

**FACTORS AFFECTING HIGHLY ACTIVE ANTI-RETROVIRAL THERAPY
ADHERENCE IN A RURAL AREA IN BOTSWANA**

by

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SUPERVISOR: PROF VJ EHLERS

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**FACTORS AFFECTING HIGHLY ACTIVE ANTI-RETROVIRAL THERAPY
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DECLARATION

I declare that FACTORS AFFECTING HIGHLY ACTIVE ANTI-RETROVIRAL THERAPY ADHERENCE IN A RURAL AREA IN BOTSWANA is my own work and that all the resources 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.

.....
Emmanuel Tshibanda Tshisuyi

.....
DATE

DEDICATION

To my dear parents Isidore (late) and Anasthasie Banfikile Tshisuyi who taught me the value of discipline and hard work; my lovely wife Bijou Mbiya; my wonderful daughters Stacia, Licia and son Emmanuel Jr; and to all people living with HIV/AIDS.

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To you all please accept my sincere gratitude and appreciation. May God bless you.

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ABSTRACT

The purpose of this study was to determine factors affecting non-adherence to Anti-retroviral therapy among AIDS patients. A cross sectional quantitative survey, was used. Structured interviews were conducted with 300 ART patients. Data were analysed using SPSS version 13 and presented in charts, graphs and frequency tables.

Motivators of good adherence were identified as disclosure of HIV positive status to more than one person, frequent adherence counselling, self-efficacy to adhere to ART, positive interactions between patients and healthcare providers; and using an adherence partner. Barriers to adherence were forgetfulness, transportation costs to and from the clinic, time away from work and side effects. There was a strong positive correlation between adherence, CD4 counts and viral load. Adherence was closely tied to immunologic and virologic improvements. Respondents with poor adherence were likely to have unsuppressed viral loads (OR 12.98, 95%, CI 4.9-34).

KEY CONCEPTS

Adherence to anti-retroviral therapy (ART), ART in Botswana, CD4 cell counts, HIV/AIDS, Viral load, perceived self-efficacy, perceived stigmatisation, Social Cognitive Theory

TABLE OF CONTENTS

CHAPTER 1

ORIENTATION TO THE STUDY

1.1	INTRODUCTION	1
1.2	BACKGROUND INFORMATION ABOUT THE RESEARCH PROBLEM	2
1.2.1	Source of and background to problem	2
1.3	RESEARCH PROBLEM	4
1.4	AIM OF THE STUDY	5
1.4.1	Research purpose	5
1.4.2	Research objectives	5
1.5	SIGNIFICANCE OF THE STUDY	6
1.6	DEFINITIONS OF KEY TERMS	6
1.6.1	Adherence	6
1.6.2	Adult patient	6
1.6.3	Anti-retroviral drugs (ARVs)	6
1.6.4	Anti-retroviral therapy (ART)	7
1.6.5	CD4 cell	7
1.6.6	CD4 cell counts	7
1.6.7	Viral load (VL)	7
1.7	FOUNDATIONS OF THE STUDY	7
1.7.1	Assumptions underlying the study	7
1.7.2	Theoretical framework	8
1.7.2.1	The Health Belief Model (HBM)	8
1.7.2.2	The theory of Planned Behaviour	9
1.7.2.3	The Informational Motivational Behaviour Model (IMB)	10
1.7.3	Concepts of the Social Cognitive Theory	11
1.8	RESEARCH DESIGN AND METHOD	12
1.9	SCOPE OF THE STUDY	13
1.10	STRUCTURE OF THE DISSERTATION	13

1.11	SUMMARY	14
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CHAPTER 2

LITERATURE REVIEW

2.1	INTRODUCTION	15
2.2	HIV PATHOGENESIS AND THE ROLE OF ANTIRETROVIRAL THERAPY	16
2.3	ADHERENCE	18
2.3.1	Adherence definitions	18
2.4	THE IMPORTANCE OF ADHERENCE	20
2.5	MEASURING ADHERENCE	21
2.6	MEASUREMENT OF ADHERENCE IN BOTSWANA	22
2.7	FACTORS AFFECTING ADHERENCE	23
2.7.1	Patients-related factors	23
2.7.1.1	Age, race and sex	24
2.7.1.2	Mental health	25
2.7.1.3	Socio-cultural issues and support	26
2.7.1.4	Education and income	27
2.7.1.5	Alcohol and drug abuse	28
2.7.2	Treatment regimens	29
2.7.3	Patient-provider relationship	30
2.7.4	Clinical settings	31
2.7.5	Disease-related factors	32
2.8	APPLICATION OF THE SOCIAL COGNITIVE THEORY TO THIS STUDY	33
2.8.1	Individual level	34
2.8.1.1	Perceived self-efficacy to adhere to ART	34
2.8.1.2	Skills or strategies applied to ART	34
2.8.1.3	Knowledge of ART	35
2.8.1.4	Outcome expectations of ART adherence	35
2.8.1.5	Interpersonal level	36
2.8.1.6	Patient-provider interaction	36

2.8.1.7	Perceived levels of social support	37
2.8.1.8	HIV and disclosure experiences	37
2.8.1.9	Community level	38
2.8.1.10	Perceived stigma towards people living with HIV	38
2.8.1.11	Perceived normative beliefs of taking ART	38
2.8.1.12	Environmental level	39
2.9	APPLICATION OF THE SOCIAL COGNITIVE THEORY AND THE HEALTH BELIEF MODEL TO ART ADHERENCE RESEARCH	39
2.10	SUMMARY	41

CHAPTER 3

RESEARCH DESIGN AND METHOD

3.1	INTRODUCTION	42
3.2	RESEARCH DESIGN	42
3.3	RESEARCH METHOD	43
3.3.1	Population and sample	44
3.3.1.1	Population	44
3.3.1.2	Sample and sampling procedure	44
3.3.1.2.1	Inclusion criteria	45
3.3.1.2.2	Exclusion criteria	45
3.3.1.3	Sample size	46
3.3.2	Data collection	47
3.3.2.1	Data collection approach and method	47
3.3.2.2	Development and testing of the data collection instrument	47
3.3.2.3	Characteristics of the data collection instrument	48
3.3.2.4	Validity and reliability of the research instrument	50
3.3.2.4.1	Reliability: Cronbach Alpha scores	51
3.3.2.5	Data collection process	51
3.3.3	Data analysis	53
3.4	ETHICAL CONSIDERATIONS	53
3.4.1	Informed consent	53
3.4.2	Anonymity	54

3.4.3	Confidentiality	55
3.4.4	Feedback	55
3.5	SUMMARY	56

CHAPTER 4

ANALYSIS, PRESENTATION AND DISCLOSURE OF THE RESEARCH FINDINGS

4.1	INTRODUCTION	57
4.2	DATA MANAGEMENT AND ANALYSIS	57
4.3	RESEARCH RESULTS	58
4.3.1	Socio-demographic characteristics	58
4.3.2	Adherence	61
4.3.2.1	Pill counts	61
4.3.2.2	Adherence by pharmacy refill appointment	62
4.3.2.3	Adherence by self-report	63
4.3.3	ART adherence correlated with patients' characteristics	64
4.3.4	Clinical data	68
4.3.4.1	Duration of ART	68
4.3.4.2	CD4 cell counts	68
4.3.4.3	Current plasma viral load	72
4.3.4.4	Current ARV treatment regimen	72
4.3.4.5	Side effects	74
4.3.4.6	Reasons for missing ART doses	76
4.3.4.7	Skills and strategies used for taking medicines regularly	77
4.3.5	Adherence and social characteristics	78
4.3.5.1	Counselling	78
4.3.5.2	Perceived self-efficacy of adherence to ART	79
4.3.5.3	Disclosure	80
4.3.5.4	Perceived stigma	82
4.3.5.5	Patient-provider relationship	83

4.3.5.6	Social information	85
4.3.5.7	Relocations and adherence	86
4.3.6	Multivariate analysis of predictors of adherence	87
4.4	SUMMARY OF RESEARCH FINDINGS	88
4.5	CONCLUSION	90

CHAPTER 5

CONCLUSIONS, RECOMMENDATIONS AND LIMITATIONS

5.1	INTRODUCTION	92
5.2	SUMMARY OF RESEARCH FINDINGS	92
5.2.1	Patients' characteristics	92
5.2.2	Treatment regimens	93
5.2.3	Patient-provider relationship	93
5.2.4	Clinical setting	94
5.2.5	Disease-related factors	94
5.3	CONCLUSIONS	95
5.4	RECOMMENDATIONS	96
5.4.1	Recommendations to improve adherence to ART	95
5.4.2	Recommendations for further studies	97
5.5	CONTRIBUTIONS OF THE STUDY	98
5.6	LIMITATIONS OF THE STUDY	99
5.7	CONCLUDING REMARKS	100
	LIST OF REFERENCES	102

LIST OF TABLES

Table 3.1:	Reliability statistics	51
Table 4.1:	Socio-demographic characteristics of the respondents	60
Table 4.2:	Patients' history of taking more than the prescribed number of pills	62
Table 4.3:	Proportion of the respondents who missed medication doses during the four days preceding the interviews	64
Table 4.4:	Association of socio-demographic variable and the pill count adherence levels	66
Table 4.5:	Adherence level correlated with the respondents' baseline CD4 counts	71
Table 4.6:	Correlation between respondents' CD4 counts and adherence levels	71
Table 4.7:	Chi-square tests	71
Table 4.8:	Respondents' plasma viral load counts	72
Table 4.9:	Distribution of the respondents' current treatment regimens	73
Table 4.10:	Respondents' ART regimen changes	73
Table 4.11:	Reasons for respondents' treatment regimen changes	74
Table 4.12:	Respondents' reported ART side effects	75
Table 4.13:	Impact of ART side effects on respondents' daily activities	75
Table 4.14:	Reasons for missing ART doses	76
Table 4.15:	Counselling prior to starting ART	79
Table 4.16:	Respondents' number of counselling sessions	79
Table 4.17:	Respondents' adherence levels and the number of people to whom they had disclosed their HIV status	81
Table 4.18:	Social and cultural factors	85
Table 4.19:	Association between relocations after starting HAART and adherence	86
Table 4.20:	Chi-square tests: association between relocation and adherence	86
Table 4.21:	Correlations between selected factors and adherence	88

LISTS OF FIGURES

Figure 1.1: Conceptual model of factors affecting adherence to ART	12
Figure 4.1: Respondents' gender distribution (N=300)	58
Figure 4.2: Respondents' marital status distribution (N=300)	59
Figure 4.3: Respondents' education levels (N=300)	59
Figure 4.4: Pill count-based ART adherence levels (N=300)	61
Figure 4.5: Proportion of missed pharmacy refill appointments (N=300)	63
Figure 4.6: Association between pill count adherence and gender (N=300)	64
Figure 4.7: Association between age and pill count adherence (N=300)	65
Figure 4.8: Loss of income during visits to the ART clinic (N=300)	66
Figure 4.9: Respondents' suggestions on how they could be helped not to lose income while accessing ART services (N=141)	67
Figure 4.10: Distribution of the adherence level by duration of treatment (N=300)	68
Figure 4.11: Respondents' baseline CD4 counts (N=300)	69
Figure 4.12: Respondents' current CD4 counts (N=300)	69
Figure 4.13: Distribution of respondents' current CD4 counts (N=300)	70
Figure 4.14: Correlation between virologic suppression and adherence levels (N=300)	72
Figure 4.15: Side effects experienced by respondents (N=300)	75
Figure 4.16: Respondents' reasons for missing ART doses (N=300)	77
Figure 4.17: Strategies used as reminders to take ART medication (N=300)	77
Figure 4.18: Distribution of respondents' adherence partners (N=300)	78
Figure 4.19: Perceived self-efficacy to adhere to taking medications in specific situations (N=300)	80
Figure 4.20: Distribution of the people to whom the respondents had disclosed (N=300)	82
Figure 4.21: Time taken to disclose HIV positive status after diagnosis (N=300)	82
Figure 4.22: Distribution of perceived stigma by the respondents (N=300)	83
Figure 4.23: Distribution of relationship between the patient and the healthcare provider (N=300)	84

LIST OF BOXES

Box 3.1:	Sampling interval	45
Box 3.2:	Sample size calculation	46
Box 3.3:	Adherence calculation	52

LIST OF ANNEXURES

ANNEXURE 1:	Map of Africa showing Botswana	128
ANNEXURE 2:	Map of Botswana	128
ANNEXURE 3:	Data collection instrument (English version)	129
ANNEXURE 4:	Data collection instrument (Setswana version)	141
ANNEXURE 5:	Informed consent form (English version)	152
ANNEXURE 6:	Informed consent form (Setswana version)	154
ANNEXURE 7:	Permission letter to the institution to conduct research	155
ANNEXURE 8:	Permission letter to the IRB to conduct the research	157
ANNEXURE 9:	Permission from HRDD	158
ANNEXURE 10:	Permission from UNISA	160
ANNEXURE 11:	Permission from the institution	161
ANNEXURE 12:	Letter from the translator	162
ANNEXURE 13:	Letter from the statistician	163

LIST OF ABBREVIATIONS

AIDS	Acquired Immuno Deficiency Syndrome
ART	Anti-retroviral therapy
ARV	Anti-retroviral
BAIS	Botswana AIDS Impact Survey
CDC	Centre for Disease Control and Prevention
CD4	T-lymphocyte CD4+
DRMH	Deborah Retief Memorial Hospital
EDM	Electronic drug monitoring
HAART	Highly active anti-retroviral therapy
HBM	Health Belief Model
HIV	Human Immunodeficiency Virus
IDCC	Infectious Disease Control Centre
HRDD	Health Research and Development Division
MCV	Mean corpuscular volume
MEMS	Medication events monitoring system
MOH	Ministry of Health
NACA	National AIDS Coordinating Agency
OI	Opportunistic infection
SCT	Social Cognitive Theory
SSA	Sub-Saharan Africa
TB	Tuberculosis
ADV L	Undetectable viral load
UN	United Nations

UNAIDS	United Nations Programme on HIV/AIDS
Unisa	University of South Africa
USA	United States of America
VL	Viral load
WHO	World Health Organization

CHAPTER 1

ORIENTATION TO THE STUDY

1.1 INTRODUCTION

The human immunodeficiency virus (HIV) causes severe damage to the immune system and eventually destroys it by using the DNA of the CD4 cells to replicate itself. In this process, the virus eventually destroys the CD4 cells (Calles, Evans & Terlonge 2010:7), rendering the person susceptible to opportunistic infections (OIs), and eventually to suffer from Auto Immune Deficiency Syndrome (AIDS). Anti-retroviral therapy (ART) is used to prolong lives of people living with HIV/AIDS. However, ART is not a cure and it must be taken every day for the entire life of the AIDS patient. As ART is becoming increasingly available and affordable to eligible people in developing countries, more attention is focused on issues related to its rational use, and particularly to ART adherence challenges. Adherence is a key element for reducing the spread of drug-resistant HIV (Steel, Nwokike & Joshi 2007:1).

Reportedly, during 2009 there were 33.3 million people globally living with HIV/AIDS, of whom 22.5 million were living in Sub-Saharan Africa (SSA) (UNAIDS 2010:23). In 2009, in Botswana, there were 300 000 adults living with HIV or one quarter of the population aged 15 years and older. Botswana has an estimated adult HIV prevalence among 15-49 year old citizens of 24.8%, the second highest in the world after Swaziland (UNAIDS 2010:180-181).

People who use ART effectively can survive for many years with this chronic disease. Although ARVs do not cure HIV, they control the virus and can reduce the level of the virus to undetectable levels in the blood. These drugs prevent the rapid multiplication of HIV and at the same time, boost the body's immune system by increasing the CD4 count, increasing the length and quality of life of people with HIV/AIDS while enabling them to lead full and productive lives (WHO 2006:26).

According to the Office of the AIDS Research Advisory Council (2008:18), the primary goals driving the decision to initiate ART are to:

- reduce HIV-related morbidity
- prolong survival
- improve quality of life
- restore and preserve immunologic functions (increase CD4 cell counts)
- maximally and durably suppress viral load
- prevent vertical HIV transmission

ART adherence levels of at least 95.0% are required to obtain and sustain benefits. Maintaining such high levels of ART adherence might be challenging in terms of pill burden, dietary restrictions and dosing frequency, required to ensure optimal treatment benefits (Altice, Mostashari & Friedland 2001:47; Poppa, Davidson, Deutsch, Godfrey, Fisher, Head, Horne & Sherr 2003:47).

1.2 BACKGROUND INFORMATION ABOUT THE RESEARCH PROBLEM

This is the part of the research problem that indicates what is known or the key research that has been done in the problem area to be discussed (Burns & Grove 2009:689).

1.2.1 Source of and background to the problem

In Botswana, the first case of HIV was diagnosed in 1985 in Selebi-Phikwe and the prevalence has increased rapidly since then (WHO 2002:6). The introduction of ART in 1996 led to a marked decrease in the morbidity and mortality rates of HIV/AIDS (Gibb et al 2003:1019).

Since 2002, the government of Botswana provides ART free of charge to all citizens of Botswana who qualify for treatment. However, there are concerns that the ART adherence levels might be sub-optimal, with potentially serious consequences (WHO

2006:83). According to the WHO (2005:12), these ART adherence rates were found to be below 95.0%, required for optimal virological suppression and treatment success.

The following are the World Health Organization (WHO) HIV/AIDS clinical stages:

Stage 1, or mild disease, is when the patient is asymptomatic or has persistent generalised lymph nodes.

Stage 2, or moderate disease, includes unexplained weight loss <10% from the base line, recurrent upper respiratory tract infections, skin infections.

Stage 3, or advanced disease, includes severe weight loss (>10% of presumed or measured body weight), unexplained chronic diarrhoea for longer than one month, unexplained persistent fever (intermittent or constant for longer than one month), oral candidiasis, oral hairy leukoplakia, pulmonary tuberculosis (TB) diagnosed during the last two years, severe presumed bacterial infections, empyema, pyomyositis, bone or joint infection, meningitis, bacteraemia, acute necrotising ulcerative stomatitis, gingivitis or periodontitis, unexplained anaemia (< 8 g/dl), and/or neutropenia (<500/mm³) and/or thrombocytopenia (<50 000/ mm³) for more than one month. According to Botswana's MoH guidelines (MoH 2008:5), HIV positive adults are eligible to start ART when their CD4 cell count is less than 250 cells/mm³ or having an AIDS defining illness according to WHO clinical stages 3 and 4 (WHO 2005).

Stage 4 or severe disease, includes HIV wasting syndrome, pneumocystic pneumonia, recurrent severe or radiological bacterial pneumonia, chronic herpes simplex infection (oral, labial, genital and/or anorectal - of more than one month's duration), oesophageal candidiasis, extrapulmonary TB, Kaposi's sarcoma, central nervous system (CNS) toxoplasmosis, HIV encephalopathy extrapulmonary cryptococcosis including meningitis, unexplained anaemia (<8 g/dl), and/or neutropenia (<500/mm³) and/or thrombocytopenia (<50 000/ mm³) for more than one month, progressive multifocal leuko-encephalopathy (PML), candida of trachea, bronchi or lungs, cryptosporidiosis,

isosporiasis, visceral herpes simplex infection, cytomegalovirus (CMV) infection (retinitis or of an organ other than liver, spleen or lymph nodes), Any disseminated mycosis (including histoplasmosis, coccidiomycosis, penicilliosis), recurrent non-typhoidal salmonella septicaemia, lymphoma (cerebral or B cell non-Hodgkin), invasive cervical carcinoma, visceral leishmaniasis (WHO/HIV/2005.02:5-6).

According to Kip, Ehlers and Van der Wal (2009a:3-7) patient-centred barriers to ART adherence in Botswana, included inadequate knowledge about ART, HIV, AIDS, CD4 cell and viral-load results, stigma, travelling costs, waiting times at clinics, side effects of ART, the use of traditional medicines, and the abuse of alcohol. Service-centred barriers included nurses' attitudes and knowledge, health workers' inability to conduct home visits and to contact defaulters, limited clinic hours, and delays in obtaining patients' CD4 and viral-load test results.

The district where this study was conducted has a population of 76 504; according to the 2001 population and housing census projection for 2008, conducted by the Central Statistics Office (CSO 2001). The HIV prevalence rate in this district was reportedly 15.8%, with the highest prevalence of 33.6% among those aged 31-49 according to the BAIS III report (CSO 2009:16, 17, 21).

1.3 RESEARCH PROBLEM

A research problem is an area of concern where there is a gap in the knowledge base needed for practice. Research is conducted to generate essential knowledge to address the practice concern, with the ultimate goal of providing evidence-based practice (Burns & Grove 2009:719).

To achieve effective treatment outcomes and realise the benefits of ART, strict adherence to treatment instructions are critical. Adherence rates of 95.0% or more are required for optimum viral suppression (Cederfjall, Langius-Eklof, Lidman & Wredling 2002:609-616; Jani 2004:9; Paterson, Swindells, Mohr, Brester, Vergis, Squire,

Wagener & Singh 2000:27; Poppa et al 2003:47; Simone, Frick, Pantalone & Turner 2003:185).

Maintaining such high levels of ART adherence might be challenging in terms of pill burden, dietary restrictions and dosing frequency, required to ensure optimal treatment benefits (Altice et al 2001:47; Poppa et al 2003:47). Failure to suppress viral replication leads to the development of drug-resistant HIV strains, limiting the effectiveness of therapy, and exposing other members of these communities to ART-resistant HIV strains. Sub-optimal adherence to ART is the strongest predictor of failure to achieve viral suppression below the level of detection and often underlies treatment failure (WHO 2006:264). Therefore, this study sought to determine factors that influence ART adherence levels among patients attending one clinic in Botswana.

1.4 AIM OF THE STUDY

The aim of this study was to contribute to the existing body of knowledge about factors influencing ART adherence levels among adults in Botswana.

1.4.1 Research purpose

The purpose of this study was to identify factors affecting ART adherence levels, and the impact on immunological and virological responses in adult patients in one rural district in Botswana. The ultimate purpose of this study is to use this knowledge to enhance the ART adherence rate among adult patients at the participating clinic, and possibly also at other clinics in Botswana, and in other SSA countries.

1.4.2 Research objectives

Specific objectives of this study were to:

- Identify factors influencing patients' ART adherence levels

- determine the association between ART adherence and immunological and virological responses
- recommend possible interventions in order to improve ART adherence levels at the participating clinic

1.5 SIGNIFICANCE OF THE STUDY

If this study could identify factors affecting ART adherence at the participating clinic in Botswana, negatively or positively, then this information could assist healthcare providers to understand and address these factors, and thereby enhance ART adherence levels which will improve these patients' quality of life, and save much money for Botswana's healthcare services.

1.6 DEFINITIONS OF KEY TERMS

1.6.1 Adherence: It refers to the ability of the person living with HIV/AIDS to be involved in choosing, starting, managing and maintaining a given therapeutic combination medication regimen to control viral (HIV) replication and improve immune function (Jani 2004:3). Effective use of ARVs requires an adherence of at least 95.0%. In this study adherence is measured as the regular and consistent collection of ARVs from the pharmacy.

1.6.2 Adult patient: Any patient aged 21 years and older receiving ART at the participating clinic.

1.6.3 Anti-retroviral drugs (ARVs): These are medications used to treat AIDS. There are different classes of ARVs and they act at different stages of the HIV life cycle (WHO 2006:24).

