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THE UNIVERSITY OF THE WITWATERSRAND

THE SCHOOL OF PUBLIC HEALTH

A STUDY ON THE BARRIERS TO ANTI – RETROVIRAL THERAPY ADHERENCE AMONG HUMAN IMMUNODEFIENCY VIRUS – INFECTED ADOLESCENTS IN GABORONE (BOTSWANA)

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A research report submitted to the Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, in partial fulfillment of the requirements for the degree of Masters of Public Health in the field of Health Measurement

22nd February, 2012

DECLARATION

I, Maimouna Ndiaye, declare that this report is my own work. It is being submitted for the degree of Masters in Public Health in the field of Health Measurement in the University of the Witwatersrand, Johannesburg. It has not been submitted before for any degree at this or any other University.

Signature:

Date: 22nd February, 2012

DEDICATION

To my late sister, Fatoumata Ndiaye, (10/11/1969–10/02/2008)

ABSTRACT

Introduction: Barriers associated with good adherence to Antiretroviral Therapy (ART) among human immunodeficiency virus (HIV) infected adolescents are multiple and complex. Those barriers contribute to low adherence levels putting infected adolescents at risk of developing resistance and decreasing their survival time. Patients care givers psychosocial and demographic variables, medication related factors and health care delivering factors are among the barriers that correlate with non adherence to antiretroviral drugs (ART's) among HIV infected adolescents. Those barriers vary across individuals within the same population of adolescents.

This study was conducted to determine the level of adherence among HIV infected adolescents on ART and to identify barriers associated with non adherence among this population attending the Botswana Baylor Children's Clinical Center of Excellence (COE) in Gaborone, Botswana.

Materials and methods: A cross sectional analytical study using quantitative data was performed. A structured, self administrated questionnaire adapted from the AIDS Clinical Trials Group (ACTG) was used to identify the barriers while the socio-demographic and clinical data were retrieved from study participants' medical records. The adherence level was estimated using the pharmacy pill count technique. The adolescents aged 13 to 18 years receiving ART for more than 6 months and attending the ART National Program at the time of the study and who did assent and had their care givers consent to participate in the study were included in the analysis.

Results: A high adherence level (75.6%) was reported among the study participants. Besides gender, no other socio-demographic and clinical variables showed association with non adherence. Male adolescents were found to be 70% less likely to adhere to their medication than their counterpart females [p= 0.020, OR=0.30, 95% CI (0.10 – 0.85)]. Furthermore adolescents

who missed a dose because their pills were not collected from the pharmacy either by themselves or by their care givers were 77 % less likely to adhere to their ART medication than those who did not miss a dose because they had their medication collected [p= 0.019, OR= 0.23, 95%CI (0.064 – 0.837)].

Conclusion: A high proportion of HIV infected adolescents attending the Baylor Center of Excellence ART National Program were adherent to their medication. Despite the high level adherence to ART among this age group, interventions to improve adherence level should be designed with a focus on male adolescents and to reinforce counseling of care givers and adolescents about the hazards of poor adherence to treatment. Further research is however, needed to elucidate more about the two main barriers that were found to be significantly associated with non adherence among adolescents at Botswana Baylor Children's Clinical Center of Excellence: male-gender and medication collection from the pharmacy.

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This degree is a contribution to my personal and professional development as a pharmacist and my hope that findings from this study improve the quality care of HIV infected patients as well as improve the health system in the Republic of Botswana.

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CHAPTER 1:INTRODUCTION

1.1 BACKGROUND

The accessibility of anti retroviral therapy (ART) has transformed the Acquired Immuno deficiency Syndrome (AIDS) from a debilitating and fatal disease to a chronic and manageable one (1).

However, despite the encouraging increases in the accessibility of ART, global donations, the affordability and use of generic drugs by governments, the proportion of people in need remains high. In 2005, it was estimated that 200,000 children below 15 years were receiving treatment worldwide out of the 2.1 million children that were infected with the Human Immunodeficiency Virus (HIV). The daily infection rate was estimated at 1,500 children (1). Among those children infected, 2 million live in Sub-Saharan Africa (2, 3).

