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Self reported factors influencing adult patients' adherence to antiretroviral therapy at St Rita's Hospital

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CHAPTER 1: INTRODUCTION

1.1 BACKGROUND

Data published by UNAIDS in 2008 suggest that the number of people newly infected with HIV and the number of people living with HIV/AIDS has reached a plateau and is probably decreasing in comparison to previous years,[1] in South Africa and globally.

In 2005, the number of people living with HIV/AIDS was estimated to be 39.5 million compared to 33.2 million in 2006[2] and 33 million in 2007[1]. Around 22.5 million people (68% of the global total) were estimated to be living with HIV/AIDS in sub Saharan Africa in 2006[2]. This decreased to 22 million in 2007[1]. The number of AIDS deaths in 2006 was reported to be 2.1 million[2], decreasing to 2 million in 2007[1]. Of these 2 million deaths, 75% occurred in sub Saharan Africa, the region most affected by the AIDS epidemic[1]. However, the number of people in sub Saharan Africa newly infected with HIV increased from 1.7 million in 2006[2] to 1.9 million in 2007[1]. This increase in the number of new HIV infections does not represent an increase in all countries in the region but, rather, in specific countries.

The epidemic differs significantly from country to country in both scale and scope[1]. One of the worst affected sub Saharan African countries is South Africa

with a population of 44.3 million people in 2005[3] and 48.5 million in 2007[3]. More than 18% of adults (aged 15 to 49 years) remain infected with HIV (estimates were 18.8% in 2005 and 18.1% in 2007)[2.]

The observed increase in the absolute number of people living with HIV/AIDS from 2001 to 2005[4] led to the emergence of an international consensus on the need to fight HIV/AIDS with a comprehensive response. The response comprises treatment, care, prevention and impact mitigation which involves initiatives to ameliorate the impact of the epidemic by addressing the existing inequities of wealth, ethnicity, class, age and geographical location, all of which help to fuel the epidemic [4]. The backbone in the fight against HIV/AIDS is prevention, followed by access to and use of, highly active antiretroviral therapy (HAART).

Projections made in early 2000 suggested that, without comprehensive treatment interventions, the death rate attributable to HIV/AIDS was likely to reach 800 000 in South Africa by 2010.[5] Increasing access to HAART, which has proven effective in decreasing morbidity and mortality attributable to HIV/AIDS, was advocated as a means of decreasing the projected escalation in the number of deaths due to HIV/AIDS by 2010.[6-8] This provided a window of opportunity in the international public health arena and efforts were focused on providing funding for HIV/AIDS with a view to increasing access to treatment, care and prevention for the people who need it most.

The WHO and UNAIDS set a challenge for the UN system and the global community through its '3 by 5' programme[4] which set a target of providing ART to 3 million people living with HIV/AIDS in low and middle income countries by the end of 2005[4]. The programme, even though aimed at treating around half of the number of people in need, was laudable in that it was a global concerted effort to get as many people as possible on life saving antiretroviral therapy (ART).

Other international initiatives, such as the US President's Emergency Plan for AIDS Relief (PEPFAR)[9], the United Nationa's Global Fund to fight AIDS, tuberculosis and malaria [10], and other national and international programmes and initiatives came on board to try and expand the uptake of ART.

In 2002, the number of people estimated to be on HAART in sub Saharan Africa doubled from 150 000 to 310 000 in just over six months[11]. During the same period, the number of people receiving treatment increased by more than 10 000 in Botswana, Kenya, Uganda, Zambia and South Africa[11]. These countries exceeded 10% coverage in 2002 alone[11].

In the latter half of 2004, the number of people on HAART in developing countries increased from 440 000 to an estimated 700 000. Although this was a major increase in HAART coverage, the achievement could not be considered to

have made a major impact as this represented around 12% of the approximately 5.8 million people that were estimated to need HAART[11] at the time.

In South Africa, the implementation of the operational plan for comprehensive HIV and AIDS care, management and treatment[12] in 2004 increased HAART uptake dramatically from 55 000 in 2004 to 207 000 in 2005.[2-4] This number further increased to 325 000 in 2006 and was estimated to be around 460 000 in 2007[13]. The figure is expected to reach around 791 000 by 2010[14]. Despite the increase in HAART coverage in 2005, only about 15% of those in need of HAART received it, leaving around 1.4 million people in need of treatment[2,13]. In sub Saharan Africa, HAART coverage was about 11% with around 4.7 million people estimated to be in need of HAART in 2005[14].

Concerns about the rapid expansion of access to HAART began to emerge as there were doubts about the ability of African patients, many of whom are poor and lack formal education, to adhere to ART[15]. Apart from living in poor socio-economic conditions and lacking in education, the varying dosing schedules, dietary restrictions and adverse effects were thought to constitute serious challenges to those receiving HAART[16,17]. Unlike treatment for most clinical conditions, ART requires an unprecedented high level of adherence for an indefinite time period to achieve desired results[18]. Consistently high levels of adherence are necessary to achieve reliable viral suppression and prevent resistance, disease progression and death[19-23]. Near perfect adherence levels of

≥ 95% have been shown to optimize outcomes of HAART, thereby minimizing HIV drug resistance, and decreasing disease progression, hospitalization and death[19,22,24,25]. Assumptions were made that such high levels would not be achieved in resource-poor settings and hence there should be caution in expanding access to HAART[26]. Recent studies from Africa refuted this, showing excellent adherence and virologic outcomes[26,27,28]. However, these studies were carried out in urban settings. No such studies have been performed in rural settings.

1.2 STATEMENT OF THE PROBLEM

The positive impact of treatment with ART on the health-related quality of life of people living with HIV/AIDS has been documented[29]. In countries with resources and experience in ART a lower proportion of people progress to AIDS and the age-adjusted death rate from HIV/AIDS has declined by more than 70% [29].

The greatest patient-enabled predictor of treatment success for those on HAART is good adherence[15]. Near perfect adherence levels (of ≥95%) are needed to optimize the benefits of HAART and significantly reduce morbidity and mortality.[19,25,32,33] Poor adherence to ART is the second strongest predictor of progression to AIDS and death after CD4 count[22,30.31]. Non-adherence to antiretrovirals (ARVs) has been implicated in the development of antiretroviral resistant viruses, increased rates of hospitalization and longer hospital stays[22,34].

1.3 JUSTIFICATION FOR THE STUDY

There is no 'gold standard' for the assessment of adherence to HIV/AIDS medications. There is also no single optimal tool that enhances adherence to HIV/AIDS treatment regimens [35]. Mills *et al*.[15] and Chesney[35] have shown that adherence to HIV/AIDS treatment is more than simply remembering to take medications, but rather a complex issue involving social, cultural, economic and personal factors that need to be addressed.

Although important barriers to adherence are consistent across multiple settings and countries, studies have also shown that adherence levels and factors that influence it differ in different subgroups [21,36-38].

Mills *et al*. [15] Orell *et al*. [26,27] and Nachega *et al*. [28] have all shown that high levels of adherence to ARVs is achievable and is being achieved in resource poor settings. They have also shown that adherence is not a barrier to successful ART in South Africa. However, these studies were all carried out in urban settings. About 46% of South Africans live in rural areas where there is a major shortage of health care workers which has led to consistently lower levels of service delivery[39,40].