1.6.4 Anti-retroviral therapy (ART): The standard ART consists of at least three antiretroviral drugs (ARVs) to maximally suppress the HI virus and stop the progression of AIDS (WHO 2006:24)

1.6.5 CD4 cell: These are immune system cells, which fight infections. The number of CD4 cells decrease when a person suffers from HIV, making him/her susceptible to opportunistic infections.

1.6.6 CD4 cell counts: This is a useful and reliable monitoring test commonly used as a surrogate for ART adherence (Poppa et al 2003:55). It is also used to determine the stage of the disease and monitor response to therapy. It is one of the criteria that can be used for deciding when to start ART. The normal CD4 cell count is about 1000 cells/mm³ (WHO 2006:23). Treatment commences when the CD4 count is 250 cells/mm³ or less in Botswana. CD4 cell counts increase with adherence to ART while it decreases with non-adherence and/or ART resistant HIV strains (Poppa et al 2003:55).

1.6.7 Viral load (VL): This is the term used to describe the amount of HIV in the blood. The result of a viral load test is described as the number of copies of HIV RNA per millilitre (copies/ml). VL goes below the level of detection (less than 400 copies/ml) by six months after starting ART (MOH 2005:18), provided the patient adheres to the prescribed ART regimen and responds to the ARVs.

1.7 FOUNDATIONS OF THE STUDY

1.7.1 Assumptions underlying the study

The study's objectives are based on the assumptions that adherence to ART will be predicted by increases in the CD4 cell counts and suppression of viral loads; and adherence is measured by regular collection of ARVs from the pharmacy. The patients who collect their refills regularly, and maintain high adherence rates, are expected to show immunological recovery and virologic suppression as reflected in the increases in

the CD4 cell counts and undetectable viral loads respectively. The study will use routinely collected data recorded on patients' medical records and pharmacy refills as stipulated in the ART guidelines. Thus the results of this study will be dependent on the quality of these two data sources.

1.7.2 Theoretical framework

This study integrated social support with constructs from the Social Cognitive Theory to explore the determinants of ART adherence. The Social Cognitive Theory looks at the multifaceted causal structure in the regulation of human motivation, action and well-being and offers predictors of adherence and guidelines for its promotion. Social support is a key component of many behavioural theories because it accounts for a great deal of variance between those who do and those who do not exhibit desirable behaviours. The core determinants include knowledge of health risks and benefits of different health practices, perceived self-efficacy enabling one to exercise control over one's health habits, outcome expectations about the expected costs and benefits for different health habits, the health goals people set for themselves, the concrete plans and strategies for realising them, and the perceived facilitators and social and structural impediments to achieving the desired changes (Bandura 2004:144-145).

The Health Belief Model, the Theory of Planned Behaviour and the Informational Behavioural Motivational Model are three social cognitive theories briefly reviewed in this chapter to conceptualise the phenomenon of ART adherence.

1.7.2.1 The Health Belief Model

The Health Belief Model (HBM) states that health-related action depends on the simultaneous occurrence of three factors. These factors are the existence of sufficient motivation (or health concern) to make health issues salient; the belief that one is susceptible to a serious health problem, that is a sense of a perceived threat; and the belief that following a particular health recommendation would be beneficial in reducing

the perceived threat at an acceptable cost, that is the perceived barriers that must be overcome in order to follow the health recommendation. For persons receiving ART, HIV positive status, CD4 count, viral load and quality of life constitute the health concern; the prospect of deterioration in health status, leading ultimately to death, is the perceived threat; and factors such as stigma might be the perceived barriers (Vincke & Bolton 2002:487-495, Malcolm, Rosen & Stone 2003: 251).

1.7.2.2 The Theory of Planned Behaviour

This is a theory about the link between attitude and behaviour. Attitudes towards the behaviour, normative support for the behaviour, and perceived behavioural control over the behaviour, notion of self-efficacy, are predictors of intentions. Intentions, in turn, are the most proximal predictor of actual behaviour (Armitage & Conner 2001:477). Perceived self-efficacy is concerned with people's beliefs in their capabilities to exercise control over their own functioning and over events that affect their lives (Bandura 1997:204).

According to the Social Cognitive Theory (Bandura 1997), a personal sense of control facilitates a change of health behaviour. Self-efficacy pertains to a sense of control over one's environment and behaviour. Self-efficacy beliefs are cognitions that determine whether health behaviour change will be initiated, how much effort will be spent, and how long it will be sustained in the face of obstacles and failures. Self-efficacy influences the effort one exerts to change risk behaviour and the persistence to continue striving despite barriers and setbacks that might undermine motivation. Self-efficacy is directly related to health behaviour, but it also affects health behaviours indirectly through its impact on goals.

In general, a positive attitude toward behaviour is associated with its practice while a negative attitude is not (Horne, Clatworthy, Polmear & Weinman 2001:66). With regard to adherence to ART, negative attitudes toward ART have been shown to be associated with non-adherence among a general sample of HIV positive patients in the United

States (Viswanathan, Anderson & Thomas 2005:306) and among African American women of child bearing age (Richter, Sowell & Pluto 2002:25-33).

ART adherence self-efficacy relates to a patient's sense of his or her ability to take medication in the way it is prescribed. Self-efficacy to engage in health behaviours has been shown to be robustly associated with a healthy lifestyle among patients with diabetes (Syrjälä, Ylostalo, Niskanen & Knuutila 2004:109-114) and among patients with hypertension (Ogedegbe, Mancusi, Allegrante & Charlson 2003:520:529). It is therefore necessary to examine the extent to which perceived self-efficacy is associated with ART adherence.

1.7.2.3 The Informational Motivational Behavioural Model

According to the Informational Motivational Behavioural Model (IMB), information, motivation, and behavioural skills are the fundamental determinants of behaviour which, in the present instance, is adherence to ART (Fisher, Fisher, Bryan & Misovich 2002:178).

Both information about the role of ART adherence leading to optimal health outcomes, and motivation to engage in adherence behaviour, influence whether individuals will be inclined to engage in adherence-related acts, such as clinic attendance and regular pill-taking. Therefore the behavioural skills associated with adherence, such as being able to travel to appointments and remembering to take medication, as well as a sense of self-efficacy for doing these acts, comprise a prerequisite of ART adherence. In terms of the IMB model, these behavioural skills determine whether well-informed and well-motivated persons will indeed adhere to their medication regimens (Fisher & Fisher 1992:462).

ART adherence might be influenced largely by the extent to which the health system helps to create a health enabling environment.

1.7.3 Concepts of the Social Cognitive Theory

- **Behavioural capability:** knowledge and skill to perform a given behaviour; promote mastery learning through skills training
- **Emotional coping responses:** strategies or tactics that are used by a person to deal with emotional stimuli; provide training in problem solving and stress management
- **Environment:** factors physically external to the person; provides opportunities and social support
- **Expectancies:** the values that the person places on a given outcome and incentives represent outcomes of change that have functional meaning
- **Expectations:** anticipatory outcomes of a behaviour, implying positive outcomes of healthful behaviour
- **Self-control:** personal regulation of goal-directed behaviour or performance; providing opportunities for self-monitoring, goal setting, problem solving, and self-reward
- **Self-efficacy:** the person's confidence in performing a particular behaviour; approach behavioural change in small steps to ensure success
- **Situation:** perception of the environment; address misperceptions and promote healthful reforms

Five major categories suggested by multiple authors are characteristics of the patient, disease-related factors, features of the regimen, aspects of the patient-provider interaction and conditions of the social environment (Golin et al 1996:1153-64). Based on a review of the literature, as well as prior qualitative and quantitative observational studies about medication taking among persons living with HIV, Golin et al modified a previous conceptual model of treatment adherence to identify determinants of medication taking related to ART. This revised model, shown in Figure 1.1, integrates the social cognitive theory with empirical studies of ART adherence to suggest that patients' adherence is affected by both their motivation and self-efficacy, or confidence in their ability to take their medication (Paterson et al 2000:21-30; Chow et al 1993:171-175; Gifford et al 2000:386-395; Bandura 1977:191-215). Furthermore, motivation and

self-efficacy are influenced by multiple factors within these five categories. Each factor in the model can reciprocally influence the others. This model was used as a conceptual basis for developing the structured interview schedule.

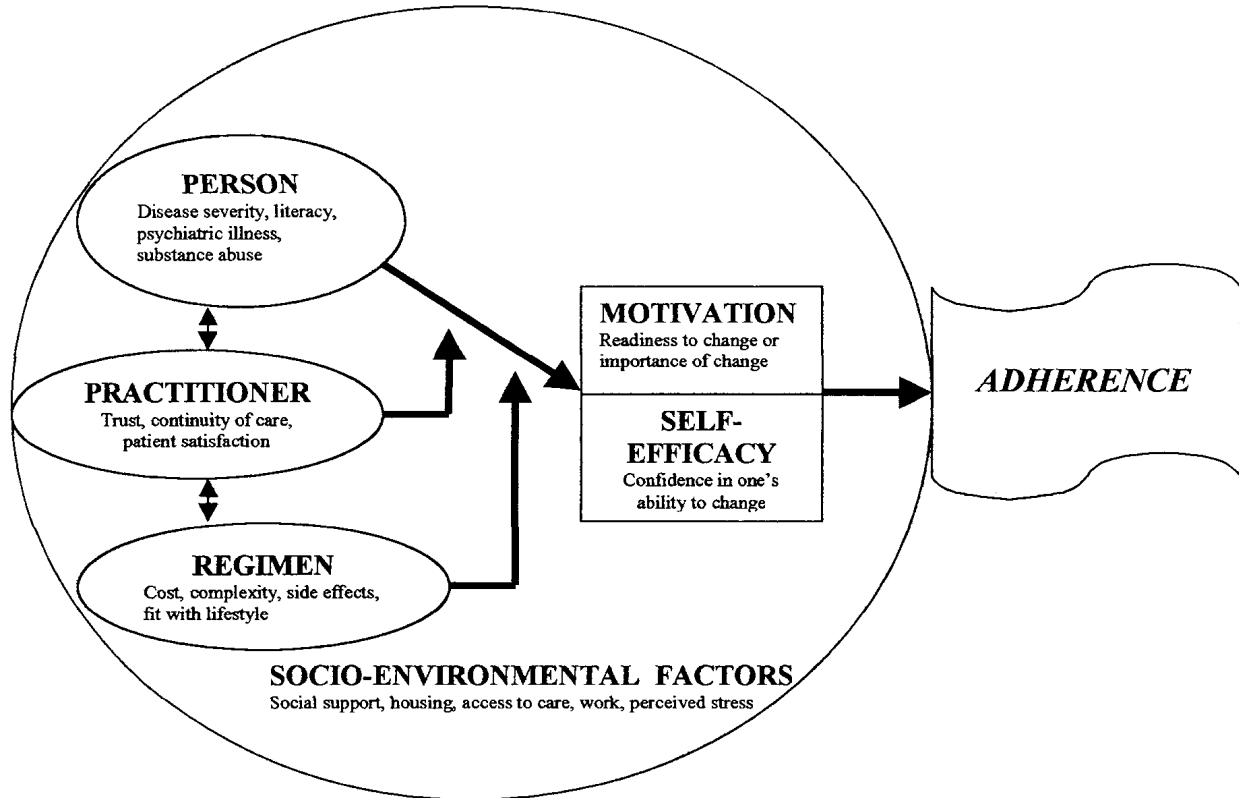


Figure 1.1: Conceptual model of factors affecting adherence to antiretroviral therapy

Source: <http://www.liebertonline.com/action/showImage?doi=10.1089/108729104323038900&iName=master.img-000.png&w=444&h=289>

1.8 RESEARCH DESIGN AND METHOD

The research methodology outlines the process of the research and the tools needed to achieve the research objectives (Mouton 2001:56).

A cross-sectional quantitative survey, using a self-developed structured interview schedule, based on the literature review, comprising open and closed ended items, was adopted for this research. Eligible patients, during their routine visits to the clinic were selected using systematic random sampling and interviewed by a trained research

assistant who was fluent in both English and Setswana. Participation in the study was voluntary and only respondents who signed consent were interviewed.

1.9 SCOPE OF THE STUDY

During this study period, about 2 000 adult patients (aged 21 years and older) were on ART for at least six months at the study site and 300 patients, who met the inclusion criteria, were recruited. The study covered demographic information, clinical information, counselling information, adherence information, perceived self-efficacy to adhere to the prescribed ART regimen, skills and strategies applied for taking medication, disclosure issues, perceived stigma, side effects, patient-provider communication, and social information. The results from this study may only apply to the study population at one clinic in Botswana.

1.10 STRUCTURE OF THE DISSERTATION

This dissertation has been structured into five chapters. This section covers a discussion of the general organisation of this dissertation.

Chapter 1 provides an orientation to and background information about the study. The research methodology and conceptual frameworks applicable to this study are briefly outlined. Definitions of key concepts are also provided.

Chapter 2 discusses the literature reviewed on ART adherence globally, in SSA and in Botswana.

Chapter 3 reflects the research methodology adopted by this study.

Chapter 4 reports on the results, analysis and discussions of the findings.

Chapter 5 presents the conclusions and limitations of the study, as well as recommendations to improve ART adherence at one clinic in Botswana and for future research.

1.11 SUMMARY

The effectiveness of ART depends on patients' abilities to maintain at least 95.0% adherence levels. Strict adherence to ART results in suppression of viral load, improved immune response (evidenced by increased CD4 counts) resulting in reduction in morbidity and mortality due to HIV/AIDS. This study aimed to identify factors that promote adherence and barriers that hinder adherence in order to propose changes to enhance patients' ART adherence levels.

The next chapter presents a discussion about the literature reviewed about ART adherence globally, in SSA and in Botswana.

CHAPTER 2

LITERATURE REVIEW

2.1 INTRODUCTION

A literature review is an organised written presentation of what has been published on a topic by scholars and includes a presentation of research conducted in a selected field of study. The review is organised into sections that present themes or identify trends. The purpose is not to list all the material published, but rather to synthesise and evaluate the information, based on the focus of the review (Burns & Grove 2009:92).

The purpose of a literature review is to provide better insight into dimensions and complexities of the research problem. A literature review further equips the researcher with a complete and thorough justification for subsequent steps to be followed in the research process. Gaps in some previous research reports can be identified through a literature review, aiming at refining and redefining the research questions (De Vos, Strydom, Fouché & Delpont 2002:66-67).

The research topic and related aspects are studied in depth and discussed in the literature review chapter. The literature review will focus on biomedical aspects of infection caused by the HIV type-1 and on ARVs' mode of action. This chapter will also clarify the concepts of adherence, measurement of adherence and importance of adherence. Some of the modifying factors that impact on adherence will be identified from previous studies, and discussed.

2.2 HIV PATHOGENESIS AND THE ROLE OF ANTIRETROVIRAL THERAPY

To understand antiretroviral medication, it is important to first understand HIV pathogenesis. A well functioning immune system protects the human body from external infections. The white blood cells' pool of lymphocytes constitutes the key components of immunity (Mindel & Tenant-Flowers 2001:1291). The two types of lymphocyte cells are the B cells and the T cells. The B cells are formed in the bone marrow and produce antibodies in response to antigen exposure. The T cells are produced in the thymus gland. The two subtypes of T cells are the regulators, helpers or CD4 cells that recognise the presence of a foreign antigen, and the fighters, effectors, cytotoxic or CD8 cells that bind directly with the foreign antigen in order to destroy it. The HI virus is classified as a retrovirus and replicates in the host CD4 cells (Bartlett & Finkbeiner 2001:10).

Once into a host CD4 cell, HIV removes its outer coating and converts its ribonucleic acid (RNA) to deoxyribonucleic acid (DNA) with the help of the enzyme reverse transcriptase. The viral DNA is now able to enter the nucleus of the CD4 cell. The viral enzyme integrase then inserts the viral DNA into the CD4 cell's DNA and the CD4 cell becomes a factory used to produce more HIV. The role of ART is to target each step of this process by preventing each of the above mentioned steps from taking place. At present, the different classes of ARVs that have been approved are classified as fusion, reverse transcriptase, and protease inhibitors, which are used in combination to stop viral entry into CD4 cells, viral replication and exit of new HIV from the CD4 cells (Calles et al 2010:7-14).

Entry inhibitors or fusion inhibitors are an antiretroviral class of drugs interrupting the process of attachment, binding, and fusion. These medications inhibit the virus from completing the steps needed to infect the CD4 cells (Tolle, Schwarzwald & Calles 2010: 68-69).

The reverse transcriptase inhibitors are classified as nucleoside reverse transcriptase inhibitors (NRTIs) and non nucleoside reverse transcriptase inhibitors (NNRTIs), or nucleotide reverse transcriptase inhibitors (NtRTIs); all working on inhibiting the functions of enzyme reverse transcriptase. The NRTIs contain nucleotides, a type of building material used by enzyme reverse transcriptase to convert RNA into DNA (Balint 2001:17-27). The NNRTIs attach themselves to the enzyme reverse transcriptase and block it from converting RNA into DNA (Tolle et al 2010: 66).

The protease inhibitors prevent the protease enzyme from cleaving large HIV precursor proteins into smaller functional units, a process that causes the production of defective virus particles incapable of infecting the CD4 cells and of replicating (Tolle et al 2010:67)

These different classes of antiretroviral drugs are prescribed in combination from at least two classes to avoid the development of resistance, hence the name highly active antiretroviral therapy (HAART) (CDC 2005b:1-45).

The CD4 cell count and the viral load determine prognostic information in terms of stages of HIV disease, as well the suggested course of treatment. A person infected with HIV can have a healthy immune system as indicated by a CD4 count of 500-1600 cells/ mm³ (normal range), where the immune system is able to defend itself against most antigens. A declining CD4 count suggests HIV disease progression where the patient infected with HIV has increased susceptibility to infections (CDC 2005b:1-45).

A CD4 cell count below 200 cells/mm³ is indicative of a weakening immune system, where the person infected with HIV is at an increased risk of AIDS defining opportunistic infections or neoplasms, associated with a failing immune system. The introduction of ART makes it possible to slow down the breakdown of the immune system and facilitate immune recovery to a normal range. However, the efficacy of ART depends on near perfect adherence to the prescribed regimen as directed by the healthcare provider (Lewthwaite & Wilkins 2005:10-13).

2.3 ADHERENCE

The efficacy of ART depends on maintaining an optimal level of ARV drugs in the blood stream to adequately resist viral replication. This level of consistent and optimal presence of drugs in the blood stream is achieved by adherence to a prescribed regimen of ARVs (Bangsberg, Perry, Charlebois, Clark, Roberston, Zolopa & Moss 2001:1181-1183).

Paterson et al (2000:21-30) identified the need for adherence, when they found that 81.0% of patients with >95.0% adherence showed complete viral suppression as compared to 6.0% with less than a 70.0% rate of ART adherence.

2.3.1 Adherence definitions

Machtiger and Bangsberg (2005:3) define medication adherence as the extent to which a patient takes medications as prescribed by the healthcare provider.

Jani (2004:1) defines medication adherence in HIV/AIDS care as the ability of the AIDS patient to choose, start, manage and maintain a given therapeutic combination medication regimen to control viral (HIV) replication and improve his/her immune function.

In a study done by Weiser, Wolfe, Bangsberg, Thior, Gilbert, Makhema, Kebaabetswe, Dickenson, Mompati, Essex and Marlink (2003:282), adherence in relation to ART, is defined as taking 95.0% of prescribed doses over the previous year which is equivalent to not missing one dose in a ten day period. An ART adherence level of at least 95% is usually accepted as indicating ART adherence.

In this study adherence to ART was defined as the patient's regular pharmacy appointments to collect the prescribed ARVs. The pill count for each visit was recorded

and the adherence level for each patient was then calculated and assessed whether it was 95.0% or lower.

According to the WHO (2006:28), there are challenges in dealing with the long term adherence to medications, especially in chronic diseases. A review of published empirical studies (over 500 studies) done over 50 years (from 1948 to 1998) showed that adherence ranged from as low as 4.6% to 100%. Eight reviewed articles revealed that the mean reported ART adherence in these studies was 88.0% (DiMatteo 2004:200-209). This was below the required adherence level of >95.0% to achieve the maximum benefit from ART as stated in the study by Paterson et al (2000:21).

Machtiger and Bangsberg (2005:3) stated that non adherence to ART is common in all groups of treated individuals. Lack of strict adherence to ART is considered to be one of the key challenges to AIDS care worldwide (Weiser et al 2003:281; Kgatlwane, Ogeny, Ekezie, Madaki, Moyo & Moroka 2006:9).

Gill, Hamer, Simon, Thea and Sabin (2005:1243-1249) noted that, in Senegal, 95.0% of patients had adherence levels exceeding 80.0% after one month of therapy but after 18 months, only 80.0% remained above that level. The 80.0% level of adherence would not be sufficient to prevent treatment failure or the development of drug resistance, because the percentage of patients with undetectable viral loads fell from 80.0% to 59.0% over that period of time.

A cross sectional study done in Botswana on barriers to ART adherence revealed that the majority of the patients found it difficult to achieve 95.0% adherence (Weiser et al 2003:284). Adult patients receiving ART for at least three months were eligible to participate in this study. Levels of adherence of people receiving ART in three clinics in Botswana were reported. The patients were asked to indicate their adherence over the previous day, previous week, previous month, and previous year. Healthcare providers (doctors, nurses, pharmacy technicians and pharmacists), were asked to indicate their assessment of patients' adherence levels over the previous year. Adherence was

defined as taking 95.0% of the prescribed doses over the past year. The findings indicated that only 54.0% of patients were more than 95.0% adherent to their prescribed doses of ARVs.

2.4 THE IMPORTANCE OF ADHERENCE

The goals of ART are the suppression of viral replication, restoration of the immune response, a halt in the progression of disease, increased survival rates, reduced morbidity and a better quality of life. Maximum and sustainable suppression of VL replication to below the level of detection is necessary to achieve these biological and chemical goals (WHO 2006:263).

Non adherence to ART leads to potential viral resistance, treatment failure, disease progression and spread of drug resistant strains to sexual partners. Resistant strains of HIV can be transmitted to newly infected individuals who will therefore have fewer treatment options from the start of their HIV infections (Kgatlwane et al 2006:7; Harries, Nyangulu & Hargreaves 2001:411).

In a study done in Pittsburgh, United States of America, Paterson et al (2000:20) reported that patients with adherence rates of 95.0% or greater had fewer hospitalisation days than those with lower adherence rates. In addition, no opportunistic infections or deaths occurred among those patients with adherence rates of 95.0% or more.

Friedland, Abdool-Karim, Lalloo, Jack, Gandhi and El Sadr (2004:424) studied 20 patients who received ART through directly observed treatment (DOT) in South Africa. The findings showed enhanced immunological and virological responses among the 17 patients who completed the study. They achieved a viral load of <50 copies/ml and a mean increase in CD4 cell counts of 148 cells/mm³. This was in agreement with other studies, indicating that adherence correlated with immunological and virological responses (Ickovics & Meade 2002:98; Paterson et al 2000:27).

In a study on the emergence of drug resistant HIV strains in Botswana, Vardavas and Blower (2007:2) showed that if the evolved drug resistant strains were 25.0% as transmissible as the existing strains, then the transmitted resistance would have reached at most just below 3.0% by 2009. If the evolved drug resistant strains were 50.0% as transmissible as the existing strains, then the transmitted resistance would have reached 6.0% by 2009. Levels of transmitted resistant strains were predicted to have reached 13.0% by 2009 if the drug resistant strains remained as resistant as the existing strains were during 2007. Higher rates are expected if the drug resistant strains are more transmissible than the existing strains.

