Adherence to antiretroviral treatment amongst patients at Lesetlhana Clinic in South East District, Botswana

A mini-dissertation submitted by

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(Department of Pharmacy)

Supervisor: Professor JC Meyer

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DECLARATION

I declare that the mini-dissertation hereby submitted to the Sefako Makgatho Health Sciences University, for the degree of Master of Science (Medical) in Pharmacy, in the Faculty of Health Sciences, School of Health Care Sciences, Department of Pharmacy, has not previously been submitted by me for a degree at this or any other university; that it is my work in design and execution, and that all material contained herein has been duly acknowledged.

__________________________________
Surname, Initials (Title)          Date
DEDICATION

I thank God the Almighty for giving me the strength, perseverance and guidance during the whole period of this research.

To my wife Margie, my daughter Tumelo, my son Mubiana, and my niece Elizabeth, I thank you all for your support, resilience and encouragement for me to pursue my studies, even during hard times.
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# ABBREVIATIONS AND ACRONYMS

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<th>Description</th>
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<tbody>
<tr>
<td>AIDS</td>
<td>Acquired Immune Deficiency Syndrome</td>
</tr>
<tr>
<td>ART</td>
<td>Antiretroviral Treatment / Therapy</td>
</tr>
<tr>
<td>ARVs</td>
<td>Antiretroviral</td>
</tr>
<tr>
<td>CD4+</td>
<td>CD4+ T Lymphocytes</td>
</tr>
<tr>
<td>DHMT</td>
<td>District Health Management Team</td>
</tr>
<tr>
<td>EDM</td>
<td>Electronic Drug Monitoring</td>
</tr>
<tr>
<td>HAART</td>
<td>Highly Active Antiretroviral Therapy</td>
</tr>
<tr>
<td>HIV</td>
<td>Human Immunodeficiency Virus</td>
</tr>
<tr>
<td>KITSO</td>
<td>Knowledge, Information and Technology Shall Overcome (HIV and AIDS)</td>
</tr>
<tr>
<td>MOH</td>
<td>Ministry of Health</td>
</tr>
<tr>
<td>MEMS</td>
<td>Medication Event Monitoring System</td>
</tr>
<tr>
<td>NACA</td>
<td>National AIDS Coordinating Agency</td>
</tr>
<tr>
<td>SMUREC</td>
<td>Sefako Makgatho University Research Ethics Committee</td>
</tr>
<tr>
<td>TDM</td>
<td>Therapeutic Drug Monitoring</td>
</tr>
<tr>
<td>UNAIDS</td>
<td>United Nations Joint Programme on AIDS</td>
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<td>WHO</td>
<td>World Health Organization</td>
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GLOSSARY OF TERMS

Adherence

Adherence is defined by the World Health Organisation (WHO, 2003) as “the extent to which a patient’s behaviour (taking medication, following a diet and/or executing lifestyle changes) corresponds with agreed recommendations from a health care provider.”

Antiretroviral therapy / treatment (ART)

Antiretroviral therapy / treatment (ART) refers to treatment with drugs that specifically target the human immunodeficiency virus (HIV). There are different classes of antiretroviral (ARV drugs), which act in different ways to interfere with the activities of the virus in the body (WHO, 2006).

Highly active antiretroviral therapy (HAART)

The combination use of three ARV drugs from different pharmacological classes, in order to suppress the viral load for the most sustained period of time, is referred to as HAART (WHO, 2006).

Optimal adherence

Optimal adherence, for the purpose of this study, is referred to as adherence levels greater or equal to 95% (Hansana et al., 2013).

Sub-optimal adherence

Sub-optimal adherence, for the purpose of this study, is referred to as adherence levels below 95% (Monjok et al., 2010; Paterson et al., 2000).
ABSTRACT

Introduction: Adherence to antiretroviral therapy (ART) plays a major role in the success of individual treatment and antiretroviral (ARV) programmes. While ART has improved the lives of many people, lack of adherence to ART is still a major challenge to Acquired Immune Deficiency Syndrome (AIDS) care and has serious public health consequences. The challenges of adherence to ART include factors related to patients and their families, socioeconomic factors, medication, and health care systems. These factors are interrelated and multidimensional, having implications for interventions to improve ART adherence. Limited studies have been published concerning rates of adherence to ART in Botswana and currently there is no "gold standard" or consensus for measuring ART adherence. This study investigated the adherence rates of patients at Lesetlhana Clinic, in South East District, Botswana, using three adherence methods and factors which possibly affect non-adherence to ART.

Objectives: To determine the proportion of patients with adherence levels above or equal to 95% and to identify factors which contribute to ART non-adherence.

Method: A quantitative descriptive study was conducted at Lesetlhana Clinic, Botswana, amongst 304 adult patients being on ART for ≥3 months. Three months’ retrospective data on pill count adherence were collected from patients’ clinic records. A mean adherence percentage was calculated. Self-reported adherence over the last 30 days, using two measures (set of four adherence questions; rating scale with 6 response options) and factors contributing to non-adherence were collected with a structured questionnaire administered in an interview. A composite (overall) adherence score based on all three measures was calculated for each patient. Proportions of adherent (≥95%) patients were calculated for each individual measure and for the composite score, and compared pairwise with the Fischer’s Exact test. with p<0.05 considered as statistically significant. Factors affecting adherence were summarised as frequency percentages. Ethical clearance for the study was granted by the Sefako Makgatho University Research Ethics Committee (SMUREC/H/19/2015:PG). Permission to conduct the study at the clinic was obtained from the Coordinator of South East District Health Management Team and the Ministry of Health of Botswana. All participants provided written informed consent for participation.

Results: Females predominated (66.1%) and the mean age was 40.4 (SD: 9.3) years. Mean duration on ART was 52.5 (SD: 33.9) months. Distance travelled to the clinic was an average of 5.9 (SD:10.5) km. Half of the participants (51.7%) had not completed their secondary education and most were either employed (47.7%) or self-employed (16.4%).
Although mean pill count adherence (3 months) was 98.0% (SD:2.2), 88.2% of patients were categorised as ≥95% adherent with the pill count, 80.6% with the self-report questions and 78.9% with the self-reported rating scale. Adherence with the composite measure was significantly lower (60.9%; p<0.001; Fisher’s Exact) compared to all other measures. Adherence challenges were reported by 87 (29%) patients. Most common challenges were ‘arriving home late’ (33.3%) and ‘forgetfulness’ (23.0%).

**Conclusion:** Mean pill count adherence was high compared to the percentage of patients categorised as ≥95% adherent. Three individual adherence measures yielded different results and all significantly higher than a composite (overall) measure. Adherence challenges were identified despite high mean pill count adherence. The results illustrated the importance of adherence monitoring, using a combination of adherence measures, which would allow the strengths of one method to compensate for the weaknesses of another method. The factors which contribute to non-adherence identified in this study should be targeted in future interventions.

**Recommendations:** Due to single adherence measures being prone to weaknesses, adherence should be measured on a monthly basis with more than one method, to identify patients who are sub-optimally adherent. Individual adherence counselling should be part of routine practice, to identify patients with adherence challenges. Patients would benefit from regular group discussions on adherence at the clinic, which will allow active participation of patients in such discussions. Factors which contribute to non-adherence to ART, identified in this study, should be used as a guideline for future strategies to enhance adherence.
CHAPTER 1
INTRODUCTION

1.1 INTRODUCTION

This chapter describes the background and rationale for the study and provides the problem statement and research question. The aim of the study and objectives to be achieved are given. The chapter ends with an overview of the importance of the study and an outline of the dissertation.

1.2 BACKGROUND AND RATIONALE FOR THE STUDY

Acquired Immune Deficiency Syndrome (AIDS) is one of the most destructive epidemics the world has ever witnessed (Reda & Biadgilign, 2012). Antiretroviral therapy (ART) has shown to delay progression to AIDS, resulting in a greater and more sustained virologic and immunologic response (Zulu et al., 2009) and better survival (Birungi et al., 2011). However, strict adherence to ART is central to therapeutic success and key to sustained HIV suppression, reduced risk of drug resistance, improved overall health, quality of life and survival (Chesney, 2006; WHO, 2003). Studies on adherence to ART in developed and developing countries have demonstrated that high levels of adherence (≥95%) are associated with improved virological, immunological and clinical outcomes and are necessary in order to maximize the benefits of ART (Ostenberg & Blaschke, 2005; Paterson et al., 2000; Peltzer et al., 2010; WHO, 2006). Levels of adherence below 95% can easily lead to drug resistance and may cause treatment failure (Baptiste, 2008; Ndubuka & Ehlers, 2010; Paterson et al., 2000; Peltzer et al., 2010).

Varying levels of adherence to ART amongst individual patients have been observed by the pharmacist at Lesetlhana Clinic, in South East District, Botswana. Pill counts are done when patients visit the clinic to refill their prescriptions. Pill count results and the number of pills dispensed at a particular visit are then entered onto the dispensing computer system for each patient. Based on this information, adherence levels are generated by the computer for each patient visit. Suboptimal levels of adherence (<95%) have been noted in a number of patients, according to these adherence levels generated by the computer. This information however, has not been analysed formally to determine overall adherence and the extent of sub-optimal adherence for the patients at Lesetlhana Clinic.
To date, only a few studies have been conducted in Botswana concerning rates of adherence to ART. In these studies, the average adherence rates varied and were reported as 86.0% (Ehlers & Tshisuyi, 2015), 77% (Kgatlwane et al., 2005), 83.0% (Nwokike, 2003) and 54% (Weiser et al., 2003). In another study conducted in Gaborone, the mean adherence rate was 97% (Gregory et al., 2008). Although the level of adherence measured is affected by the method of assessment, there is a remarkable difference in adherence among these studies. Hence, further assessment of adherence using different methods of measurement is necessary. Furthermore, since adherence changes over time, it needs to be monitored consistently. This study aimed to determine to what level patients at Lesetlhana Clinic are adhering to their ART and identify contributing factors to non-adherence.

1.2 RESEARCH QUESTION

What is the level of adherence of patients taking ART at Lesetlhana Clinic, in Botswana and which factors possibly contribute to non-adherence?

1.3 AIM OF THE STUDY

The aim of the study was to determine the levels of adherence to ART amongst patients at Lesetlhana Clinic and identify factors which contribute to non-adherence.

1.4 OBJECTIVES OF THE STUDY

The objectives of the study were as follows:

- To determine the proportion of patients at Lesetlhana Clinic with adherence levels within each of the following categories:
  - Adherence ≥95%
  - Adherence <95%
- To identify factors which contribute to non-adherence to ART

1.5 IMPORTANCE OR SIGNIFICANCE OF THE STUDY

This study about adherence to ART is very important, because adherence can affect the success or failure of therapy. While ART has improved the lives of many people worldwide, lack of adherence to ART is still a major challenge to AIDS care (Bangsberg et al., 2000; Kgatlwane et al., 2005).
Chapter 1: Introduction

Antiretroviral therapy has been available in the public sector in Botswana since 2002. However there is continuously a concern about the level of adherence. Studies done in Botswana have reported adherence levels of 77% (Kgatlwane et al., 2005) and 83% (Nwokike, 2004) in the public sector and 54% (Weiser et al., 2003) in the private sector. These levels are below 95%, the adherence level required for treatment success.

The results obtained from this study illustrated the importance of continuous adherence monitoring, using a combination of adherence measures. As there is no gold standard for adherence measurements yet, using a combination of methods would allow the strengths of one method to compensate for the weaknesses of another. Furthermore, factors contributing to non-adherence to ART identified in this study will assist in making recommendations pertaining to the development of strategies to maintain adherence to ART.

The information can also be used to develop guidelines and educational materials for patients that can be used in the clinic to promote adherence counselling before patients are initiated on ART. The results will also contribute to the pool of adherence studies conducted in Botswana, so that comparisons can be made with previous studies and progress monitored.

1.6 OUTLINE OF THE DISSERTATION

The dissertation consists of five chapters. Chapter 1 gives an introduction to the dissertation and provides the aim and objectives of the study. Chapter 2 includes a review of the literature on the study topic. Chapter 3 describes the methodology used in this study in detail. The results of the study and a discussion thereof are presented as a manuscript in Chapter 4. Chapter 5 contains the limitations of the study, recommendations offered and the final conclusion of the study.
CHAPTER 2
LITERATURE REVIEW

2.1 INTRODUCTION

In this chapter, the literature pertaining to the study topic is reviewed. The chapter starts with a description of the HIV and AIDS situation in Botswana, followed by a review of antiretroviral treatment (ART). The methods of adherence measurement are reviewed, with emphasis on the pill count and patient self-report. The chapter ends with a review of the factors which affect adherence to ART.

2.2 HIV AND AIDS SITUATION IN BOTSWANA

The first case of human immunodeficiency virus (HIV) infection and Acquired Immune Deficiency Syndrome (AIDS) in Botswana was diagnosed in 1985. Since then the prevalence of HIV has risen significantly to amongst the highest in the world (National AIDS Coordinating Agency (NACA), 2012). From 2003, Botswana provides free ART to its citizens, as well as regular CD4+ count testing and viral load tests (NACA, 2012).

Following the introduction of ART, in the last number of years, HIV prevalence has declined in Botswana from 37.3% in 2004 (UNAIDS, 2004) to 25.2% in 2014 among adults aged 15 to 49 years old (UNAIDS, 2014). According to UNAIDS statistics of 2014, the number of people living with HIV in Botswana is 390 000. The number of deaths due to AIDS is 5 100 and the number of orphans who died due to AIDS by 2014 is 67 000 (UNAIDS, 2014). The number of children aged 0 to 14 years living with HIV is 16 000 while the number of adults aged 15 and older living with HIV is 380 000 (UNAIDS, 2014). More than half (55.38; 210 000) of adults aged 15 years and up living with HIV are women (UNAIDS, 2014). From these figures it is evident that women are more affected by AIDS than men.