It has been shown that ART based on triple therapy (three different drugs, up to three different classes or highly active antiretroviral therapy, HAART) compared to double and mono-therapy, has been significantly associated with an increase in survival among HIV infected patients who are adherent to the treatment (4). Adherence to the medication is a shared responsibility between the health care provider and the patient that involves the process of: taking the right dose at the prescribed time, following food restrictions, and not skipping doses as the result of irregularity in routines (5). The risk of death has been found to be lowered by 64% in people on ART (3, 4) and by fivefold in child (6). For this reason, ART is recommended for all infants, children, adolescents and adults infected with HIV (7). In 2007, WHO and UNAIDS estimated that 370,000 children were in need of ART (8), which represented only 6% of the total number of people on ART (9).

A good and sustained adherence to ART remains the key factor for any successful ART. It is now well known that failure to adhere to treatment allows the rapid replication of the virus and the generation and the spread of resistant strains that are no longer responsive to available anti-retroviral drugs (ARVs), posing great risk of public health (4).

Maintaining adherence to ART is a challenge for individuals with chronic diseases, even when the regimen is simple and the patient is asymptomatic (6). Children and adolescents may face obstacles to achieve adherence.

A successful treatment outcome for a child on ART relies on the commitment and involvement of the care givers (8). Adolescents at this time of their age are already faced with the natural challenges of adolescence and do not want to be different or perceived different from their peers (5).

1.2 BACKGROUND INFORMATION ON BOTSWANA HIV & AIDS

In response to the HIV epidemic that was threatening the country with extinction of its population, Botswana was the first African country to provide anti-retroviral drugs to all HIV positive individuals in need. The National Program launched its six year (2003-2009) National Strategic Framework in response to HIV and AIDS in 2003.

Currently, the population of Botswana is less than 2 million. In 2007, an estimated 300,000 people were living with HIV, thus, representing a prevalence rate of 23.9%. The latest survey, Botswana AIDS Impact Survey III in 2008 has shown a prevalence rate of 17.9% and an incidence rate of 2.9% (10). The result of that survey has shown a trend of infection with an increase of the prevalence with age with a peak in the group age 30 to 45 years (40%) and for

the incidence with a peak in the group age between 45 to 49 years of age (7.3%). The age group between 15 to 19 years has presented with the lowest incidence rate (0.7%).

Children are highly affected by the burden of the disease. 16 % of children aged between 0-18 years are orphans (10).

The creation of the Botswana Baylor Children Clinical Center of Excellence (COE) in 2003 has been an important step in the management of pediatric HIV in Botswana. This center, which is the product of a public private partnership between the Baylor College of Medicine, one of the United States premier medical schools, the Princess Marina Hospital, and the Government of Botswana, is the first of its kind in Africa. The center has been created to provide a comprehensive care that comprises: primary, specialized medical care and psycho-social services for the HIV infected infants, children and families. Today, an average of 1972 children aged between 0 and 19 years of age are attending the COE.

To cater for the needs of the growing population of HIV infected adolescents that are attending the COE, an adolescent clinic was opened in 2005.The clinic, in addition to the medical treatment, is providing specialized care and support to help adolescents with coping strategies to overcome the challenges associated with puberty and adolescence and to live positively with HIV. In 2011, 641 teenagers aged between 13 to 18 years were enrolled in the ARV National Program.

1.3 PROBLEM STATEMENT

Adherence to therapy is a universal challenge with all illnesses in all age groups (11). However, in the context of HIV/AIDS, ART is a lifelong therapy that has shown to improve the quality of life of people (adults and children) infected by HIV. Consequently, a perfect adherence (process

of taking 95% of ARV's prescribed) to the ART has to be maintained consistently in order to prevent resistance to the drugs and the progression of the disease to death (4). In Sub Saharan Africa, it has been shown that adherence to ART among HIV infected adults is much higher than that of their counterparts in North America (80% and 55%, respectively) (12) and much higher than that of the children (3, 13).