A recent review of four comprehensive care management and treatment sites in Gauteng revealed that the service delivery to patients on ARVs was suboptimal. Amongst other things, the ever increasing number of patients against a

background of decreasing staff strength, as well as space shortages, had led to poor service delivery[41]. It is therefore possible that poor service delivery might have an impact on ART adherence, and that results from urban settings might thus not be replicable in rural settings. This study investigated if these excellent outcomes also exist in a rural setting.

It is also important to identify factors that might influence adherence in rural settings in South Africa, with a view to modifying these factors and hence improving adherence. This study investigated which factors play a role in adherence in this setting.

This study was done in St. Rita's Regional Hospital which is situated in Sekhukhune district, Limpopo Province. It is deeply rural and is classified as a presidential nodal rural area because it is over 100km from the provincial capital, Polokwane and over 60km from the nearest town, Groblersdal. Since the commencement of ART roll-out in this district in September 2004, there has been a steady increase in the number of patients enrolled into the programme[42]. The programme has also been expanded to some surrounding clinics and sub-districts. Despite this, no studies have been carried out to evaluate patients' adherence to ART and the factors that might be influencing it.

CHAPTER 2: LITERATURE REVIEW

2.1 Rates of Adherence

Early reports by Orell *et al.*[27] in 2003 showed that adherence is not a barrier to successful ART in South Africa. Adherence rates of higher than 90% were recorded through self reported adherence questionnaires and pill counts. A relatively high proportion of the participants (about 71%) achieved undetectable viral load. In 2004 Nachega *et al.*[28] confirmed this in their study on self reported levels of adherence to ART among HIV-infected adults in Soweto. About 80% of the participants had adherence levels higher than 95% and about 9% of the participants recorded adherence levels of between 90%-95% respectively.

In 2006, Mills *et al.*[15] performed a meta-analysis of 31 studies from North America and 27 studies from sub Saharan Africa to compare adherence to ART in the two regions. Patient self reports were used to assess adherence in 71% of the North American studies and in 66% of the African assessments. A pooled analysis of the North American studies showed that about 55% of the population achieved adequate levels of adherence compared to about 77% in the sub Saharan African studies. These findings indicate that acceptable levels of adherence can be achieved in sub Saharan African settings and that adherence to ART remains a concern in North America. This led to a lot of attention being given to adherence to ART because concerns about the feasibility of ART in Africa had been expressed earlier[15,26,43]. In 2003 The New York Times

highlighted this by running a headline story titled ‘Africans outdo US patients in following Aids Therapy.[44]

The consistently higher levels of adherence observed in sub Saharan Africa were attributed to patients being motivated by the devastating effects of HIV/AIDS in their everyday lives[45]. Gill *et al.*[46] noted that the results from the early sub Sahara African studies might not be generalizable as most of the participants were enrolled in ongoing randomized trials and might have benefited from the structural support provided by the trials. They also noted that those studies that were not clinical trials and reported high levels of adherence in general, relied on patients’ self reports without surrogate markers, followed small numbers of patients for short periods, and were cross sectional analyses; thus, they could not comment on sustained adherence rates.

Mills *et al*.[15] agreed with this in their review of adherence to ART in sub Saharan Africa and North America. They further stated that, because the African studies were carried out in tertiary hospitals in large cities very early during the ARV roll out, the patients might have experienced dramatic improvement in their health status and may have thus been better motivated. They cautioned that these benefits may be reversed when patients start experiencing long term adverse effects of therapy as well as when treatment access is rolled out to various rural district hospitals where the impact of socio-economic factors such as unemployment, illiteracy, poverty and physical barriers to health might be seen.

The concerns of Mills *et al.*[15] and Gill *et al.*[46] have been confirmed as there are now increasing reports of declining adherence over time in longitudinal studies in various regions on the continent. Laurent *et al.*[47] from Senegal noted that more than 95% of their patients had adherence exceeding 80% after one month on ARVs but only 80% of this group maintained these high adherence levels after 18 months. In addition, the proportion of patients with undetectable viral load fell from 79.6% to 59.3%. Akam[48] reported similar results viz. an adherence level of 68% through a self report method in Cameroon. Similar to Laurent *et al.*'s study, the adherence level declined over time. Eholie *et al.*[49] from the Ivory coast reported that 52% of their patients were poorly adherent and that HIV was detectable even among those reporting over 90% adherence.

In South Africa, apart from studies done by Orell *et al.*[27] and Nachega *et al.*[28] which recorded adherence levels of 93.5% and 88% respectively, Darder *et al.*[50] recorded an adherence level of 88%. Brown *et al.*[51] recorded adherence levels of 76% whilst Ferris *et al.*[52] recorded adherence levels of 77%.

The apparently higher levels of adherence that were recorded in the South African studies in relation to the studies from Senegal, Cameroon and the Ivory Coast were attributed to a difference in the study designs and the methods used to assess adherence. Whilst Laurent *et al.*[47] and Akam[48] undertook longitudinal studies, the South African studies had a cross-sectional design.

Most of the above studies used self report with one or two surrogate markers to measure adherence. There have been a handful of studies where more than two surrogate markers have been used in parallel to self reports. Oyugi *et al*.[53] in Uganda who measured adherence via self report, pill count, visual analogue score and electronic drug monitoring, recorded adherence levels of 85%, 86%, 88% and 82%, respectively. These results imply a high degree of concordance even though they applied to only 46% of the study participants who completed 24 weeks of study.

In the South African studies that measured adherence with two surrogate markers, the associations were poor at times. Orell *et al*.[27] used pill counts and viral load estimations as surrogate markers and recorded adherence levels of 93.5% for pill count and 70.9% for viral load. Nachega *et al.*[28] recorded 88% adherence by self report and 73% using undetectable viral load.

At other times, the results were highly discordant. Ferris *et al*.[52] reported a striking 100% of patients reporting adherence and only 57% actually achieving undetectable viral load. This significant disparity between self reported adherence and clinical success is reminiscent of studies from the United States by Liu *et al*.[54] and Arnsten *et al*.[55] who recorded low and discordant levels of adherence using different surrogate markers a few years after the introduction of HAART. Their studies were among those compared to the African studies when the conclusion was reached that ‘Africans outdo US following AIDS therapy.[44]

The similarity of study results from sub Saharan Africa after a few years of ART and those of Liu *et al*.[54] and Arnsten *et al*.[55] highlights the caution sounded by Mills *et al*.[15] that the apparently higher levels of adherence recorded in the African studies might have been due to better motivation and dramatic improvements, and that the impact of socio-economic factors e.g. poverty, unemployment etc. might actually lead to a reversal of these gains and hence, later studies might record levels similar to those from the United States.

In conclusion, adherence is proving to be very challenging in sub Saharan Africa. Early reports about 'excellent adherence rates', especially in comparison with North America, should be interpreted cautiously. Also, interpretation of studies showing good results with self reported adherence but poor results with undetectable viral load should be seen as unreliable. There is therefore an urgent need for more studies on adherence in sub Saharan Africa in general, and South Africa in particular.