2.3 ANTIRETROVIRAL TREATMENT FOR HIV INFECTION

In 2002, Botswana became the first country in sub-Saharan Africa to launch a free national ART programme in the public health sector (Kgatlwane et al., 2005). Access to HIV treatment in Botswana has been improving in recent years. Currently, access to ART is extremely high with more than 95% of all adults and children in need of treatment receiving it (UNAIDS, 2013). National treatment guidelines now recommend the Test and Treat All strategy (MOH Botswana, 2015).
Chapter 2: Literature Review

The standard first line regimens for newly diagnosed treatment-naïve patients are as follows:

- Tenofovir + Emtricitabine or Lamivudine + Efavirenz (as a single dose called Atripla®)
- If the patient is intolerant to Efavirenz, and if baseline CD4+ cell count is less than 250 cells (women) or less than 400 cells/µL (men): Tenofovir + Emtricitabine or Lamivudine + Nevirapine

The standard second line regimen for those who fail the first line regimen is as follows:

- Zidovudine + Lamivudine + Aluvia (also known as Kaletra)

2.4 ADHERENCE TO ANTIRETROVIRAL TREATMENT

2.4.1 Definition of adherence

Adherence is a concept with social and emotional components. Adherence is defined in Stedman’s Medical Dictionary as follows (Williams & Wilkins, 1995): “The extent to which the patient continues the agreed-upon mode of treatment under limited supervision when faced with conflicting demands”.

The WHO (2003) defines adherence as follows: “The extent to which a patient’s behavior (taking medication, following a diet and/or executing lifestyle changes) corresponds with agreed recommendations from a health care provider”.

The term 'medication adherence' in HIV and AIDS care specifically refers to the ability of the person living with HIV and 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). Adherence is therefore regarded as the “extent to which a client’s behavior coincides with the prescribed health care regimen as agreed through a shared decision-making process between the client and the health care provider” (KITSO Manual, 2004).

2.4.2 Importance of adherence

The introduction of ART and multidrug regimens, or highly active antiretroviral therapy (HAART) has substantially improved the survival of persons infected with HIV (Hansana et al., 2013). These drug regimens however are complex. This, alongside issues of toxicity, side
effects, disruptions to a patient’s daily life and difficulties in returning for scheduled follow-up consultations, often makes maintaining adherence over the long term challenging. Yet the individual and public health benefits of ART are adherence dependent (Adefolalu & Nkosi, 2013; Hansana et al., 2013).

The study of Paterson et al. (2000), has been referred to widely, in establishing the level required for optimal adherence necessary to maintain viral suppression (≥95%). Understanding the pathogenesis of HIV has suggested that adherence to ART of at least 95% or greater is required to keep the viral load at undetectable levels for as long as possible to prevent drug resistance and to maintain the functionality of the immune system (Okafor & Ekwunife, 2013). Accepted wisdom is that if rates of ART adherence are less than 90-95%, treatment can fail, and the virus may become resistant (Baptiste, 2008; Chalker et al., 2009). Knowing the percentage of adherence and understanding the predictors of non-adherence, are the initial steps in an attempt to improve adherence to ART (Okafor & Ekwunife, 2013). Sustaining adherence to ART over the long-term requires accurate and consistent monitoring, and this is a particular challenge for countries in sub-Saharan Africa (Nachega, Mills & Schechter, 2010). It is further challenged by various social and clinical obstacles (Nachega, Mills & Schechter, 2010) where inadequate suppression of viral replication by ART is a result of poor adherence to therapy, low potency of the ARV regimens, viral resistance to ART medications, and pharmacokinetic interactions (Friedland & Andrews, 2001) causing inadequate drug delivery (Nachega, Mills & Schechter, 2010).

Adherence levels change over time. Clinical experience and research indicate that adherence is a “moving target”; the longer the patient stays on treatment the poorer the adherence is likely to become (Adefolalu & Nkosi, 2013; Cauldbeck, Connor, Connor, Saunders, et al., 2009; Ickovics & Meade, 2002). Generally, adherence rates are higher among patients who are taking medication for acute medical conditions compared to those with chronic medical conditions (Adefolalu & Nkosi, 2013; McDonald, Garg & Haynes, 2002). Furthermore, adherence levels among patients with chronic diseases, no matter how impressive adherence is initially, have been reported to drop dramatically after six months on ART (Dulmen, Sluijs, Dijk, Riddet, Heerdink & Bensing, 2007). A review of adherence for chronic diseases such as hypertension and diabetes reported that achieving adherence rates above 80% is difficult, even in resource-rich countries (Machttinger & Bangsberg, 2006). Hence, it is crucial to be able to accurately monitor ART adherence rates and immediately address identified problems (Chalker et al., 2009).

Adherence to ART for patients with HIV and AIDS is different from that for other chronic diseases such as hypertension and diabetes, because it should be greater or equal to 95%
for treatment to succeed (Baptiste, 2008). Particularly in Africa, studies have reported very high levels of adherence to ART of between 85% and 99% (Baptiste, 2008, Bezabhe et al., 2013; Elul & Asiimwe, 2011; Machtinger & Bangsberg, 2006; Nachega et al., 2009). A major review on studies conducted on ART adherence that involved 72 developed countries and 12 developing countries, five of which were African, estimated adherence level among people living with HIV and AIDS in sub-Saharan Africa at 77%, surprisingly higher than 55% in North America (Mills et al., 2006).

Sub-optimal adherence has been associated with rapid disease progression, poor immunologic response, increased drug resistance, and increased risk of mortality, complicating further treatment and increasing the risk of transmission of resistant virus (Chaiyachati et al., 2011, Elul & Asiimwe, 2011; WHO, 2006). Antiretroviral adherence is the second strongest predictor of progression to AIDS and death, after CD4+ count (Machtinger & Bangsberg, 2006). Promoting adherence is especially important as these treatments become increasingly available and affordable for people living with HIV (PLHIV) in developing countries (Bangsberg, Moss & Deeks, 2004; UNAIDS, 2009). Adherence monitoring and evaluation of ART are therefore essential in the management of HIV and AIDS (Lyimo et al., 2011; Monjok et al., 2010).

2.4.3 Adherence levels

Previous research indicate that despite earlier fears of poor medication adherence, patients in developing countries are able to achieve adherence levels similar to or higher than those of patients in developed countries (Reda & Biadgilign, 2012). For instance, a review by Vreeman and colleagues (2008) indicated that the majority of the studies in developing countries report adherence levels of more than 75% (range 45-100%), while in developed countries the majority report less than 75% (Reda & Biadgilign, 2012; Vreeman et al., 2008).

In Africa, some studies indicated the following adherence levels: Rwanda 91% (Mussime et al., 2011), Nigeria 86% (Iroha et al., 2010), Kenya 84% (Okonji et al., 2010), Uganda 100% (Senkomago et al., 2011).

Another systematic review by Mills et al. (2006) obtained a pooled estimate of adequate adherence by sub-Saharan Africa patients of 77% and 84.3% (Okafor & Ekwunife, 2013), whereas the figure for North American patients in 2006 was 55%.

In a recent study conducted in Botswana, the adherence level was 86.0% (Ehlers & Tshisuyi, 2015). The other findings for Botswana are 77.0% by Kgatlwane et al., (2005); 83.0% by Nwokike (2004); and 54.0% by Weiser et al., 2003).
Some caution is needed in comparing adherence rates across studies, as the methods of measuring adherence (self-report vs. pill counts or medication electronic monitoring system [MEMS]) and settings (such as free ART vs. non-free, rural vs. urban) can affect findings (Hansana et al., 2013).

2.5 METHODS OF ADHERENCE MEASUREMENT

Currently there is no "gold standard" or consensus for measuring ART adherence (Berg & Arnsten, 2006; Bezabhe et al., 2013; Chesney, 2006; Elul & Asiimwe, 2011). Previous studies have used a wide range of methods to measure adherence at the individual level with variable sensitivity and specificity. Methods include patient self-report, pharmacy refill records, pharmacy insurance claims, pill counts, medication electronic monitoring systems (MEMS), measurement of drug plasma levels, therapeutic drug monitoring (TDM), changes in CD4+ count and changes in viral load (Bezabhe et al., 2013; Elul & Asiimwe, 2011; Muyingo et al., 2008; Uzochukwu et al., 2009). According to Gill et al. (2005) the hierarchy of adherence measures ranks physician and self-assessment report the least accurate, pill count intermediate and unannounced pill counts and electronic drug monitoring, the most accurate adherence measure (Bangsberg, 2009; Chkhartishvili et al., 2014).

It has been found that the use of more than one measure of adherence allows the strengths of one method to compensate for the weaknesses of the other and to more accurately capture the information needed to determine adherence levels (Sahay et al., 2011; Vitolins et al., 2000). The self-report remains the most frequently used adherence measure because of its low cost and simplicity. Although the accuracy of self-reported adherence has been questioned because of social desirability and recall bias, several approaches have shown good correlation with objective adherence measures and viral suppression (Degnan et al., 2010; Oyugi et al., 2004).

For the purpose of this dissertation, pill counts, self-report and composite adherence measures are discussed in more detail in this section.

2.5.1 Pill counts

Due to their relative low-cost and simplicity, the most commonly used measures of ART adherence are pill counts (Elul & Asiimwe, 2011; Muyingo et al., 2008). Pill counts, which involve counting the number of pills that remain in the patient’s bottles, have been widely used to measure adherence to medication in clinical settings. Pill counts are done during patients’ visits to health facilities when they come for a follow-up appointment and/or refill of their
medication. The patient returns the actual pill container in order for the clinician to physically count the left over pills. The return of excess pills provides real evidence of non-adherence (Berg & Arnsten, 2006; Osterberg & Blaschke, 2005; Sendagala, 2010).

Pill counts however, has weaknesses because patients can deliberately remove and dump some pills before their next clinical visit so as to appear to be adherent (Awolola, Meyer, Summers & Johnson, 2014). Because of this, pill counts can overestimate adherence. In addition, the method does not provide information on other aspects of taking medication, such as dose timing and drug holidays, which are vital in determining the clinical result (Sendagala, 2010; Williams et al., 2013). Pill count adherence is usually calculated by dividing the difference between the number of pills taken home and the current pill count, by the number of pills that should have been taken during the period since the last clinic visit (Bezabhe et al., 2013). The following formula is used to assess adherence using the pill count (Chesney, 2006):

\[
\% \text{ Adherence} = \frac{\text{Number of pills taken home} - \text{number of pills returned}}{\text{Number of pills that should have been taken}} \times 100
\]

Unannounced pill counts, at patients’ homes, were developed to check the practice of pill dumping, but it has the tendency to affect the trust between the patient and health care provider, which may eventually hinder adherence (Adefolalu et al., 2013; Machtinger & Bangsberg, 2006).

2.5.2 Patient self-report

Patient self-report is the longest standing and most widely used method to assess medication adherence in both the research and practice setting because of its low cost and simplicity (Williams et al., 2013). A number of factors can compromise the accuracy of self-report and should be avoided. These include poor framing of the question which could result in responses being influenced by social desirability (Steel et al., 2007; Williams et al., 2013).

With self-report the patient is asked to recall medication-taking behaviour over a short period of time, usually a 3-day, 7-day or 30-day period (Steel et al., 2007; Thompson et al., 2012). Self-reported adherence is often over-reported and dependent on the structure of the adherence question asked (Berg et al., 2010). The advantage of self-reported adherence is that it is easy to use and gives the health care worker the opportunity to immediately intervene and counsel the patient in the case of non-adherence (Berg et al., 2010). An important strength of self-report is that it maps very well into standard practice and costs relatively little to implement. Furthermore, it is the only assessment available that asks subjects directly about adherence, while other measures directly assess proxies of adherence (Williams et al., 2013).
Questions on self-report in ART adherence are readily accessible, inexpensive, and easily and quickly administered in clinical settings (Chaiyachati et al., 2011). They are thus a feasible method to monitor adherence in sub-Saharan Africa, where neither the human resources to perform more time-consuming adherence assessment (such as counting of antiretroviral pills or reviewing pharmaceutical records) nor the financial resources to conduct more costly assessment (such as electronic monitoring or monitoring of blood ART concentrations) may be available (Chaiyachati et al., 2011).

2.5.3 Composite measure of adherence

The Oxford Advanced Learner’s Dictionary of Current English (2001), defines composite as “Something made by putting together different parts or materials”. The composite adherence is the adherence obtained by putting together different methods of assessing adherence to ART.

Although some of the adherence measurement tools have been validated to be sensitive in measuring adherence, the majority of the tools currently used cannot meet all the features for an ideal tool, hence there is no “gold standard” in the measurement of adherence (Steel, Nwokike & Joshi, 2007). Because of the weaknesses of each individual measure, there is a possibility that the best method of assessing adherence includes multiple measures (Steel, Nwokike & Joshi, 2007).

2.6 FACTORS AFFECTING ADHERENCE TO ART

The factors affecting adherence to ART are normally classified according to five dimensions namely, health system/health care team, social/economic factors, therapy-related factors, patient-related factors and condition-related factors (WHO, 2003).
2.6.1 Social and economic dimension

The social and economic factors which affect adherence include English proficiency, low health literacy, lack of family or social support network, unstable living conditions, homelessness and medication costs (Krueger et al., 2005; Osterberg & Blasche, 2005; WHO, 2003).

Other socio-economic factors considered as barriers to adherence to ART in a number of studies in Africa are the cost of ART, availability and accessibility to ARV drugs (Adefolalu & Nkosi, 2013; Hardon et al., 2007; Hawkins et al., 2007; Iliyasu et al., 2005; Mukhtar-Yola et al., 2006; Tuller et al., 2009; Weiser et al., 2003). There are also some indirect costs associated with ART which influence adherence; these are the time taken off work, the time spent in hospital and inability to provide for the family when affected by opportunistic infections (Adefolalu & Nkosi, 2013; Castro, 2005; Hardon et al., 2007).

2.6.2 Health care system dimension

Providers' characteristics and clinical settings affect the patient's adherence to ART. The patient’s satisfaction with the level of care has been found to correlate with increased adherence (Gauchet, Tarquino & Fischer, 2007). The characteristics of clinical setting that could affect adherence are a friendly and supportive environment, non-judgmental health care providers, suitable appointment schedule and confidentiality in service provision (Simoni et
Long waiting times, poor staff attitudes, shortage of drugs and other barriers decrease patient’s adherence to ART and also result in poor clinic attendance (Hawkins & Murphy, 2007). The other factors affecting adherence are disparity between the health beliefs of the health care provider and those of the patient, lack of positive reinforcement from the health care provider, weak capacity of the system to educate patients and provide follow-up, lack of knowledge on adherence and of effective interventions for improving it, patient information materials written at too high literacy level, restricted formularies; changing medications covered on formularies, high drug costs, poor access or missed appointments and lack of continuity of care (Krueger et al., 2005; Osterberg & Blasche, 2005; Vermiere et al., 2001; WHO, 2003).