Since ART has been shown to improve outcome of the disease, adherence is a strong indicator of therapeutic impact (11). Three main factors have been identified to be barriers to a good adherence to ART among HIV infected adolescents. There are factors related to children themselves and care givers to on whom the children rely for their treatment, those related to the drugs and the complexity of the regimen, and those associated with the environment (system of care) (8). In addition to that, there is no gold standard technique that accurately measures the level of adherence to ART (14). This is critical as adolescence is a period of great change where teenagers are under physical and emotional changes (increased autonomy, rapid growth, sexual maturity) and trying to cope with new responsibilities and external factors that they do have less control of. For that reason, factors that could result in low medication adherence in adolescence must be a matter of concern, because they are the ones who could benefit from a successful ART to prolong their life expectancy as there still is no cure for the disease.

1.4 JUSTIFICATION

ART treatment in Botswana is one of the success stories of Africa. According to WHO, 95 % of people in need of treatment have had access to ART in Botswana. In 2005, 54,378 adults and 4,582 children were treated with ARVs. By 2007, the number of people on ART had increased to

84,000, and there are today more than 30 sites where ARVs are dispensed by personnel trained in HIV management (15).

Despite all the great effort that Botswana has made in combating HIV/AIDS, the achievement of national pediatric HIV care and treatment is lacking behind: lack of structure, data and policies (15).

Studies done on adolescent adherence to ART have always shown a suboptimal adherence to ART among HIV infected adolescents compared to that of adult (3,12 and 13). However, very few studies have been done to depict the major factors that could prevent HIV infected adolescents to maintain an optimal adherence to the medication. In Southern Africa in particular, no study has investigated barriers that could be associated with HIV infected adolescents adherence to ART, the majority of the studies have focused on assessing the correlation between the suboptimal adherence and the virological and immunologic outcome to ART. In Botswana, only one study has been done which focused on the relationship between HIV disclosure, pediatric ART adherence, perceived stigma and gender in Botswana (16), but that study was not focused on adolescent's adherence to ART.

Presently, in addition to the population of HIV infected adolescents that is enrolled in the National ARV Program at COE, there is an increasing number of young HIV infected children that is growing to become adolescents, still no studies have been done to assess the adherence level among adolescents on ART at COE and to investigate potential barriers/factors that may influence their adherence to the medication.

Therefore, this study aims to assess the adherence level to ART and to identify barriers/factors associated with adherence among the HIV infected adolescents that are enrolled in the Botswana

National ARV Program and are attending the comprehensive healthcare facility, COE, in Gaborone.

CHAPTER 2: LITERATURE REVIEW

Botswana has the highest HIV/AIDS prevalence rate among Sub-Saharan African countries (17). In 2007, an estimated 300,000 people were living with HIV representing a prevalence rate of 23.9% (10). The results of the latest survey, the Botswana AIDS Impact Survey III 2008 showed a prevalence rate of 17.9% and an incidence rate of 2.9% (10). This reveals a trend toward an increasing prevalence rate with age with a peak in the age 30 to 45 years (40%) group and increasing incidence with a peak in the age group between 45 to 49 years of age (7.3%). The age group between 15 to 19 years presented with the lowest incidence rate (0.7%) in this survey.

Children are highly affected by the burden of the disease. Sixteen (16 %) percent, ninety three thousand (93 000) children between 0-18 years of age are orphans (10, 18) and two and a quarter million young people in the fifteen (15) year old age group in Botswana are infected with the HIV/AIDS virus (10,17).

The National ART Program has made tremendous success in availing treatment to 95 % of the population. In 2009, more than 95% (8409) of HIV infected children less than 15 years of age were on anti-retroviral therapy (ART) in Botswana and the prevalence rate of HIV infected children born from infected mother was reduced to 3.8% (17). However, other programs such as prevention through AIDS education in schools and in the community have not made significant impact (10).