2.2 Factors Influencing Adherence to Antiretroviral Therapy

Ickovics and Meisler identified four distinct groups of factors that affect adherence[57] viz patient related factors, patient provider relationship, regimen factors and general socio-environmental factors.

a. Patient factors

Ickovics and Meisler.[56] classified patient related factors into two main groups, viz demographics (age, gender, race, employment status, educational level and housing status) and psychosocial (family and social support, mental health and substance abuse) factors.

There have been conflicting reports about the association between socio-demographic factors and adherence. In resource-rich settings where this association has been studied extensively, younger non-white race (ethnicity) and unstable housing have been consistently associated with non-adherence. Other factors, such as educational level and gender, have not been associated with difficulties relating to adherence[22,31,57,58].

The association between psychosocial factors and adherence is more consistent. Good support from family and the primary care provider has been shown to have a positive impact[60]. Conversely, poor family support, being secretive about HIV status, having a concurrent addiction, depression, a feeling of being overwhelmed, etc., have been associated with poor adherence[59,60].

b. Patient provider relationship

Experience from studying chronic diseases such as tuberculosis, asthma, etc. has shown that patients on chronic medications encounter significant problems

with adhering to their treatment but that these problems can be ameliorated by a good patient provider relationship[59,61]. In a study on the general care of patients living with HIV/AIDS, Tomlinson *et al*.[62] found that 53% of the HIV positive patients studied would like their General Practitioner (GP) to be involved in their care. Sinn,[63] in her study on encouraging adherence to antiretroviral drug regimes, enumerated many difficulties faced by patients, such as simply forgetting to take pills. She was of the opinion that these difficulties might have been overcome by consultation with a sympathetic GP and called for more involvement of GPs with patients on ART. Gifford *et al*.[64] reported that patients who knew that their provider 'knew them as a person' were more likely to be adherent to ARVs. These patients also missed fewer appointments, and reported less social stress and more positive beliefs about HAART. Such patients were also less likely to use alcohol, less likely to drop out, and reported a higher quality of life, generally. There was also a higher level of undetectable plasma viral load among this group. Conversely, dissatisfaction with prior experience in the health care system has been shown to have an adverse effect on adherence[62].

c. Regimen factors

Mills *et al*.,[60] in their systematic review of patient-reported barriers and facilitators to ART in both developed and developing nations, enumerated numerous regimen related factors that facilitate adherence to ART. These comprise a belief in the efficacy of HAART, 'having faith' in the treatment, understanding the need

for strict adherence, having a simple regimen, learning to balance HAART with daily schedules, incorporating ARVs into daily routine, and making use of reminder tools. Regimen-related barriers to successful ART that they enumerated include difficulty in understanding treatment instructions and the need for adherence, beliefs about the efficacy of ART, treatment side effects (real or anticipated), and complicated regimens. Other regimen-related barriers to successful ART adherence include beliefs about taste, size, frequency of dosing, a decreased quality of life while taking medications, feeling too sick, and being uncertain about potential long-term effects of HIV treatment.

Other factors, such as difficulty in incorporating work and family responsibilities with HAART, as well as simply running out of medications or having irregular supplies, were also mentioned. Studies by Patterson *et al*.[19] and Golin *et al*.[25] support this. They particularly highlighted dosing frequency, pill burden and the long-term side effects of treatment as major barriers to adherence.

d. General socio-environmental factors

Mills *et al*.[60] enumerated socio-environmental factors, such as being away from home, being too busy or distracted to properly comply, as well as issues of access, financial constraints and disruptions in access to medication, as important barriers to adherence. Golin *et al*.[25] enumerated similar reasons and also highlighted ‘change in daily routine’ and ‘simply forgetting’ as important barriers to adherence.

A study on comprehensive care, management and treatment sites in Johannesburg, and highlighted a very important socio-environmental factor barrier to antiretroviral therapy. In their report, Schneider *et al*.[41] found 'space and staff shortage, services being cut back and general staff burnout and dissatisfaction' due mainly to patient overload, to impact negatively on monitoring and evaluation systems thereby making them weak across all the sites'.

The major problem, highlighted by the study was that demand was now outstripping supply and, as such, the recommendation of the operational plan for comprehensive HIV and AIDS care by the Department of Health, that there should be an average of 12.5 staff per 500 patients,[65] was no longer practicable as health care staff saw 50 to 200 patients daily. The report also highlighted the lack of the use of viral load to guide treatment due to cost concerns, as well as a lack of mechanisms to trace defaulters. These challenges might have a huge impact on adherence.

2.3 Measurement of Adherence

There is no 'gold standard' for the measurement of adherence to HIV/AIDS medications[35], although several measurement methods have been used. In selecting adherence assessment approaches, the method used depends on the purpose for which the assessment is to be made. The general consensus is to divide the use of such assessments into clinical and research settings[35]. Methods

of measuring adherence can be broadly divided into two categories[66], viz. direct and indirect methods.

a. Direct measures

* **Directly observed therapy** – this is an accurate method of assessing adherence whereby the observer sees and records the patient taking the medication. It is, however, not practical, especially when pills need to be taken several times a day for long periods [66].

* **Biomedical assay of blood and urine analysis** – this refers to the concentration of ARVs in the patient's blood or urine. It is an objective way of assessing adherence and does not depend on the patient's report[66]. It is, however, not always accurate due to pharmacokinetic factors, difficulties with timing of tests, pill ingestion times and susceptibility to 'white coat effects'. It is also an expensive method and not always readily available.

b. Indirect measures

* **Medication Event Monitory System (MEMS)**

The MEMS is an electronic system that utilizes a computer microchip embedded in a specially designed pill bottle cap that records the time and duration of each bottle opening. Its benefits include objectivity, the identification of specific patterns of medication taking over time, higher rates of missed doses detected as compared to other measures, and that fact that it is fairly tamper-proof.

Graphs of MEMS data can provide behavioural feedback useful for patient's motivation[66]. It appears to be the most sensitive of methods used to measure and monitor adherence[19,28,38,67] and has been referred to, by Berg *et al*,[55,68] as a potential 'gold standard' for adherence assessment; when used properly, they can provide detailed longitudinal data that can be fairly accurate[35.] The major drawbacks of the MEMS include:

- It is expensive and cumbersome, particularly when multiple medications are used.
- Accuracy is compromised by how often the patient opens the bottle and removes a pill (or not) but does not take the medication.
- The use of blister packs and medications in liquid formulations are excluded because the patient has to open a bottle to withdraw medications.
- The interpretation and management of data from MEMS studies can be a challenge.

It is thus mainly used in clinical trials in resource rich countries.