### 2.6.3 Condition-related dimension

The factors affecting adherence under this dimension are chronic conditions of the patient, lack of symptoms, severity of symptoms, depression, psychotic disorders and mental retardation or developmental disability (Krueger et al., 2005; Osterberg & Blasche, 2005; Vermiere et al., 2001; WHO, 2003). The prior opportunistic infections in an HIV patient before initiating ART have the potential of influencing adherence as the patient may perceive the disease to be severe enough to require good adherence to treatment in order to achieve the desired treatment outcome (Cauldbeck et al., 2009; Adefolalu & Nkosi, 2013).

### 2.6.4 Therapy-related dimension

Antiretroviral therapy is a complex treatment which is characterized by pill burden, dietary restrictions and timing of medicine intake (Adefolalu & Nkosi, 2013). The numerous and potential side effects contribute to irregular drug use and deliberate discontinuation of medication intake by some patients (Waters, 2007; Weiser et al., 2003). Regimens with significant side effect profiles are usually associated with poor adherence (Caulbeck et al., 2009; Glass et al., 2010). Health care providers should consider the circumstances of patients when prescribing ART (Harries et al., 2010); a potent combination therapy may not fit into a patient’s schedule and may affect the adherence to such medication. The rate of adherence to a once-daily ART regimen has been found to enhance adherence than a twice-daily regimen (Parienti et al., 2009). Other therapy-related factors which affect adherence to medication are duration of therapy, frequent changes in medication regimen, lack of immediate benefit of therapy, medication with social stigma attached to use, actual or perceived unpleasant side effects, treatment interferes with lifestyle or requires significant behavioural changes (Krueger et al., 2005; Osterberg & Blasche, 2005).
2.6.5 Patient-related dimension

Socio-demographic factors such as age, gender, socio-economic status, level of education, income and ethnicity have been used in studies to understand their influence on adherence (Rougemont et al., 2009; Gordillo et al., 1999). Psychosocial factors like drugs and alcohol use, social stability, depression and psychiatric illness have also been used in other studies to find out if there was a correlation between any of them and adherence to ART (Adefolalu & Nkosi, 2013; Berg et al., 2009). What studies have found are barriers to adherence such as substance abuse, unstable housing, depression, mental illness, fear of disclosure of HIV status, decreased quality of life, work and family responsibility (Mills et al., 2006; Protopopescu et al., 2009; Glass et al., 2010).

Other factors which affect adherence are visual impairment, hearing impairment, cognitive impairment, impaired mobility or dexterity and swallowing problems (WHO, 2003).

Psychological or behavioral factors include knowledge about the disease, perceived risk or susceptibility to disease, understanding the reason medication is needed, expectations or attitudes toward treatment, perceived benefit of treatment, confidence in ability to follow the treatment regimen, motivation, fear of possible adverse effects, fear of dependence, feeling stigmatized by the disease, frustration with health care providers, psychosocial stress, anxiety, anger and alcohol or substance abuse (Krueger et al., 2005; Osterberg & Blasche, 2005; WHO, 2003).

Other patient factors which mainly affect adherence include fear of disclosure and wanting to avoid taking medication in public places, feeling depressed, hopeless, or overwhelmed, forgetting to take medication at the specified time (Castro, 2005; Mills et al., 2006). The likelihood of a patient’s adherence to a given regimen declines with polypharmacy, the frequency of dosing, severity of side effects and the complexity of the regimen (Nakiyemba et al., 2005).

Some of the subjective reasons for non-adherence often cited by patients are distress due to side effects, lack of insight and non-belief in treatment, substance abuse, low self-esteem and inability to identify the stressors of life (Sahay et al., 2011). Other situations include consistent under-or over-dosing, abrupt over-dosing (neglecting to take medication properly for a period of time, then over-dosing just before a visit to the clinic), drug holidays, random administration (taking drugs whenever the thought occurs), incorrect administration because of not comprehending the physician’s prescription and prematurely terminating the medication without consulting the health care provider (Chesney, 2003; Kagee, 2008).
2.7 SUMMARY

In this chapter the HIV and AIDS situation in Botswana was described. The HIV prevalence declined in Botswana from 37.3% in 2004 to 25.2% in 2014 among adults aged 15 to 49 years old. The level of adherence required to continuously suppress HIV and improve immune function is 95% and more. The levels of adherence to ART need to be monitored regularly because adherence changes over time. Various methods of adherence measurement are available, such as the pill count and the patient self-report. The pill count and self-report methods of assessing adherence to ART are simple and easy to administer in resource constrained settings. The challenges of adherence include factors related to patients and their families, socio-economic factors, medication and the health care system. Some of the specific reasons for non-adherence which have been reviewed are drugs not being available in the clinic, personal financial problems, forgetfulness, being away from home, running out of pills and medication side effects.

In the next chapter, the research methodology of this study will be described in detail.
CHAPTER 3

METHODOLOGY

3.1 INTRODUCTION

This chapter presents the method used to conduct the study. The chapter starts with a description of the study design, followed by an outline of the study site. A discussion of the study population and sample selection is provided. The data collection process and data collection instruments are discussed in detail. The data analysis procedures and measures used to ensure reliability and validity of the data are presented in the subsequent sections. The chapter is concluded with a discussion of the ethical considerations of the study.

3.2 STUDY DESIGN

The design of the study was quantitative, descriptive and cross-sectional. Prospective data on adherence were obtained from patients’ self-report of their adherence, by using a structured questionnaire administered in an interview. Retrospective data on pill count adherence were collected at the dispensary by reviewing patients’ adherence charts, included in their clinic records. Data on demographic information and factors which contribute to non-adherence were collected during the interview.

3.3 STUDY SITE

The study was conducted at Lesetlhana Clinic, in South East District, Botswana. The clinic is approximately 35 kilometres from Gaborone. The clinic has one medical practitioner, pharmacist and pharmacy auxiliary, eight registered nurses, four midwives, a driver and three cleaners and watchmen who change shifts. The clinic offers the following services: youth friendly services; sex reproductive services; HIV testing services, cervical cancer screening; Expanded Programme on Immunisation; child welfare clinic; diabetic and hypertensive clinic; and family planning services. The clinic has the Infectious Disease Control Centre where they offer HIV and AIDS services, a pharmacy and a dispensary. Enrolment for ART at the clinic started in June 2009. The total number of patients on ART at the time of the study at Lesetlhana Clinic was 556. Patient reviews and dispensing of ARVs are done three times in a week, on Tuesdays, Wednesdays and Thursdays.
3.4 STUDY POPULATION

The target population for this study included all adult patients enrolled on ART at Lesetlhana Clinic at the time of the study.

3.5 SAMPLE SELECTION

Considering a two-sided 95% confidence level and 5% margin of error, with a total population of 556 patients active on ART, the sample size was calculated as 228 patients. For a lower margin of error (3.84%) a larger sample of 300 patients was required (Raosoft® Sample size calculator). The final sample for the study included 304 patients on ART.

To achieve the required sample size, all the patients attending the clinic and who met the inclusion criteria were invited to participate in the study. Patients who agreed to participate and provided written informed consent were enrolled in the study, until the required sample size of 304 patients was reached.

The following inclusion criteria were used during patient recruitment:

- Patients on ART who were ≥18 years
- Patients who have been on ART for ≥3 months
- Patients with adherence charts available in their records for the three months prior to the study
- Patients who provided written informed consent

The following exclusion criteria applied:

- Patients who have been transferred to the study site within the three months prior to the study
- Patients who were too ill to participate in an interview

3.6 DATA COLLECTION PROCEDURES

3.6.1 Data collection period

Data collection started after ethical clearance for the study was obtained from Sefako Makgatho University Research Ethics Committee. Data collection took place on clinic days (3
days/week) over a period of four months (July 2015 to October 2015) until the required sample size of 304 participants was reached.

3.6.2 Data collectors

All the data were collected by the researcher and three data collectors who were also fluent in Setswana (most common language spoken in the area).

3.6.3 Data collection training

The researcher and the data collectors were trained in interview techniques, prior to the commencement of data collection. One of the data collectors has a registered nurse while the other two were health education Assistants. During the training, discussions included how to establish willingness for participants to enroll into the study and how to conduct the interviews and collect the data. The questions included in the interview were discussed and reviewed in order to get a clear understanding. The different ways of possibly interpreting the questions were discussed and consensus was reached amongst the data collectors.

3.6.4 Participant enrolment

The data collectors introduced themselves to all potential participants and informed them of the study by giving them a study information leaflet (see Appendix 1a and 1b). The participants were also informed that their adherence would be assessed using their previous pill count records available in the computer, as well as through self-report of adherence during the interview. Potential participants, who needed any clarification about the study, were allowed to ask questions. Those who agreed to participate in the study were then requested to provide written informed consent (see Appendix 2a and 2b).

3.6.5 Data collection process and instrument

Enrolled patients were interviewed using a structured questionnaire (see Appendix 3a and 3b). The patients were approached in the clinic on the days they came for their clinic review or refill of their ARVs. This happened when they were waiting for their turn to be reviewed by the medical practitioner or have their drug refill from the pharmacy. If not possible, patients were interviewed when they were about to leave the clinic.

Demographic data, the patient’s self-report adherence data and information about factors contributing to non-adherence were obtained during the interview with the patient, using a structured questionnaire (see Appendix 3a and 3b), while the patient’s pill count adherence was obtained retrospectively from the computer data base. The questionnaire was available
in English and in Setswana so that participants could respond in their language of preference. The study participants were informed that the adherence assessment was not punitive but rather aimed at determining what challenges they were facing to achieve optimal adherence. Each patient was assigned a study identification number which assisted the researcher to match patient information from the questionnaire and that from the computer, as well as to maintain patient confidentiality.

With the first adherence self-report measure, the researcher and the data collectors guided the study participants through four questions to which they had to respond either “yes” or “no”. An adherent patient would respond “no” to all questions. The non-adherent patient would respond “yes” to one or more questions. This type of question helps to validate responses, since many patients tend to respond “yes” to any questions posed to them by a health care professional, in order to please the health care worker (Steel et al., 2007). The questions examined whether the patient forgot to take his/her medication, whether the patient stopped taking his/her medicine when they felt better, whether the patient missed their medication in the past four days, and whether the patient stopped taking medication when they feel worse (see Appendix 3a and 3b).

With the second self-report adherence measure, study participants were asked to rate their adherence to ARVs in the last 30 days, by using six response options. The options were as follows: very poor, poor, fair, good, very good and excellent. Study participants would select only one of the six options (see Appendix 3a and 3b).

After the patient interview was concluded, adherence information from pill counts was obtained retrospectively from patient records for the three months prior to enrolment in the study (see Appendix 3a and 3b). Information was obtained from the ART dispensing software referred to as ‘PIMS II Data Base Version 2.6’. This dispensing tool keeps all adherence records of patients based on pill count data. The patient’s file number was used to retrieve the information. As part of standard clinic practice, adherence is calculated by the computer, based on a pill count done during each visit to the clinic. After the interview, the researcher reviewed each participant’s pill count adherence records on the computer for the three months period prior to enrolment in the study (see Appendix 3a and 3b).

3.7 PILOT STUDY

A pilot study was conducted one week prior to the commencement of data collection, to determine the feasibility and acceptability of the data collection instruments. The pilot study was conducted at Taung Clinic, situated 5 km from Lesetlhana Clinic. Ten patients were
randomly selected to participate in the pilot study. No changes were made to the data collection instruments, since there were no challenges observed.

3.8 DATA ENTRY AND ANALYSIS

Data were captured and entered into Microsoft Excel™ spread sheets. The statistical analysis was performed on Statistical Analysis Software (SAS institute Inc., Carey, NC, USA), Release 9.3 running under Microsoft Windows for a personal computer in consultation with a statistician. Demographic data and factors affecting adherence were summarised and expressed as frequency percentages, means with standard deviations and medians with inter quartile range as appropriate.

Mean adherence was calculated for the three months’ retrospective pill count adherence data. Responses to the rating scale were expressed as frequency percentages and also converted to numeric values to express self-reported adherence as a percentage for each patient. A composite (overall) adherence score based on all three measures was calculated for each patient, based on the criteria as shown in Table 3.1.

Table 3.1: Outcome criteria for ≥95% composite (overall) adherence

<table>
<thead>
<tr>
<th>Adherence measure</th>
<th>Outcome criteria for ≥95% adherence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pill count</td>
<td>Monthly pill count of all antiretrovirals and % adherence calculated for regimen</td>
</tr>
<tr>
<td>Adherence questions</td>
<td>Do you find it difficult to remember to take your medication?</td>
</tr>
<tr>
<td></td>
<td>Do you stop taking medication when you feel better?</td>
</tr>
<tr>
<td></td>
<td>Do you stop taking medication when you feel worse?</td>
</tr>
<tr>
<td></td>
<td>Have you missed &gt; 3 doses in the last 30 days?</td>
</tr>
<tr>
<td>Self-report rating scale</td>
<td>Options for rating scale</td>
</tr>
<tr>
<td></td>
<td>Excellent</td>
</tr>
<tr>
<td></td>
<td>Very good</td>
</tr>
<tr>
<td></td>
<td>Good</td>
</tr>
<tr>
<td></td>
<td>Fair</td>
</tr>
<tr>
<td></td>
<td>Poor</td>
</tr>
<tr>
<td></td>
<td>Very poor</td>
</tr>
</tbody>
</table>

Patients were categorised into two categories for each measure of adherence, namely ≥95% adherent or <95% adherent. The proportion of adherent (≥95%) patients were calculated for
each individual measure and for the composite score, and compared pairwise with the Fischer Exact test with p<0.05 considered statistically significant.

3.9 RELIABILITY AND VALIDITY

The pilot study which was conducted at Taung clinic before the actual study commenced helped to increase the reliability and validity of the data collection instrument. The fact that the pilot study was conducted at a different clinic prevented the study participants from informing others about the nature of questions in the study.

The questionnaires were available in both English and Setswana. This ensured that the same information was given to all study participants. The data collectors were encouraged to establish a comfortable, conducive and trusting atmosphere in which participants could honestly discuss non-adherence issues. The data collectors were trained in interview techniques in order to ensure the reliability of data collection. The researcher and data collectors wrote their names on the questionnaires that they administered to allow follow-up with the data collector in case of any queries. The researcher was always on site on data collection days to ensure that the questionnaires were properly completed and that patients’ responses were not forced in any way.

Two adherence methods, namely the pill count and a self-report, were used in order to increase the validity of the study results (Steel & Josh, 2007). This was further strengthened by using a composite measure of adherence.