In the area of child care, the national pediatric HIV care and treatment in Botswana is lagging behind due to lack of structure, lack of data and lack of policies (15). The Children's Care Act of 2009 is the only law that focuses on the care and support of orphans and other vulnerable children.

As there is no cure yet for the disease, adherence to ARV medication is essential for HIV infected children and adolescents to prolong life expectancy and maintain good health. In 2011, among 893 adolescents between 13 and 18 years of age attending the COE, 587 (65.7 %) were secondarily infected and 288 (32.3%) prenatally infected. Adherence to ARV medication is a shared responsibility between the health care provider and the patient involving behavior changes such as taking the right dose at the prescribed time, following food restrictions, and not skipping doses as a result of irregular routines (5).

Child and more particularly adolescent adherence have not been widely studied (11) in contrast to the number of studies conducted on adult adherence. Currently, existing study findings on barriers to child and adolescent adherence to ART were influenced by the culture of a specific ethnic group or population making results invalid for other populations even in the same country (7, 14). Generally the literature has shown that three main factors may either negatively or positively affect child and adolescent adherence to ART (4). These factors are related to the patient and the family or care givers, drug regimen complexity, and health care delivery systems (4).

2.1 PATIENT AND CARE GIVER RELATED FACTORS

Adherence issues in children are principally related to the caring of a child with HIV/AIDS and the transition from childhood to adolescence. Those factors are demographic and psycho-social.

Studies have found that impaired cognitive and behavior problems, mental health disorders, substance abuse and structural barriers affect the psycho-socio development of the child and impact negatively on young children/adolescent's adherence to ART (14)

First, behavioral problems have been shown to be related to non adherence. Many studies conclude that high self efficacy to adhere to ART and high outcome expectancy regarding effectiveness to ART are the most important predictors of medication adherence. Self efficacy or acceptance of the treatment is defined as ‘‘one’s sense of being able to adhere to the medication prescribed” while the outcome expectancy is “the belief in the treatment outcome to improve the health status” (14).

However, as the child matures into adolescence and is faced with the natural challenges of adolescence, studies have shown that association between an increase of autonomy and the adolescent’s refusal to take their medicine. Other contributing factors are related to the regimen fatigue (16), clinical stage of the disease and changes in the health status (improvement as well as deterioration) (4).

Studies have also shown that mental health disorders could also impact negatively on non adherence. There are five types of mental health disorders that impact on the adolescent’s adherence to ART. These are attention deficit/hyperactivity disorder, anxiety disorder, mood disorder, developmental delay and schizophrenia. Among these are mood disorders of which the depressive symptom has been found to be the most common disorder affecting HIV infected adolescents. It also happens to be the most difficult mental health disorder to diagnose in children (5, 6 and 14). Mental health disorders are generally related to the care giver’s stressful life events that could impact negatively on psycho-social adjustment of the child and adolescent’s (6, 19). It has been shown that an adolescent who is not aware of the care giver’s stressful life and his/her history of drug abuse has a better adherence to ART (20).

Structural barriers are also found to be associated with adolescent’s non adherence to ART. The different structural barriers encountered among HIV infected adolescents on ART, are related

both to children/adolescents and their care givers. These factors are various even though their influence on adolescent ART's adherence varies between regions.

In USA, a study conducted on adolescent adherence to ART showed that with the exception of homelessness, all remaining structural barriers identified affect adolescent adherence to the medication (14). The barriers identified by the study were lack of medical insurance, lack of transportation to the clinic or getting medication prescription filled, lack of job or attendance in school, lack of a relationship with the family or with other children. However, in Brazil, homelessness is a structural barrier that could interfere with an adolescent's adherence to their medication. Homeless HIV infected adolescents that stay in support houses (shelters for children affected and infected by HIV/AIDS and are offered out of hospital care, food, transportation to hospital visit and enrolled at school) are faced with the stigma and discrimination associated with HIV/AIDS in the society (21).