2.5 MEASURING ADHERENCE

Measures of adherence can be divided into two categories: subjective (patient self-reports) and objective (pill counts, pharmacy refill records and biological markers). Validation of adherence measures is generally done by looking at the correlation of the measures with patients' VL and/or CD4 counts (Montessori et al 2004:229-238).

Various strategies are available and have been used in clinical settings to monitor adherence to ART (AIDS Read 2000; Jani 2004:17; Paterson et al 2000:25). These strategies include medication event monitoring systems (MEMS), pill counts, self reports, pharmacy refill data, provider estimates, and directly observed therapy (DOT) or directly administered antiretroviral therapy (DAART). Clinical studies employ a number of methods, either alone or in combination, to measure medication adherence.

Different adherence measures applied to the same patients, suggested different levels of adherence. It has been reported that adherence might be underestimated by MEMS and overestimated by pill counts and patients' self reports (Liu, Golin, Miller, Hays, Beck, Sanandaji, Christian, Maldonado, Duran, Kaplan & Wenger 2001:973).

The relative accuracy of adherence measures ranks from physician assessment and self-assessment being the least accurate, to pill counting being intermediate and electronic drug monitoring being the most accurate (Gill et al 2005:1243-1249). Electronic drug monitoring systems (such as electronic recording in the bottle's cap of every opening of the bottle) more accurately predicts undetectable viral loads (UDVL) than self-reports or pill counts. Its main advantages are that it provides data on the timing of doses taken and permits monitoring over long periods. Since adherence can be known precisely, the link between adherence levels and undetected viral load can be established with a high degree of confidence.

Arsten, Demas, Farzadegan, Grant, Gonvevitch and Howard (2001:1417-1423) noted that patients whose electronic drug monitoring data indicated high adherence levels (above 90.0%) were more likely to achieve undetected viral load than patients whose self-reports indicated the same level of adherence.

2.6 MEASUREMENT OF ADHERENCE IN BOTSWANA

The Botswana HIV/AIDS guidelines (2002:5-7) recommend two or more of the following methods for adherence monitoring:

- Careful drug history regarding missed or incorrect doses (self-reporting)
- Directly observed therapy (DOT) by a nurse, pharmacist; or modified DOT, where a family member or a friend directly observes the patient taking his/her medication
- Pill count (patient is asked to bring back all the remaining pills)
- Blood drug level measurements, where available
- Assessment of mean corpuscular volume (MCV), in zidovudine containing regimens
- Periodic viral load determinations and CD4 cell counts
- Healthcare workers' assessments of patients' ART adherence at every routine visit

2.7 FACTORS AFFECTING ADHERENCE

Numerous factors affect ART adherence including behavioural, socio-demographic and health system factors. Reviews indicate that these factors can be placed into five categories such as patient-related factors, treatment regimens, patient-provider relationships, clinical settings, and disease-related factors (Ammassari et al 2002:123; Chesney 2000:171; Poppa et al 2003:48; Reiter, Stewart, Wojtusik, Hewitt, Segal-Maurer, Johson, Fisher, Zackin, Masters & Bangsberg 2000:67; WHO 2006b:89).

According to Weiser et al (2003:285-7), adherence rates in Botswana were comparable with adherence rates in most developed countries but patients in Botswana had to overcome financial constraints (44.0%), stigma (15.0%), travel/migration challenges (10.0%) and side effects of ARVs (9.0%).

2.7.1 Patient-related factors

A number of patient-related factors have been studied in relation to adherence to medications. These include socio demographic factors (age, sex, race, income, education, literacy, housing, HIV risk factors) and psychological factors (mental health, substance abuse, health beliefs, self-efficacy, socio-cultural issues and support, knowledge and attitudes about HIV and its treatment) (Carriere, Caillefon & Le Moing 2002:232; Machtinger & Bangsberg 2005:9; WHO 2006:88).

Patients' health beliefs and knowledge have been studied in various ways. Underlying the various models that address health beliefs is the assumption that an individual, faced with constraints, has preferences and must make choices to maximise benefits and minimise costs. The HBM asserts that adherence and other health-related behaviours are determined by one's beliefs concerning the severity of the illness, one's personal susceptibility, and one's evaluation of the costs and benefits of the recommended action (Moatti & Souteyrand 2000).

Bandura (1997) defined self efficacy beliefs as people's beliefs about their capabilities to exercise control over events that affect their lives. Self-efficacy beliefs determine an individual's choices of activities, coping, how much effort an individual will spend, and how he/she will persist in the face of obstacles (Bandura 1977:193).

Gifford et al (2000) examined predictors of adherence to ART among a mixed sample of 133 HIV-positive adults. Only self-efficacy and convenience of medication regimens remained significant in the final multivariate analysis of this study's results.

In a study of adherence among 72 women living with HIV/AIDS, Kalichman et al (2001) examined the relevance of the Information-Motivation-Behavioural Skills Model on adherence. Measures included assessments of treatment information, motivation to take medications, and adherence self-efficacy. Structural modelling indicated that self-efficacy was the only variable that had a direct effect on treatment adherence, while treatment motivation to take medications had direct effects on self-efficacy and indirect effects on adherence. The direct and indirect effects of treatment information were not significant.

Tuldra et al (2000:224) found that self efficacy was strongly and independently associated with adherence, in their controlled study of an intervention to improve adherence involving 116 HIV positive patients in Spain.

2.7.1.1 Age, race and sex

Studies report conflicting evidence about the association between socio-demographic factors and adherence behaviour. Some studies reported that certain socio-demographic variables influence ART adherence. However, others did not show such associations (Tadios & Davey 2006:243; Amico, Rivet, Harman & Johnson 2006: 285-297; Nachega, Michael, Dowdy, Lo, Omer, Leon, Chaisson & Gary 2006:1-7; Berg, Demas, Howard, Schoenbaum, Gourevitch & Arnsten 2004:1111-1117; John, Kaplan,

Sheldon, Li, Wilson 2004:1096-1103; Carballo, Cadarso-Suarez, Carrera, Fraga, de la Fuente, Ocampo, Ojea & Prieto 2004:587-99).

According to Catz, Kelly, Bogart, Benotsch & McAuliffe (2000:124-133), gender and other kinds of demographic variables have not traditionally been associated with adherence.

In a meta-analysis of ART adherence in which 31 studies from North America and 27 studies from SSA regions were incorporated, it was demonstrated that high levels of adherence could indeed be achieved in African settings (Mills et al 2006:679-690).

In a series of studies in several resource poor countries such as Rwanda (Demeester et al 2005:113-114), Haiti (Koenig, Leandre & Farmer 2004:21-25), and Uganda (Weidle et al 2006:1587-1594), it was demonstrated that high levels of ART adherence could be achieved, even in resource limited countries.

2.7.1.2 Mental Health

Depression and other psychiatric illnesses have been shown to be related to poor adherence to ART regimens as well as having a significant impact on the overall quality of life for PLWH in both high income and resource limited countries (Amberbir Woldemichael, Getachew, Girma & Deribe 2008:265; Byakika-Tusiime, Crane, Oyugi, Ragland, Kawuma, Musoke & Bangsberg 2009:82-91; Dalessandro et al 2007:58-61; Starace et al 2002:136-139; Hinkin et al 2002:1944-1950). In a review of various studies documenting the challenges to ART adherence, mental health problems such as depression, hopelessness, anxiety, avoidance, substance abuse, and other psychological problems were identified as the most common barriers (Fogarty et al 2002:93-108) that affect ART adherence levels negatively.

The relatively high rates of depression among South African women undergoing HIV testing (Rochat, Richter, Buthelezi, Tomkins, & Stein, 2006: 1376-1378), indicates that depression might pose a barrier to ART adherence. Symptoms of depression have been associated with lower CD4 counts (Seldjeski, Delahanty & Bogart 2005:728-736). There is consistent evidence that mental status, specifically depressive illness, plays a role in affecting ART adherence levels negatively (Kilbourne et al 2005:202-210; Seldjeski et al 2005:728-736).

2.7.1.3 Socio-cultural issues and support

Other factors included fear of disclosure and wanting to avoid taking medication in public places, feeling depressed, hopeless, or overwhelmed, having a concurrent addiction, forgetting to take medication at the specified times (Starace et al 2002:136-139; Castro 2005:338; Mills et al 2006:438).

Social support for adherence is defined as encouragement from family and friends for the patient to co-operate with the recommendations and prescriptions of a healthcare professional (DiMatteo 2004:207-218). Positive social support, including being married, is associated with ART adherence (Holstad, Pace, De, & Ura 2006:4-15; Parruti et al, 2006:48-56). However, in a qualitative study of HIV positive women, participants reported that ruptures in positive social support such as the death of a spouse, the end of an intimate relationship, and family conflict resulted in some questioning their need to adhere to their prescribed ART regimens (Wood, Tobias & McCree 2004:909-913), affecting their ART adherence levels negatively.

There are many other barriers such as being suspicious of the treatment and/or the medical establishment, wanting to be free of medication or preferring a natural approach (due to treatment fatigue); feeling that treatment is a reminder of HIV status, wanting to be in control, not understanding treatment instructions, still doubting or being unable to accept the HIV positive status and lack of self worth (Castro 2005:338; Mills et al 2006:438).

Persons living with HIV are often subject to stigmatisation and discrimination. It has been noted that stigma might be a barrier to ART adherence mainly due to the interaction between adherence and disclosure of one's HIV positive status (Klitzman et al 2004:628-640).

The threat of social stigmatisation might prevent people living with HIV/AIDS to disclose their HIV status. This might serve as a barrier to ART adherence. In a study done by Rintamaki, Davis, Skripkauskas, Benett and Wolf (2006:366) in Chicago, the effects of social concerns on treatment adherence were evaluated. People with high stigma concerns were 3.3 times more likely to be non-adherent to their medication regimens than those with low concerns.

Weiser et al (2003:285) noted that the negative repercussions of stigma included broken marriages and relationships, rejection by family, ostracism by the community and loss of employment. However, only 15.0% of patients reported stigma to interfere with their ability to take their treatment as prescribed. As a result, many patients kept their HIV status a secret from their families and communities.

Other factors that may affect ART adherence include attempts to hide the medication, changing the dosing schedules, or suppressing observable side effects of treatment. It has been suggested that disclosure to others might result in negative attitudes that could inhibit adherence (Klitzman et al 2004:628-640).

2.7.1.4 Education and income

Patient-level socioeconomic factors, such as income and education, have been shown to contribute to suboptimal ART adherence, while a high level of education seems to have a positive impact (Stone 2004:400-404, Mills et al 2006:438). Poor literacy abilities have been associated with low levels of understanding of medical instructions and adherence to ART (Kalichman, Benotsch, Suarez, Catz & Miller, 2000:325-331).

Yet, specific psychosocial interventions, designed specifically for patients with low literacy abilities, have been shown to yield adequate levels of ART adherence (Kalichman, Cherry & Cain 2005:3-15).

Poverty in itself is likely to affect adherence, as financial resources might have to be directed elsewhere, funds for travel to the ART clinic might be unavailable, and child-care might not be readily accessible for parents who needed to attend ART clinics. The competing demands of several responsibilities such as work and family life, along with the stresses associated with poverty and difficult life circumstances such as unemployment, might cause ART adherence to assume a low priority among all other responsibilities (Simoni, Frick, Lockhart & Liebovitz 2002:431-439).

As shown by Kagee, Le Roux, and Dick (2007:444-460), transport problems and the need to take time off work without pay to attend clinic appointments were serious barriers to adherence among patients with hypertension and diabetes, to the extent that many failed to arrive for appointments or refill their prescriptions. Conversely, a study in Cape Town, found no association between socioeconomic status and ART adherence (Orrel, Bangsberg, Badri & Wood 2003:1369-1375).

2.7.1.5 Alcohol and drug abuse

Drug abuse and alcohol consumption are factors that further threaten optimal adherence to ART. Studies have consistently shown that active alcohol use and substance abuse make it more difficult for patients to adhere to ART (Gill et al 2005:1243-1249; Weiser, Leiter, Heisler, McFarland, Percy-de Korte, DeMonner, Tlou, Phaladze, Lacopino & Bangsberg 2006:1940-1948; Chander, Lau & Moore 2006:411-417).

In a study by Christiansen, Vik and Jarchow (2002:393-404), heavy drinkers had lower adherence self-efficacy than those who drink less or who drink only in social situations.

A systematic review in 2009 found that ART patients who used alcohol were 50–60% less likely to adhere to their prescribed medications than those patients who did not use alcohol (Hendershot, Stoner, Pantalone & Simoni 2009:180-202).

In a study conducted among 1 889 ART patients, difficulties in obtaining medication were associated with non-adherence among heavy drinkers while a poor fit of the regimen with the patient's lifestyle was associated with non-adherence among drug users who drank heavily (Tucker et al 2004:363-370). Similarly, among a sample of ART patients whose use was electronically monitored, those with poor adherence had higher rates of substance abuse than those with higher ART adherence levels (Levine et al 2006:329-335).

In Botswana nearly 40.0% of the respondents admitted missing a dose because of alcohol consumption (Kip et al 2009a:153). Similar studies also indicated that alcohol use is associated with reduced ART adherence levels (Gill et al 2005:1243-1249).

2.7.2 Treatment regimens

Various combinations of ARVs are available, but side effects and negative interactions between medications are still an issue impacting on effective treatment and medication adherence. Pill burden (number of pills per day) has been a strong indicator of adherence failures, along with dosing frequency and side effects. Newer medication formulations, combining two or more drugs such as Trizivir (abacavir, AZT and lamivudine), dosed at one tablet twice a day and Atripla (Tenofovir, Entricabine and Efavirenz) dosed once a day, have reduced the number of pills to be taken daily, dosing three to four times a day and food restrictions. The combination of drug amounts, types, and eventual viral mutations leading to alterations in medication regimens, could none the less affect adherence. The numbers of pills and dosing schedules have decreased since the first use of AZT, but new regimes created concerns regarding medication induced medical conditions such as nausea, vomiting,

fatigue, headaches, anaemia and fat redistribution (lipodistrophy) (Zive & Learned 2005:16-21).

Some common barriers pertaining to beliefs/perceptions about medications include side effects, complicated regimens, the taste and size of the pills, dosing frequency, and/or pill count. When individuals on ART start feeling healthy, they might reduce their number of pills and/or the frequency of taking these pills, affecting ART adherence negatively (Castro 2005:338; Mills et al 2006:438). Other barriers include doubting the efficacy of ART, having a decreased quality of life; uncertainty about the long term effects and unwanted changes in body image, such as body fat redistribution (Mills et al 2006:438).

Weiser et al (2003:287) reported that 30.0% of Botswana's ART patients believed that they had swallowed too many pills every day and 5.0% stated that the large number of pills interfered with their ability to take the treatment. These authors also reported that side effects did not pose a large barrier to adherence in Botswana as fewer than 10.0% of ART patients in Botswana indicated that side effects were a significant barrier to adherence.

2.7.3 Patient-provider relationship

Positive interaction between patients and providers has been consistently associated with better adherence to ART in North American studies (Burke-Miller et al 2006:1044; Heckman et al 2004:219-230; Wroth & Pathman 2006:478-486). In the United States, a friendly, supportive, and non-judgmental attitude of healthcare providers and facility staff reportedly contributed to improved ART adherence (Altice et al 2001:47-58; Beach, Keruly & Moore 2006:661-665). When healthcare providers use communication tools that empower patients to be involved in their own care, health outcomes could be improved (Trummer et al 2006:299-306).

In Botswana, a study done by Weiser et al (2003:284), found that most interviewed patients had excellent relationships with their healthcare practitioners and felt respected and supported by their caretakers. The doctor-patient relationship has also been shown to be strongly associated with improved ART adherence levels (Ciechanowski, Katon, Russo & Walker 2001:29-35).

Indeed, medical providers should regard communicating with patients about ART adherence as an essential component of the healthcare service (Roberts 2002:43-50). While the provider-patient relationship might ostensibly constitute an example of social support, it also extends beyond this. The healthcare worker is often seen as a person with authority, in possession of specific expertise, and in whom the patient invests hope for assistance during the recovery process (Bury 2004).

On the other hand it has been shown that good intentions of medical providers, to emphasise the importance of ART adherence, might actually undermine adherence (Tugenberg, Ware & Wyatt 2006:269-274). Moreover, physicians' estimation of the adherence level of their patients were reportedly not always accurate (Murri et al 2004:1104-1110).

2.7.4 Clinical settings

Kgatlwane et al (2006:6) highlighted that patients' ART adherence levels might be influenced by health system barriers, such as access to the facility and to medication, the overall environment of the facility, and support services that are incorporated into care.

In a study by the WHO (2006:9), patients' long waiting times at clinics was found to be a major challenge to ART adherence. Patients have expressed difficulty balancing their need for transportation to the clinic and any medication costs against the need to pay for food, school fees, and other necessities for themselves and their families. As a result, some patients have missed pharmacy pick-ups and other follow-up appointments

(Hardon et al 2007:658-665; Stout et al 2004:297-304). According to Weiser et al (2003:283), in a study done during 2000 in Botswana, having to travel long distances for services can hinder adherence to ART.

2.7.5 Disease-related factors

Disease characteristics influence rates of ART adherence in several ways. These include the stage and duration of HIV infection, associated opportunistic infections, and HIV-related symptoms (Machtiger & Bangsberg 2005:5). Opportunistic infections (OIs), which interfere with cognitive functions, include cryptococcal meningitis, toxoplasmosis, progressive multifocal leuko-encephalopathy (PML), and central nervous system lymphoma (Clifford 2002:537-550). In the context of ART adherence, neuro-cognitive deficits, particularly everyday functioning abilities such as memory, learning and executive functioning, can contribute to ART non-adherence. According to Hinkin et al (2002:1944-1950), 34.0% of the respondents (n=46) were cognitively impaired and reported a 73.0% ART adherence rate, which is both inadequate for therapeutic gains and in the zone of development of potential drug resistance. Cognitively impaired individuals reported more difficulties with increasingly complex regimens, requiring more than twice daily dosages. This study found that cognitive dysfunctions contributed to lowered adherence and that neuro-cognitive deficits lead to poor adherence. However, inadequate ART adherence levels can also contribute to the development and/or aggravation of neuro-cognitive deficits.

Some studies, however, showed that patients who had serious OIs might perceive their illness to be severe and adhere better to their treatment, although the results have been mixed in terms of the strength and direction of this association (Gifford et al 2000:386-395; Paterson et al 2000:21). Adherence was reportedly better among patients who had spent fewer days in the hospital with opportunistic infections (Paterson et al 2000:21).

Overlapping toxicities of medications used to treat AIDS defining illnesses such as tuberculosis (TB), a common OI in resource-limited settings, could also result in similar challenges with concurrent treatment of HIV and TB (Pepper et al 2007:980-989). This is the case because both ARVs and anti-TB drugs can produce side-effects, aggravated by the more severely ill PLWHA affected by both HIV and TB.

2.8 APPLICATION OF THE SOCIAL COGNITIVE THEORY TO THIS STUDY

This study integrated social support with constructs from the Social Cognitive Theory to explore the determinants of ART adherence. Social support is defined as assistance that is given through formal or informal relationships with the intention of being helpful to the beneficiary (Heaney & Israel 2002), and has been categorised into four broad forms of supportive behaviours (emotional, instrumental, informational and appraisal) (Ferguson et al 2002:607-617).

Social cognitive theory is a behavioural theory that integrates intrapersonal and interpersonal levels of the social ecological framework and situates them together in a dynamic environment. The organising concept of Social Cognitive Theory is reciprocal determinism, which asserts continual interaction between the behaviour, the person, and the physical and social environment (Baranowski et al 2002:165-184).

Albert Bandura (1977:191-215), who has been refining the Social Cognitive Theory since the 1970s, has identified five core constructs of the Social Cognitive Theory:

- Knowledge of health risks and benefits of a specific behaviour
- Self-efficacy to perform a behaviour
- Outcome expectations of a behaviour
- Goal setting and strategies to attain a goal of health behaviour
- Perceived facilitators and obstacles to performing a behaviour

2.8.1 Individual level

Psychological and behavioural factors at the individual level are important for explaining ART adherence. All the individual-level determinants are informed by the Social Cognitive Theory.

2.8.1.1 Perceived self-efficacy to adhere to ART

Self-efficacy is defined as the confidence a person feels about performing a particular activity, including confidence in overcoming the barriers to performing that behaviour (Baranowski et al 2002:165-184). Bandura (2004) asserted that self-efficacy is perhaps the strongest determinant influencing whether or not a person will undertake a particular behaviour.

For people who have never previously taken chronic medications, the idea of taking pills every day, for the rest of one's life, could be daunting. This is particularly the case in the face of disrupting circumstances, such as experiencing side effects, travelling, or trying to hide one's HIV status, especially from significant other people such as spouses or family members. Adherence requires confidence that one can take the pills every day, even in the face of difficult circumstances. Self-efficacy has been associated with adherence in several studies (Catz et al 2000:124-133; Chesney 2000:S171; Gifford et al 2000:386-395; Godin et al 2005:493-504; Wilson et al 2004:251-257), including one study in a developing country (Pineiro et al 2002:1173-1181).

2.8.1.2 Skills or strategies applied to ART

The Social Cognitive Theory identifies goal-setting and specific strategies to achieve goals as important for achieving behaviour change (Bandura 1977:191-215). Qualitative studies have identified the use of skills and strategies to ensure adherence including: pillboxes, alarm devices, carrying pills in a bag, and associating pill taking with other daily activities (Adam, Maticka-tyndale & Cohen 2003:263-274; Golin, Isasi, Bontempi,

& Eng 2002:318-329; Kumarasamy et al 2005: 530-533; Ryan & Wagner 2003:795-806). In a study in Costa Rica, people who set out their pills on a daily basis had better adherence levels than people who did not use this strategy (Stout et al 2004:297-304). In a prospective study in the United States, patients who used some adherence aids had significantly better adherence levels than patients who used no adherence aids (Golin et al 2002b:756-765).

2.8.1.3 Knowledge of ART

The Social Cognitive Theory views knowledge of the risks and benefits of a given health behaviour as a precondition for embarking on changing behaviours (Bandura 1977). For ART adherence, it is important that people have some basic comprehension of the mechanisms of ART, that they understand the long term nature of ART, and that they grasp the potential negative impact of non-adherence. One study, that specifically considered the association between knowledge of ART and adherence, found that people with better ART knowledge were less likely to miss pills, compared to people with less ART knowledge (Weiser et al 2003:281-288). In a longitudinal study in the United States, patients who had poor knowledge of their ART regimens, eight weeks after initiating treatment, demonstrated poorer adherence levels than those with better understanding of these issues (Burke-Miller 2006:1045).

2.8.1.4 Outcome expectations of ART adherence

Outcome expectations are what people expect will happen if they perform a given behaviour. Outcome expectations may be either positive (expecting good things) or negative (expecting bad things). Positive outcome expectations increase the pros of performing behaviour and therefore create incentives to perform a given behaviour. These incentives may take the form of physical outcomes, social outcomes or self-sanctions (Fishbein et al 2001). Negative outcome expectations increase the cons of performing behaviour and therefore present barriers to achieving behaviour. When people begin taking ART, they would probably have some positive expectations of

taking the drugs. For example, they might expect that their health will improve, that they will be able to return to work, or that they will live longer.

They might also have negative expectations, such as experiencing side effects, disrupting their normal daily routines, or having people find out that they are HIV-positive. The balance of positive to negative outcome expectations, which might change over time, could influence patients' motivation levels to adhere to ART. In a study in Brazil, low positive outcome expectations were associated with poor ART adherence levels (Pinheiro et al 2002:1173).