Entered data were checked for correctness and completeness before commencement of data analysis, to ensure the reliability of the entered data.

3.10 BIAS

The study site is one of the researcher's places of work. The researcher recognised this as a potential source of bias. Therefore, bias was minimized through the practice of professionalism, maintaining medical ethics and ensuring patient confidentiality and privacy.

Self-report measures of adherence are subject to bias because patients usually over-estimate their adherence. The researcher recognised this and encouraged study participants to respond honestly.

Selection bias was reduced by including all patients who met the inclusion criteria in the study.
3.11 ETHICAL CONSIDERATIONS

Ethical clearance for the study was obtained from the Sefako Makgatho University Research Ethics Committee, prior to the commencement of data collection (SMUREC/H/19/2015: PG) (see Appendix 4). Permission to carry out the study at the site was obtained from both the Coordinator of South East District Health Management Team and the Ministry of Health in Botswana (see Appendix 6 and 7).

Written informed consent was obtained from participants (see Appendix 2a and 2b) after they were given information about the study (see Appendix 1a and 1b) and prior to participation in the study. Participants were informed of their right to withdraw from the research at any time if they so wished.

The participants were assured of confidentiality and privacy of their responses and other information in the research. To ensure this, each participant was assigned a unique study identification number instead of using their names.

3.12 SUMMARY

The study was conducted at Lesetlhana clinic, in the South East District of Botswana. The number of participants who gave their written consent and met the inclusion criteria was 304. The study design was quantitative, descriptive and cross-sectional survey. Data were collected over a period of four months, from July, 2015 to October, 2015. Adherence data were collected based on pill counts for the three months prior to study enrolment and using two self-report adherence measures with a questionnaire administered in ARV interview. Factors which possibly cause non-adherence to ART were also determined with the interview. Ethical clearance to conduct the study was granted by the Sefako Makgatho University Research Ethics Committee.

The results of the data collected over the four month study period, will be presented and discussed as a manuscript for publication in Chapter 4.
CHAPTER 4

RESULTS AND DISCUSSION

4.1 INTRODUCTION

The results and discussion of this study are presented in the format of a manuscript, which will be submitted for publication to African Journal of AIDS Research (AJAR), a peer reviewed and accredited journal. The reference list of the manuscript contains all the references used in the manuscript, formatted according to the journal guidelines. These references are also included in the reference list of the dissertation, formatted according to the Harvard citation style, as required by the university.

The journal's guidelines for authors are included as Appendix 8 to the dissertation. For the purpose of the dissertation, tables appear in the text, and not as a separate file, as specified by the journal.

The results of the study were already presented as a poster at the 2nd MURIA Group Symposium, University of Botswana, Gaborone, July 25-27, 2016. A copy of the poster appears in the last section of this chapter.

4.2 MANUSCRIPT FOR PUBLICATION

4.2.1 Manuscript

The manuscript which will be submitted to the African Journal of AIDS Research (AJAR) appears in this section.
Adherence to antiretroviral treatment amongst patients at a clinic in South East District, Botswana: A multi-measure approach to guide future practice

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Chapter 4: Results and Discussion

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Number of figures: 1
Abstract

Adherence to antiretroviral treatment amongst patients at a clinic in South East District, Botswana: A multi-measure approach to guide future practice

Strict adherence to antiretroviral therapy (ART) is important for sustained HIV suppression, reduced risk of drug resistance, and improved quality of life. Currently there is no "gold standard" or consensus for measuring ART adherence. This study investigated adherence rates and factors affecting non-adherence amongst 304 adult patients on ART at Lesetlhana Clinic, Botswana, using a multi-measure approach. One objective and two subjective adherence measures were used in a quantitative descriptive study design. Three months' retrospective pill count data (objective) were collected from electronic pharmacy dispensing records and mean adherence percentage calculated. Self-reported adherence using two subjective measures (set of four questions; rating scale) and factors contributing to non-adherence were collected in an interview with a structured questionnaire. Proportions of adherent (≥95%) patients were calculated according to each measure, and for a composite score based on all three measures. Ethical clearance and written informed consent were obtained. Although mean pill count adherence (3 months) was 98.0% (SD:2.2), 88.2% of patients were categorised as ≥95% adherent with the pill count method, 80.6% with the self-report questions and 78.9% with the self-report rating scale. Adherence with the composite measure was significantly lower (60.9%; p<0.001). Challenges with adherence as reported by 87 patients, included arriving home late (33.3%), forgetfulness (23.0%), visiting or attending functions (19.5 %), alcohol (18.4%) and medication side-effects (16.1%). Results illustrated the importance of adherence monitoring, using a multi-method adherence measurement approach, which would allow the strengths of one method to compensate for the weaknesses of another method.

Key words: Adherence; Botswana; challenges; composite measures; HIV/AIDS; pill count; rating-scale; self-reporting
Introduction

The introduction of antiretroviral therapy (ART) and multidrug regimens, or highly active antiretroviral therapy (HAART) has substantially improved the survival of persons infected with HIV (Hansana et al., 2013). Factors such as side effects of antiretroviral (ARV) medicines, disruptions to the patient’s daily life and difficulties in returning for scheduled follow-up consultations, often make maintaining adherence over the long term challenging. Yet the individual and public health benefits of antiretroviral treatment (ART) are adherence dependent (Adefolalu and Nkosi, 2013; Hansana et al., 2013).

Although the minimum adherence threshold for clinical effectiveness of ART remains unclear, existing data suggest that it is necessary to take a high proportion (≥95%) of ARV doses to maintain suppression of viral replication (Paterson, 2000; Chesney, 2006; Baptiste, 2008). Sub-optimal adherence has been associated with rapid disease progression, poor immunologic response, and increased risk of mortality, complicating further treatment and increasing the risk of transmission of resistant virus (WHO, 2006; Chaiyachati et al., 2011; Elul and Asiimwe, 2011).

The factors affecting adherence to ART are normally classified according to five dimensions namely, health system/health care team, social/economic factors, therapy-related factors, patient-related factors and condition related factors (WHO 2003). Non-adherence is also linked to patients’ forgetfulness. Due to absence of reminders, patients report with no cogent reason that they forget to take their medicines on one or more occasion (Okafor and Ekwunife, 2013).

Currently there is no "gold standard" or consensus for measuring ART adherence (Berg and Arnsten, 2006; Chesney 2006; Elul and Asiimwe, 2011; Bezabhe et al., 2013; Lam and Fresco, 2015). Methods to measure adherence include patient self-report, pharmacy refill records, pharmacy insurance claims, pill counts, medication electronic monitoring systems (MEMS), measurement of drug plasma levels, therapeutic drug monitoring (TDM), changes in CD4 count and changes in viral load (Muyingo et al., 2008; Uzochukwu et al., 2009; Elul and Asiimwe 2011; Bezabhe et al., 2013).
Due to their relative low-cost and simplicity, the most commonly used measures of ART adherence are pill counts (Muyingo et al., 2008; Elul and Asiimwe, 2011). Pill counts are done during patients’ visits to health facilities when they come for a follow-up appointment and/or refill of the medication. Pill count adherence is usually calculated by dividing the difference between the number of pills taken home and the current pill count, by the number of pills that should have been taken during the period since the last clinic visit, multiplied by hundred (Bezabhe et al., 2013). The sensitivity of pill counts for detecting non-adherence is compromised when patients remove pills from their containers without taking them, referred to as “pill dumping” or “decanting”. This practice leads to an overestimation of adherence (Adefolalu et al., 2013; Awolola et al., 2014), especially if patients fear a bad response from health workers during dispensing if they have not achieved optimal adherence (Katlwane et al., 2005).

Patient self-reporting is the longest standing and most widely used method to assess medication adherence in both the research and practice setting because of its low cost and simplicity (Williams et al., 2013).

The majority of the adherence measurement tools currently used cannot meet all the features of an ideal tool, which also explains why there is no gold standard in the measurement of adherence (Steel et al., 2007; Lam and Fresco, 2015). This study aimed to determine the level of adherence to ART amongst adult patients at Lesetlhana Clinic, using three different adherence measures, and to identify factors which contribute to non-adherence. We attempted to overcome the weaknesses of different measures of adherence by combining adherence scores from the different measures into a composite adherence score.

**Methods**

**Study setting**

The study was undertaken at Lesetlhana Clinic, in South East District, Botswana. The clinic is approximately 35 kilometres from Gaborone, the capital city. Enrolment on ART at the clinic started in June 2009, with a total of 556 patients on ART at the time
of the study. Patient reviews and dispensing of ARVs at the clinic are undertaken three times per week, on Tuesdays, Wednesdays and Thursdays.

**Study design**
The design of the study was quantitative and descriptive. Three different measures, two subjective and one objective, were used to measure adherence to ART. A structured questionnaire, administered in an interview, included two patient self-report measures (subjective) and questions on factors which contribute to non-adherence. Data on pill count adherence (objective) were collected retrospectively from patients’ computerised pharmacy dispensing records.

**Study population, sample and enrolment**
The target population for this study included all adult patients enrolled on ART at Lesetlhana Clinic at the time of the study. Inclusion criteria were patients on ART ≥18 years, patients who have been on ART for ≥3 months, and patients with adherence charts available in their records for the three months prior to the study. Exclusion criteria were patients who have been transferred to the study site within the three months prior to the study and patients who were too ill to participate in an interview and those who did not give informed consent.

Considering a two-sided 95% confidence level and 5% margin of error, with a total population of 556 patients active on ART, a sample size of 228 patients was calculated. For a lower margin of error (3.84%) a larger sample of 300 patients was required (Raosoft® Sample size calculator). To achieve the required sample size, all the patients attending the clinic and who met the inclusion criteria were invited to participate in the study. Patients who agreed to participate and subsequently provided written consent were enrolled in the study, which resulted in a final sample of 304 patients.

**Data collection process and instrument**
Data were collected on clinic days (3 days/week) over a period of four months (July to October 2015) by four trained data collectors. Enrolled patients were interviewed using a structured questionnaire. Data collectors were fluent in English and Setswana.
(most common language spoken in the area), which allowed participants the option to respond in their language of preference. Interviews took place while patients were waiting for their consultation with the medical practitioner, or to have their prescription refilled at the pharmacy, or on exit from the clinic. Participants were informed that the adherence assessment was not punitive but rather aimed at determining what challenges they were facing to achieve optimal adherence. There was no financial reward for taking part in the interviews.

Demographic data, self-report adherence data and information about factors contributing to non-adherence were obtained during the patient interview, while patients’ pill count adherence data were obtained retrospectively from the computer database. With the first adherence self-report measure, data collectors guided participants through four questions to which they responded “yes” or “no” (see Table 1). An adherent patient would respond “no” to all questions. The non-adherent patient would respond “yes” to one or more questions. This type of question helps to validate responses, since many patients tend to respond “yes” to any questions posed to them by a health care professional, in order to please the health worker (Steel et al., 2007). The questions examined whether the patient forgot to take his/her medication, whether the patient stopped taking his/her medicine when they felt better, whether the patient missed their medication in the past four days, and whether the patient stopped taking medication when they feel worse. With the second self-report adherence measure, patients were asked to rate their adherence to ARVs in the last 30 days, by selecting one of six response options (see Table 1).

After the patient interview was concluded, adherence information from pill counts was obtained retrospectively from patient records for the three months prior to enrolment in the study. The ART dispensing software referred to as ‘PIMS II Data Base Version 2.6’ was used for this purpose. As part of standard clinic practice, adherence is calculated by the computer, based on a pill count done during each visit to the clinic.  

**Data analysis**
Data were entered into Microsoft Excel™ spread sheets. Statistical analysis was performed on Statistical Analysis Software (SAS institute Inc., Carey, NC, USA), Release 9.3, in consultation with a statistician. Demographic data and factors affecting adherence were summarised and expressed as frequency percentages.

Mean adherence was calculated for the three months’ retrospective pill count adherence data. Responses to the rating scale were expressed as frequency percentages and also converted to numeric values to express self-reported adherence as a percentage for each patient. A composite (overall) adherence score based on all three measures was calculated for each patient, using the criteria as shown in Table 1.

Table 1: Outcome criteria for ≥95% composite (overall) adherence

<table>
<thead>
<tr>
<th>Adherence measure</th>
<th>Outcome criteria for ≥95% adherence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pill count</td>
<td>Average adherence for 3 months ≥95%</td>
</tr>
<tr>
<td>Monthly pill count of all antiretrovirals and % adherence calculated for regimen</td>
<td></td>
</tr>
<tr>
<td>Adherence questions</td>
<td>Answered ‘NO’ to all questions</td>
</tr>
<tr>
<td>Do you find it difficult to remember to take your medication?</td>
<td></td>
</tr>
<tr>
<td>Do you stop taking medication when you feel better?</td>
<td></td>
</tr>
<tr>
<td>Do you stop taking medication when you feel worse?</td>
<td></td>
</tr>
<tr>
<td>Have you missed &gt; 3 doses in the last 30 days?</td>
<td></td>
</tr>
<tr>
<td>Self-report rating scale</td>
<td>Adherence rated as ‘Excellent’</td>
</tr>
<tr>
<td>Options for rating scale</td>
<td></td>
</tr>
<tr>
<td>Excellent</td>
<td></td>
</tr>
<tr>
<td>Very good</td>
<td></td>
</tr>
<tr>
<td>Good</td>
<td></td>
</tr>
<tr>
<td>Fair</td>
<td></td>
</tr>
<tr>
<td>Poor</td>
<td></td>
</tr>
<tr>
<td>Very poor</td>
<td></td>
</tr>
</tbody>
</table>

Patients were categorised into two categories for each measure of adherence, namely ≥95% adherent or <95% adherent. The proportion of adherent (≥95%) patients were
calculated for each individual measure and for the composite score, and compared pairwise with the Fischer Exact test (p<0.05 statistically significant).

**Ethical considerations**
Ethical clearance for the study was obtained from the Sefako Makgatho University Research Ethics Committee (SMUREC/H/19/2015: PG), prior to the commencement of data collection. Permission to carry out the study at the site was obtained from both the Ministry of Health in Botswana and the Coordinator of South East District Health Management Team in Botswana. Written informed consent was obtained from participants after they were given information about the study and prior to participation in the study. Participants were assured of confidentiality of their responses and informed of their right to withdraw from the study at any time if they so wished. Each participant was assigned a unique study number and no personal information was recorded.