Stressful events as identified in studies such as, the day to day or routine changes, dropping school or repeating a grade in school, housing and financial problem, a poor caregiver, unstable physical and mental status, the death of a parent, changes in family structure and the lack of nutritional support of the care giver (20) may result in a decrease of adolescent's adherence to ART (6, 19). However, it seems that there is no association between an HIV infected child's cognitive impairment and medication adherence (22). A child with cognitive impairment has less knowledge about the medication and has limited ability to understand the intermediate and long term consequence of non adherence (6, 22).

Furthermore, gender (female adolescent) and the age (older) of the child seems to correlate negatively with adherence to ART (6, 23 and 24).

Good communication between the care givers and the child/adolescent is another psycho-social factor that influences positively on HIV infected adolescent adherence to ART (21). These factors influence mainly adolescence's adherence to medication in two ways.

Firstly, good and open communication between care givers and the child creates a supportive environment that contributes to the psycho-socio development of the child (21). The child not only gains knowledge about the disease and the medication during his illness experience, but as the child grows older and becomes aware of environment changes, the open communication seems to help the child build the self-confidence to fight the forces of stigma and discrimination. This helps to reduce the confusion and distress (for things that have been kept in secrecy from him) and exhibit positive attitudes that prevent unhealthy, risky behaviors such as unsafe sexual practice and treatment adherence problems (21, 16).

Additionally, good and open communication between care givers and the child has been demonstrated to be a useful in easing the process of disclosure by the care giver (21). "The proper time approach" for disclosure of a child's HIV/AIDS status remains controversial (21) and caregivers who fear to disclose the child HIV status delay the process. The disclosure process is viewed today to be an important support mechanism for adherence as a child gets mature and starts questioning the care giver about the medication (22). In sub- Sahara Africa, a child is under the care of the family. This family structure may be characterized as an extended, conservative unit, comprised of parents, grand–parents, uncles, and aunts.

In the era of HIV/AIDS, the care giver is the usually the one who is physically able to administer or ensure that the patient is taking his medication as prescribed. In Sub-Sahara Africa, the aunt may have the authority or a say on matters regarding a child but she may not necessarily be the care giver (25). In most cases, grand-parents are the care givers of orphans who have lost their

parents because of AIDS and their attitude or behavior towards the medication can impact the child's adherence to ART (25). However, as the child grows older, the close supervision of the care giver tends to diminish. Studies conducted on pediatric adherence to ART in the Ivory Coast have shown a correlation between the non adherence to ART of older children and the lack of supervision by the care giver (9).

Higher education of the care giver and a care giver who is not the biological parent of the child are other factors that seem to improve children adherence to medication (24). Studies conducted in Southern Africa, Botswana, have shown that young children whose care givers were their grandmothers had better adherence to ART medication than those whose care givers were their biological mothers. In addition to that, the same study showed that young children that were adherent to their medication had care givers with excellent adherence self efficacy and a strong bond with the medical team especially the nurses at COE. However, contrary to pediatric adherence study conducted in South Africa, Cape Town, the study in Botswana did not show any association between young children's adherence to ART and the care giver's level of education, age, and his HIV status (16). The Cape Town study has shown that it is the caregiver's overall education and not just his ability to describe a regimen (health literacy) that impacts more on treatment adherence (26). In addition, the Botswana's study has shown that a care giver perceived stigma from the family had a positive impact on the child adherence to ART. The conclusion was that understanding of HIV/AIDS and the adherence to ART by the care giver assisted in keeping the child's disease secret from the stigmatizing family (16).

The care giver's belief and trust in the medication have also been associated with children's adherence to ART. Mistrust of western medicines by African and African-American care givers have resulted in suboptimal adherence of children on ART in Africa (27).