* **Pharmacy refill record**

The pharmacy refill or log record has been used to measure adherence in some settings. This method uses refill data to calculate adherence. If patients do not refill at the appropriate times, e.g. if it takes a patient a longer time to refill treatment than expected, it is assumed that the patient is not taking medications

or is skipping some doses[71]. The advantage of this method is that it does not rely on patient report and it is less intrusive. Its major drawback is that it underestimates the adherence of patients who refill medications elsewhere, e.g. if they have to travel out and refill their medications outside the hospital pharmacy. [66]

* **Visual Analogue Scale (VAS)**

The Visual Analogue Scale (VAS) was recently validated as a tool to measure and monitor adherence to antiretroviral therapy.[72] The tool asks participants to "put a cross on the line below, at the point showing your best guess about how much of each drug you have taken in the last 3 or 4 weeks. For example, 0% means you have taken no drug, 50% means you have taken half your drug, and 100% means you have taken every single dose of your drug."[72]

The VAS is simple, quick, inexpensive and a valid instrument to accurately measure and monitor adherence. The major advantage over other adherence measuring instruments is that it can easily be self-administered, thereby saving the time of both researchers and participants.[72] Its major drawback is that barriers to adherence cannot be elucidated from these scores.

* **Pill count**

Pill counts are usually conducted in clinics or at unannounced home visits. Adherence with pill count is usually measured by counting the remaining pills,

and it is assumed that the pills in excess of what should have been taken represent missed doses. 'Pill dumping', the practice whereby patients remove pills without necessarily taking them, is an important drawback for this method. Also, assessments can be impractical if the assessment period does not coincide with prescription refills or if there are too many pills to fit into containers. Although it is inexpensive and relatively easy, it does not provide information about whether the pills are actually taken or if they have been taken according to schedule. Although VAS and pill counts suffer from similar drawbacks, VAS provides more valid information. Thus, pill count is usually used as an adjunct to other methods which estimate adherence.[25,38]

* **Service utilization records**

These can be used to assess adherence by calculating the percentage of appointments kept. This provides a direct measure of appointment adherence and an indirect measure of medication adherence. The records are only as accurate as the record-keeping system and the record review can be time-consuming and expensive. [66]

* **Patient self-report**

The patient' self-report is a relatively simple and efficient method of measuring and monitoring adherence in a clinical setting. In this method, adherence is assessed on patients' responses to a questionnaire and/or interview, or extracts from diaries. It is an inexpensive and necessary component of adherence

assessment. The most commonly used form of questionnaire was developed and validated by the Adult Aids Clinical Trial Group (AACTG) [35]. The problem with this method lies with recall and comprehension. To improve the accuracy of recall, different recall periods have been used. The general consensus, however, is that the shorter the recall period, i.e. less than a week[35] or less than a month, the greater the chance of accuracy.[70] Reporting accuracy may be improved upon if you 'give the patient the permission' to admit skipping a dose, use the patient's language, and provide recall cues over a brief time period.[67]

Several comparison studies have concluded that adherence is overestimated with patient self-report in comparison with the other objective measures such as MEMS. [55,64,67,70] Adherence behaviour varies from time-to-time and, therefore, a single adherence assessment does not necessarily correlate with consistent adherence beavhiour.[22]

It is, however, important to note that, despite its flaws, self- reported adherence is significantly associated with viral suppression, whilst self-reported non-adherence is associated with virologic failure.[55,70,71] This therefore makes it an appropriate tool to measure and monitor adherence. This study utilized self-report to measure adherence because it is a cheap and reliable method, providing valuable information by means of a questionnaire without the need for expensive laboratory or clinical investigations.

In conclusion, adherence is proving to be a weak point in antiretroviral therapy roll-out. To achieve the near perfect adherence apparently necessary for optimal effects, individuals often require assistance. To provide this assistance, adherence needs to be measured accurately. No studies have provided data on which surrogate markers of adherence best predict undetectable viral load, and all methods have advantages and disadvantages. A combination of different methods has been proposed for measuring adherence.[35] The selection of the methods to be used will depend on the focus of the research.

CHAPTER 3: METHODS

3.1 DEFINITION OF TERMS

- **Adherence**: "The ability of the person living with HIV/AIDS to be involved in choosing, starting, managing and maintaining a given therapeutic combination medication regimen to control viral (HIV) replication and improve immune function."[64]
- **Virologic failure**: Failure to achieve a viral load of <400 copies/ml within 4-6 months of starting therapy.[73-75]
- **Plasma viral load**: The measure of the quantity of HIV RNA levels in the plasma component of blood.
- **Antiretrovirals (ARVs)**: Drugs used for the treatment of HIV.

3.2 STUDY AIM

To identify factors that influence adherence in order to improve adherence to ARVs at St. Rita's Regional Hospital

3.3 STUDY OBJECTIVES

- To determine the demographic profile of adult patients on antiretroviral therapy at St. Rita's Regional Hospital.
- To measure self-reported adherence among adult patients attending the Dira go Direge Clinic at St. Rita's Regional Hospital.
- To correlate self-reported adherence with plasma viral load.

- To identify factors that influence adherence to antiretroviral therapy among adult patients at Dira go Direge Clinic of St. Rita's Hospital.

3.4 STUDY DESIGN

This was a cross sectional analytical study of patients living with HIV/AIDS, carried out at the Dira go Direge Clinic (which caters for patients living with HIV/AIDS) at St. Rita's Regional Hospital in Glen Cowie, Limpopo Province.

3.5 STUDY SETTING

St. Rita's Regional Hospital is located in Glen Cowie which is situated in Sekhukhune district, in the southern part of Limpopo Province. Sekhukhune district has an estimated population of 1 041 454 which makes up about 19% of the total population of Limpopo Province[3]. St. Rita's Regional Hospital was established in 1926. On average, about 200 patients are treated in the out-patient department, about 100 are treated in the HIV clinic and about 30 patients are treated in the Accident and Emergency Department on a daily basis. The hospital serves as a referral centre for six district hospitals and 16 clinics. It has 400 approved and 326 active beds. Limpopo province has an estimated HIV prevalence of 19.6% which is the second lowest prevalence among South African provinces.[74]

The Dira go Direge Clinic serves as the referral clinic for patients who either want to commence treatment with ARVs or are already receiving treatment. The clinic

was established in September 2004 to implement the governments roll out for ARVs. It started its first group of patients on ARVs in late September 2004. About 80 patients on average visit the clinic on a daily basis to receive treatment. The clinic runs for four days in a week, i.e. Mondays to Thursdays. Fridays are reserved for ward rounds in the sub acute ward and also for data collection and analysis.

Adherence counselling at the clinic is offered by lay counsellors who explain the role of ARVs in disease management as well as the need for 100% adherence and the implications of non-adherence. In addition, they explain what is required of the patients during each visit to the clinic.

At the time this study was carried out, three classes of ARVs were available in the public sector. These were:

(i) Nucleoside reverse transcriptase inhibitors (NRTIs)

- Thymidine analogues
    - · Zidovudine (AZT)
    - · Stavudine (D4T)
    - · Abacavir (ABC)
- Non-thymidine analogues
    - · Lamivudine (3TC)
    - · Didanosine (DDI)

(ii) Non-nucleoside reverse transcriptase inhibitors:

- Efavirenz (EFV)
- Nevirapine (NVP)

(iii) Protease inhibitors:

- Lopinavir/ritonavir (Kaletra)

The nucleotide reverse transcriptase inhibitors, Tenofovir and Emtricitabine, were not yet available in public hospitals in Limpopo at the time this study was conducted.

3.6 STUDY POPULATION

The study population comprised all adult patients 18 years or older who had been on ARVs for more than one year, and who were currently receiving antiretroviral therapy at St. Rita's Regional Hospital. At the time of the study, this population was 1 000 patients.