2.8.1.5 Interpersonal level

People live in a social environment where they are constantly being influenced by other people. It is critical to understand how these interpersonal aspects could influence ART adherence. Although all the variables are measured at an individual level, their influences, and subsequent interventions, occur at an interpersonal level.

2.8.1.6 Patient-provider interaction

A good relationship between patients and healthcare providers is recognised as being vitally important for positive health outcomes (Golin, Thorpe & DiMatteo 2008:210-214; Lewis, DeVellis & Sleath 2002:260-264). When healthcare providers use communication tools that empower patients to be involved in their own care, health outcomes can be improved (Trummer et al 2006:300-305). Positive interaction between patients and providers has been consistently associated with better adherence to ART in North American studies (Burke-Miller et al 2006:1046-1041; Heckman et al 2004:220-228; Wroth et al 2006:478-486). Adherence could be improved when patients feel free to ask questions and can honestly share their experiences with healthcare providers, and when providers listen to their patients and impart relevant information and skills (Schneider et al 2004:1096).

2.8.1.7 Perceived levels of social support

Social support is positive assistance that is intentionally given by one person to another. In general, social support has been associated with adherence to medications (DiMatteo 2004:218) and in particular, with adherence to ART (Ammassari et al 2002:S123-S127). The mechanisms through which social support exerts an influence on adherence have not been studied sufficiently. DiMatteo (2004) suggests that instrumental support might lead directly to adherence through the provision of practical support, while the relationship between emotional support and adherence might be mediated by a reduction in stress and depression, or an increase in self efficacy or self esteem.

2.8.1.8 HIV and ART disclosure experiences

Because of community level stigma and fear of negative repercussions, many people might not disclose their HIV positive status to others (Blacker 2004:S19-26; Chandra et al 2003:207-215; Petrak et al 2001:69-79). Among women receiving HIV testing in a Dar es Salaam clinic, only 64% of those who tested positive disclosed their HIV status to their sexual partners (Maman et al 2003:373-382). Among women who did not disclose their HIV positive status, most reported that they were afraid of their partners' reactions. If the response to the disclosure of one's HIV positive status to others, including family members, partners, friends and neighbours, is supportive and understanding, then disclosure might increase support for taking ART effectively.

Failing to disclose one's HIV status, might make it difficult to take ART on a regular basis, both because of not wanting to take ART in front of others and lacking outside cues for assistance. A qualitative study among ART patients in the rural areas of the USA found that many patients missed doses because of fear of being identified as HIV-positive (Golin et al 2002a:218). In Botswana, 69.0% of ART patients did not disclose their HIV status to their families and 94.0% did not disclose to other people in their lives ($p=0.07$) (Weiser et al 2003:285).

2.8.1.9 Community level

While interpersonal influences deal with dyads, community influences deal with broader issues of group norms and cultural expectations. While the variables are measured at an individual level, their influences, and therefore subsequent interventions, occur at community level.

2.8.1.10 Perceived stigma towards people living with HIV

The term “stigma” originates from the Greek language and refers to a tattoo mark branded on the skin of an individual as a result of some incriminating action, identifying the person as someone to be avoided (Visser, Makin & Lehobye 2006). Researchers distinguish between perceived or felt stigma and enacted stigma, which refers to identifiable forms of discrimination. In a mixed-methods study conducted on HIV stigma in Ethiopia, Tanzania and Zambia, people living with HIV/AIDS faced physical isolation from their family members, friends and communities when their HIV status was known (Nyblade et al 2003). Both perceived and enacted stigma led to isolation and a sense of hopelessness and resulted in the loss of access to physical and social resources. The study found that stigma resulted in people delaying HIV care until absolutely necessary and not getting the consistent care that was required. This impact of stigma could prevent ART patients from regularly attending clinic appointments and picking up their medications on time. In a South African study, ART patients who reported that they were afraid of being stigmatised by their sexual partners reported worse adherence levels than patients who did not express a fear of being stigmatised (Nachega et al 2004:1053).

2.8.1.11 Perceived normative beliefs of taking ART

Normative beliefs refer to people’s beliefs about whether individuals in their reference group would approve or disapprove of a given behaviour. Normative beliefs make up a

core construct of the theory of reasoned action (Montano & Kasprwyk 2002:67-98), and are also inherent in the theoretical framework of social influence/interpersonal communication (Lewis et al 2002:254). Normative beliefs of taking ART refer to whether people believe that others around them (family members, friends, religious leaders and physicians) approve or disapprove of their taking ART.

2.8.1.12 Environmental level

The Social Cognitive Theory asserts that obstacles can make it nearly impossible to perform health-related behaviours, even if all other facilitators are in place. An obvious obstacle is the physical accessibility of the ART clinic. Even with the strongest motivation, if people are not able to keep their clinic appointments and pick up prescriptions on time, adherence would be impossible. Clinic accessibility could be a barrier if patients live far from the clinic, and if they cannot return for clinic appointments and drug pick-ups, if they cannot afford transportation to the clinic, or if the clinic has operating hours that are incompatible with patients' schedules. Difficulty finding or affording transportation to the clinic has been documented to negatively influence ART adherence (Hardon et al 2007:664; Stout et al 2004:300).

2.9 APPLICATION OF THE SOCIAL COGNITIVE THEORY AND THE HEALTH BELIEF MODEL TO ART ADHERENCE RESEARCH

The Social Cognitive Theory constructs are used to investigate congruent and incongruent beliefs held by HIV positive individuals with regards to antiretroviral drugs. Research on conditions such as diabetes and hypertension has shown that patients from diverse populations often have complex mixes of medically accurate and inaccurate beliefs.

The Social Cognitive Theory has attempted to explain health-related behaviours that influence prevention and promotion of personal health (All, Nishakawa, Vinson & Huycke 2004). It assumes that good health is a goal of most persons and that their

perceptions of susceptibility, seriousness, benefits, barriers and self-efficacy impact on the likelihood of a person sustaining actions that are health-related by adhering to their prescribed ARV treatment.

The Social Cognitive Theory is particularly applicable to adherence issues in HIV positive individuals. Therefore, this study will apply the Social Cognitive Theory in an effort to demonstrate the relationship between adherence, the health beliefs and self-efficacy of HIV positive individuals and how these influence their subsequent health behaviours by identifying the factors that might impact on patients' ability to adhere to their ART regimens.

The Health Belief Model has been applied to a broad range of health behaviours and subject populations. Three broad areas were identified by Conner and Norman (1996), namely:

- Preventive health behaviours, such as health promoting (diet and exercise) and health risk (smoking) behaviours as well as vaccination and contraceptive practices.
- Sick role behaviours, referring to compliance with recommended medical regimens such as ARVs), usually following professional diagnosis of the illness.
- Clinic use, which includes physician (or clinic) visits for various reasons.

Thus, the HBM is relevant to the Botswana context with a medley of cultures with their various beliefs. These beliefs might contribute to delayed presentation at hospitals and clinics as well as adherence failure.

Research done with other models has provided many insights into the determinants of people's motivations to adopt a whole range of health-related behaviours (Becker, Haefner & Maiman 1977). Positive correlations exist between patients' adherence levels and their health beliefs.

2.10 SUMMARY

Taking ART is a lifelong responsibility and an ART adherence level of 95.0% or more is crucial to maintain viral suppression and increase immunologic responses; and also to reduce morbidity and mortality caused by AIDS. Regular assessments of patients' adherence to ART for optimal treatment outcomes with multiple adherence measures are necessary.

Research is needed to identify factors affecting ART adherence to enable clinicians to use this information and engage in open discussions with patients to promote ART adherence levels.

Chapter 3 will discuss the research methodology adopted by this study.

CHAPTER 3

RESEARCH DESIGN AND METHOD

3.1 INTRODUCTION

This chapter describes the design and methodology that was adopted by this study. This chapter looks at research design and method, sampling techniques, study population, ethical considerations, data collection, data analysis, and internal and external validity of the study.

3.2 RESEARCH DESIGN

The research design is the blueprint for conducting a study that maximises control over factors that could interfere with the validity of the findings (Burns & Grove 2009:696) or the entire strategy followed from identification of the problem to final plans for data collection (Burns & Grove 2005:211). Strydom, Fouche and Delport (2002:137) define a research design as a specification of the most adequate operations to be performed in order to test specific hypotheses under given conditions.

A cross sectional quantitative survey, using structured interview schedules to collect data, was used in this study. A cross-sectional study is used to examine groups of subjects in various stages of development simultaneously with the intent of inferring trends over time (Burns & Grove 2009:694). According to Grimes and Schulz (2002:58), cross-sectional studies are done to examine the presence or absence of disease and the presence or absence of an exposure at a particular time.

A quantitative study is a formal, objective, systematic study process to describe and test relationships and to examine cause and effect interactions among variables (Burns &

Grove 2009:717). This study systematically and objectively analysed data obtained from respondents to identify the barriers and motivators to ART adherence. Statistics were used to describe and summarise the data.

A survey is a data collection technique in which questionnaires or personal interviews are used to gather data about an identified population (Burns & Grove 2009:724). Primary data were collected through interviewing respondents and secondary data were collected through reviewing medical and pharmacy refill records of the respondents after getting permission from the healthcare institution's management and consent from the respondents.

3.3 RESEARCH METHOD

This section specifies the method of data collection, as well as the variables or characteristics measured. It describes measuring instruments, provides an indication of their reliability and validity of the instrument, and also indicates the desired characteristics (inclusion and exclusion criteria) of the respondents and the setting in which the study was conducted.

The setting refers to the location for conducting research, such as a natural, partially controlled, or highly controlled setting (Burns & Grove 205:751). The study was conducted at the Infectious Disease Control Centre (IDCC) clinic located at the district hospital where HIV patients are consulted every working day and where patients receive ART.

3.3.1 Population and sample

3.3.1.1 Population

According to Stommel and Wills (2004:441), a study population is defined as any universe of subjects, cases, units, or observations containing all possible members. Burns and Grove (2009:714) define a population as all elements including individuals, objects, events, or substances that meet the sample criteria for inclusion in a study; sometimes referred to as target population. This group, called the study population or target population, should be clearly defined in respect of person, place and time, as well as other factors relevant to the study (Katzenellenbogen et al 2007:94).

The study population for this study comprised adult ART patients who had been on ART at the participating clinic for at least six months by 31 October 2011. The study site's July 2011 report indicated that 3 501 patients were receiving ART at this clinic (MOH 2011:4). Out of these 3 501 patients, approximately 2 000 patients had been receiving ART for more than six months at this clinic by 31 October 2011, and were at least 21 years old, comprising the target population for this study.

3.3.1.2 Sample and sampling procedure

Sampling is a process of selecting subjects, events, behaviours, or elements for participation in a study (Burns & Grove 2009:35). Sampling involves selecting a group of people, events, behaviours or other elements with which to conduct a study. Sampling theory determines mathematically the most effective way to acquire a sample that would accurately reflect the population under study. The key concepts of sampling theory are population, elements, sampling criteria, representativeness, sampling errors, randomisation, sampling frame and sampling plan (Burns & Grove 2009:343).

Eligible patients, attending routine visits at the clinic, were selected using systematic sampling until the required sample size had been obtained. The sampling interval K of 7 was calculated using the following formula: K equals N (N=2000) divided by n (n=300).

Box 3.1: Sampling interval

$$\text{Sampling interval } K = \frac{N}{n}$$

Where k = sampling interval;
N is the sampling frame , and
n is the sample size

Burns and Grove (2009:344-345) define eligibility or sampling criteria as a list of characteristics essential for membership or eligibility in the target population. Eligibility criteria include both inclusion and exclusion criteria

3.3.1.2.1 Inclusion criteria

Inclusion sampling criteria are characteristics that an element or a subject must possess to be part of the target population (Burns & Grove 2009:345). The inclusion criteria for this study were:

- patients aged ≥ 21 years old on ART for at least six months by 31st October 2011
- having at least two CD4 cell counts and one viral load result during the last six months
- agreeing to participate in the study and willing to sign the consent form.

3.3.1.2.2 Exclusion criteria

Exclusion sampling criteria are characteristics that can cause a person or element to be excluded from the target population (Burns & Grove 2009:345). The exclusion criteria for this study were:

- Patients younger than 21 years of age
- Clients who had been on ART for less than 6 months by 31st October 2011
- Clients without at least two CD4 cell counts and one VL result during the last six months

3.3.1.3 Sample size

A sample is a subset of the population that is selected for a study and a sample size refers to the number of respondents recruited and consenting to take part in a study (Burns & Grove 2009:721).

Using the accrual rate for the site, it was estimated that by August 2011 approximately 2 000 patients would have received ART at the site and would have been on ART for at least 6 months, representing 60.0% of those on ART cumulatively. Using an estimated 80.0% adherence rate for Botswana (MoH 2006b) and worst acceptable 75.0%, an estimated minimum sample size of 245 was calculated using the method of Israel (1992:2) (Box 3.2). In order to cater for a potential non-response of 20.0%, the final sample size estimate comprised 295 respondents.

Box 3.2: Sample size calculation

$$\text{Sample size (n)} = \frac{Z^2 pq}{e^2}$$

where Z^2 = is the abscissa of the normal curve that cuts off an area α at the tails ($1 - \alpha$ equals the desired confidence level, e.g., 95%) = 1.96; e is the desired level of precision (in this case 5%); p is the estimated proportion of good adherence (0.8) in the population, and q is $1-p$.

3.3.2 Data collection

Data collection is a precise, systematic gathering of information relevant to the research purpose or the specific objectives, questions, or hypotheses of a study (Burns & Grove 2009:695). It is the process by which information is obtained about the characteristics of individuals being studied (Katzenellenbogen et al 2007:106). Perceived self-efficacy to adhere to the prescribed ART regimen was measured using 10 items that addressed respondents' confidence levels. Patients' health beliefs were also addressed in this data collection tool.

3.3.2.1 Data collection approach and method

A structured interview schedule, with mostly closed-ended and some open-ended response options, was developed specifically for this study. A structured interview uses strategies that enable the researcher to control the interview process (Burns & Grove 2009:724). While conducting structured interviews, the interviewer followed the structured format to prevent him from placing his own interpretation on the questions. The interviewer asked questions in a standard way, with the same clarifications for each respondent, and he also recorded the verbal responses to open-ended questions in a uniform way.

3.3.2.2 Development and testing of the data collection instrument

A structured interview schedule in Setswana was developed specifically for this study, based on the literature review, comprising open and closed ended items. The English structured interview schedule was translated by a proficient English-Setswana translator (see Annexure 12 for a letter from the translator). A research assistant, trained by the researcher, conducted the structured interviews with the patients.

A pre-test was conducted by interviewing 10 patients, who were excluded from participation in the actual study. This enabled the researcher and the research assistant

to identify any potential comprehension problems, recording problems and to estimate the time needed to complete each structured interview. The researcher did not encounter any major problems that could lead to the interview schedule's modification. Each interview took from 22 to 40 minutes.

3.3.2.3 Characteristics of the data collection instrument

The structured interview schedule was divided into sections assessing respondents' health beliefs, self efficacy and social support systems. Questions were also asked to obtain information about issues pertaining to demographics, clinical aspects, counselling experiences, adherence levels, perceived self-efficacy to adhere to the prescribed ART regimen, skills and strategies for taking medication, disclosure issues, perceived stigma, side effects, patient-provider communication, and social aspects. The order of the questions was specified. The structured interview schedule had ten (10) sections (see Annexure 3 and 4).

Section A dealt with demographic information. It asked information about gender, age in years, marital status, educational level, employment status, income, loss of income and residential address.

Section B dealt with clinical information. It asked about duration on HAART, initial and current CD4 cell counts, current plasma viral load, current treatment regimen, reasons for change of treatment regimen (if appropriate) and pharmacy refill records.

Section C dealt with counselling information. It asked who was the treatment adherence partner or supporter, who did the counselling before the ART initiation and how many times the patient had been counselled since he/she started ART.

Section D dealt with adherence information. It asked about the number of appointments missed, self-report medication adherence (four days' recall period), and the last part of this section asked about issues that made the patients miss their medications which

included feeling better, clinic accessibility, availability of food, depression, pill burden, lack of care or support, hospitalisation, inability to understand the instructions, alcohol use, forgetfulness, running out of pills, side effects and alternative treatments used by the patient.

Section E dealt with perceived self-efficacy to adhere. It had 10 questions asking about the level of confidence to take medication.

Section F dealt with skills and strategies applied to taking medication. It had six questions asking about different skills and strategies used by patients to take their prescribed medications.

Section G dealt with disclosure issues. It asked about the number of people each patient had told about his/her HIV status, the time taken before disclosure and to whom they had disclosed their HIV positive status.

Section H dealt with perceived stigma. It had 11 questions asking how worried the patient was about different circumstances.

Section I dealt with side effects and asked about nausea, vomiting, diarrhoea, headache, skin rashes, dizziness, depression and nail discolouration. It also asked if these side effects affected the patient's daily activities.

Section J dealt with patient-provider communication. It had 11 questions asking about how satisfied patients were with the healthcare providers.

Section K dealt with social information and it had 11 questions asking about traditional medicine use, alcohol and cigarette consumption, number of sexual partners and their HIV status.

3.3.2.4 Validity and reliability of the research instrument

Validity refers to the degree to which a measure adequately reflects the actual meaning of the concept under consideration (Babbie & Mouton 2001:122). Face validity refers to how much a measure covers the range of meanings included within the concept (Babbie & Mouton 2001:123). According to De Vos (2007:161), face validity concerns the superficial appearance or face value of a measurement procedure.

Content validity is concerned with the adequacy of coverage and representativeness of the content area being measured. The content of the structured interview schedules was based on the contents covered by studies reported in the literature review. Construct validity determines whether the instrument measures the theoretical construct that it purports to measure (Babbie & Mouton 2009:663). In this study, five healthcare providers, trained and knowledgeable about ART issues, were consulted and agreed that the instrument appeared to address ART adherence issues.

The reliability of a data collecting instrument refers to the accuracy or precision of an instrument (De Vos et al 2002:168-169). It is a matter of whether a specific method, if applied to the same object, would give the same results (Babbie & Mouton 2001:119-120).

A pre-test was conducted on 10 patients and the results were not included in the data analysis of the actual study. This enabled the researcher and the research assistant to identify any potential comprehension problems, recording problems and to estimate the time needed to complete each structured interview.

The reliability coefficients are important indicators of an instrument's quality. Unreliable measures do not provide adequate tests of a researcher's hypotheses. If the data fail to confirm a prediction, it could be that the instruments were unreliable and not necessarily that the relationship did not exist. Knowledge about an instrument's reliability is thus

critical for interpreting research results, especially if research hypotheses are not supported.

Cronbach's alpha is a statistical estimate used as a measure of reliability of a psychometric instrument (Vehkalantahnti, Puntamen & Tarkkonen 2006:6). The SPSS version 13 was used to estimate the Cronbach's alpha coefficient for the data collection instrument (structured interview schedule). According to Burns and Grove (2005:374), a reliability coefficient of 0.70 is sufficient for a newly developed psycho-social instrument.

3.3.2.4.1 Reliability: Cronbach Alpha scores

Reliability analysis allows you to study the properties of measurement scales and the items that make them up. The reliability analysis procedure calculates a number of commonly used measures of scale reliability and also provides information about the relationships between individual items in the scale. The Cronbach Alpha scores were used to assess the reliability of likert scales used to measure "perceived self-efficacy" (section E), "perceived stigma (section H)" and "perceived patient provider communication" (section J). The Cronbach Alpha of 0.85 was acceptable based on the classification by Cortina (1993).

Table 3.1: Reliability Statistics

Cronbach's Alpha	Cronbach's Alpha Based on Standardized Items	N of Items
.850	.796	24

3.3.2.5 Data collection process

Every morning the clinic nurse informed all eligible ART patients about the study and, if they were interested in participating, he/she referred them to the interviewer who conducted individual structured interviews, in Setswana or English, after being trained by the researcher. The interviews took place in a private office and no disturbances

occurred during the interviews. The researcher checked the completed interview schedules at frequent intervals to identify and address any potential problems/shortcomings in the data collection process.

Pill counts from January 2011 to the date of interview were recorded from each patient's records and adherence percentages were calculated by counting the remaining doses of medication and assuming that remaining pills, exceeding the expected number, represented missed doses. The percentage of adherence was calculated by subtracting the number of remaining pills from the number of dispensed pills, divided by the expected number of pills to be taken and the result multiplied by 100. The expected number of pills to be taken was calculated by multiplying the number of days (including missed clinic attendance days) by the prescribed number of tablets to be taken per day.

Box 3.3: Adherence calculation

$$\% \text{ adherence} = \frac{\text{Dispensed} - \text{returned}}{\text{Expected to be taken}} \times 100$$

Pharmacy refill records covering the period between 1 January 2011 and the day of interview were recorded. Exact dates when ARVs were collected from pharmacy were compared with the expected refill dates as previously appointed. The adherence was calculated by dividing the respondent's number of pharmacy refills that occurred the same day as appointed by the total number of expected pharmacy refill appointments, multiplied by 100.

Self-report adherence was assessed by asking respondents if they had missed any medication doses during the four days preceding the interview. A categorical variable was constructed reflecting two levels of adherence during a four day period namely "missed" and "not missed" taking medication doses during the past four days.

The completed structured interview schedules were kept securely locked up and were handled in a very confidential manner. Only the researcher and the statistician had access to the completed interview schedules.

3.3.3 Data analysis

The p-value was set at <0.05 for statistical significance. Descriptive statistics were used for analysing the sample's demographic characteristics. Statistical analysis methods were used to measure associations using SPSS version 13. Associations between social factors and adherence were determined using Chi-squares or Fishers exact test, where expected values were less than five. The 95.0% confidence intervals were estimated using the binomial exact methods. A statistician assisted with the analysis and interpretation of the data (see Annexure 13: letter from the statistician).

The outcome measure of adherence was based on the pharmacy refill data, the pill counts and the self report, and the correlation of these measures to the changes in the patients' CD4 cell counts and the viral load results.

3.4 ETHICAL CONSIDERATIONS

Permission to carry out the study was granted by the University of South Africa (see Annexure 10), the Botswana Ministry of Health (see Annexure 9) and the participating healthcare institution's management (see Annexure 11) with names deleted to guarantee anonymity. (The researcher and his supervisor have copies of the original permission granted in case of queries).

3.4.1 Informed consent

Burns and Grove (2009:704) defined informed consent as a prospective respondent's agreement to voluntarily participate in a study, which is reached after assimilating

essential information about the study. It was also defined by Stommel and Wills (2004:439), as the disclosure statement to be signed by each respondent that contains a clear account of all the risks and benefits involved in the participation in a particular research study.

Signed informed consent (see Annexure 5 and 6 for an informed consent form in English and Setswana) was obtained prior to conducting any structured interview. The signed, informed consent also guaranteed the confidentiality agreement on the side of the researcher. Participation in the study was voluntary and refusal to participate in the study had no effect whatsoever on any patient's treatment. No respondent was coerced to answer any specific question that he/she did not want to answer.

Each respondent was informed about the interview procedure, and its potential risks and benefits. No risks were anticipated as only interviews were conducted. However, if any respondent might get upset or experience any negative reaction during or as a result of the interview, the researcher was available to assist such a patient and to refer the patient to the relevant healthcare provider, if that should be deemed necessary. No remuneration was paid but patients might benefit in future if factors that promote or hinder ART adherence could be identified and addressed as a result of this study.