**Results**
**Socio-demographic characteristics**
A total number of 304 patients participated in the study, of whom females predominated (66.1%). The socio-demographic characteristics of participants are summarised in Table 2.
Table 2: Socio-demographic characteristics of participants (n=304)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>n</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>103</td>
<td>33.9</td>
</tr>
<tr>
<td>Female</td>
<td>201</td>
<td>66.1</td>
</tr>
<tr>
<td>Age (years)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>18 to &lt;30</td>
<td>42</td>
<td>14.0</td>
</tr>
<tr>
<td>30 to &lt;45</td>
<td>168</td>
<td>55.0</td>
</tr>
<tr>
<td>45 to &lt;60</td>
<td>86</td>
<td>28.0</td>
</tr>
<tr>
<td>60 and above</td>
<td>8</td>
<td>3.0</td>
</tr>
<tr>
<td>Marital status</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Single</td>
<td>208</td>
<td>68.4</td>
</tr>
<tr>
<td>Married</td>
<td>79</td>
<td>26.0</td>
</tr>
<tr>
<td>Divorced</td>
<td>5</td>
<td>1.6</td>
</tr>
<tr>
<td>Separated</td>
<td>3</td>
<td>1.0</td>
</tr>
<tr>
<td>Widowed</td>
<td>9</td>
<td>3.0</td>
</tr>
<tr>
<td>Highest level of qualification</td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>13</td>
<td>4.3</td>
</tr>
<tr>
<td>Primary completed</td>
<td>49</td>
<td>16.1</td>
</tr>
<tr>
<td>Secondary incomplete</td>
<td>95</td>
<td>31.3</td>
</tr>
<tr>
<td>Secondary completed</td>
<td>86</td>
<td>28.3</td>
</tr>
<tr>
<td>Tertiary completed</td>
<td>61</td>
<td>20.1</td>
</tr>
<tr>
<td>Employment</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Employed</td>
<td>142</td>
<td>47.7</td>
</tr>
<tr>
<td>Self-employed</td>
<td>50</td>
<td>16.4</td>
</tr>
<tr>
<td>Unemployed</td>
<td>112</td>
<td>38.8</td>
</tr>
<tr>
<td>Social assistance</td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>297</td>
<td>97.7</td>
</tr>
<tr>
<td>Pension</td>
<td>7</td>
<td>2.3</td>
</tr>
<tr>
<td>Distance to clinic</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Less than 5 km or walking distance</td>
<td>222</td>
<td>73.0</td>
</tr>
<tr>
<td>5-12 km</td>
<td>44</td>
<td>14.5</td>
</tr>
<tr>
<td>More than 12 km</td>
<td>38</td>
<td>12.5</td>
</tr>
</tbody>
</table>

**Antiretroviral treatment**

Table 3 shows the ART regimens and the duration that patients have been on treatment. Nearly two thirds (60.8%) of the patients were on a fixed-dose combination containing tenofovir, emtricitabine and efavirenz (Atripla®) and the majority (76.0%) were on ART for more than two years.
Chapter 4: Results and Discussion

Table 3: Antiretroviral treatment and duration on treatment (n=304)

<table>
<thead>
<tr>
<th>Antiretroviral treatment regimen</th>
<th>n</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tenofovir + Emtricitabine + Efavirenz (fixed-dose combination)</td>
<td>185</td>
<td>60.8</td>
</tr>
<tr>
<td>Tenofovir + Emtricitabine + Nevirapine</td>
<td>28</td>
<td>9.2</td>
</tr>
<tr>
<td>Tenofovir + Emtricitabine + Lopinavir/Ritonavir</td>
<td>5</td>
<td>1.6</td>
</tr>
<tr>
<td>Zidovudine + Lamivudine + Efavirenz</td>
<td>21</td>
<td>6.9</td>
</tr>
<tr>
<td>Zidovudine + Lamivudine + Nevirapine</td>
<td>53</td>
<td>17.4</td>
</tr>
<tr>
<td>Zidovudine + Lamivudine + Lopinavir/Ritonavir</td>
<td>12</td>
<td>3.9</td>
</tr>
</tbody>
</table>

Duration on antiretroviral treatment (months)

<p>| | | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>3 to &lt;12</td>
<td>18</td>
<td>6.0</td>
</tr>
<tr>
<td>12 to &lt;24</td>
<td>50</td>
<td>16.0</td>
</tr>
<tr>
<td>24 and above</td>
<td>236</td>
<td>76.0</td>
</tr>
</tbody>
</table>

**Antiretroviral treatment adherence levels**

Results of the pill counts for three months are presented in Table 4. The average adherence in month 1 for all the 304 patients was 98.1% and the average adherence in the second month was 98.0%. The average adherence in the third month was 98.0% for all the 304 patients.

Table 4: Mean and median adherence (%) for 3-month retrospective pill counts (n=304)

<table>
<thead>
<tr>
<th></th>
<th>Mean (SD)</th>
<th>Median (IQR)</th>
<th>Minimum</th>
<th>Maximum</th>
</tr>
</thead>
<tbody>
<tr>
<td>Month 1</td>
<td>98.1 (3.0)</td>
<td>100.0 (97.5; 100)</td>
<td>82.0</td>
<td>100</td>
</tr>
<tr>
<td>Month 2</td>
<td>98.0 (3.0)</td>
<td>99.0 (97.5; 100)</td>
<td>80.0</td>
<td>100</td>
</tr>
<tr>
<td>Month 3</td>
<td>98.0 (3.4)</td>
<td>100.0 (97.0; 100)</td>
<td>73.0</td>
<td>100</td>
</tr>
<tr>
<td>Average</td>
<td>98.0 (2.2)</td>
<td>98.7 (97.7; 99.3)</td>
<td>87.0</td>
<td>100</td>
</tr>
</tbody>
</table>

A composite (overall) adherence score based on all three measures for each patient was calculated according to the criteria as shown in Table 1. Figure 1 shows the proportions of patients ≥95% adherent for each individual measure as well as for the composite measure. Although the mean pill count adherence (3 months) was 98.0%,
88.2% of patients were categorised as ≥95% adherent with the pill count, 80.6% with the self-report questions and 78.9% with the rating scale. Adherence with the composite measure was significantly lower (60.9%; p<0.001) compared to all other measures.

![Bar chart showing adherence rates](image)

**Figure 1:** Percentage of patients categorised as ≥95% adherent according to the different measures (n=304)

**Factors contributing to non-adherence**

Table 5 shows a summary of the factors contributing to non-adherence. Among the factors which contribute to non-adherence to ART, arriving home late (9.5%) ranked the highest, followed by forgetfulness (6.6%), visiting or attending a function (5.6%), the use of alcohol (5.2%) and side effects of ARV medicines (4.6%).
Table 5: Adherence challenges experienced (n=87)

<table>
<thead>
<tr>
<th>Adherence challenge</th>
<th>n</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arriving home late</td>
<td>29</td>
<td>33.3</td>
</tr>
<tr>
<td>Forgetfulness</td>
<td>20</td>
<td>23.0</td>
</tr>
<tr>
<td>Visiting or attending a function</td>
<td>17</td>
<td>19.5</td>
</tr>
<tr>
<td>Alcohol</td>
<td>16</td>
<td>18.4</td>
</tr>
<tr>
<td>Side effects</td>
<td>14</td>
<td>16.1</td>
</tr>
<tr>
<td>Depressed</td>
<td>10</td>
<td>11.5</td>
</tr>
<tr>
<td>Lack of family/friend support</td>
<td>10</td>
<td>11.5</td>
</tr>
<tr>
<td>Lack of food</td>
<td>9</td>
<td>10.3</td>
</tr>
<tr>
<td>Lack of money</td>
<td>6</td>
<td>6.9</td>
</tr>
<tr>
<td>Stigma</td>
<td>5</td>
<td>5.7</td>
</tr>
<tr>
<td>Misunderstood instructions</td>
<td>3</td>
<td>3.4</td>
</tr>
<tr>
<td>Too many pills</td>
<td>2</td>
<td>2.3</td>
</tr>
<tr>
<td>Other</td>
<td>13</td>
<td>14.9</td>
</tr>
</tbody>
</table>

Note: Some patients provided more than one answer

Discussion

Three methods of measuring adherence were used, that is the pill count, the self-report with four questions, and the self-rating scale. In the pill count assessment, the overall adherence for all the three months was 98.0%. This result is similar to the adherence level finding of Ndubuka and Ehlers, 2011 in Botswana of 96.2%. The minimum adherence in the study was 73.0% and the maximum adherence was 100%. Finally, 269 (88.5%) of the patients had high adherence (≥95%), while 35 (11.5 %) of the patients had low adherence (>90% but<95%).

The adherence levels for each method were very high in comparison to the composite adherence. In the pill count method, the average adherence for the participants was 98.0 %. This is comparable to the findings of Ehlers and Tshisuyi, 2015, who found an adherence level of 97.6 %, using the pill count method and 96.2% (Ndubuka and Ehlers, 2011). The adherence level from the self-report, using four questions was 80.6%. This is less than what was found by Bangsberg et al. (2000) of 89 %. However,
the adherence in this study is higher than the 78% adherence reported by Arsten and colleagues (2001).

With the self-rating scale, the adherence level for the study participants was 78.9%. This is lower than Hong et al., 2012 finding of 84.7%, using the same rating scale. All the three measures have both strengths and weaknesses. Recognition of the limitations of each method resulted in the determination of the composite adherence rate with the belief that this would allow the strengths of one method to compensate for the weaknesses of the other methods.

This result is similar to that found in a study in Zambia (Birbeck et al., 2009). However, the composite adherence for the three assessment methods is 60.9%. This means 185 (60.9%) of the patients had adherence rate ≥95 % (high). The composite adherence rate was lower than the adherence rates of the individual adherence instruments. The main reason is that, in the composite adherence assessment, when the results are spread over three columns, the scores in the right column are favoured. In the classification of the composite adherence, when a patient’s adherences is high from two methods in the left column and lower from one method in the right column of adherence assessment, the lower adherence in the right column is considered to be the true adherence of the patient (Steel et al., 2007). This method lowered the Composite adherence. However, this classification of the composite adherence is different from that by Katlwane, et al., 2005 and Ndubuka and Ehlers, 2010, who added the adherence from the different adherence instruments and divided by the number of adherence methods in order to get the composite adherence.

In this study, factors found to contribute to non-adherence (Table 5) are arriving home late, forgetfulness, visiting or going for a function, alcohol, side effects and stigma. Other factors were depression, lack of food, lack of money, lack of family support and misunderstanding instructions. In a recent study (Heestermans et al., 2016), it was found that the factors contributing to non-adherence were the use of alcohol, male gender, depression, discrimination and stigmatisation, and poor social support. This is similar to other studies (Baptiste, 2008; Hansana et al., 2013).
We are aware that we only conducted this study within one clinic in Botswana. However in view of the nature of the clinic, i.e. not in rural Botswana, and the number of patients involved, we believe the findings are robust and give guidance to the authorities in Botswana of measures to further enhance adherence rates given the continued high prevalence of HIV in Botswana.

**Conclusion**

In this study, pill count adherence rates were high, which is encouraging. However, adherence rates were lower when using the agreed measure of ≥95% adherence. Three individual adherence measures yielded different results when using the agreed cut-off level and all significantly higher than a composite (overall) measure. The findings illustrated the importance of adherence monitoring, using a combination of adherence measures, which would allow the strength of one method to compensate for weaknesses of another method. We suggest this becomes normal practice in the future in order to enhance overall adherence rates.

**References**


Chapter 4: Results and Discussion


4.2.2 Letter to the editor

A cover letter to the editor of the African Journal of AIDS Research (AJAR), which will accompany the manuscript, is included in this section.
Editor in Chief  
Expert Review of AIDS Research in Africa

Dear Sir

RE: SUBMISSION OF A MANUSCRIPT FOR PUBLICATION

I am pleased to submit an original research article entitled “Adherence to antiretroviral treatment amongst patients at a clinic in South East District, Botswana: A multi-measure approach to guide future practice” for consideration of publication in Expert Review of AIDS Research in Africa.

With the submission of this manuscript I would like to declare that the above-mentioned manuscript has not been published elsewhere, accepted for publication elsewhere or under editorial review for publication elsewhere, and that my Institution (Lesetlhana Clinic) has granted permission for publication of this article.

I further declare that all the authors have critiqued and approved the content of the manuscript and have contributed significantly to the work. The authors have no conflict of interest to disclose and no sponsorship was received for the study.

Thank you for your consideration of our manuscript.

____________________________________
Angel Lubasi (first author)
Date: 11/01/2017
Tel: +267 5390297; Cell: +267 72877316
4.3 POSTER PRESENTATION

The results of the study were presented as a poster, at the 2nd MURIA Group Symposium, University of Botswana, Gaborone, July 25-27, 2016. The details of the poster presentation were as follows:

“Adherence to antiretroviral treatment amongst patients at a clinic in South East District, Botswana.”

Lubasi A, Meyer JC.

A copy of the poster is included on the next page.
Chapter 4: Results and Discussion

Adherence to antiretroviral treatment amongst patients at a clinic in South East District, Botswana

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2Lesotho Clinic, South East District, Botswana
Email: ajlsbasi21@yahoo.com

Introduction

The introduction of antiretroviral therapy (ART) substantially improved the survival of people infected with HIV. Factors such as side effects, disruptions to the patient’s daily life and difficulty in returning for scheduled follow-up consultations, are known challenges to maintaining long-term adherence. Yet the individual and public health benefits of ART are contingent on strict adherence (90%) to ART.

Self-optimal adherence can easily lead to drug resistance, may cause treatment failure and has serious public health consequences, necessitating continuous monitoring. Limited studies have been published concerning rates of adherence to ART in Botswana and currently there is no “gold standard” or consensus for measuring ART adherence.

Objectives

- To determine adherence to ART amongst patients at Lesotho Clinic, Botswana
- Using pill counts, two self-report measures and a composite measure
- To identify possible factors contributing to non-adherence

Results

Table 1: Socio-demographic characteristics of patients (n=504).