3.7 SAMPLING

From the estimated study population of 1 000 patients, the appropriate sample size was calculated using Epi-Info as show in Table I

Table I: Sample Size Calculation

Parameter	Value
Reference population (number of people on treatment for one or more years)	1000
Expected prevalence of adherence	85%
Worst acceptable deviation	90%
Study power	80%
Confidence level (Alpha level = 0.05)	95%
Effective sample size	169
Anticipated non-response (10%)	17
Total sample size	186

The expected prevalence was put at 85% as adherence studies carried out in USA, Cape Town and Johannesburg reported adherence levels to be in the range of 75% to 95%[13,15,26-28]. The worst acceptable prevalence from 85% that the researcher desired was put at 90%. This means that if 85% is the true prevalence rate, 5% would be the margin of error for the confidence interval.

Although the sample size was calculated as 169, we collected data from 188 participants as most participants approached were willing to participate in the study. Eligibility criteria for the study were:

1. Being on ARV for one year or above
2. 18 years or above
3. Willingness to participate in the study

Systematic random sampling was used to recruit participants with a sampling interval of 5 (because total sample size was 186 and the reference population was 1000). Patients are recorded on the clinic's ARV register, according to the date of commencement of ARV. The patients' names on the register were allotted numbers. The first 10 numbers were put into a hat and a number was randomly chosen as a starting point. This patient was approached for interview. Subsequently, every fifth name after this was selected. This process continued until all participants were recruited.

3.8 DATA COLLECTION TOOL

The measurement tool used was a version of the Adult AIDS Clinical Trials Group Adherence Questionnaire. The Adult AIDS Clinical Trials Group developed and validated a baseline adherence questionnaire to assess self-reported adherence among adult patients on ARVs in the USA[70] (see Appendix 1). This instrument has been modified and validated repeatedly to increase its sensitivity and specificity.[67,69] The time frames usually used in self-reported adherence questionnaires are for the past three or past seven days. Longer periods of up to one month may also be used as well. Both time frames have been validated against MEMS[69].

The questionnaire used for this study is an abbreviated version of this self-reported adherence to antiretroviral therapy developed by the Adult AIDS Clinical

Trials Group (see Appendix 1). Questions not relevant to this study were excluded from the questionnaire and the one week adherence measurement was used to increase recall. The questionnaire sought information on:

1. Socio-demographic variables
2. Important motivation and satisfaction information
3. One-week adherence
4. Reasons for non-adherence

Participants were asked about their adherence to ARVs in the preceding week. Because adherence was defined as taking at least 95% of the medication for the period, skipping a dose for the preceding week was defined as non-adherence.

The socio-demographic variables that were measured included: gender, age, marital status, educational level, occupation, income and membership of AIDS support groups. Psychological variables included motivation to take medications, disclosure and satisfaction with support from members of family and clinic staff. Descriptive statistics and stratified analyses were carried out to assess the effects of these variables on adherence.

3.9 DATA COLLECTION PROCESS

Data collection for this study was in two phases:

3.9.1 Phase 1: Face-to-face interviews

Face-to-face structured interviews were carried out to identify missed doses over one week. Interviews were administered by the researcher and a trained assistant. Interviews were conducted in the language of the participant and responses from the participants were translated from their language to English by the assistant. These responses were filled into the questionnaires by the researcher. Patients who were fluent in English were interviewed by the principal researcher alone.

The data collection process lasted 12 weeks.

3.9.2 Phase 2: Record review

After the interview, the same patient's record was reviewed. The patient's baseline and most recent viral load were recorded. At the initiation of treatment, baseline tests, including liver function tests, CD4 counts and viral load are usually carried out for every patient. This is repeated at 10 weeks and then at six monthly intervals to ascertain response to treatment according to the South African Department of Health recommendations. The changes in patients' viral load were compared to self-reported adherence obtained from the face-to-face interviews.

Non-adherence (virologic failure) was taken as failure to achieve a viral load of <400 copies/ml within 4-6 months of starting therapy.[73-75]

3.10 PILOT STUDY

A pilot study was carried out on 10 patients from the clinic who did not take part in the main study, to test the method for data collection (logistics) and to modify the questionnaire where necessary. The pilot study identified some key terminologies in the questions that needed clarification and these were amended accordingly.

3.11 SOURCES OF BIAS

A single adherence assessment gives only a snapshot of adherence behaviour. It has been recognized that individual adherence behaviour can differ over time and usually deteriorates with time[76]. Recall bias becomes a major problem when adherence is measured over long periods. Therefore, questions in the questionnaire were limited to a maximum time frame of one week (past seven days). This time frame has been validated against the MEMS and was found to have similar results.[67]

Interpretation of questions from one language to another is bound to differ from one individual to the other. To reduce such measurement errors, only one

assistant was used and the principal researcher provided her with training and closely supervised her interviews.

3.12 ETHICS

This study was approved by the Committee for Research on Human Subjects (Medical) of the University of the Witwatersrand. Permission to carry out this study was also granted by St. Rita's Regional Hospital (see Appendix 6) and Limpopo province Department of Health (see Appendix 7).

Participation was voluntary and all information was treated with utmost confidentiality. Patients who agreed to participate in the study were taken to a designated private room in the clinic where the interviews were conducted. Before administering the questionnaire, the purpose and nature of the study was explained to the participants using a standard guideline (see Appendix 2). Possible risks, benefits and rewards for participation to the patients were explained and addressed in this standard guideline. Each questionnaire was given a unique study number, and only the researcher had access to the personal information of the participants. Written Informed Consent was sought and obtained from all the participants (see Appendix 3). The principal researcher's contact details were made available to all the participants so that help and/or further information with regards to the study can be offered (see Appendix 4).

3.13 DATA ANALYSIS

The study data were entered into Epi-Info version 3.3.2. Statistical analyses were carried out in STATA version 9 (STATA Corporation, Tx, USA). Statistical analyses carried out included:

1. Descriptive statistics (mean and simple frequencies using charts and tables) for description of the socio-demographic variables.
2. Prevalence of one-week adherence and 95% confidence intervals.
3. Descriptive statistics to describe adherence by important demographic, social and psychological variables.
4. Correlation between adherence prevalence and changes in viral load.
5. Simple frequencies to describe common reasons given for non-adherence.

Hypothesis testing for association was done using chi-square test and student t-test. Chi-square tests were used to assess for significant differences in adherence prevalence for categorical variables while t-tests were used for continuous variables. Odds ratio was also calculated as a measure of association for categorical variables. The basic principle of the analyses was to assess if the people reporting adherence differed significantly from those who did not report adherence in terms of important explanatory variables like motivation and satisfaction.

All hypothesis testing was carried out at an alpha-level of 0.05. Any p-value less than 0.05 reflected statistically significant differences. The Fisher's exact p-value was reported in many cases because of the small expected frequencies in the cross-tabulation cells. Multiple logistic regressions could not be carried out due to small numbers. The small numbers in some of the cells was due to the very high prevalence of adherence.

CHAPTER 4: RESULTS

The number of eligible patients who were contacted for the study was 193, of whom188 consented to participate in the study. This was a response rate of 97%.