3.4.2 Anonymity

Anonymity means that the respondent should not be identifiable at any time by anyone reading the research reports (Holland & Rees 2010:98). It also means that no subject's identity can be linked, even by the researcher, with his or her individual responses (Burns & Grove 2009:688).

Prior to the interviews, all respondents were requested not to make any reference to colleagues or to their clinic numbers. Respondents were assured that all information gathered was treated carefully and anonymity was maintained by de-identifying health data and no names were used. Each respondent was assigned a code number for data

processing purposes only. A red dot on the right hand side corner of the back side of the patient's file indicated that the patient had been interviewed, avoiding the risk of interviewing any patient more than once. The relevant information from the patient's file such as the CD4 and VL counts were entered directly from the file, avoiding the necessity of retracing any patient's file and also making a list correlating the interview number with any patient number irrelevant and unnecessary.

Every signed consent form was sealed in an envelope and placed into a sealed container. The completed interview schedules were placed into another sealed container. This ensured that no signed consent form could be linked to any specific completed interview schedule to maintain anonymity.

3.4.3 Confidentiality

Confidentiality is essential in order to protect people, especially if they are disclosing sensitive information as part of the research (Holland & Rees 2010:99). It is defined by Burns and Grove (2009:693), as management of private data in research so that subjects' identities are not linked to their responses.

The individual interviews were conducted privately in a specific room. It was ensured that the interviews were inaudible to all other persons. During this study all respondents were verbally reassured about the confidentiality of the information provided. The researcher requested respondents not to discuss the content of the interview with other patients. No unauthorised person could access the signed consent forms or the anonymously completed interview schedules which were kept securely locked up.

3.4.4 Feedback

Feedback would be provided to all stakeholders. Copies of the dissertation will be given to Botswana's Ministry of Health, the participating hospital and respondents who requested such reports, after the acceptance of the dissertation. This opportunity was

offered to every interviewee. Any articles published, based on this study's findings, will also be supplied to the relevant authorities.

3.5 SUMMARY

This chapter described the steps that were followed by the researcher during the research process. A cross sectional quantitative survey was used to determine factors affecting ART adherence by AIDS patients. Only structured interviews, conducted with 300 respondents, were used to collect data. The ethical principles, adhered to throughout this study, were also explained in this chapter. The researcher gave significant attention to ethical procedures and practices, such as informed consent, non-coercion of participation and of answering any specific question, and maintaining privacy and confidentiality. Statistical analysis methods were used to analyse and summarise the data using SPSS version 13.

Chapter 4 deals with the presentation, analysis and discussion of the data collected from 300 structured interviews and patients' records.

CHAPTER 4

ANALYSIS, PRESENTATION AND DISCUSSION OF THE RESEARCH FINDINGS

4.1 INTRODUCTION

This chapter provides a summary of the results of the study. A total of 300 respondents consented to participate in the study. Clinical data were also extracted from patients' medical records, including pharmacy refill frequencies and dates. In order to understand the factors affecting adherence, the univariate data analysis examined adherence estimates, the characteristics of the respondents, service providers, and social behaviours associated with ART adherence. This chapter also presents the results of the multivariate analyses exploring the independent predictors of adherence such as age, CD4 cell count and viral load.

4.2 DATA MANAGEMENT AND ANALYSIS

Data were coded and captured electronically. Accurate coding was ensured by entering data from the interview schedules into an excel spreadsheet. Data entries were checked by the statistician. Data were then cleaned and exported to SPSS version 13 for analysis. Adherence rates, measured via pill counts, were defined as the number of doses taken divided by the number of doses prescribed. Respondents were categorised as being adherent (taking $\geq 95.0\%$ of pills) or non-adherent (taking $\leq 94.9\%$ of pills).

Medication refill appointment records are a coarse measure of adherence. Respondents were given one or two months' supplies of ARVs at a specific clinic visit and therefore had to collect their medication refills every one or two months. Adherence was then calculated based on pharmacy refill records. The adherence level by self report (four days' recall period) was calculated to obtain the short term adherence level.

Descriptive statistics were used to analyse socio-economic and demographic

characteristics of the respondents as well as other variables. Bivariate analysis was used to examine the potential factors affecting the different measures of adherence. Chi-square tests or Fisher's Exact tests were used to test the associations between the different variables and adherence levels.

Respondents' current viral load data (categorised as <400 copies/mm³ meaning suppressed and ≥ 400 copies/mm³ meaning detectable viral load) and CD4 cell count data (categorised as < 200 or ≥ 200) were analysed descriptively. Data were analysed descriptively and cross tabulated with adherence using proportions and Chi square tests of independence.

4.3 RESEARCH RESULTS

4.3.1 Socio-demographic characteristics

Table 4.1 summarises the socio-demographic characteristics of the 300 respondents. There were more female (74.3%; n=223) than male (25.7%; n=77) respondents (see figure 4.1). Many males were not willing to participate in the study, and refused to sign the informed consent forms, explaining why fewer males than females participated in the study.

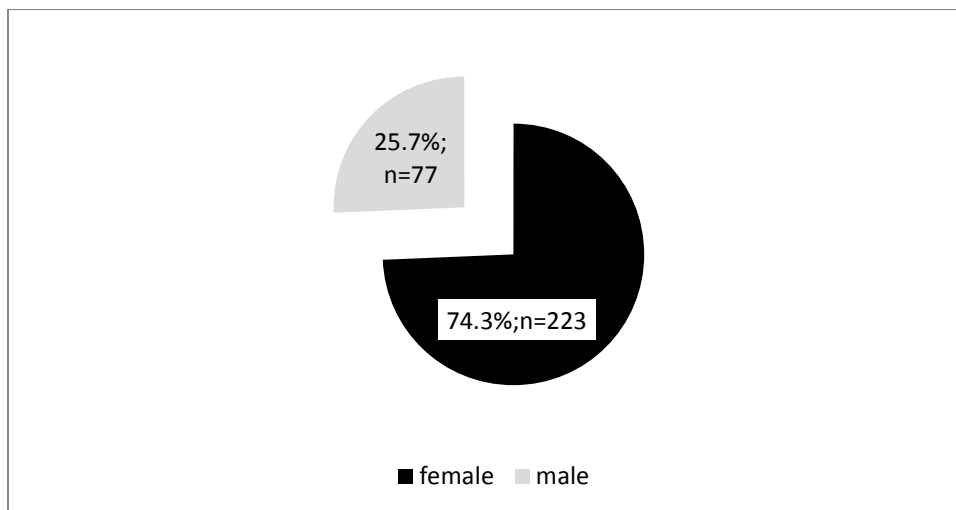


Figure 4.1: Respondents' gender distribution (N=300)

Of the 300 respondents, 195 (65.0%) had never been married, 46 (15.3%) were married, 42 (14.0%) were cohabiting and 17 (5.7%) were divorced, widowed or separated (see figure 4.2).

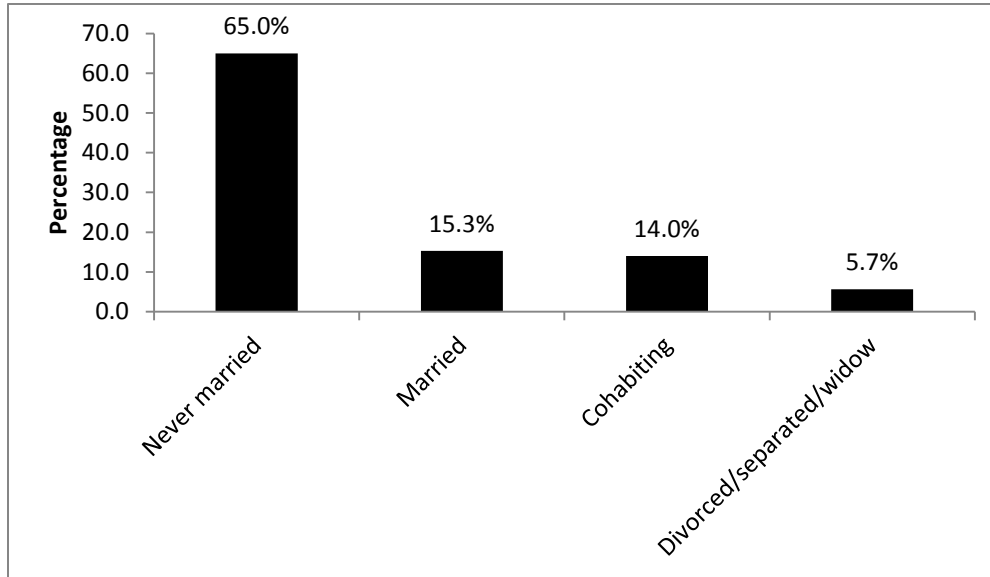


Figure 4.2: Respondents' marital status distribution (N=300)

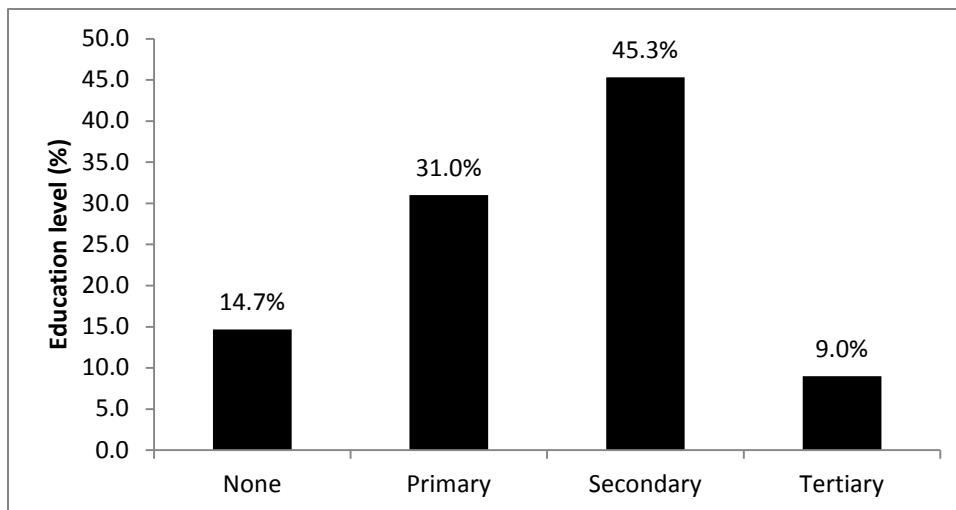


Figure 4.3: Respondents' education levels (N=300)

Figure 4.3 shows the respondents' highest levels of education, with 45.3% (n=136) of the respondents having received secondary education, 31.0% (n=93) having received primary education, 14.7% (n=44) had no education and 9.0% (n=27) reportedly had tertiary education. Of the respondents 56.7% (n=170) had no monthly income, 16.0% (n=48) earned less than a thousand pula a month, 14.3% (n=43) earned between 1 000 and 1999 pula, 5.7% (n=17) earned between 2 000 and 2999 pula, and 7.3% (n=22) earned at least 3000 pula per month. Of the respondents 52.7% (n=158) were unemployed whereas 47.3% (n=142) were employed.

Table 4.1: Socio-demographic characteristics of the respondents (n=300)

Variable	Number (N = 300)	Percentage
Gender		
Female	223	74.3
Male	77	25.7
age (years)		
21 – 30	54	18.0
31 – 40	118	39.3
41 – 50	73	24.3
51 – 60	39	13.0
> 60	16	5.3
Marital status		
Never married	195	65.0
Married	46	15.3
Cohabiting	42	14.0
divorced/separated/widow	17	5.7
Education status		
None	44	14.7
Primary	93	31.0
Secondary	136	45.3
Tertiary	27	9.0
Employment Status		
Employed	142	47.3
Unemployed	158	52.7
Income (Pula)		
No income	170	56.7
< 1000	48	16.0
1000 – 1999	43	14.3
2000 – 2999	17	5.7
>= 3000	22	7.3

4.3.2 Adherence

Adherence was measured using pill counts, pharmacy refill records and patient self reports methods from January 2011 until the time of the interview. Adherence was defined as taking 95.0% or more of the prescribed doses or attending 95.0% or more of the pharmacy refill appointments on the expected date, while levels of ART adherence of 94.9% or lower were considered to be non-adherent.

4.3.2.1 Pill counts

Pill count adherence was calculated by counting the remaining doses of medication and assuming that the remaining pills, in excess of the expected number, represented missed doses. The percentage of adherence was calculated by subtracting the number of remaining pills from the number of dispensed pills, divided by the expected number of pills to be taken and the result multiplied by 100.

The mean ART adherence, as measured by pill counts was 97.6% (95% CI 97.3-98.1) with a standard deviation of 3.7%. The median adherence level was 99.0% (IQR 97-100). Most respondents (86.0%; n=258) had optimal recommended average adherence of greater than or equal to 95.0% throughout the observation period (see figure 4.4). Kgatlwane et al (2006:9) reported 75.0% adherence rates and Weiser et al (2003:281) reported 56.0% adherence rates.

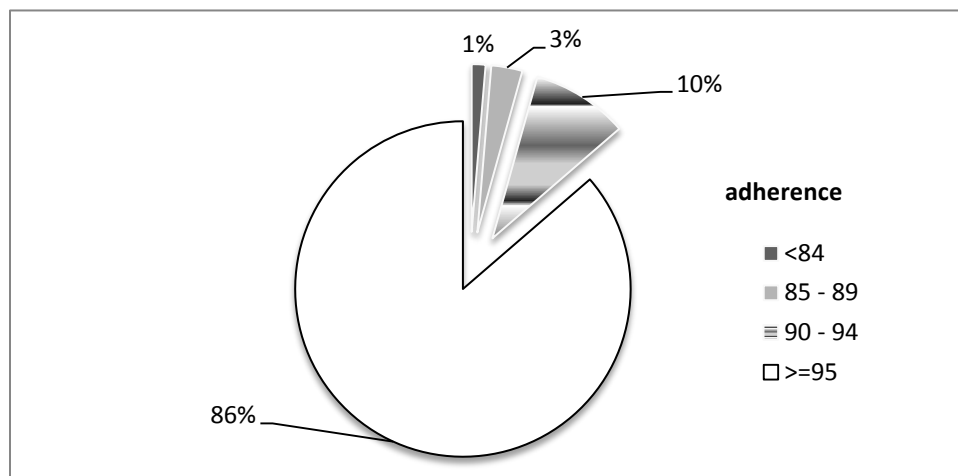


Figure 4.4: Pill count-based ART adherence levels (N=300)

Consequently this study's pill count based ART adherence rates appear to be better than those reported by previous studies. However, these other studies were reported more than five years prior to the current study.

Table 4.2 shows that a proportion of patients (32.7%; n=98) had a history of taking more than the prescribed number of pills. This was observed indirectly, since they returned fewer pills than expected and according to them, they had taken these tablets.

Table 4.2: Patients' history of taking more than the prescribed number of pills (N=300)

History of taking more than the prescribed number of pills	Frequency	Percent
Yes	98	32.7
No	202	67.3
Total	300	100.0

4.3.2.2 Adherence by pharmacy refill appointment

Recorded pharmacy refill records covered the period between 1 January 2011 and the day of interview. Exact dates when ARVs were collected from the pharmacy were compared with the expected refill appointment dates. The adherence was calculated by dividing the respondent's number of pharmacy refills that occurred on the appointment day by the total number of expected pharmacy refill appointments, multiplied by 100.

The medical records' analysis indicated that a total of 47.0% (n=141) of the patients reported ever missing refill appointments and 53.0% (n=159) reported never missing refill appointments (see figure 4.5).

Based on review of medical records, 53.0% (n=159) of the respondents reported never missing refill appointments, 33.3% (n=100) missed fewer than 25.0% of their appointments, 12.7% (n=38) missed 26.0%-50.05% and 1.0% (n=3) missed more than 50.0% of their pharmacy refill appointments (see figure 4.5).

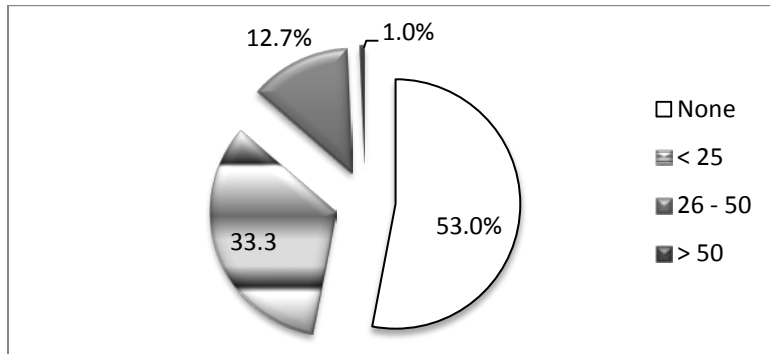


Figure 4.5: Proportion of missed pharmacy refill appointments (N=300)

4.3.2.3 Adherence by self-report

The respondents were asked whether they had missed any medication doses during the four days preceding the interview. A categorical variable was constructed reflecting two levels of adherence during a four day period namely “missed” and “not missed” taking medication doses during the past four days. Only 4.0% (n=12) reported having missed medication doses and 96.0% (n=288) reported that they had never missed any medication doses during these four days (see table 4.3). Kgatlwane et al (2006:9) reported 96.0% adherence based on self reports of a two day period recall method in Botswana. Nachegea et al (2004) reported 88.0% ART adherence rates of patients in South Africa based on self reports relevant to the preceding month. Studies conducted in Botswana have reported adherence levels of 83.0% (Nwokike 2004) in the public sector and 54.0% (Weiser et al 2003:281) in the private sector, based on patients’ self-reports.

The current study’s ART adherence rates are higher than the adherence rates reported by other studies conducted in Botswana by Nwokike et al (2004) and Kgatlwane et al (2006). However, the current study’s data were collected during 2011, seven and five years after the other two studies respectively. The current study’s ART adherence

levels were higher than those found in other countries (Bangsberg et al 2001; Chesney 2000; Liu et al 2001; Nemes et al 2004; Safren et al 2005; Nachega et al 2004).

Table 4.3: Proportion of the respondents who missed any medication during the four days preceding the interviews (N=300)

Did you miss any medication in the past 4 days?	Frequency	Percent
No	288	96.0
Yes	12	4.0
Total	300	100.0

4.3.3 ART adherence correlated with patients' characteristics

Of the 223 female respondents, 197 (88.3%) had a high level of adherence and 62 (80.5%) out of 77 males respondents also had high adherence levels, but there was no significant association between gender and adherence ($\chi^2 = 2.97$; $p = 0.085$; see figure 4.6).

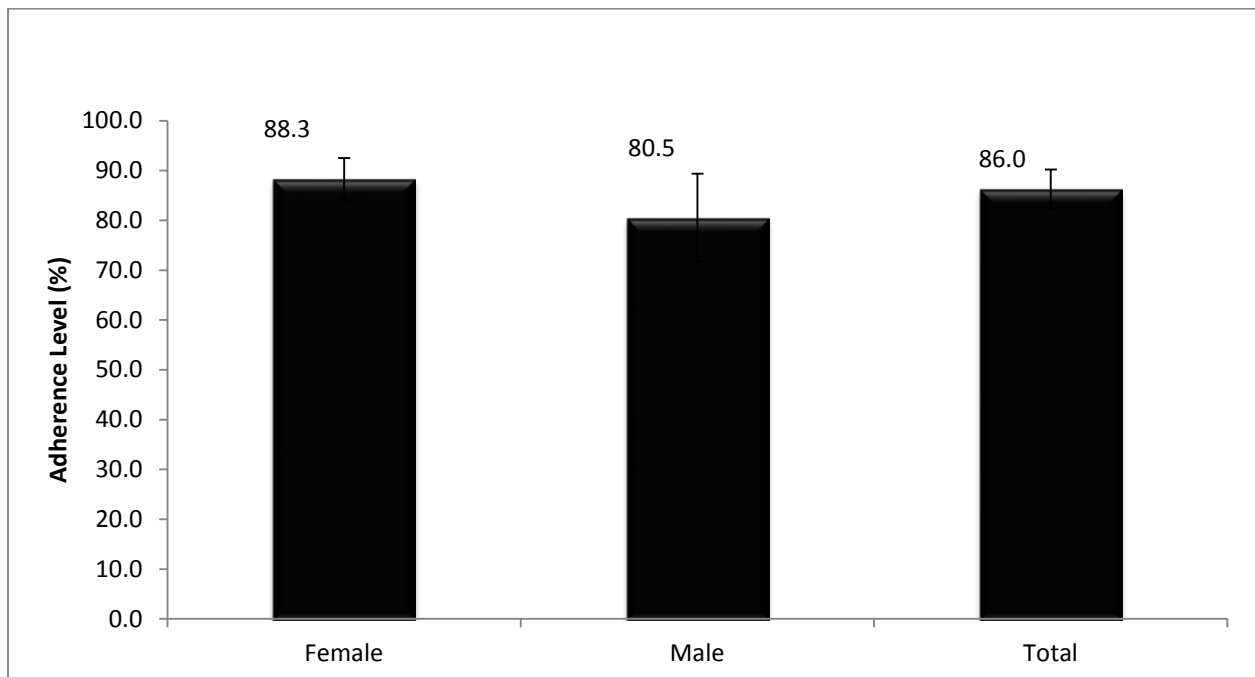


Figure 4.6: Association between pill count adherence and gender (N=300)

Although the 54 younger respondents aged 21-30, and the 16 who were older than 60 years of age, had lower adherence levels of 83.3% and 81.3% respectively, as shown in figure 4.7, no statistically significant trend was observed ($\chi^2 = 1.11$; $p = 0.89$). Nemes et al (2004) as well as Orrell et al (2001) found that younger age was associated with poorer ART adherence levels, using multivariate analyses models, based on their data collected in Brazil.

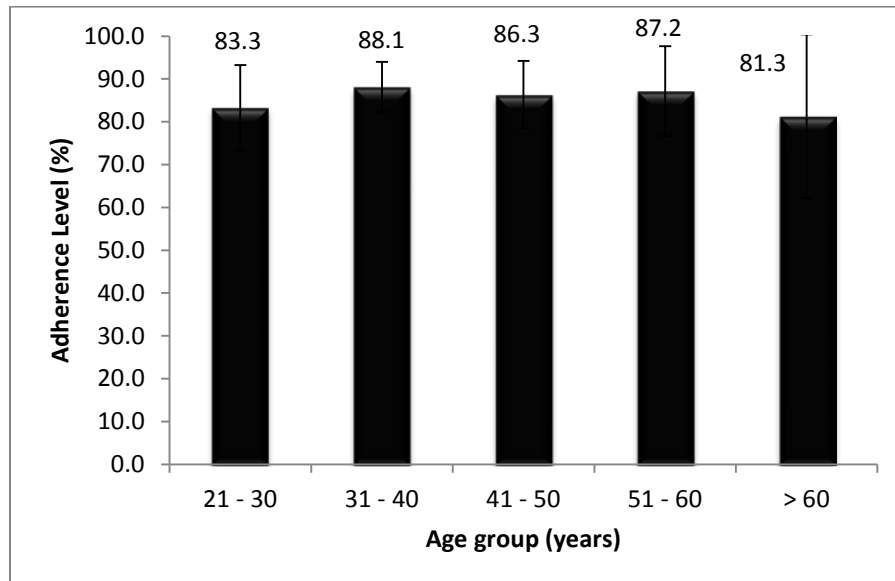


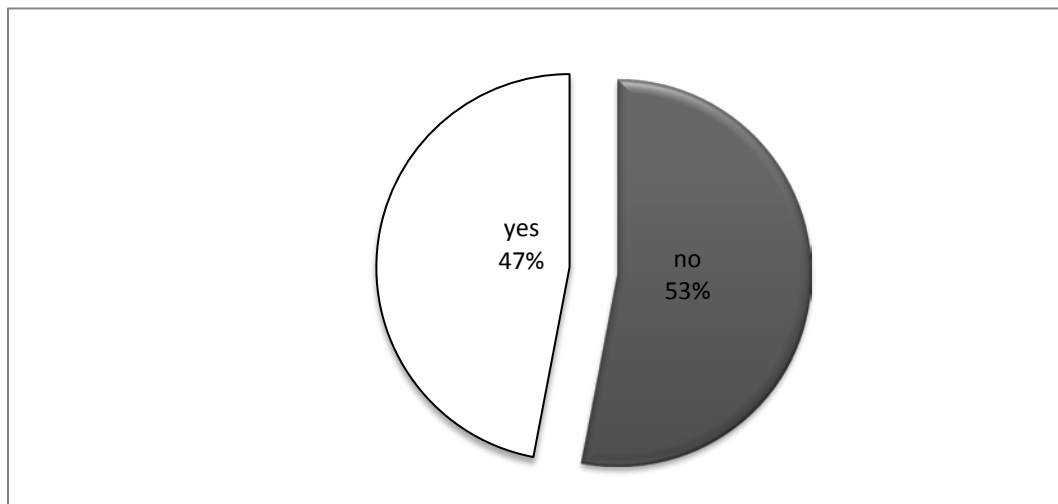
Figure 4.7: Association between age and pill count adherence (N=300)

Similarly there was no significant association between employment status, loss of income, education status, marital status and monthly income (see table 4.4). Although there was no significant association, there was a general lower adherence with increasing income.