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Male (%)</th>
<th>Female (%)</th>
<th>Total (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>18-30</td>
<td>31-60</td>
<td>61-80</td>
</tr>
<tr>
<td>Education</td>
<td>No education</td>
<td>14.7%</td>
<td>13.4%</td>
</tr>
<tr>
<td>12th &amp; Above</td>
<td>86.3%</td>
<td>86.2%</td>
<td>86.3%</td>
</tr>
<tr>
<td>Marital status</td>
<td>Single</td>
<td>31.7%</td>
<td>30.8%</td>
</tr>
<tr>
<td>Employed</td>
<td>142 (77)</td>
<td>256 (66)</td>
<td>398 (79)</td>
</tr>
<tr>
<td>Self-reported employed</td>
<td>90 (66%)</td>
<td>147 (65)</td>
<td>237 (56)</td>
</tr>
<tr>
<td>Unemployed</td>
<td>112 (35%)</td>
<td>109 (34)</td>
<td>221 (44)</td>
</tr>
<tr>
<td>Female preponderance</td>
<td>96.4%</td>
<td>96.5%</td>
<td>96.4%</td>
</tr>
<tr>
<td>Mean age (years)</td>
<td>49.4 (n=37)</td>
<td>35.3 (n=13)</td>
<td>42.8 (n=50)</td>
</tr>
</tbody>
</table>

Table 2: Art adherence and regimen (n=330).

<table>
<thead>
<tr>
<th>Adherence treatment</th>
<th>No (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Average pill adherence (months)</td>
<td>1 (n=1)</td>
</tr>
<tr>
<td>12th &amp; Above</td>
<td>31 (10)</td>
</tr>
<tr>
<td>24th &amp; Above</td>
<td>228 (73)</td>
</tr>
<tr>
<td>Age (years)</td>
<td>31-60</td>
</tr>
<tr>
<td>61-80</td>
<td>106 (34)</td>
</tr>
<tr>
<td>Education</td>
<td>No education</td>
</tr>
<tr>
<td>12th &amp; Above</td>
<td>108 (34)</td>
</tr>
<tr>
<td>Marital status</td>
<td>Single</td>
</tr>
<tr>
<td>Employed</td>
<td>146 (45)</td>
</tr>
<tr>
<td>Self-reported employed</td>
<td>90 (66)</td>
</tr>
<tr>
<td>Unemployed</td>
<td>110 (35)</td>
</tr>
<tr>
<td>Female preponderance</td>
<td>96.4%</td>
</tr>
<tr>
<td>Mean age (years)</td>
<td>49.4 (n=37)</td>
</tr>
</tbody>
</table>

Composite (overall) adherence

Although mean pill count adherence (3 months) was 98.0% (SD:2.2), a total of 46.8% of patients were classified as 25% adhérent with the pill count adherence questions and 78.0% with the rating scale. Adherence with the composite measure was significantly higher (89.9%, p<0.01); Fischer’s Exact compared to all other measures.

Table 3. Outcome criteria for 25% and composite (overall) adherence

<table>
<thead>
<tr>
<th>Pill count</th>
<th>Composite (overall) adherence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Average</td>
<td>Average</td>
</tr>
<tr>
<td>88.2%</td>
<td>88.2%</td>
</tr>
<tr>
<td>88.2%</td>
<td>88.2%</td>
</tr>
<tr>
<td>73.9%</td>
<td>73.9%</td>
</tr>
<tr>
<td>69.4%</td>
<td>69.4%</td>
</tr>
</tbody>
</table>

Adherence challenges

Table 4. Types of adherence challenges experienced (%)

<table>
<thead>
<tr>
<th>Adherence challenges</th>
<th>% of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Average pill adherence (months)</td>
<td>1 (n=1)</td>
</tr>
<tr>
<td>12th &amp; Above</td>
<td>31 (10)</td>
</tr>
<tr>
<td>24th &amp; Above</td>
<td>228 (73)</td>
</tr>
<tr>
<td>Age (years)</td>
<td>31-60</td>
</tr>
<tr>
<td>61-80</td>
<td>106 (34)</td>
</tr>
<tr>
<td>Education</td>
<td>No education</td>
</tr>
<tr>
<td>12th &amp; Above</td>
<td>108 (34)</td>
</tr>
<tr>
<td>Marital status</td>
<td>Single</td>
</tr>
<tr>
<td>Employed</td>
<td>146 (45)</td>
</tr>
<tr>
<td>Self-reported employed</td>
<td>90 (66)</td>
</tr>
<tr>
<td>Unemployed</td>
<td>110 (35)</td>
</tr>
<tr>
<td>Female preponderance</td>
<td>96.4%</td>
</tr>
<tr>
<td>Mean age (years)</td>
<td>49.4 (n=37)</td>
</tr>
</tbody>
</table>

Table 5. Types of adherence challenges experienced (%)

<table>
<thead>
<tr>
<th>Adherence challenges</th>
<th>% of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Average pill adherence (months)</td>
<td>1 (n=1)</td>
</tr>
<tr>
<td>12th &amp; Above</td>
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</tr>
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</tr>
<tr>
<td>Education</td>
<td>No education</td>
</tr>
<tr>
<td>12th &amp; Above</td>
<td>108 (34)</td>
</tr>
<tr>
<td>Marital status</td>
<td>Single</td>
</tr>
<tr>
<td>Employed</td>
<td>146 (45)</td>
</tr>
<tr>
<td>Self-reported employed</td>
<td>90 (66)</td>
</tr>
<tr>
<td>Unemployed</td>
<td>110 (35)</td>
</tr>
<tr>
<td>Female preponderance</td>
<td>96.4%</td>
</tr>
<tr>
<td>Mean age (years)</td>
<td>49.4 (n=37)</td>
</tr>
</tbody>
</table>

Table 6. Types of adherence challenges experienced (%)

<table>
<thead>
<tr>
<th>Adherence challenges</th>
<th>% of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Average pill adherence (months)</td>
<td>1 (n=1)</td>
</tr>
<tr>
<td>12th &amp; Above</td>
<td>31 (10)</td>
</tr>
<tr>
<td>24th &amp; Above</td>
<td>228 (73)</td>
</tr>
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<td>Age (years)</td>
<td>31-60</td>
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</tr>
<tr>
<td>Education</td>
<td>No education</td>
</tr>
<tr>
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</tr>
<tr>
<td>Marital status</td>
<td>Single</td>
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<td>146 (45)</td>
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</tr>
<tr>
<td>Unemployed</td>
<td>110 (35)</td>
</tr>
<tr>
<td>Female preponderance</td>
<td>96.4%</td>
</tr>
<tr>
<td>Mean age (years)</td>
<td>49.4 (n=37)</td>
</tr>
</tbody>
</table>

Discussion and conclusion

In this study, pill count adherence was high and similar to the results of two other pill count studies previously conducted in Botswana. Mean pill count adherence was high compared to the percentage of patients categorised as 25% adherent. Three individual adherence measures yielded different results and at significantly higher than a composite (overall) measure. Adherence challenges were identified despite high mean pill count adherence. Results illustrated the importance of adherence monitoring, using a combination of adherence measures, which would allow the strengths of one method to compensate for the weaknesses of another method.

Recommendations

Due to single adherence measures being prone to weaknesses, adherents should be monitored on a monthly basis with more than one method, to identify patients who are sub-optimally adherent. Individual adherence counseling should be part of routine practice, to identify patients with adherence challenges. Patients would benefit from regular group discussions on adherence at the clinic, which will allow active participation of patients in such discussions. Factors which contribute to non-adherence to ART identified in this study, should be used as a guideline for group adherence discussions at the clinic.
CHAPTER 5
SUMMARY OF RESULTS, LIMITATIONS, RECOMMENDATIONS
AND CONCLUSIONS

5.1 INTRODUCTION

This chapter presents a summary of the results, followed by the limitations of the study. This is followed by the recommendations based on the study. In the last section of the chapter the final conclusion for the study is presented.

5.2 SUMMARY OF THE RESULTS

A total number of 304 patients who met the inclusion criteria participated in the study. Females (66.1%) in this study predominated over males (33.9%), which is similar to the patient distribution reported by previous Botswana studies (Kgatlwane et al., 2005; Ndubuka & Ehlers, 2011). The mean and median age of the participants in this study was 40 years and 39 years (SD: 9.2) years and 39 (IQR: 33-46) years respectively, ranging from 21 years to 70 years. Just more than half (55.0%) of the participants were between the ages of 30 and 45 years.

Two thirds (68.4%) of participants were single and the vast majority (95.7%) had some form of education, with 48.4% having completed secondary education or holding a tertiary qualification. Nearly two thirds of the participants were either employed (46.7%) or self-employed (16.5%). Only a third (36.8%) of the participants were unemployed. Two hundred and ninety seven (97.7%) patients received no social assistance while seven (2.3%) were on pension assistance.

The number of patients who travelled less than 5 kilometres was 222 (73.0%) and the patients who travelled more than 12 kilometres was 38 (12.5%). The farthest distance travelled to the clinic was 80 kilometres and the shortest distance to the clinic was 0.5 kilometre.

Only 18 (6.0%) participants were on treatment for less than 12 months, whereas the majority (76.0%) have been on treatment for more than 24 months at the time of the study.

Levels of adherence to ART were determined with the use of three methods, namely pill counts, self-report assessment and use of the rating scale.

Results of the pill counts for three months are presented as follows: The average adherence in month 1 for all the 304 patients was 98.1% and the average adherence in the second month
was 98.0%. The mean value for month 2 does not differ significantly from the mean value at Month 1 (paired t test, p=0.765). The average adherence in the third month was 98.0% for all the 304 patients. Again, the mean value for month 3 does not differ significantly from the mean value at month 1 (paired t test, p=0.667). The Overall average adherence for all the three months was 98.0%.

In the second adherence assessment with four questions, 245 (80.6%) of the patients had High adherence (≥95%) while 59 (19.4%) had Low adherence (≥90%< 95%).

In the third adherence assessment with the self-rating scale, 240 (78.9%) of the patients had High adherence (≥95%) while 64 (21.1%) of the patients had Low adherence (≥90%< 95%). The median adherence was 95%, the minimum adherence rate was 80% and the maximum adherence in the rating scale was 95%.

The adherence assessments from the three adherence methods were combined to make a composite adherence. The composite adherence for the study population was 60.9%. Adherence with the composite measure was significantly lower (60.9%; p<0.001; Fischer’s Exact) compared to all other measures. This means 185 (60.9%) of the participants had adherence greater than 95% (High adherence). The number of patients with moderate adherence was 118 (38.8%). Only one (0.3%) patient had low adherence rate, that is below 90%.

The four adherence rate assessments were considered independent and they were compared pairwise by the Fisher Exact test, with the following results: the adherence rate for the pill count differed significantly from the Self-report (p=0.014; Fisher Exact test). The adherence rate of the pill count differed from the Rating scale (p=0.003 Fisher Exact test). Also, the Composite adherence rate differed significantly with the Rating scale (p<0.001 Fisher Exact test). Therefore, the Self-report and the Rating scale were similar in the results they produced (p=0.687, Fisher Exact test).

A total of 87 participants mentioned that they had adherence challenges. The challenges experienced were: arriving home late as the highest, 29 (33.3%), followed by forgetfulness (23.0%), visiting or attending functions (19.5%). Other challenges were: use of alcohol, side effects, depression, lack of family support, lack of food, lack of money, stigma and misunderstanding instructions.
5.3 LIMITATIONS OF THE STUDY

- A limitation of the study is that it was conducted at only one clinic offering ART, in Botswana, hence the results cannot be generalised to other health facilities.
- Another limitation of the study is that viral load test results were not available. Adherence data could therefore not be correlated with viral load outcomes.

5.4 RECOMMENDATIONS

The following recommendations are made based on the results of the study:

- Due to single adherence measures being prone to weaknesses, adherence should be measured on a monthly basis with more than one method to identify patients who are sub-optimally adherent.
- Health talks should be introduced at least once a week to discuss the importance of adherence with patients.
- Health talks concerning factors which contribute to non-adherence to ART which have been identified in the study should be discussed with patients.
- There is need to conduct similar studies in other facilities to allow for the comparison of findings across facilities.

5.5 CONCLUSIONS

In this study, pill count adherence was high and similar to the results of two other pill count studies previously conducted in Botswana. Although the single adherence methods yielded high results, single methods are prone to weaknesses. Mean pill count adherence was high compared to the percentage of patients categorised as ≥95% adherent. Three individual adherence measures yielded different results and all significantly higher than a composite (overall) measure. This study shows that a single method to measure adherence is not adequate, because it may have weaknesses. A number of factors can affect adherence and can only be identified through a study. In this study the critical barriers to adherence identified were arriving home late, forgetfulness, visiting or going out for a function, use of alcohol, side-effects, lack of food, depression, lack of money, stigma, misunderstanding instructions and lack of family support.
Struggles to determine the level of adherence among patients on ART is complicated by the general practical difficulties of adherence assessment. There is no gold standard for measuring adherence.

More studies of this nature should be conducted so that results can be compared.
REFERENCES


Adeyinka, T.A. 2011. Investigation of the method of “mixed “pill counts as a tool to detect deliberate masking of non-adherence to antiretroviral therapy at Ntschembo Clinic, Mamelodi Hospital. MSc (Med) in Pharmacy Dissertation. Pretoria: Department of Pharmacy, University of Limpopo, Medunsa Campus.


References


UNAIDS – see Joint United Nations Programme on HIV/AIDS.


Appendix 1a: Study information leaflet (English)

My name is Angel Lubasi. I am a student at Sefako Makgatho Health Sciences University in South Africa, pursuing a Master’s degree in Clinical Pharmacy. As part of my study, I am required to conduct a research study. I have chosen to do a study on adherence to antiretroviral treatment (ART) at Lesetlhana clinic. We are inviting all adults who attend Lesetlhana clinic and those who have been on antiretroviral treatment for more than three months; to participate in this study.

I am going to give you information about the study and invite you to be part of this project. In case there is something you do not understand, please feel free to ask me any question you may have.

The aim of this study is to determine patients’ adherence to their ARVs in the past month by using a questionnaire to ask them a few questions in an interview. We will also review patients’ adherence records of the past three months, as recorded in the computer. During the interview we will ask patients about the challenges they experience in taking their ARVs. All answers to the questions during the interview will be written on the questionnaire. The interview will take not more than 10 minutes of your time while you wait for other services.

Your participation in this research is voluntary, and you can withdraw your participation at any time without giving reasons. You are free to ask any questions and all your responses and information will be kept confidential. The information gathered in this research will help us to improve our services and we believe that it will improve your wellbeing.

This study poses no risk to your health and has no financial gain. The results of this study will be shared with you and may be shared with authorities who take care of your health. You are free to ask questions and for any further clarification, you may contact me on phone number at 72877316.

This research protocol has been reviewed and approved by the Sefako Makgatho University Research and Ethics Committee (SMUREC) and the Coordinator of the South East District Health Management Team.