4.1 SOCIO-DEMOGRAPHIC CHARACTERISTICS OF STUDY PARTICIPANTS

The mean age of the participants was 39 and about 75% of the participants were females. About 65% of the participants had at least primary education (the level of education that is usually associated with literacy) and 57% had never been married. The majority (90%) of study participants had a total monthly household income of less than R1 000 and a similar proportion was unemployed. About 73% belonged to an AIDS support group. Of the remaining 27%, reasons given for non-membership included lack of information (16%), lack of time (7%), lack of money (3%) and lack of interest (1%).

The mean duration the patients had been on ARVs was 1.9 years and 43% had been on ARVs for more than two years.

Table II: Socio-demographics of study participants

Characteristics	n (%)
Age (188)	
≥40 years	77 (41)
<40 years	111 (59)
Gender (186)	
Male	47 (25)
Female	139 (75)
Education (188)	
> Primary	123 (65)
≤ Primary	65 (35)
Marital status (170)	
Married	62 (34)
Single	108 (57)
Divorced/Widowed	16 (8)
Living together	2 (1)
Employment status (194)	
Employed	18 (10)
Unemployed	166 (90)
Total household income per month (183)	
<1000 rand	164 (89)
≥ 1000 rand	19 (10)
Belongs to AIDS support group (188)	
Yes	136 (73)
No	51 (27)
Duration on ARV therapy	
> 2 years	81 (43)
1 - 2 years	107 (57)

4.2 SELF REPORTED PREVALENCE OF ARV ADHERENCE

4.2.1 Ever missed/skipped medication

Prior to being asked about one-week adherence, participants were asked when last they had skipped/missed a dose of their ARV drugs. This was to validate the response to the questions on one-week adherence. The majority of the participants (74.5%) reported that they had never skipped/missed their medications.

Table III: Proportion of study participants who had ever missed/ skipped a dose of their ARV medication

Characteristics	**n (%)**
Never missed	140 (74.5)
Ever missed	48 (25.5)
Total	188 (100)

Among the participants who missed at least a dose of their medication, 12.8% did so during the preceding week, and 14.8% during in the past month whilst 76% missed at least a dose for more than a month prior to the interview date.

A t-test showed there was no significant differences in the mean duration on ARV treatment between participants who ever missed a dose and those who had not ($p = 0.8785$) (Table IV).

Table IV: Difference in the duration on ARV between participants who never missed

	N	mean duration	mean diff	P value
Never missed	140	23.3	0.2	0.8785
Ever missed	48	23.1		

4.2.2 Prevalence of one-week adherence

The prevalence of one-week adherence was very high and satisfactory; 96.8% with a 95% confidence interval of 93.2 - 98.8%.

4.3 CORRELATION BETWEEN SELF-REPORTED ADHERENCE AND PATIENT VIRAL LOAD

4.3.1 Viral load results – for all participants and by adherence

To assess the correlation between self-reported adherence and patient viral load (PVL), PVL results were analyzed in two stages. In the first stage, PVL was analyzed as a continuous variable, reporting means and t-test results. In further analyses, PVL was analyzed categorically using chi-squared test because, for a sizeable proportion (77%) of the study participants, latest PVL results were below detection limit.

In the first set of analyses, PVL results were log-transformed to base 10. Table V shows that the latest PVL for all study participants were significantly lower than baseline values ($p < 0.001$). Also, latest PVL (mean = 2.7) were significantly

lower than baseline rates (mean = 4.7) for participants who were adherent to their medication (p-value < 0001). However, there was no significant difference for patients that were not adherent. The very small numbers in the latter group calls for caution in result interpretation.

Table V: Baseline and latest log patient viral load for all study participants by adherence group

Measurement	N	Mean (std dev)	Range	p-value
All participants				
Baseline viral load	188	4.8 (1.1)	1.4 – 6.6	< 0.001
Latest viral load*	43	2.8 (1.3)	1.4 – 5.6	
Adherence = Yes				
Baseline viral load	41	4.7 (1.3)	1.4 – 6.6	< 0.001
Latest viral load	41	2.7 (1.3)	1.4 – 5.6	
Adherence = No				
Baseline viral load	2	4.8 (0.6)	4.4 – 5.2	< 0.9663
Latest viral load*	2	4.8 (0.7)	4.3 – 5.3	

* Viral load was below detection limit (BDL) for 145 participants

In further correlation analyses, PVL was treated as a categorical variable. In one analysis, PVL was categorized as lower than baseline levels or not. In the second analysis, PVL was categorized as below detection limit or not. Both analyses showed similar results. Although these were not statistically significant, those patients who were adherent were about 1.7 times more likely to have a latest PVL below detection limit, and were also about five times more likely to have their latest PVL lower than their baseline PVL than those who were not adherent.

Table VI: Comparison between one-week adherence to ARVs and changes in patient viral load

Characteristics	N	BDL* (%)	OR	p-value	BBL** (%)	OR	p-value
All participants	188	77			96		
Adherence							
Yes	182	77	1.7	0.5363	96	5	0.1268
No	6	67			83		

*BDL – Below detection limit; *BBL – Below baseline level

4.3.2 Sensitivity and specificity of self-reported adherence

This relationship between self-reported adherence and viral load change is summarized using diagnostic indicators (sensitivity, specificity and predictive values) (Table VI). For this analysis, decrease in baseline PVL load is assumed to be the gold standard.

Table VII: Diagnostic agreement between self-reported adherence and changes in viral load

		Viral load decrease		
One-week adherence		Yes	No	Total
	Yes	175	7	182
	No	5	1	6
Total		180	8	188

Using a decrease in viral load as a tool, the prevalence of adherence in this study was about 96% (180/188). This is very close to the 97% reported by participants.

However, the overall agreement between both tools was about 94% (176/188). This is due to a few false positives and false negatives. Seven people who were classified as non-adherent by viral load decrease reported adherence (false positives) while five people classified as adherent by viral load decrease reported non-adherence (false negatives). The sensitivity of self-report was very high (97%) with a positive predictive value of 96% while the specificity was very low (13%) with a negative predictive value of 17%.

4.4 PATIENT REPORTED FACTORS THAT INFLUENCE ADHERENCE TO ARV THERAPY

4.4.1 Determinants of adherence

Stratified analyses were carried out to assess the effect of important explanatory variables on one-week adherence. Because only 6 of the participants were non-adherent, observed differences were not expected to be statistically significant. However, the analyses were carried out to assess the size and direction of any observed differences. In instances where cross-tabulation cells had no frequencies, odds ratios were not computed.

4.4.1.1 Socio-demographic variables

Table VIII summarizes the relationship between self-reported adherence and important explanatory variables. All the 62 respondents who were married, reported one-week adherence while most of the 108 people who were single (94%) reported one week adherence. Participants who had been on ARVs for

longer than two years were about four times more likely to be adherent than those who had been for less.