Table 4.4: Association of socio-demographic variables and pill count adherence levels

Variable	N	No. Adherent (>= 95%)	Percent Adherent 95%	(>= χ^2 (association))	p-value
Marital status					
Never married	195	168	86.2	0.86	0.993
Married	46	40	87.0		
Cohabiting	42	36	85.7		
divorced/separated/widow	17	15	88.2		
Income					
no income	170	149	87.6	0.89	0.925
< 1000	48	41	85.4		
1000 – 1999	43	37	86.0		
2000 – 2999	17	14	82.4		
>= 3000	22	18	81.8		
Loss of income					
No	159	138	86.8	0.60	0.806
Yes	141	121	85.8		

As many as 47.0% (n=141) of the respondents in the study reported experiencing a loss of income while accessing ART services and 53.0% (n=159) were not concerned about loss of income while coming to the clinic (see figure 4.8).

**Figure 4.8: Loss of income during visits to the ART clinic (N=300)**

Respondents provided suggestions on how they could be assisted (see figure 4.9) to enhance their ART adherence levels. Some respondents lost income due to taking time off work or failure to obtain the appropriate permission to attend the ART clinic, or the inability to use sick leave or clinic attendance slips as they had their own businesses or they were paid on a daily basis, forfeiting part of their income to attend the ART clinic. This was also reported by Kgatlwane et al (2006:102) who reported that some employers in Botswana would not give their employees time off to attend ART clinics.

Some of the suggestions provided by 141 respondents to assist them to improve their adherence levels, without incurring losses of income, included: employees should not lose payment for attending the ART clinic (37.6%; n=53), services should be provided closer to respondents' homes (28.4%; n=40), transportation should be provided for patients to and from ART clinics (22.0%; n=31), and employment opportunities should be created for ART patients (12.2%; n=17).

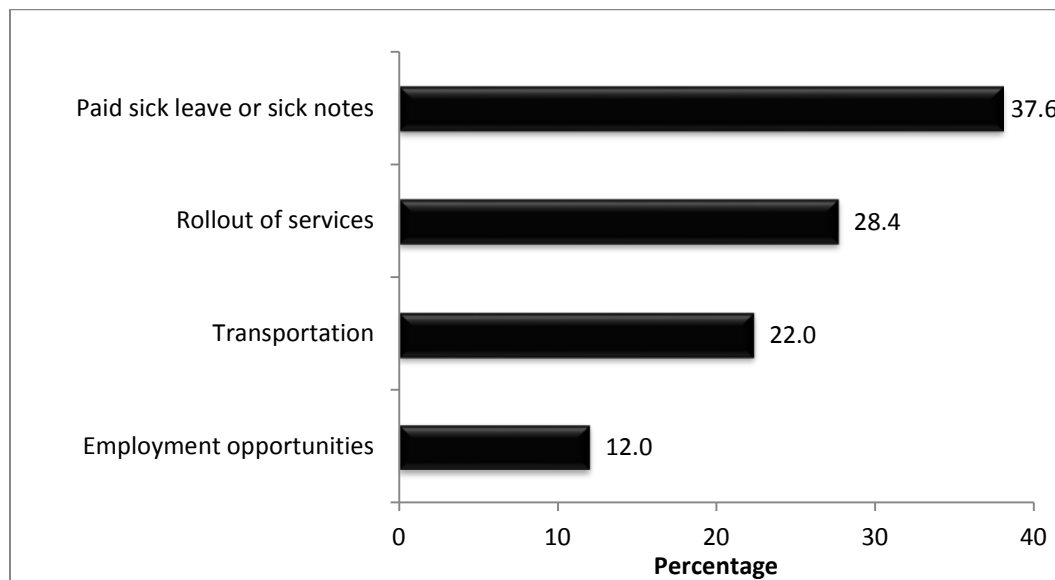


Figure 4.9: Respondents' suggestions on how they could be helped not to lose income while accessing ART services (N=141)

4.3.4 Clinical data

4.3.4.1 Duration of ART

Respondents (70.7%; n=212) who had been on ART for more than 24 months, had an average adherence level of 88.4%; those from 19 to 24 months (4.3%; n=13) had 86.7%; from 13 to 18 months (3.7%; n=11) had 73.3% and those from 6 to 12 months (6.3%; n=19) had an average adherence level of 75.0% (see figure 4.10). Kgatlwane et al (2006:38), in their study in Botswana, did not find any significant differences. There was also no association between duration of ART and adherence levels in the studies reported by Diabate et al (2007) and Orrel et al (2003).

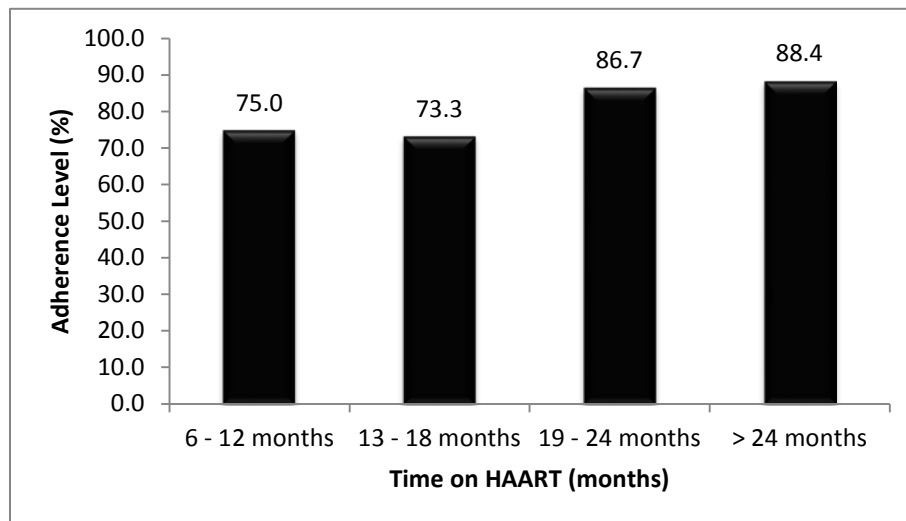


Figure 4.10: Distribution of the adherence level by duration of treatment (N=300)

4.3.4.2 CD4 cell counts

Of the patients, 52.7% (n=158) had recorded baseline CD4 counts ranging from 51 to 100 cells/ul, 35.7% (n=107) had baseline CD4 counts of equal to or less than 50 cells/ul and 11.6% (n=35) had baseline CD4 counts greater than 100 cells/ul (see figure 4.11). The median baseline CD4 cell count was 134 cells/ul (IQR 67–180).

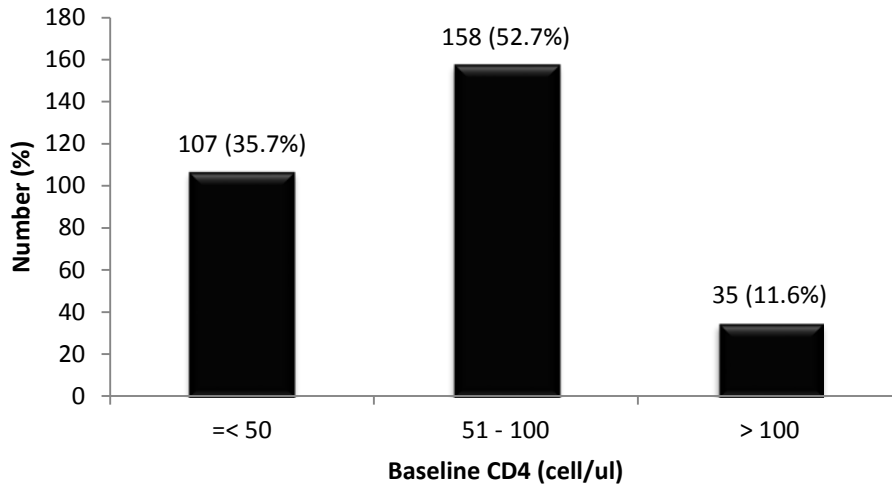


Figure 4.11: Respondents' baseline CD4 counts (N=300)

The majority of the respondents (87.3%; n=262) had current CD4 counts of greater than 200 cells/ul indicating the success of treatment, 9.0% (n=27) had CD4 cell counts ranging from 101 to 200 cells/ul, 2.3% (n=7) had CD4 counts ranging from 51 to 100 cells/ul and 1.3% (n=4) had CD4 cells counts of equal to or less than 50 cells/ul (see figure 4.12). Immunological failure is defined as the persistent decline in the CD4 cell count as measured on at least two separate occasions (Starace 2002:S137). Immunological failure also occurs if the CD4 cell count falls steadily or fails to reach 200 cells/ul after six months on ART (MOH 2005:20).

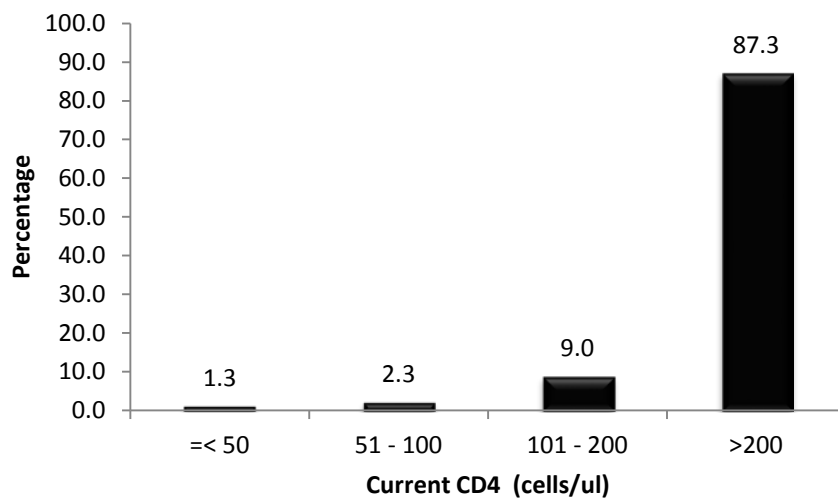


Figure 4.12: Respondents' current CD4 counts (N=300)

Figure 4.13 shows the distribution of respondents' current CD4 counts (at the time of conducting the structured interviews) with the majority of respondents (82.0%; n=246) having current CD4 counts equal to or greater than 250 cells/ul and 18.0% (n=54) having current CD4 cell counts of less than 250 cells/ul.

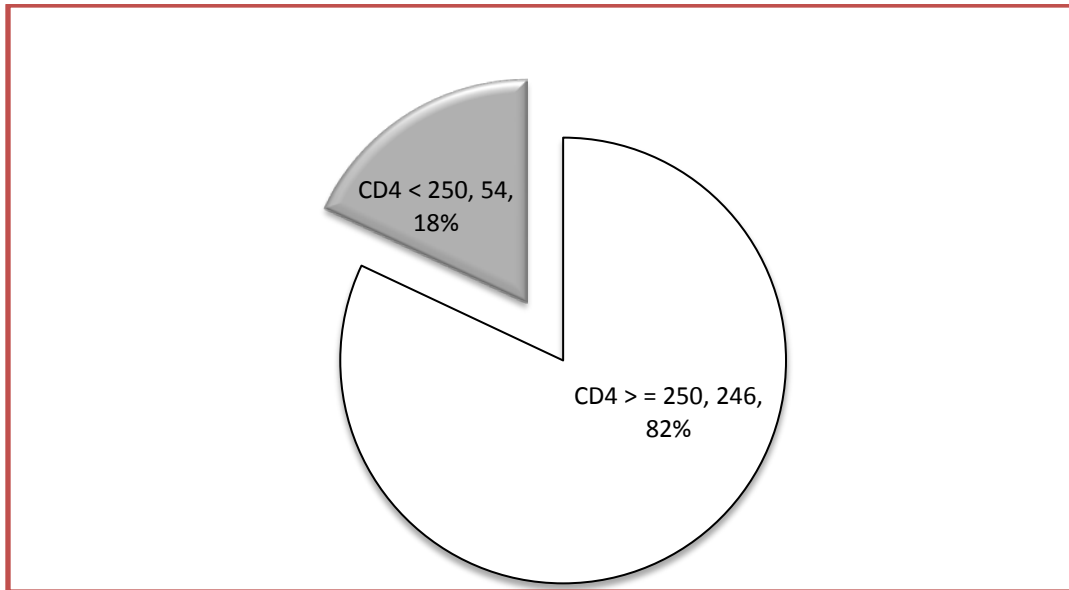


Figure 4.13: Distribution of respondents' current CD4 counts (N=300)

Adherence was more than 80.0% across all baseline CD4 strata (see table 4.5). Of the respondents (35.7%; n=107; see figure 4.11) with baseline CD4 counts of equal to or less than 50 cells/mm³, 83.2% (n=89, see table 4.5) had optimal adherence levels equal to or greater than 95.0%. Of the respondents (52.7%; n=158; see figure 4.11) with CD4 counts from 51 to 100 cells/mm³, 142 (89.9%; see table 4.5) had optimal adherence; and of those (11.6%; n=35; see figure 4.11) with CD4 counts of more than 100 cells/mm³, 28 (80.0%, see table 4.5) had optimal adherence equal to or greater than 95.0%.

Table 4.5: Adherence level correlated with the respondents' baseline CD4 counts (N=300)

Baseline CD4	>=95% adherence	<95% adherence	N	% Adherence (>= 95%)
=< 50	89	18	107	83.2
51 - 100	142	16	158	89.9
=> 101	28	7	35	80.0
Total	259	41	300	

Respondents' current CD4 cell counts (at the time of conducting the interviews) were marginally associated with adherence to ART ($\chi^2 = 3.99$; $P = 0.046$) (see tables 4.6 and 4.7). The test for association p-values was almost equal to 0.05.

Table 4.6: Correlation between respondents' CD4 counts and adherence levels

CurrentCD4 Category	>=95% adherence	<95% adherence	Total
> 200	230	31	261
<= 200	29	9	38
Total	259	40	299

Pearson Chi-Square 3.99 ($P = .0.046^*$ marginally significant); Fisher's Exact Test = 0.047* (significant)

Table 4.7: Chi-Square Tests

	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	3.990(b)	1	.046*		
Continuity Correction(a)	3.036	1	.081		
Likelihood Ratio	3.459	1	.063		
Fisher's Exact Test				.070	.047*
Linear-by-Linear Association	3.977	1	.046		
N of Valid Cases	299				

a Computed only for a 2x2 table

b 0 cells (.0%) have expected count less than 5. The minimum expected count is 5.08.

*P-value < 0.05 (significant relationship)

4.3.4.3 Current plasma viral load

The majority of respondents (93.3%; n=280) had current virologic suppression (undetectable viral load) as only 6.7% (n=20) had detectable VL (see table 4.8). Viral loads of less than 400 copies/mm³ were considered as being undetectable and viral loads of more than 400 copies/mm³ were considered to be detectable.

Virologic failure is said to occur when the VL is not reduced to less than 400 copies/mm³ by six months after ART initiation or when, after initial suppression to less than 400 copies/mm³, VL again becomes detectable any time while on ART (MOH 2005:20).

Table 4.8: Respondents' plasma viral load counts

Viral Load Level	Frequency	Percent
undetectable (suppressed)	280	93.3
detectable (not suppressed)	20	6.7
Total	300	100.0

Among the 20 respondents who were not virologically suppressed, 12 (60.0%) had sub-optimal ART adherence levels and respondents with sub-optimal ART adherence are likely to be unsuppressed (OR 12.98 95% CI 4.9 – 34.0 p < 0.001). And 29 (10.4 %) of respondents with suppressed viral load had sub-optimal ART adherence levels.

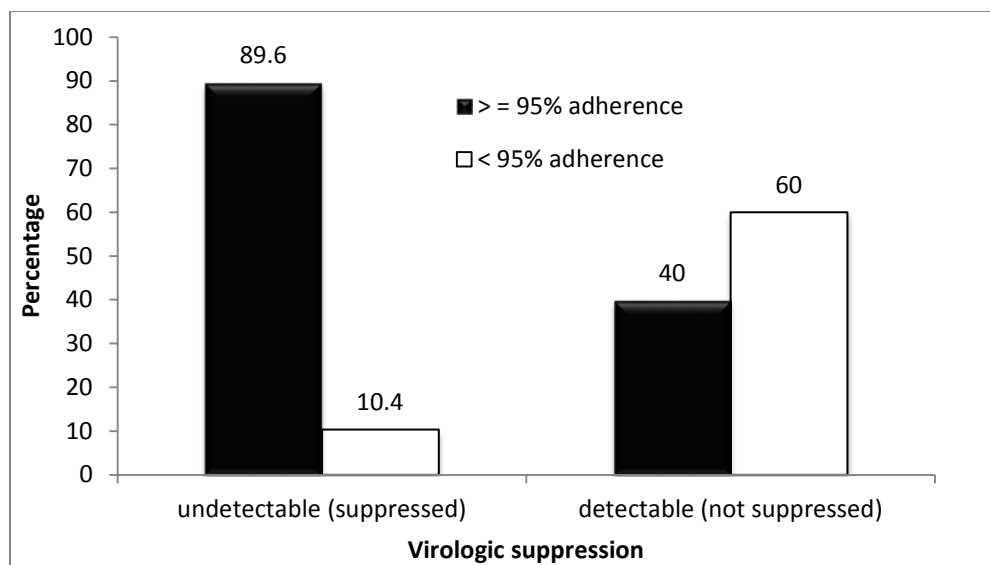


Figure 4.14: Correlation between virologic suppression and adherence levels (N=300)

4.3.4.4 Current ARV treatment regimen

Most respondents (89.0%; n=267) were still on the first line ART regimen (see table 4.9), 9.3% (n=28) were on the second line and 1.7% (n=5) were on the third line ART regimen.

Table 4.9: Distribution of the respondents' current treatment regimens

	Frequency	Percent
First line	267	89.0
Second Line	28	9.3
Third line	5	1.7
Total	300	100.0

Most respondents (82.3%; n=247) had not changed or modified their treatment regimens and 17.7% (n=53) had their regimens changed (see table 4.10). Thus 82.3% (n=247) of the respondents did not require any ART regimen changes.

Table 4.10: Respondents' ART regimen changes

Regimen changed/modified	Frequency	Percent
No	247	82.3
yes	53	17.7
Total	300	100.0

Out of the 53 respondents who had their ART regimens changed or modified, this was done for 20 (37.7%) respondents due to virologic failure, 15 (28.3%) reportedly suffered from drug toxicity, 4 (7.5%) had clinical failures, 3 (5.7%) had immunological failure and 8 (15.1%) reported other reasons like pregnancies or changed treatment guidelines (see table 4.11). Three (5.7%) of these 53 respondents did not provide any reasons for their regimen changes.

Table 4.11: Reasons for respondents' treatment regimen changes

Reasons for Regimen Change	Frequency	Percent
Virologic failure	20	37.7
Immunological Failure	3	5.7
Clinical Failure	4	7.5
Toxicity	15	28.3
Other	8	15.1
No response	3	5.7
Total	53	100.0

4.3.4.5 Side effects

Each respondent could report more than one ART side effect, explaining why a total of 459 side effects were recorded. However, the percentages for the respective side effects were calculated, based on the total number of respondents (N=300), because the variable of interest was the number and percentage of respondents suffering from one or more side effects. (Consequently these percentages do not add up to 100%). The most common side effects experienced by the respondents were dizziness (30.3%; n=91), headaches (27.3%; n=82) and nausea (23.0%; n=69) as shown in figure 4.15. Skin or nail discolouration were reported by 18.7% (n=56), depression by 16.7% (n=50), skin rashes by 15.3% (n=46), vomiting by 14.3% (n=43), diarrhoea by 7.3% (n=22) and other side effects were reported by 4.0% (n=12).

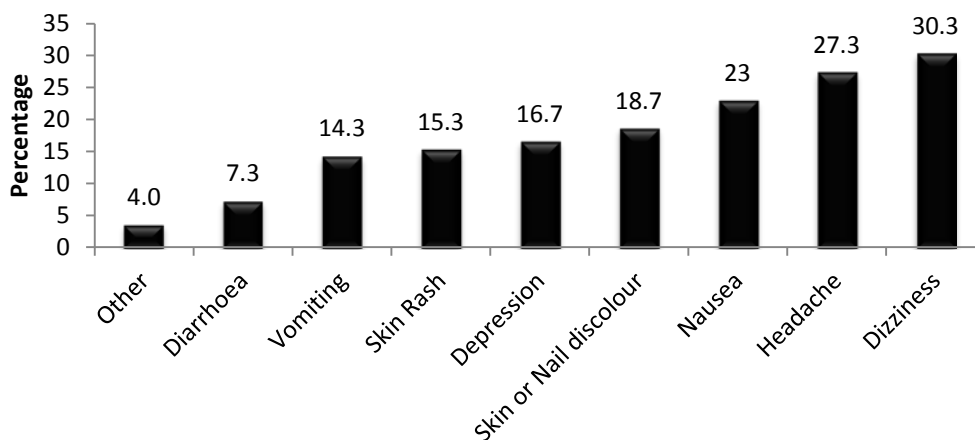


Figure 4.15: Side effects experienced by respondents (N=300)

A total of 10.7% (n=32) respondents reported that the side effects affected their daily activities but 89.3% (n=268) did not report daily activities being affected by medication side effects (see table 4.12 and 4.13).

Table 4.12: Respondents' reported ART side effects (N=300)

Daily activities affected by medication	Frequency	Percent
No	268	89.3
Yes	32	10.7
Total	300	100.0

Table 4.13: Impact of ART side effects on respondents' daily activities (N=300)

Daily activities affected by medication	Number of respondents		Total
	> = 95% adherence	< 95% adherence	
No	232	36	268
Yes	27	5	32
Total	259	41	300

No significant correlation was identified between respondents' reported impact of ART side effects on their daily activities and their ART adherence levels. Diabate et al (2007) and Orrell et al (2003) in their studies also found no association between side effects and ART adherence levels.