Thank you for your time.
Angel Lubasi

Appendix 1b: Study information leaflet (Setswana)
Leina la me ke Angel Lubasi. Ke moithuti kwa University ya Sefako Makgatho kwa Aforika Borwa. Ke moithuti wa Master’s degree in Clinical Pharmacy. Ke tlamega go dira patlisiso kana tshekatsheko e le nngwe ya karolo ya ithutuntsho ya me. Ke ikgethetse go dira patlisiso ka selekanyo se balwetse ba tsaya diritibatsi ka sone mo kokelong ya Lesetlhana. Re laletsa batsadi botlhle ba ba kopang thuso ya tsa botsogo mo kokelong ya Lesetlhana Clinic le ba ba setseng ban a le kgwedi tse tharo le go feta mo lenaneong la diritibatsi.

Ke tla go tthalosetsa ka patlisiso e, e bile ke go laletsa go tsaya karolo. Fa go na le sengwe se o sa se thaloganyeng gololesega go ka mpotsa potso e o ka tswang o na le yone.

Maikaelelo a patlisiso e ke go sekaseka selekanyo se balwetse ba tsereng diritibatsi ka sone mo kgweding e e fetileng ka go le botsa dipotso. Re tlaa lebelela le ka fa o tsereng diritibatsi ka teng mo kgweding tse tharo tse di fetileng mo dibalamakgolo. Potsolotso e, e tlaa akaretsa dipotso ka dikgweltho tse le kopanang le tsone fa lo tsaya diritibatsi. Dikarabo tsothle di tlaa kwalwa mo pampitshaneng ya potsolotso. Potsolotso e, ga e na go tsaya metsotso e e fetang lesome jaaka o emetse dithuso tse dingwe mo kokelong.

Go tsaya karolo gago mo patlisisong e, ke boithaopo. O ka ikgogela morago nako nngwe le nngwe o sa fe mabaka ape. O gololesegle go ka botsa potso nngwe le nngwe le dikarabo tse o tlaa di fang e tlaa nna sephiri. Maduo a tshekatsheko e, a tlaa re thusa go tokafatsa ditirelo tsa rona, gape re dumela fa di tlaa tokafatsa le botsogo jwa gago.

Tshekatsheko e, ga e na go tsenya botsogo jwa gago mo diphatseng ka tsela epe, e bile ga e duelelwe. Re tlaa kgagana maduo a patlisiso le wena ga mmogo le ba ba go neelang dithuso tsa botsogo. O gololesegle go ka botsa potso, e bile fa o batla go thalosetswa sengwe, o ka ntshwara mo mogaleng wa 72877316.

Patlisiso e sekasekiliwe e bile e thlomamisitswe ke ba Sefako Makgatho University Research and Ethics Committee (SMUREC) le botsamaisi jwa botsogo mo kgaolong ya South East, e bong South East District Health Management Team.

Ke lebogela nako ya gago.

Angel Lubasi
Appendix 2a: Consent form (English)

SEFAKO MAKGATHO HEALTH SCIENCES UNIVERSITY ENGLISH CONSENT FORM

Statement concerning participation in a Research Project

Name of Project: Adherence to antiretroviral treatment amongst patients at Lesethana Clinic in South East District, Botswana

I have read the information on the aims and objectives of the proposed study and was provided the opportunity to ask questions and given adequate time to rethink the issue. The aims and objectives of the study are sufficiently clear to me. I have not been pressurized to participate in any way.

I understand that participation in this Study is completely voluntary and that I may withdraw from it at any time and without supplying reasons. This will have no influence on the regular treatment that holds for my condition neither will it influence the care that I receive from my regular doctor.

I know that this Study has been approved by the Sefako Makgatho University Research Ethics Committee (SMUREC), Sefako Makgatho Health Sciences University. I am fully aware that the results of this study will be used for scientific purposes and may be published. I agree to this, provided my privacy is guaranteed.

I hereby give consent to participate in this Study

............................................................  ............................................................
Name of patient/volunteer  Signature of patient or guardian

............................................................  ............................................................  ............................................................
Place  Date  Witness

Statement by the Researcher

I provided verbal and/or written information regarding this Study
I agree to answer any future questions concerning the Study as best as I am able.
I will adhere to the approved protocol.

............................................................  ............................................................  ............................................................  ............................................................
Name of Researcher  Signature  Date  Place
SEFAKO MAKGATHO HEALTH SCIENCES UNIVERSITY SETSWANA CONSENT FORM

Seteitemente se se ka ga go tsaya karolo mo Porojeke ya Patlisiso

Leina la Patlisiso: Adherence to antiretroviral treatment amongst patients at Lesetlhana Clinic in South East District, Botswana

Ke buisitse tshedimosetso mo e patlisiso e e tshitshintsweng mme ke fiowe tšhono ya go botsa dipotso le go fiwa nako e e lekaneng ya go akanya gape ka nthla e. Maitlhomo le maikemisetso a patlisiso e a thaloganyega sentle. Ga ke a patelediwa ke ope ka tselo epe go tsaya karolo.

Ke thaloganya gore go tsaya karolo mo Patlisiso ke boithaopo le gore nka ikgogela morago mo go yona ka nako nngwe le nngwe kwa ntle ga go neela mabaka. Se ga se kitla se nna le seabe sepe mo kalafong ya me ya go le gale ya bolwetsi Jo ke nang le jona e bile ga se kitla se nna le thiotheletso epe mo thokomelong e e amogelang mo ngakeng ya me ya go le gale.

Ke a itse gore Patlisiso e e rebotswe ke Patlisiso le Molao wa Maitsholo tsa Khampase ya Sefako Makgatho Health Sciences, Research Ethics Committee (SMUREC), Yunibesithi ya Sefako Makgatho Health Sciences. Ke itse ka botlalo gore dipholo tsa Patlisiso di tla dirisetswa mabaka a saentifiiki e bile di ka nna tsa phasaladiwa. Ke dumelana le seno, fa fela go netefadiwa gore se e tla nna khupamarama.

Fano ke neela tumelelo ya go tsaya karolo mo Patlisiso e.

............................................................
Leina ka molwetse/moithaopi
............................................................
Tshaeno ya molwetse kgotsa motlamedi

............................................................
Lefelo.
............................................................
Letlha
............................................................
Paki

Seteiteimeka Mmatlisisi

Ke tlametse tshedimosetso ka molomo le/kgotsa e e kwadilweng malebana le Tekelelo / Patlisiso / Porojeke* e. Ke dumela go araba dipotso dingwe le dingwe mo nakong e e tlang tse di amanang le Tekelelo / Patlisiso / Porojeke* ka moo nka kgongang ka teng.

Ke tla tshegetsa porotokolo e e rebotsweng.

............................................................
Leina la Mmatlisisi
............................................................
Tshaeno
............................................................
Letlha
............................................................
Paki

............................................................
Lefelo
Appendix 3a: Structured questionnaire (English)

Adherence to antiretroviral treatment amongst patients at Lesetlhana Clinic in South East District, Botswana

Data collector: _______________________

Date: _______________________

Patient study ID: __________

- Greet the patient and introduce yourself.
- Establish willingness to participate in the study.
- If willing to participate, give the patient the study information leaflet.
- Patient to sign consent form.
- Tick the appropriate box or provide the necessary information.

Socio-demographic data

<table>
<thead>
<tr>
<th>Gender:</th>
<th>Male</th>
<th>Female</th>
</tr>
</thead>
</table>

Distance from home: __________ km

Date of birth: yyyy mm dd

Date ART initiation: yyyy mm dd

Marital status:

- Single
- Married
- Divorced
- Separated
- Widowed

Highest level of education:

- None / primary not completed
- Primary completed
- Secondary incomplete
- Secondary completed (Grade 12)
- Tertiary or vocational

Employment:

- Employed
- Self-employed
- Unemployed

Social assistance:

- Pension
- Child support grant
- Disability grant
- None

Adherence challenges

Taking medication daily can sometimes be difficult. What do you think makes you sometimes fail to take your medicines?

*Data collector:* Tick the appropriate box or use the ‘Other’ box to write down the response. Repeat the question again to ensure the patient has provided all the information. DO NOT PROMPT
Adherence self-report

Most people with HIV have many pills to take at different times during the day. Many people find it hard to always remember to take their pills. It is important for me to understand how you are really doing with your medicines. Do not worry about telling me if you do not always take all your doses. I need to know what is really happening not what you think I want to hear. You will not be victimised in anyway. We would like to help you to take your medicines in the way you are supposed to, so that you can get the best out of your treatment.

Data collector: Mark the patients’ response to the following questions.

<table>
<thead>
<tr>
<th>Question</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>1  Do you sometimes find it difficult to remember to take your medication?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2  When you feel better, do you sometimes stop taking your medication?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3  Sometimes if you feel worse when you take the medication, do you stop taking it?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4  Did you miss three or more doses in the last 30 days?</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

In the last 30 days (4 weeks), how good a job did you do at taking your ARVs (HIV medicines) in the way you were supposed to?

Data collector: Tick the appropriate box

Excellent
Very good
Good
Fair
Poor
Very poor

Pill count record (To be collected retrospectively from electronic patient records)
<table>
<thead>
<tr>
<th>Antiretroviral Treatment Regimen</th>
<th>% Adherence</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Month 1</td>
</tr>
<tr>
<td>Antiretroviral medicines</td>
<td>Date:</td>
</tr>
<tr>
<td>Zidovudine 300 mg / Lamivudine 150 mg</td>
<td></td>
</tr>
<tr>
<td>Nevirapine 200 mg</td>
<td></td>
</tr>
<tr>
<td>Atripla (Emtricitabine/ Tenofovir/ Efavirenz 200/300/600 mg)</td>
<td></td>
</tr>
<tr>
<td>Truvada (Emtricitabine 200 mg/ Tenofovir 300 mg)</td>
<td></td>
</tr>
<tr>
<td>Aluvia 200/50 mg (Lopinavir/ Ritonavir 200/50 mg)</td>
<td></td>
</tr>
<tr>
<td>Efavirenz 600 mg</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td></td>
</tr>
</tbody>
</table>

Appendix 3b: Structured questionnaire (Setswana)
Adherence to antiretroviral treatment amongst patients at Lesetlhana Clinic in South East District, Botswana

Data collector: _______________________
Date: _______________________
Patient study ID: __________

- Dumedisa molwetse, o mo ikitsise gore o mang.
- Tlhomamisa gore molwetse o na le keletso ya go tsaya karolo mo potsolotsong.
- Fa a supa gore o na le keletso ya go tsaya karolo mo neele pampitshana ya potsolotso
- Molwetse o tshwanetse go saena pampitshana e e supang fa a dumela go tsaya karolo mo potsolotsong.
- Tshwaya kana o fe karabo e e tshwanetseng.

Socio-demographic data

<table>
<thead>
<tr>
<th>Gender:</th>
<th>Munna</th>
<th>Musadi</th>
<th>O tshotswe leng?</th>
<th>yyyy</th>
<th>mm</th>
<th>dd</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sekgala go tswa ko lwapeng:</td>
<td>_______ km</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>O simolotse diritibatsi leng?</th>
<th>yyyy</th>
<th>mm</th>
<th>dd</th>
</tr>
</thead>
</table>

A o nyetswe?

Ga ke a nyalwa
Ke nyetswe
Ke kgagane le rrre yo o ntsereeng/mme yo ke mo ntseng
Ke mo nyalong mm eke kgagane le mme yo ke mo ntseng/rrre yo o ntseng
Ke tihokaletaetswe ke rrre yo o ntseng/mme yo ke mo ntseng

O fleets kae ko sekolong?

Ga ke a tsena sekolo/ga ke a fetsa dithuto tsana sekolo se se potlana
Ke feditse sekolo se se potlana
Ga ke a fetsa dithuto tsa sekolo se se golwane(form five)
Ke feditse dithuto tsa sekolo se se golwane(form five)
Ke tsene ko mmadikolo

Tiro:

Ke a bereka
Ke a ipereka
Ga ke bereka

Dithuso tse o di amogelang:

Madi a bagodi
Madi a go thusa bana
Dithuso tsa ba a le bogole
Ga go na thuso epe e ke e amogelang
Dikgwetlho tse o kopanang le tsone tse o fa o tsaya melemo

Go tsaya melemo letsatsi le letsatsi go thata nako dingwe. O tsaya gore ke eng se se go itsang go ka tsaya melemo ya gago sentle?

**Data collector:** Tick the appropriate box or use the ‘Other’ box to write down the response. Repeat the question again to ensure the patient has provided all the information. DO NOT PROMPT

<table>
<thead>
<tr>
<th>Ditlamorago tse di sa siamang tsableme</th>
<th>Go nwa bojalwa</th>
</tr>
</thead>
<tbody>
<tr>
<td>Go lebala go tsaya melemo</td>
<td>Go tlhoka dijo</td>
</tr>
<tr>
<td>Dipilisi tse di ntsi</td>
<td>Go tlhoka madi go ya go tsaya melemo</td>
</tr>
<tr>
<td>Go sa thaloganya ditaelo</td>
<td>Go etela ditsala</td>
</tr>
<tr>
<td>Go tsena thari ko lwapeng</td>
<td>Go kgethololwa</td>
</tr>
<tr>
<td>Go tlhoka thotoetso go tswa mo go ba losika</td>
<td>Go tlhoka thotoetso go tswa mo ditsaleng</td>
</tr>
<tr>
<td>Go gatelelwa mo maikutlong</td>
<td></td>
</tr>
</tbody>
</table>

Mabaka a mangwe ntle ga a kwadilweng fa godimo:

---

**Adherence self-report**

Batho ba le ba ntsi ba ba tshelang ka mogare wa HIV ba nwa dipilisi tse di ntsi ka nako tse di farologaneng mo letsatsing. Bontsi jwa bone bo bona go le thata go gakologelwa go tsaya dipilisi. Go botlhokwa thata gore ke thaloganye gore o tsaya melemo ya gago jang. O seka wa tshaba go mpolelela fa o sa tseye melemo ya gago sentle. Ke tlhoka go itse gore go diragalang tota, e seng se o akanyang gore ke eletsa go se utlwa. Maduo a potsolotso e, ga a na go dirisiwa kgathanganong le wena ka tsela epe. Re eletsa go go thusa go nwa melemo ya gago ka tsela e e tshwanetseng gore o kgone go akola maduo a go tsaya melemo ya gago.