Table VIII: Bivariate analysis showing the relationship between adherence and important explanatory variables

Characteristics		**Adherent**			
	N	**[a]Yes (%)**	**[b]No**	**OR**	**p-value (Fisher's)**
Age					
≥40 years	77	97	3	1.56	1.000
<40years	111	96	4		
Gender					
Male	47	100	0	*	0.340
Female	139	96	4		
Education					
>Primary	123	98	2	1.94	0.418
≤Primary	65	95	5		
Marital status					
Married	62	100	0	*	0.087
Single	108	94	6		
Employment status					
Employed	18	100	0	*	1.000
Unemployed	166	96	4		
Total household income					
≥1000 rand	164	100	0	*	1.00
<1000 rand	19	96	4		
Belongs to AIDS Support Group					
Yes	136	97	3	1.32	0.665

Characteristics		Adherent			
	N	[a]Yes (%)	[b]No	OR	p-value (Fisher's)
No	51	96	4		
Duration on ARV Therapy					
>2 years	81	99	1	3.92	0.238
1 -2 years	107	95	5		

* Odds ratio not calculated due to some cells having no values
[a] Adherence = Yes
[b] Adherence = No

4.4.1.2 Other important variables

This section of the results shows the distribution of other important explanatory variables, such as motivation and satisfaction. One hundred and eighty six participants (99%) said they had disclosed their HIV status to somebody (table IX).

Table IX: Basic description of study participants by three psychological factors

Characteristics	n (%)
Disclosure of HIV status (188)	
Yes	185 (99)
No	2 (1)
Satisfaction with family support	
Very satisfied	159 (85)
Satisfied	17 (9)
Not satisfied	11 (6)
Satisfaction with clinic staff support	
Very satisfied	175 (93)
Satisfied	11 (6)
Not satisfied	1 (1)

4.4.1.3 Psychological factors

Cross-tabulation could not be done by these factors as most respondents indicated that they were motivated and satisfied with support from their family members and clinic staff. About 99% said they were motivated or highly motivated to take their pills regularly.

4.4.2 Reasons for non-adherence

Participants who were non-adherent (6) were asked to indicate from a list of statements what their reasons were for missing their drugs. Figure 1 summarizes responses.

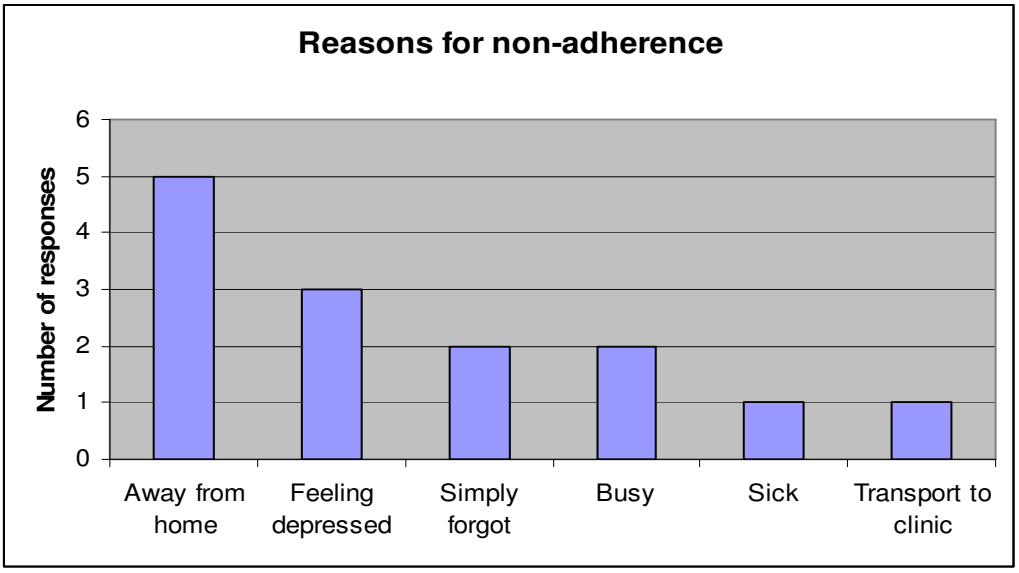


Figure 1: Reasons reported for non-adherence

CHAPTER 5: DISCUSSION

This study assessed the prevalence of self-reported adherence to antiretroviral therapy among adult patients attending St Rita's HIV clinic and compared the reported adherence to plasma viral loads, in patients who were adherent to their medication and those who were not. The influences of psychological factors and socio-demographic factors on adherence were also explored.

5.1 SOCIO-DEMOGRAPHIC CHARACTERISTICS

Gender and education levels are generally not associated with adherence.[17, 19, 25] In this study, it was found that people who achieved post-primary education were twice as likely to be adherent to ARVs than those who did not. This difference, although not statistically significant, is in keeping with other studies. [17, 18, 25]

The higher adherence rates reported in married participants as compared to those who were single is in keeping with other studies which have shown that having strong family and good network support is influential in facilitating adherence.[61] Family support has been shown to have a positive impact on adherence[60]. The fear of stigma prevents disclosure to family members and loved ones. Nachega *et al*[28] in their study on adherence to antiretroviral therapy in HIV-infected adults in Soweto, South Africa, reported that the odds of obtaining a >95% level of adherence decreased considerably with an increased fear of stigmatization (rejection, violence or both) by the participant's sexual partner.

These studies highlight that, despite continued educational campaigns and the availability of treatment, enduring stigma might be an important contributing factor to non-disclosure which leads to non-adherence.

The high proportion of study participants reporting disclosure, satisfaction and motivation might also explain the high level of adherence reported in this study as other studies have also reported that disclosure, patient satisfaction and motivation impact positively on the level of adherence.[17, 18, 25]

About 73% of the participants belonged to an AIDS support group. Those who did not belong to an AIDS support group gave reasons such as lack of information, lack of time, financial constraints and lack of interest. Membership to an AIDS support group was seen to slightly increase the likelihood of adherence. Nachega *et al*.[13] and Mills *et al*.[60] reported similar findings. Routinely encouraging patients to belong to an AIDS support group is a potentially explorable but less utilized method to improve adherence among patients on antiretroviral therapy, particularly in the setting of this study. Nachega *et al*.[13] in their qualitative study on the use of treatment supporters to improve adherence to antiretroviral therapy in HIV-infected South African adults, reported that a major social barrier for attaining excellent adherence is the stigma associated with HIV/AIDS. Helping patients cope with, and overcome the barriers posed by social stigma, is one of the themes of AIDS support groups.

5.2 PREVALENCE OF ARV ADHERENCE

5.2.1 Prevalence of One Week Self-reported Adherence

The prevalence of one week adherence was 96.8% (95% CI: 93.2-98.9%). The majority of the participants (about 75%) reported that they had never missed their medications. The results of those (25%) who have missed their pills in the past indicate that, although a sizeable proportion of the participants had missed a dose of their medication sometime in the past, this seemed to reduce with time. This suggests that the nearer the patient's appointment time to the hospital visit, the more likely they are to be adherent to their medication, as tests for surrogate markers like viral load and CD4 count could be taken and the patients might not want to be 'caught out'. It could also be a reflection of recall problems which got worse with increasing time. This correlates with the findings of Arnsten *et al.*[55], Liu *et al*.[77] and McNabb.[78]

There were no statistically significant differences between participants who had ever missed a dose and those who did not by the duration they had been on ARVs. However, people who had been on ARVs longer than two years were about four times more likely to be adherent than those who were not. This suggests that the longer the participants have been on ARVs, the more likely they are to be adherent. This corresponds to the findings of Mills *et al*.[15] and Carlucci[24]. The most likely explanation for this is that the patients in sub-Saharan Africa are early in therapy, and are thus still experiencing dramatic increases in health status, which usually precedes long-term adverse effects of therapy[15]. It

has also been explained that Africa regimens are relatively simpler than those in North America and thus could be easier to follow and maintain over time[15]. Another plausible explanation for this is that patients who have stayed longer in therapy might have developed and perfected coping mechanisms that help them to remember, for example, the time to take their medications or how to include their medications in their luggage when travelling and also how to adjust their dosing schedule to their itinerary when out of station.