4.3.4.6 Reasons for missing ART doses

The top three common reasons, reported by 57 respondents, for missing ART doses were forgetfulness (6.3%; n=19), running out of pills (4.0%; n=12) and depression (3.3%; n=10). No respondent complained of pill burden as a reason for missing medications (see figure 4.16). Each respondent could report more than one reason for missing ART doses, explaining why a total of 315 reasons for missing ART doses were recorded. However, the percentages for the respective reasons were calculated, based on the total number of respondents (N=300), because the variable of interest was the number and percentage of respondents missing ART doses due to one or more reasons. Kgatlwane et al (2006:35), in a study done in Botswana, found that the most common reasons cited for missing medication doses were: forgetfulness (18.0%), costs and logistics (13.0%), work and home duties (12.0%), stigma (7.0%), lack of support (4.0%), lack of food (2.0%), alcohol abuse (2.0%) and they also reported that pill burden was not a problem.

Table 4.14: Reasons for missing ART doses

Reason for missing ART dose	Frequencies	Percentage (N=300)
Too many pills	0	0.0
Did not understand instructions	2	0.7
Lack of Food to take Meds	3	1.0
Clinic not accessible	4	1.3
Lack of care/suport	4	1.3
Hospitalised	4	1.3
Alcohol use	4	1.3
Felt better	5	1.7
Side effects	5	1.7
Depressed	10	3.3
Ran out of pills	12	4.0
Forgot	19	6.3
No response	243	81.0

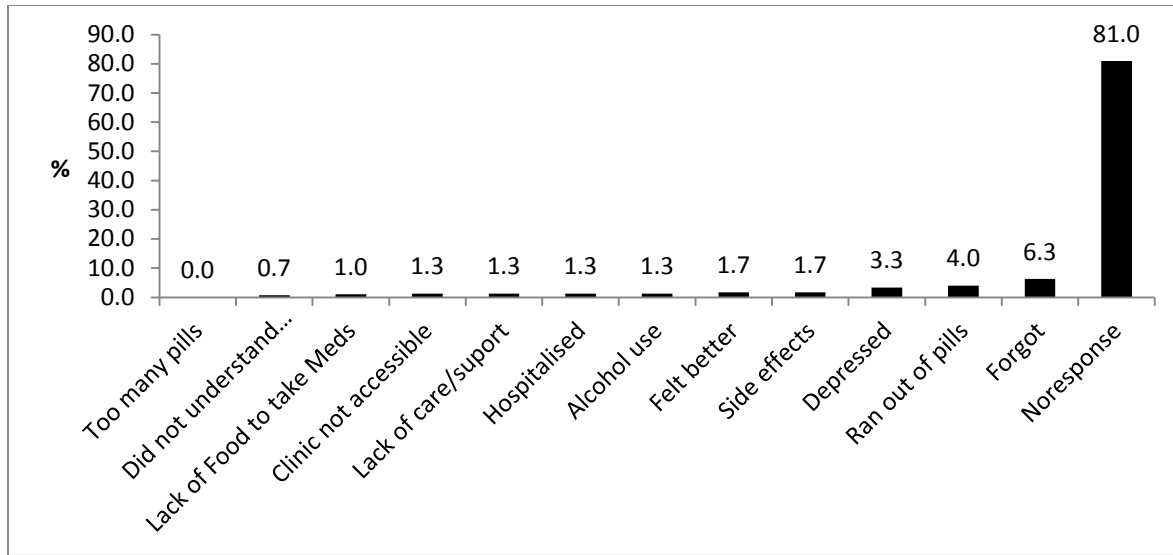


Figure 4.16: Respondents' reasons for missing ART doses (N=300)

4.3.4.7 Skills and strategies used for taking medicines regularly

Each respondent could report more than one strategy used for taking medicines regularly. However, the percentages for the respective strategy were calculated, based on the total number of respondents (N=300), because the variable of interest was the number and percentage of respondents using one or more strategies. (Consequently these percentages do not add up to 100%).

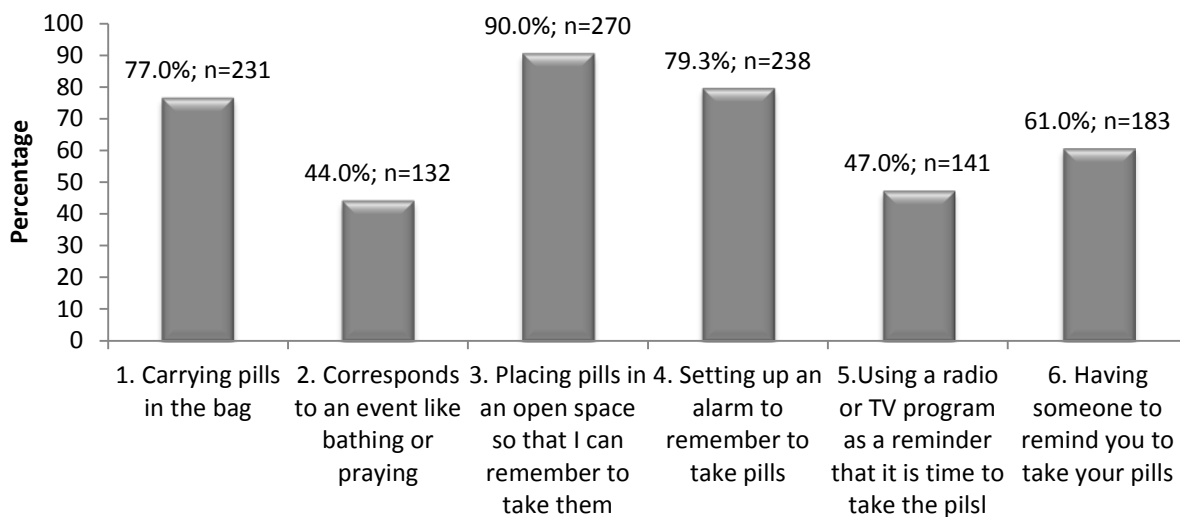


Figure 4.17: Strategies used as reminders to take ART medication (N=300)

Most respondents used a variety of ways of reminding themselves to take their medication (see figure 4.17). The most common strategies were putting pills in an open place (90.0%; n=270), setting alarms (79.3%; n=238) and carrying pills if away from home (77.0%; n=231).

4.3.5 Adherence and social characteristics

4.3.5.1 Counselling

Before a patient is initiated on HAART, adherence counselling is done by a social worker or a nurse in the presence of a treatment adherence/supporter partner to determine each patient's readiness to begin treatment. Adherence partners were respondents' mothers (20.0%; n=60), children (17.7%, n=53), spouses (16.0%, n=48), brothers or sisters (13.3%, n=40), friends (9.3%, n=28) and fathers 0.7% (n=2), who came as adherence partners (see figure 4.18). Kip et al (2009:154) found that mothers (24.0%; n=96) and sisters (12.0%; n=48) were mostly chosen as ART adherence buddies in Botswana. The use of family members and peers to enhance ART adherence has emphasised the importance of social support in the treatment of HIV patients (Kgatlwane et al 2006:55). Low social support was found to be a significant predictor of poor adherence in a study conducted in the Ivory Coast (Diabate et al 2007), but was not significant in a study in Uganda (Byakika-Tusiime et al 2009).

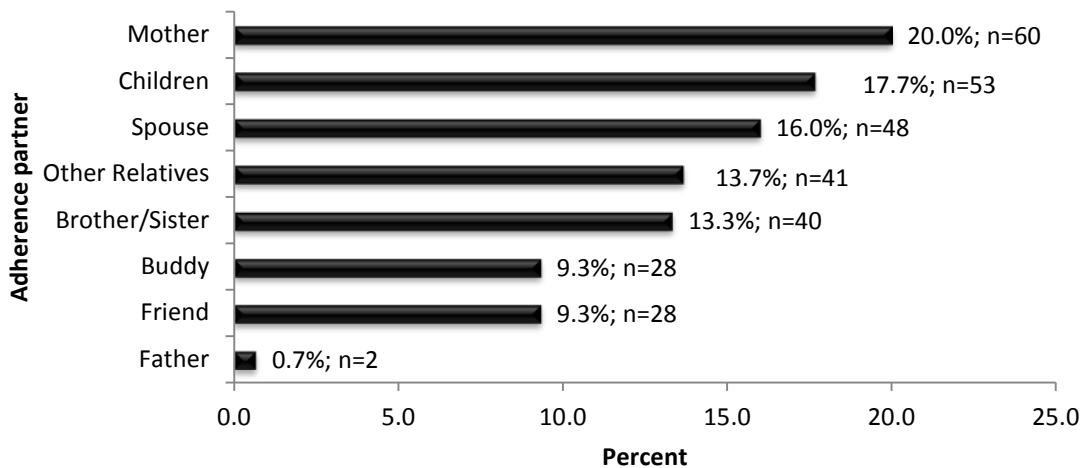


Figure 4.18: Distribution of the respondents' adherence partners (N=300)

Almost all respondents (99.7%; n=299) were counselled before ART (see table 4.14). However, 58.0% (n=174) have reportedly been counselled once only since the start of treatment and 42.0% (n=126) were counselled more than once (see table 4.15). However, there was no significant association with ART adherence ($p = 0.151$).

Table 4.15: Counselling prior to starting ART

Counselled before ART	Frequency	Percent
No	1	.3
yes	299	99.7
Total	300	100.0

Table 4.16: Respondents' number of counselling sessions

Frequency of counselling	Number	Percent
1	174	58.0
2	28	9.3
3	10	3.3
4	6	2.0
≥ 5	82	27.3
Total	300	100.0

4.3.5.2 Perceived self-efficacy to adhere to ART

Respondents were asked to grade their level of confidence pertaining to their perceived self efficacy to adherence, using a ten items in the structured interview schedule. Most respondents (average of 94.7%, see figure 4.19) had high levels of confidence in this study sample. Similarly, Kip et al (2009a:155) also found that self efficacy was high in their study. Self-efficacy has been associated with adherence in several studies (Catz et al 2000; Chesney et al 2000; Gifford et al 2000; Godin et al 2005; Wilson et al 2004).

As indicated in figure 4.19, 10.3% (n=31) of the respondents had low confidence levels to take their treatment when they did not have food, 9.0% (n=27) had low confidence

when they were with someone who did not know that they were HIV positive and 6.3% (n=19) had low confidence levels when they were busy at work.

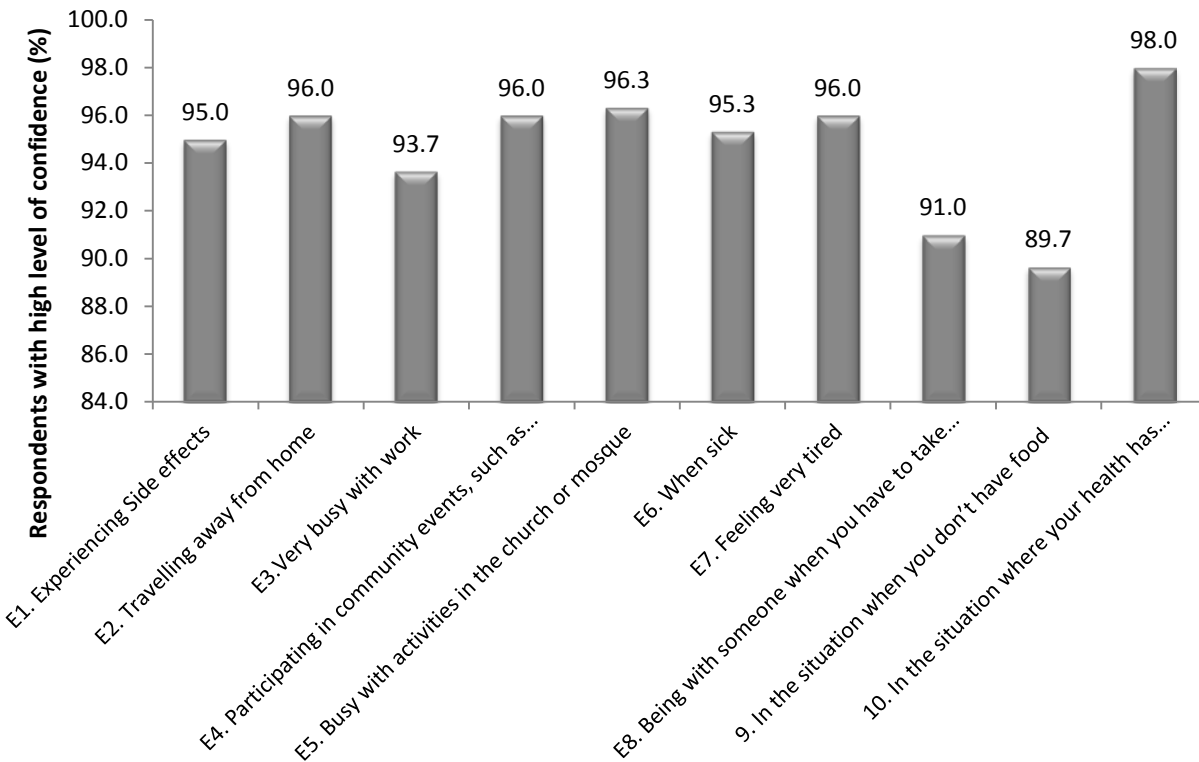


Figure 4.19: Perceived self-efficacy to adhere to taking medications in specific situations (N=300)

4.3.5.3 Disclosure

Reportedly 63.0% (n=189) of the respondents had disclosed their HIV positive status to five or more people (see table 4.16) and their adherence level of 89.0% (95% CI 84 – 93) was significantly higher ($P < 0.005$) than those respondents (8.7%; n=26) who had disclosed only to one person whose adherence level was 65.0% (95% CI 44 – 83). Disclosure of HIV status was measured in a Botswana study and showed a trend of non-disclosure being associated with poorer adherence. Kip et al (2009a:154) reported that the majority (93.5%; n=374) of their respondents had adherence buddies, indicating that they had disclosed their HIV status and ART regimen at least to their buddies. In another study, 69.0% of the patients did not disclose their HIV positive status to their

families, and 94% did not disclose to people in their community (Weiser et al 2003:285). These findings were not supported by another study on AIDS patients in North America, among whom 67.7% reported fear of disclosure (Mills et al 2006).

Table 4.17: Respondents' adherence levels and the number of people to whom they had disclosed their HIV positive status

No of please disclosed to	Frequency	Percent	Valid Percent	Cumulative Percent	Adherence % (>= 95%)	Confidence interval (%)
1	26	8.7	8.7	8.7	65.0	44.3 - 82.8
2	25	8.3	8.3	17.0	80.0	59.3 - 93.2
3	26	8.7	8.7	25.7	92.0	74.9 - 99.1
4	34	11.3	11.3	37.0	88.0	72.5 - 96.7
> 5	189	63.0	63.0	100.0	89.0	83.5 - 92.9
Total	300	100	100			

Consistent with the profile of adherence partners, the respondents had disclosed their HIV positive status to grandparents and parents-in-law (61.0%; n=183), mothers (35.3%; n=106), spouses or partners (26.0%; n=78), friends (24.7%; n=74), brothers and/or sisters (16.3%; n=49), fathers (13.0, n=39), sons and/or daughters (12.0%; n=36). Some respondents reported that they disclosed to more than one person or category of people. However, the percentages for the respective category were calculated, based on the total number of respondents (N=300), because the variable of interest was the number and percentage of respondents having disclosed to one or more categories of people. (Consequently these percentages do not add up to 100%) (see figure 4.20).

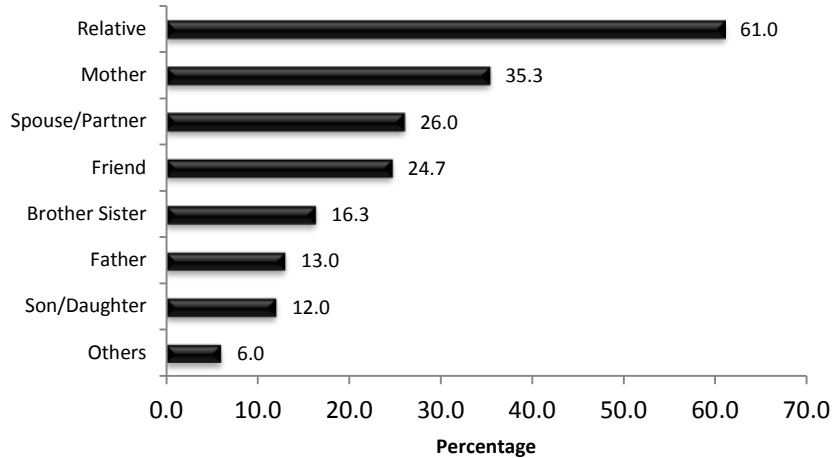


Figure 4.20: Distribution of the people the respondents disclosed to (N=300)

Respondents were also asked how long they took before they disclosed their HIV status. Reportedly 55.3% (n=166) disclosed their HIV positive status on the same day that the diagnosis had been made, 11.0% (n=33) took less than one week, 7.0% (n=21) did so a week after the diagnosis, 17.7% (n=53) within 1 to 12 months and 9.0% (n=27) disclosed more than 1 year after knowing their HIV positive status (see figure 4.21).

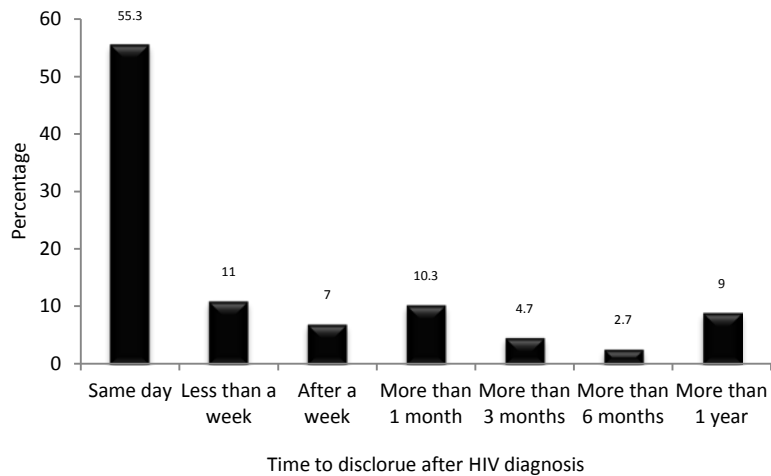


Figure 4.21: Time taken to disclose HIV positive status after diagnosis (N=300)

4.3.5.4 Perceived stigma

The respondents were asked how worried they were about a variety of stigma-related issues (see figure 4.22). Most respondents reported very low levels of perceived stigma (average 15.7%; see figure 4.22). Only 20.0% (n=60) of the respondents were worried about being shunned by the community, 21.0% (n=63) were worried about being teased or insulted and 18.0% (n=54) were worried about losing respect from their family members. In an open-ended question of why patients missed ART doses in Botswana, 15.0% reported missing doses due to stigma (Weiser et al 2003) and Kgatlwane et al (2006:35) indicated that 7.0% reported that stigma contributed to their patterns of skipping medication doses.

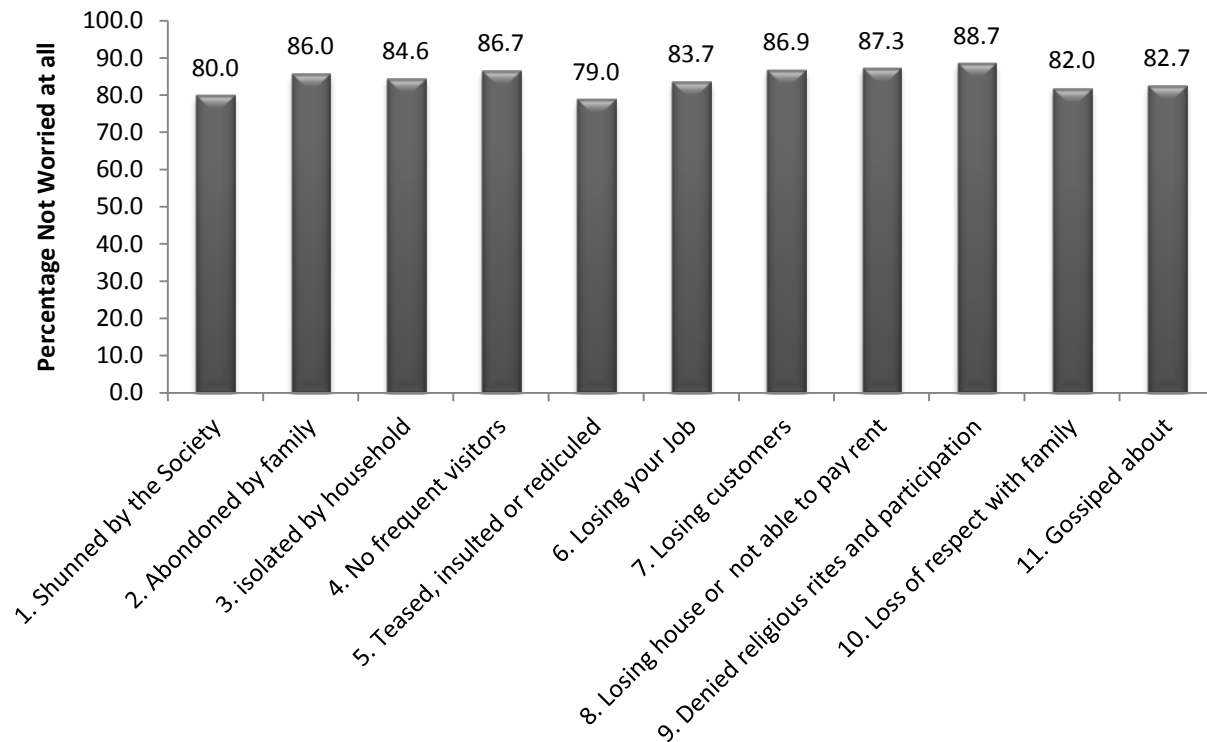


Figure 4.22: Distribution of perceived stigma by the respondents (N=300)

4.3.5.5 Patient-provider relationship

As indicated in figure 4.23, most respondents (74.7%; n=224) could always meet the hospital staff whenever they needed help, 76.3% (n=229) reported that the time they were given while being attended to, was sufficient and 78.0% (n=234) reported that hospital staff understood their difficulties.