**Data collector:** Mark the patients’ response to the following questions.

<table>
<thead>
<tr>
<th>Potsa</th>
<th>Ee</th>
<th>nnya</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>A nako dingwe o bona go le thata go tsaya melemo ya gago?</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>A o emisa go nwa melemo ya gago fa o ikutiwa o le botoka?</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>A o emisa go tsaya melemo ya gago fa o bona o sa nne botoka?</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>A o paletswe ke go tsaya dipilisi gararo le go feta mo malatsing a masome mararo a a fetileng?</td>
<td></td>
</tr>
</tbody>
</table>
Mo malatsing a masome a mararo a a fetileng o bona o dirile go le kae go nwa diritibatsi ka tsela e e tshwanetseng?

**Tshwaya karabo e e tshwanetseng:**

| Ke dirile go le go ntle thata |
| Bontletota |
| Bontle |
| Selekano |
| Palelwa |
| Ke paletswe thata |

---

**Pill count record** *(To be collected retrospectively from electronic patient records)*

<table>
<thead>
<tr>
<th>Antiretroviral Treatment Regimen</th>
<th>% Adherence</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Month 1</td>
</tr>
<tr>
<td>Antiretroviral medicines (Regimen (Tick))</td>
<td>Date:</td>
</tr>
<tr>
<td>Zidovudine 300 mg / Lamivudine 150 mg</td>
<td></td>
</tr>
<tr>
<td>Nevirapine 200 mg</td>
<td></td>
</tr>
<tr>
<td>Atripla (Emtricitabine/ Tenofovir/ Efavirenz 200/300/600 mg)</td>
<td></td>
</tr>
<tr>
<td>Truvada (Emtricitabine 300 mg/ Tenofovir 300 mg)</td>
<td></td>
</tr>
<tr>
<td>Aluvia 200/50 mg (Lopinavir/ Ritonavir 200/50 mg)</td>
<td></td>
</tr>
<tr>
<td>Efavirenz 600 mg</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td></td>
</tr>
</tbody>
</table>
Appendix 4: SMUREC Clearance Certificate

Sefako Makgatho Health Sciences University Research & Postgraduate Studies Directorate
Sefako Makgatho University Research Ethics Committee (SMUREC)
Molotlegi Street, Ga-Rankuwa 0208
Tel: (012) 521 5617/3698 | fax: (012) 521 3749
Email: lorato.phiri@smu.ac.za
P.O. Box 163 Medunsa 0204

APPROVAL NOTICE - NEW APPLICATION

12 February 2015

Mr A Lubisi
Department of Pharmacy
P.O Box 216
MEDUNSA, 0204

MEETING: 01/2015

SMUREC Ethics Reference Number: SMUREC/H19/2015: PG

Title: Adherence to antiretroviral treatment amongst patients at Lebophiwa Clinic in South East District, Botswana

Researcher: Mr A Lubisi
Supervisor: Dr JC Mayor
Department: Pharmacy
School: Health Care Sciences
Degree: Master of Pharmacy

The New Application received on 23 January 2015, was reviewed by members of Sefako Makgatho University Research Ethics Committee on 12 February 2015 and was approved on 12 February 2015.

Please note the following information about your approved research protocol:


Please remember to use your protocol number (SMUREC/H19/2015: PG) on any documents or correspondence with the REC concerning your research protocol.

Please note that the REC has the prerogative and authority to ask further questions, seek additional information, require further modification, or monitor the conduct of your research and the consent process.

After Ethical Review: Please note a template of the progress report is obtainable in the Research Office and should be submitted to the Committee before the year has expired. The Committee will then consider the continuation of the project for a further year (if necessary). Annually a number of projects may be selected randomly for an external audit. Translation of the consent document in the language applicable to the study participants should be submitted.

International Organisation: (ORG0004319), Institutional Review Board (IRB00005122), Federal Wide Assurance (FWA00009419)
Expiry date: 11 October 2016 and NHREC No: REC 210406-003

Sincerely,

PROF GA OGUNSANJO
CHAIRPERSON SMUREC

Members of the Interim Council:
Prof D Shisana (Chairperson), Ms SA Motlouu, Mr P Slik, Dr N Simelela, Prof AM Ergane, Dr E van Staden

SEFAKO MAKGATHO
HEALTH SCIENCES UNIVERSITY
SMU Research Ethics Committee
Chairperson
Date: 12 February 2015
Appendix 5: Letter to Coordinator of South East District Health Management Team

Department of Pharmacy  
Sefako Makgatho Health Sciences University  
P.O. Box 218  
Medunsa, 0204  
Tel: (012) 5214312  
Fax: (012) 5213992

The Coordinator, South East District Health Management Team  
P/B 14 Ramotswa  
Botswana  
10\textsuperscript{th} May, 2015

Dear Sir

Re: Request for permission to conduct a research study at Lesetlhana clinic

I am a postgraduate student in the Department of Pharmacy, Sefako Makgatho Health Sciences University. I hereby kindly request permission to conduct a research study at Lesetlhana Clinic, as part of the requirements for my Master’s Degree Programme.

The title of the study is: Adherence to antiretroviral treatment amongst patients at Lesetlhana Clinic in South East District, Botswana.

The study will only be conducted once I have obtained ethical clearance from the Research and Ethics Committee of the university.

Your permission to conduct the study will be highly appreciated.

Please feel free to contact me or my supervisor, for any additional information.

Yours faithfully,

Mr Angel Lubasi  
MSc (Med) Pharmacy student  
Cc: Dr JC Meyer (Supervisor)
Appendix 6: Letter from Coordinator of South East District Health Management Team

REF: SE/DHMT

To: Mr. Angel Lubasi
P. O. BOX 10494
Ramotswa.

Dear Sir,

RE: PERMISSION TO CONDUCT RESEARCH IN LESETHLANA CLINIC
ADHERENCE TO ANTIRETROVIRAL TREATMENT AMONGST PATIENTS
AT LESETHLANA CLINIC IN SOUTH EAST DISTRICT

Reference is made to your letter dated June 10th 2015.

Permission to conducting research is granted. You are expected to liaise with the facility management to make the necessary arrangements.

By copy of this letter Lesethana clinic is requested to provide you with the necessary support and assistance.

Kind regards,

Yours sincerely,

E. M. Ramoba
South East DHMT - Head
Appendix 7: MOH Botswana Clearance Certificate

REFERENCE NO: PPME 13/18/1 PS V (356) 23 June 2015

Health Research and Development Division

Notification of IRB Review: New application

Angel Lubasi
P.O. Box 10494
Ramatswa

Protocol Title:

ADHERENCE TO ANTIRETROVIRAL TREATMENT AMONGST PATIENTS AT LESETHLANA CLINIC IN SOUTH EAST DISTRICT

HRU Approval Date: 22 June 2015
HRU Expiration Date: 21 June 2016
HRU Review Type: HRU reviewed
HRU Review Determination: Approved
Risk Determination: Minimal risk

Dear Mr Lubasi

Thank you for submitting new application for the above referenced protocol. The permission is granted to conduct the study.

This permit does not however give you authority to collect data from the selected site without prior approval from the management. Consent from the identified individuals should be obtained at all times.

The research should be conducted as outlined in the approved proposal. Any changes to the approved proposal must be submitted to the Health Research and Development Division in the Ministry of Health for consideration and approval.

Furthermore, you are requested to submit at least one hardcopy and an electronic copy of the report to the Health Research, Ministry of Health within 3 months of completion of the study. Approval is for academic fulfillment only. Copies should also be submitted to all other relevant authorities.
Continuing Review

In order to continue work on this study (including data analysis) beyond the expiry date, submit a Continuing Review Form for Approval at least three (3) months prior to the protocol's expiration date. The Continuing Review Form can be obtained from the Health Research Division Office (HRDD), Office No. 7A 7 or Ministry of Health website: www.moh.gov.bw or can be requested via e-mail from Mr. Kgomo Mothanka, e-mail address: kgm.mothanka@gov.bw. As a courtesy, the HRDD will send you a reminder email about eight (8) weeks before the lapse date, but failure to receive it does not affect your responsibility to submit a timely Continuing Report form.

Amendments

During the approval period, if you propose any change to the protocol such as its funding source, recruiting materials, or consent documents, you must seek HRDC approval before implementing it. Please summarise the proposed change and the rationale for it in the amendment form available from the Health Research Division Office (HRDD), Office No. 7A 7 or Ministry of Health website: www.moh.gov.bw or can be requested via e-mail from Mr. Kgomo Mothanka, e-mail address: kgm.mothanka@gov.bw. In addition, submit three copies of an updated version of your original protocol application showing all proposed changes in bold or "track changes".

Reporting

Other events which must be reported promptly in writing to the HRDC include:
- Suspension or termination of the protocol by you or the grantor
- Unexpected problems involving risk to subjects or others
- Adverse events, including unanticipated or anticipated but severe physical harm to subjects.

If you have any questions please do not hesitate to contact Mr. P. Khulumani at pkhulumani2egov.bw, Tel +267-391467 or Lemphi Moremi at lancereel@gov.bw or Tel: +267-362754. Thank you for your cooperation and your commitment to the protection of human subjects in research.

Yours sincerely

P. Khulumani
For Permanent Secretary
Appendix 8: African Journal of AIDS Research Author Guidelines

Instructions for Authors

African Journal of AIDS Research (AJAR) publishes papers that make an original contribution to the understanding of the social dimensions of HIV and AIDS in African contexts. AJAR will publish research articles of 5 000 to 7 500 words and short communications of 2 000 words. Review papers will be considered only if they make an original conceptual or theoretical contribution to the field. Invited book reviews are also published.

Editorial policy: Submission of a manuscript implies that the material has not previously been published, nor is it being submitted elsewhere for publication. Contributions are accepted with the understanding that the authors have the authority for publication. Submission will be taken to imply transfer of copyright of the material to the publishers. NISC (Pty) Ltd. Contributions must conform to the principles outlined in Ethical Considerations in Research Publication available for download below.

Papers submitted to AJAR will be reviewed by two appropriately qualified and experienced referees to ensure that all articles accepted for publication are methodologically and conceptually sound and make an original contribution to the field. The journal adheres strictly to a double blind review process. The final decision to accept a manuscript rests with the Editor-in-Chief. Queries regarding manuscripts can be addressed to the Editorial Office at ajar.editor@nisc.co.za.

Submission: Manuscript submissions should be made online at the African Journal of AIDS Research ScholarOne Manuscripts site. New users should first create an account. Once a user is logged onto the site, submissions should be made via the Author Centre. Manuscripts must adhere to the format criteria described below, and papers failing to do so will be returned to authors to be corrected before being reviewed. Authors can make use of a language editing service to ensure that the presentation of their work is of an appropriate standard for submission.

Manuscript presentation: Submitted manuscripts should contain the following sections, each in separate files:

**Title page:** The title (max. 20 words) should be a concise description of the article content. Author names must appear only on the title page. This page should also include each author’s names (full first name and surname), each author’s full institutional affiliation, the e-mail address of the designated corresponding author. Recommended, but not required, are short biographical notes for the authors (highest academic degree, work experience, research interests) and/or any acknowledgements.

**Abstract:** This should include the title of the paper and an abstract. The abstract is a concise statement of the scope of the work, the principal findings and the conclusions and should not exceed 250 words. It should not contain references. Below the abstract, up to eight additional keywords or phrases (which are not already given in the title) should be listed in alphabetical order. Short communications also require brief abstracts (max. 150 words).

**Main text:** All papers should include Introduction and Conclusions sections, but given the diverse range of papers that might be published in AJAR, we do not prescribe a standard format for the middle section. Format – Manuscripts should be prepared in MSWord. The headings and text should be presented in 12-point Arial or Calibri font. The text should use 1.5 line spacing, with no extra line spacing, and should not include text columns, creative formatting or additional fonts. Headings should be sentence case and never numbered. There should be no more than three heading levels: (1) **bold**, (2) **bold italics**, (3) *italics*. Endnotes, not footnotes, may be used sparingly. Tables and figures (graphs, photographs or scanned images) should not be part of the text but prepared as separate files.

**Editorial style** – Manuscripts should be written in clear English (UK spelling). Consult the Oxford English Dictionary for spelling, capitalisation, hyphenation and abbreviation conventions. Consult a copy of the journal for general style conventions. Double quotation marks and regular font should be used to designate material quoted directly
from other texts. Direct speech should be italicised. Use single quotation marks to signify a quote embedded within another quotation. Double quote marks and italic font should be used to denote informants’ quotes. The period (.) must be used as the decimal indicator, and ‘thousands’ should be designated by a space rather than a comma (Example: 1 500 000). Conventions on presenting mathematical and statistical data are outlined in Guidelines for the presentation of mathematical and statistical data available for download below.

Referencing: Use APA 6 author–date style. Multiple citations in the text must be separated by semicolons and cited chronologically in the form (Habib, 1998, 2005; Bwanika & Davis, 2000; Ministry of Health, 2011). If there is more than one citation with the same publication year, these should be listed alphabetically. If previously published work is quoted directly, the citation must include the author, year of publication, and page number as in (Ajulu, 1999, p. 63). If more than five authors are cited in a reference, use only the name of the first author followed by ‘et al’. The reference list should be in alphabetical order by first author, and include all the authors of a given reference (do not use “et al.” in the list); likewise, use full journal titles. URLs may be cited only for references that are not available in print (such as a webpage) or ones that link to hard-to-find sources (e.g. municipal document), and these URLs must be up-to-date at the time of submission. Include DOIs for articles where possible.

Example reference list:


Tables and Figures – Tables and figures should contain only information directly relevant to the content of the paper. Each table and figure must include a full, stand-alone caption, and each must be sequentially mentioned in the text. Highly stylised formatting should be avoided. Tables may use thin, horizontal lines but should not include cells with shading. Authors must ensure that their figures conform to the style of the journal. Pay particular attention to line thickness, font and figure proportions, taking into account the Journal’s printed page size. Costs of redrawing figures may be charged. Please refer to Figure Guidelines for Authors: format, style and technical considerations available for download below. For digital photographs or scanned images the resolution should be at least 300 dpi for colour or greyscale artwork and a minimum of 600 dpi for black line drawings. These can be saved (in order of preference) in PSD, JPEG, PDF or EPS format. Graphs, charts or maps can be saved in AI, PDF or EPS format. MS Office files (Word, Powerpoint, Excel) are also acceptable but DO NOT EMBED Excel graphs or Powerpoint slides in a MS Word document, rather send the original Excel or Powerpoint files. More detailed technical information is given in Figure Guidelines for Authors.

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