Reports from Senegal[47] and Cameroon[48] seem to suggest the contrary. These reports showed decreasing adherence among study participants over time. Gill *et al.,*[46] in their review of adherence to antiretroviral therapy in sub Saharan Africa, believe that there has been a problem of decreasing adherence among patients on antiretroviral therapy ever since antiretroviral therapy was made available in sub Sahara Africa, as in North America. Their opinion was that publication bias in which results from less successful programs went unreported might have been responsible for the exclusion of these studies from publication. They further explained that questions about the feasibility of antiretroviral therapy in Africa by Harries *et al.*[43] and others[15,26] which led to an attempt to justify the call to make antiretroviral therapy available to sub Sahara Africa might have led to this publication bias.

The study carried out by Schneider *et al.*[41] on performance and capacity of second generation comprehensive care management and treatment (CCMT)

sites in Gauteng Province showed that the four sites assessed were running optimally for about two years. After this there was a rapid growth in patient numbers that led to space and staff shortages, a long waiting list for treatment and patients being turned away at some of the sites.

Gill *et al*.[46] also reported that most of the early studies that were carried out in Africa were cross sectional in design, hence high adherence levels might decline over time. This is in agreement with Schneider *et al*. [41]

The importance of the findings by Gill *et al*. [46] and Schneider *et al*. [41] in relation to the reports from Laurent *et al*.[47] and Akam[48] is that programme strategies that focus on maintaining high levels of adherence particularly through ongoing education especially within the first months of therapy should be introduced and incorporated into the clinic's regular programmes.

5.2.2 Prevalence of Adherence by Viral Load

The latest viral load values were significantly lower than baseline values ($p < 0.001$). This reduction in viral load for all study participants reflects the almost perfect adherence in the group (about 97%). It also reflects that all participants had been on ARVs for more than six months, a duration at which ARVs are expected to have positive effects on viral load.[73-75]

Using a decrease in viral load as a tool to assess adherence, the prevalence of adherence in this study was found to be 96% (180/88). This is very close to the

97% reported by the participants. Combining both tools (viral load and self-report) the overall agreement between both tools was 94% (176/188). Thus, the average adherence prevalence in this study is taken to be 94%. This is similar to the findings of Orell *et al.*[27] who reported an adherence prevalence of 93.5% by pill count and self-reported questionnaires.[1] The sensitivity and specificity of the patient report found in this study indicate that face-to-face adherence interview was very sensitive at identifying adherent patients but weakly specific at excluding non-adherent patients.

The average adherence prevalence from this study is higher than that reported by Nachega *et al.*[28] from Soweto, South Africa who reported 88% adherence by self-reported questionnaires and viral load. Other South African studies reported by Brown et al[55] (76%) and Ferris et al[52] (77%) also reported lower prevalence rates.

The apparent high prevalence of adherence recorded in this study might be explained by the observation made by Schneider *et al.*[41] in their report on the capacity of second generation comprehensive care management and treatment sites in Gauteng Province. At the time of their assessment, the number of patients on ARVs in each of the sites ranged from 600 to 1700 patients; health care personnel attended to 50 to 200 patients a day. During this period, services were rated as optimal and were on par with first generation model programmes. Two years later, due to an overwhelming increase in patient load, static or

decreasing staff strength, space shortages; the Department of Health's norm of 12.5 members of staff to 500 patients was not being observed.[41] This led to services being cut back, staff burn out and dissatisfaction.

At the time this study was carried out at the Dira go Direge Clinic; there were around ten staff members to 1500 patients.[42] Service delivery at this stage could be considered to be optimal and this might have impacted positively on adherence.

5.3 REASONS FOR NON-ADHERENCE

Because only about 3% of the study participants were non-adherent, observed differences were not expected to be statistically significant. However, the most common reasons indicated by the participants for non-adherence were being away from home, feeling depressed or simply forgetting to take their medications. Similar reasons were implicated by Mills *et al*.[60] in their systematic review of adherence to HAART in developed and developing nations.

Having a concurrent illness such as depression is an independent risk factor for non-adherence to ARVs[79]. This could be because patients become overwhelmed with the diseases and their treatment and may not be able to cope with treatment.

Mills *et al.*[60] reported that patients simply forgetting to take their medications or being away from home or forgetting not to take their medications with them are important barriers to adherence. The explanation for this might be that when patients start taking their treatment, they feel very weak and are reminded of the devastating effects of HIV/AIDS. This motivates them to take their treatment[28]. Patients usually get past this period after the first three months of treatment, and begin to experience marked physical improvements such as weight gain, fewer opportunistic infections, and overall improvement in qualify of life[13]. This makes them shift focus to other pre-occupations in life as they now feel strong and healthy. As such, they may not see the urgent need to adhere strictly to their ARVs.

Patient-related barriers as reported by Mills *et al.*[60] in the same study included: having a co-existing substance addiction, financial constraints, difficulty understanding treatment instructions, the need for compliance, and the presence of concurrent diseases or illnesses. Other than having a concurrent disease or illness, these reasons were not mentioned as barriers to adherence by the participants in this study.

CHAPTER 6: CONCLUSIONS AND RECOMMENDATIONS

6.1 CONCLUSIONS

This study measured the prevalence of adherence to antiretroviral therapy at St. Rita's Hospital, Glen Cowie using a one-week adherence questionnaire and a decrease in viral load within six months as a surrogate marker for adherence. The levels of adherence observed in the study were very satisfactory. Self reported adherence by questionnaire was 97% and 96% when using decrease in viral load. Adherence self-reported by questionnaire was highly correlated with adherence measured by decrease in viral load with 94% agreement.

This high level of adherence might be a reflection of patients' satisfaction with the support and effort of the clinic staff, as 93% of the respondents were very satisfied with the services that they received.

6.2 RECOMMENDATIONS

- There is need to maintain and, if possible, improve upon the high prevalence of adherence to antiretroviral therapy seen in this particular setting as well as to replicate this in similar settings.
- Adherence counseling should be provided at every visit and particularly emphasized and strengthened for patients with chronic diseases especially depression.
- Strategies to enhance adherence, such as the incorporation of adherence questionnaires at specific intervals, as is done with viral load and CD4 count, should be introduced. Adherence reminders such as medication diaries, pill boxes and cell phone alarms should be encouraged.
- All patients should be routinely encouraged to join AIDS support groups from their first visit to the clinic and information regarding this should be made available to all the patients.

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