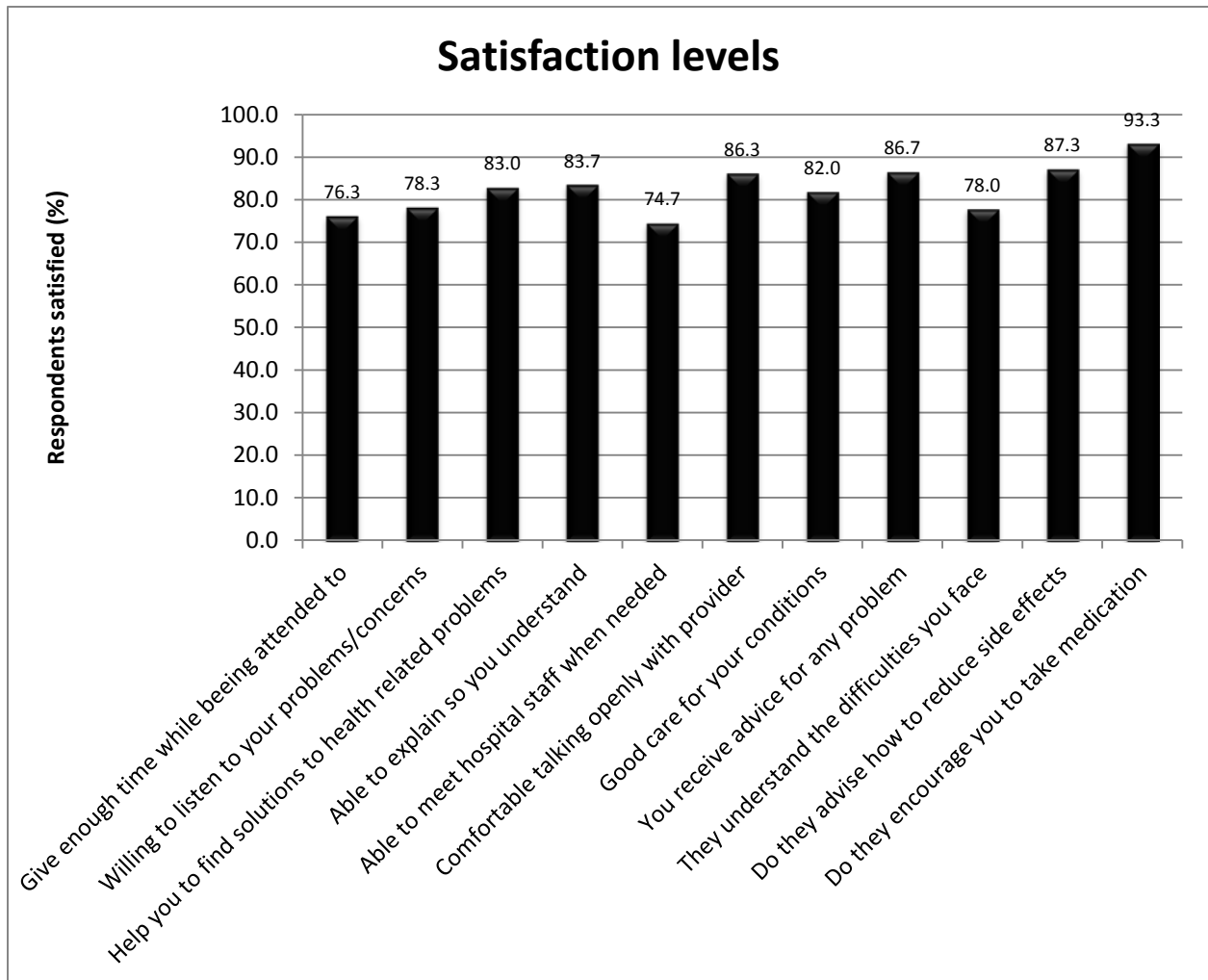


Figure 4.23: Distribution of relationship between the patient and the healthcare provider (N=300)

Most respondents (93.3%; n=280) were encouraged by hospital staff to take their medication correctly. Positive interaction between patients and providers has been consistently associated with better adherence to ART in North American studies (Burke-Miller et al 2006; Heckman et al 2004; Wroth et al 2006).

4.3.5.6 Social Information

These findings show that respondents' perception of ART was positive. Reportedly only 2.0% (n=6) of the respondents had visited traditional healers since they started taking ARVs and 1.7% (n=5) used traditional medicines together with ARVs.

Table 4.18: Social and cultural factors

Question	Answer	Frequency	Percent	P-value (Fishers ^a or Chi-square ^b)
Since you started ARV have you visited any traditional healer	No	294	98.0	0.191 ^a (ns)
	Yes	6	2.0	
Are you taking any traditional medicines together with ARVs?	No	295	98.3	0.139 ^a (ns)
	Yes	5	1.7	
Do you think traditional medicines work for you?	No	294	98.0	0.191 ^a (ns)
	Yes	6	2.0	
Do you drink alcohol?	No	252	84.0	0.425 ^a (ns)
	Yes	48	16.0	
Do you smoke cigarettes?	No	269	90.0	0.591 ^a (ns)
	Yes	31	10.0	
Number of sexual partners	None	81	27.0	0.850 ^a (ns)
	1	215	71.7	
	2	4	1.3	
How long together with current sexual partner	≤ 3 months	16	7.3	0.282 ^b (ns)
	4-6 months	16	7.3	
	7-12 months	19	8.6	
	2 - 5 years	53	24.1	
	> 5 years	116	52.7	
HIV status of partner	Positive	99	33.0	0.546 ^b (ns)
	Negative	86	28.7	
	Unknown	37	12.3	
	No response	78	26.0	

ns (non-significant P > 0.05)

Most respondents (98.0%; n=294) reportedly did not believe in traditional medicines. Only 16.0% (n=48) of the respondents admitted to alcohol consumption and 10.0% (n=31) to smoking cigarettes. Out of the 300 respondents, reportedly 71.7% (n=215)

had only one sex partner, 27.0% (n=81) had no sex partner at the time of the study and 1.3% (n=4) respondents had two or more sex partners.

Of those 220 respondents, 52.7.0% (n=116) had been together for more than five years, 24.1% (n=53) between 2 and 5 years, and 23.0% (n=51) have been together for one year or less. Of the respondents' sex partners, 33.0% (n=99) were HIV positive, 28.7% (n=86) were HIV negative and 12.3% (n=37) had unknown HIV status.

4.3.5.7 Relocations and adherence

Out of the 300 respondents, 19.0% (n=59) had relocated since they started HAART. However this did not seem to affect their adherence to medication

Table 4.19: Association between relocations after starting HAART and adherence

		adherence_cat2		Total
		> = 95% adherence	< 95% adherence	
Relocations	no	204	37	241
	yes	55	4	59
Total		259	41	300

Table 4.20: Chi-Square Tests: association between relocation and adherence

	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	2.952(b)	1	.086		
Continuity Correction(a)	2.271	1	.132		
Likelihood Ratio	3.396	1	.065		
Fisher's Exact Test				.094 (ns)	.059
Linear-by-Linear Association	2.943	1	.086		
N of Valid Cases	300				

a Computed only for a 2x2 table

b 0 cells (.0%) have expected count less than 5. The minimum expected count is 8.06.
ns (non-significant P > 0.05)

Table 4.19 shows the p-values for the Chi-square test for the association of social and cultural factors and adherence. None of the social and cultural factors had any significant association with ART adherence ($P > 0.05$).

4.3.6 Multivariate analysis of predictors of adherence

Table 4.18 shows the non-parametric correlations of selected characteristics with adherence. Correlation is a measure of an association between variables. It does not necessarily prove causality but gives evidence suggestive of possible strategies to intervene. Viral load (copies/ml) was negatively correlated ($r_s = -0.243$; $p < 0.05$), meaning higher viral load copies were associated with low adherence. This shows that low adherence was associated with failure to suppress the viral load.

As expected CD4 cell counts were also negatively significantly associated with viral load ($r_s = -0.197$; $p < 0.05$). This means that those who were sicker or with low CD4 cell counts, tended to have an unacceptably low level of ART adherence.

Table 4.21: Correlations between selected factors and adherence

			Correlations				
			Age	CD4	VL_copies	CD4 current	adh_avg
Kendall's tau_b	Age	Correlation Coefficient	1.000	-.045	-.115*	.009	.044
		Sig. (2-tailed)	.	.296	.027	.844	.351
		N	300	300	300	299	300
	CD4	Correlation Coefficient	-.045	1.000	-.043	.209**	.042
		Sig. (2-tailed)	.296	.	.356	.000	.321
		N	300	300	300	299	300
	VL_copies	Correlation Coefficient	-.115*	-.043	1.000	-.197**	-.246**
		Sig. (2-tailed)	.027	.356	.	.000	.000
		N	300	300	300	299	300
	CD4 current	Correlation Coefficient	.009	.209**	-.197**	1.000	.022
		Sig. (2-tailed)	.844	.000	.000	.	.612
		N	299	299	299	299	299
	adh_avg	Correlation Coefficient	.044	.042	-.246**	.022	1.000
		Sig. (2-tailed)	.351	.321	.000	.612	.
		N	300	300	300	299	300
Spearman's rho	Age	Correlation Coefficient	1.000	-.061	-.129*	.012	.055
		Sig. (2-tailed)	.	.296	.026	.835	.345
		N	300	300	300	299	300
	CD4	Correlation Coefficient	-.061	1.000	-.054	.310**	.058
		Sig. (2-tailed)	.296	.	.352	.000	.314
		N	300	300	300	299	300
	VL_copies	Correlation Coefficient	-.129*	-.054	1.000	-.243**	-.279**
		Sig. (2-tailed)	.026	.352	.	.000	.000
		N	300	300	300	299	300
	CD4 current	Correlation Coefficient	.012	.310**	-.243**	1.000	.031
		Sig. (2-tailed)	.835	.000	.000	.	.593
		N	299	299	299	299	299
	adh_avg	Correlation Coefficient	.055	.058	-.279**	.031	1.000
		Sig. (2-tailed)	.345	.314	.000	.593	.
		N	300	300	300	299	300

*. Correlation is significant at the 0.05 level (2-tailed).

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

4.4 SUMMARY OF RESEARCH FINDINGS

Adherence to ART is closely tied to virologic, immunologic, and clinical outcomes. Increases in adherence levels resulted in significant improvements in these outcomes. Near perfect adherence, however, is required to maximise the likelihood of long-term clinical success, which could pose challenges to many ART patients. One substantive

finding of this study is that 86.0% (n=259) of respondents had optimal ART adherence (equal or greater than 95.0%); it is higher than previously reported (77.0% by Kgatlwane et al 2006; 54.0% by Weiser et al 2003 and 83.0% by Nwokike 2003); possibly showing an improvement in ART patients' adherence levels. However the ultimate goal is to increase the adherence level to equal to or greater than 95.0% at individual level as well as at the population level.

No significant association was found between gender and adherence. Although younger and older age groups had lower adherence levels, there was no statistically significant trend observed ($\chi^2 = 1.11$; $p = 0.89$). Similarly there was no association between employment, loss of income, education status, marital status and monthly income and adherence. Although there was no significant association, there was a generally lower adherence with increasing income.

The most common side effects experienced by the respondents were dizziness, headache and nausea. The top three common reasons for missing medications were forgetfulness, running out of pills and depression. None of the participants complained of pill burden as a reason for missing medications. Change of residential address did not have any effect on adherence.

The most common strategies applied for taking medicines were setting alarm clocks, putting pills in an open place and carrying pills if away from home. Almost all the respondents (99.7%, n=299) were counselled prior to starting ART together with their adherence partners. Most of the respondents had very high levels of confidence or self-efficacy to adhere to ART in this study sample.

Most of the participants reported very low levels of perceived stigma. The effects of drugs side effects on the daily activities had no significant association with adherence. Almost all the respondents were satisfied with the quality of care services provided at the clinic. Patients who disclosed their HIV positive status to more than one person had a higher adherence level than those who disclosed to only one person.

None of the social and cultural factors such as alcohol consumption, cigarette smoking, number of sexual partners, HIV status of the partner and traditional medicines had any significant association with ART adherence levels ($P > 0.05$).

Respondents' current CD4 cell counts were associated with ART adherence ($\chi^2 = 3.99$; $P = 0.046$). There was a high virologic suppression among the respondents, with 93.0% of respondents having achieved undetectable viral load, a sign of good adherence. Respondents with poor adherence were likely to have unsuppressed VL counts (OR 12.98 95% CI 4.9 – 34).

4.5 CONCLUSION

While the findings in this study reflected results from a very small rural population, they nonetheless were supported by similar research in this area. Although the adherence rates found in this study (86.0%) are comparable to those of other studies in Botswana and other developing countries, these rates are still too low for good clinical outcomes.

HIV/AIDS is a lifelong chronic illness, but treatment continues to improve with the production and availability of newer medications. The issues relative to maintaining medication adherence now appear to include a broader spectrum of issues impacting on adherence to both address the constraints and strengthen the key facilitators of adherence

In this study the critical barriers to adherence identified were: forgetfulness, loss of income due to transport fees to the health facility and time off work, fear of discrimination and stigma, and non-supportive home and work environments.

Although side effects occurred among some users, this was not perceived as a significant barrier to adherence. Although pill burden still existed at various levels in treatment, it was not found to be a problem in this study and could not be considered as

an absolute reason for medication adherence failure. Most patients had high self efficacy and used reminders to take their ART medication.

Some respondents (32.7%; n=98) had a history of taking more than the prescribed number of pills. This was observed indirectly, since they returned fewer pills than expected and according to them, they had taken these pills. The correlation with clinical outcomes and measures of adherence, based on pill count, could be challenging if patients take more than recommended doses since the outcomes might be positive, for instance, reduction of viral load or increased CD4 counts. However, if patients take more than the prescribed number of pills, they might be more likely to suffer side effects and they might run out of pills before their next scheduled clinic visit. All patients received adherence counselling and the majority were satisfied with the health services provided at the clinic.

CHAPTER 5

CONCLUSIONS, RECOMMENDATIONS AND LIMITATIONS

5.1 INTRODUCTION

The purpose of this study was to identify factors affecting ART adherence levels, and the impact on immunologic and virologic responses in adult patients at one rural district ART clinic in Botswana.

This chapter sums up the findings of the research; outlines the implications of the study's results; provides conclusions based on the research findings; makes recommendations for improving ART services in Botswana and for further research. The limitations, impacting on the generalisability of the findings, are also specified.

5.2 SUMMARY OF RESEARCH FINDINGS

5.2.1 Patients' characteristics

Patient characteristics include socio-demographic factors (age, gender, income, education, HIV risk factors) and psychosocial factors (alcohol use, cigarettes smoking, social climate and support, attitudes about HIV and its treatment).

Females had higher adherence levels than males but it was not statistically significant. Age, education level, income or employment status, marital status, alcohol and cigarettes consumption and change of address were not significantly associated with ART adherence.

There were 86 (28.7%) discordant couples in this study and 37 (12.3%) did not know the HIV status of their partners. Patients who disclosed their HIV status to more than one person had a significantly higher adherence level than those who disclosed to only one person.

Reportedly only 2.0% (n=6) of the respondents had visited traditional healers since they started taking ARVs and 1.7% (n=5) used traditional medicines together with ARVs. Most respondents (98.0%; n=294) reportedly did not believe in traditional medicines. Only 16.0% (n=48) of the respondents admitted to alcohol consumption and 10.0% (n=31) to smoking cigarettes.

Most respondents reported low levels of stigma, supported by the fact that 55.7% (n=167) disclosed their HIV status the same day they had been diagnosed as being HIV positive.

5.2.2 Treatment regimens

In this study, no respondent complained about the pill burden as a reason for missing medication doses. The majority of the respondents (89.0%; n=267) were still taking their first line ART, while only 9.3% (n=28) were on second line regimens and 1.7% (n=5) of the respondents were on third line regimens. Of the 300 respondents, 17.7% (n=53) had their treatment regimens changed or modified since they started HAART. Of the 53 respondents who had their treatment regimens changed or modified since they started HAART, only 15 (28.3%) had their treatment changed due to drug toxicity. The most common side effects experienced by the respondents were dizziness, headache and nausea.

5.2.3 Patient-provider relationship

Most respondents were satisfied with their relationship with the healthcare providers at the clinic with a composite level of satisfaction of 82.6%. However, 25.3% (n=76) of respondents could not always meet clinic staff when they needed help, 23.7% (n=71) were not given enough time while being attended to by clinic staff and 22.0% (n=66) felt that the clinic staff did not understand their difficulties.

5.2.4 Clinical setting

Aspects of the clinical setting that might influence ART adherence levels include access to ongoing primary care, involvement in a dedicated adherence programme, availability of transportation, pleasantness of the clinical environment, convenience in scheduling appointments, perceived confidentiality, and satisfaction with past experiences in the healthcare system.

In this study, most respondents had high levels of confidence concerning their self-efficacy to adhere to ART with a composite perceived efficacy level of 94.7%. The most common strategies to take treatment were setting alarm clocks, putting pills in an open place and carrying pills if they were away from home. A total of 141 (47.0%) out of 300 interviewed respondents had experienced income losses when they came to the clinic either through transport fares or losing business while they were at the clinic or by losing payment for that particular day. Some respondents complained that multiple visits to the clinic were inconvenient because they interfered with work and income. Perceived self-efficacy was high and almost all patients (96.0%; n=288) reported not having missed a single ART dose during the four days preceding their interviews.

5.2.5 Disease-related factors

This study did not look into opportunistic infections and the symptoms of patients before and while on ART. Low baseline CD4 cell counts (less than 100 cell/ul) were characterised by increased optimal adherence levels to ART compared to their counterparts with CD4 cell counts of more than 100 cells/ul. There was a high virologic suppression among the respondents, with 93.3% (n=280) having achieved undetectable viral loads, a sign of adherence. The longer, the patients continued taking ART, the better the adherence levels.

5.3 CONCLUSIONS

Adherence is a complex issue and multi-dimensional approaches are required to address the constraints and strengthen the key facilitators of adherence. In this study, motivators of ART adherence were identified as disclosure of HIV positive status to more than one person, frequent adherence counselling, self-efficacy to adhere to ART, positive interaction between patients and providers and the use of adherence partners. Barriers to ART adherence were forgetfulness, transportation costs to and from the clinic, time away from work and side effects. There was a strong positive correlation between adherence, CD4 counts and viral load. Adherence was closely tied to immunologic and virologic outcomes.

These results could be related to the small respondent size and possible hesitation or bias on the part of those who did not want to respond openly or accurately. It is possible that this sample might have had good adherence capabilities and practices, and that the seemingly higher reporting for adherence indicated that the population was aware and adjusted to the particular physiological influences of medication used and negative impacts on variables that impacted negatively on adherence levels.

Thus, future research should be conducted on similar rural populations to further define and ascertain pertinent factors that impact on ART adherence levels.

Some of the recommendations include the development of practical guidelines for implementing adherence management strategies. These should include guidelines for continuous adherence counseling, roll out of more ART facilities closer to patients' homes, and the use of practical reminders

5.4 RECOMMENDATIONS

5.4.1 Recommendations to improve adherence to ART

Improvement in adherence to ART by adults at this ART clinic, based on the research results, might be enhanced if the following recommendations were implemented. It is recommended that:

- The continued assessment of the levels of adherence amongst patients on ART should be re-enforced at the clinic. Unless these assessments are conducted, it will be impossible for the healthcare professionals to identify non-adherent patients and to intervene to improve ART adherence levels to avoid virologic and immunologic failures as well as drug resistance.
- Practical guidelines for implementing adherence management strategies should be developed, implemented and evaluated at regular intervals.
- The patients' pill counts must be done at each clinic visit.
- Adherence counselling of patients should be done before initiation of ART for each patient.
- Intensify health education campaigns addressing stigma and promote family and community support for people living with HIV and AIDS.
- It is also crucial that factors contributing to non-adherence are explored and interventions developed to eliminate the barriers to adherence in order to improve adherence.

- There is a need to roll out ART to health centres and clinics to increase accessibility to ART and promote adherence to reduce transportation costs and time away from work.
- To reduce the travel costs to hospital and off time at work, to collect the ARVs on monthly basis which has been cited to be a barrier to adherence, the patients who adhere should be given three months' supplies. This will imply that the patient will come to the hospital only once per quarter and not every month.
- Adherence counselling should be repeated at every ART clinic and ARV pharmacy visits to reinforce the importance of adherence to ARVs.
- Patients that are stable and with good adherence can be given counselling jobs to educate and follow up those that are non adherent in order to create jobs since the majority of our respondents were unemployed.
- There is need to re-inforce couple HIV testing to encourage couples to know their partners HIV status

5.4.2 Recommendations for further studies

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

- Duplicate this study in other public health facilities prior to generalisation of these research results to all HIV/AIDS experienced patients.
- Investigate the correlation between CD4 cell counts and adherence in the private sector using medical aid scheme records for ARV refills and laboratory results.

- Identify and implement interventions that could be put in place to increase adherence to ARVs.
- Study the extent of economic impact on ART adherence at DRM.
- Study the use of traditional or complementary medicines in combination with ARVs and its relations with CD4 cell counts.
- Conduct qualitative research to determine the knowledge, attitudes and perceptions of people in the community concerning ARVs in an attempt to get their support in reducing discrimination and stigmatisation and increase adherence among all patients at DRM.
- Study the extent of depression among patients on ART at DRM and its link to non-adherence.
- Study the rate of hospitalisation among patients on ART at DRM and its correlation with non-adherence.
- Identify the major opportunistic infections experienced among patients on ART at DRM.
- Study the extent of TB and HIV/AIDS co-morbidity.
- Study the extent of morbidity and mortality among patients on HAART at DRM.

5.5 CONTRIBUTIONS OF THE STUDY

The objectives of the study which was to identify factors affecting ART adherence levels, and the impact on immunologic and virologic responses in adult patients in one rural district in Botswana, were evaluated to determine the contributions of this study.

Frequent counselling sessions, disclosure of HIV status to more than one person, high confidence in self efficacy to adhere to ART, patients' satisfaction with healthcare workers and social support contributed to ART adherence. Barriers to optimal adherence were forgetfulness, side effects, economic factors like transport and time off work which led to loss of income, stigmatisation and unsupportive families.

There was a positive relationship between adherence, CD4 cell counts and viral load. The pill counts and pharmacy refill records are a simple measurement tool of adherence which can be used to monitor adherence at the ART clinic. This should be coupled by regular CD4 cell counts and VL results to detect those patients who might have good pill count and pharmacy refill records but not necessarily taking their treatments.

5.6 LIMITATIONS OF THE STUDY

The following limitations were identified during the course of this study:

- Only voluntary interviews were conducted. Patients who agreed to be interviewed might have had the same or different experiences compared to those who refused to be interviewed. Thus the results from the study cannot be generalised to the ART patient population as such.
- The degree of cooperation and honesty of the respondents to provide accurate information regarding their ART adherence. Participants could have been dishonest in their responses to the structured interview schedule, they might have provided answers they thought will please the healthcare worker.
- A quantitative approach may not have been able to assess other ART adherence issues, such as the quality of adherence counselling given at the clinic; cultural beliefs and practices which could influence adherence.

- The study only interviewed patients currently on ART and did not include those who had discontinued treatment. It is possible that the patients who discontinued treatment could have given more information.
- The research results might only be limited to this ART clinic where the study was conducted and since the sample was small and represented only one clinic, therefore it is not a representative sample and the results are not generalisable to all ART patients in Botswana.
- Patients who were enrolled on ART at this clinic are from a lower socio-economic class and most of them are unemployed and therefore do not represent the general patients on ART because the majority of those who are employed receive their ARVs in the private sector in Botswana.
- Low CD4 cell counts and high VL indicate treatment failure which might result from HIV strains resistant to ARVs, and not necessarily from patients' ART non-adherence.
- The study focused only on ART patients. More different questions and information might have been raised by the patients' family members, treatment buddies and healthcare providers.

5.7 CONCLUDING REMARKS

Adherence remains a major challenge and continuing evaluation of the levels of adherence and appropriate intervention mapping are crucial for sustaining the ART programmes and minimise the emergence of resistant HIV strains and to preserve the current regimens. Machtiger and Bangsberg (2005:20) indicated that near perfect adherence is required to maximise the likelihood of long-term clinical success. The adherence levels found in this study were higher than those found in previous studies

done in Botswana (Nwokike et al 2003; Kgatlwane et al 2006) and other countries (Bangsberg et al 2001; Chesney 2000; Liu et al 2001; Nemes et al 2004; Safren et al 2005).

The results from this study identified some issues that impact on patients' ART adherence levels in a rural population in Botswana. However, more research is required to ascertain what individual and social factors actually help maintain ART adherence over many years. Efforts to improve the level of adherence require a collaborative approach involving the patient, the community, healthcare workers and policy makers, and a focus on addressing environmental and structural constraints

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