2.2 FACTORS RELATED TO DRUG REGIMENS

The second factor that impacts on child adherence to ART is the drug regimen. The ART medication regimen is actually a key challenge in ART adherence for all classes of age (4). It has been shown that the complexity of the drug regimen along with strict dietary instructions, storage conditions and adverse effects of drugs (toxicity) may negatively influence adherence to ART. The class of drugs may be another factor affecting adolescent adherence to ART. A study conducted in the United States (6) found an estimated rate of adherence in children to be equal in all for the first three classes of ART: non nucleoside reverse transcriptase inhibitors (NNRTI's), nucleoside analogue reverse transcriptase inhibitors (NRTI's) and the protease inhibitors (PI's), while, one conducted in the Ivory Coast (West Africa) found that children are non adherent with regimens that comprise Efavirenz, a NNRTI's (7, 9). In addition, results from studies conducted in Togo, another West African country, supported findings from the Ivory Coast study correlating imperfect adherence among children on regimens without NNRTI's. However, studies conducted in the USA have shown that children with cognitive impairment are likely to be non adherent to regimen comprising PI's (5).

Even if the pill burden of the drug regimen as a barrier to good adherence was not commonly found to be the subject of most literature studies (6), the Togo's study showed that children (0-15 years) taking more than six pills/syrup spoons per day reported a low adherence to ART (7). It has been shown that some drug regimens for children could count to a total of 14.7 capsules or

pills per day (3). The non availability of fixed dose pediatric formulations of ARV's (4, 6) still remains a major challenge to achieving acceptable adherence rates among HIV infected children on ART.

Other factors that contribute to suboptimal adherence to ART among HIV infected children are identified as regimen fatigue, increased autonomy among older children forgetting to take the medicine at the prescribed time, difficulty of integrating the regimen into a daily schedule or routine as the child grows older and is busy with other things, and failure to maintain adherence to treatment when the child is far from home (19). However, social support with medications has been shown to increase HIV youth adherence on ART (5).

2.3 FACTORS RELATED TO HEALTH CARE DELIVERY SYSTEM

The health care delivery system plays a key role in children/adolescent adherence to ART. Firstly, it involves the care giver, child and or adolescent relationship with the clinician in terms of communication, information and education. The existence of structures that address or support adolescent psycho-social issues (4), care givers on issues of adherence complexity and challenges (children refusal to take medication), disclosure of the child's HIV status and counseling on the adverse effects of the drugs, have been shown to improve adolescent adherence to ART and the emotional wellbeing of care givers (19). Other factors related to the health care delivery system involve reliable ARV supply chain management processes (4, 7 and 9), a centre for follow-up of defaulters (patients who fail to maintain 90 to 100% adherence to their medication) and management of children with failing ART regimen.

At Baylor COE the health care services include the dispensing of the ART that is ensured by the pharmaceutical officers (1 pharmacist and 1 pharmacy-technician) that have been trained in

Pediatric HIV /AIDS Management and Care. The treatment adherence counseling and support is another service offered and is provided by the nurse in charge of the national ART program. The unit assesses the readiness of the care givers before initiating the ART and also provides support for non adherent patients. Non adherent adolescents are followed by the psychologist at the psycho-social unit before becoming members to Baylor Adolescent Teen Club. The monitoring of side effects of ART is provided by the medical team. All patients are monitored by a medical doctor with the assistance of a local nurse who is fluent in Setswana, the official language. The same medical doctor monitors the side effects. The screening for HIV of children (including six weeks old new born children) and their parents are provided by the center. Holistic care services are also provided to the affected families (health education on HIV prevention, psychological support to optimize the elimination of stigma) by the centre.

Finally, even though studies have not shown an association between health literacy and children adherence to their medication, there is evidence that regular visits and interaction between the HIV infected or positive children and the health care provider can improve health literacy (22). Health literacy is 'the degree to which individual have the capacity to obtain process, and understand basic health information to make appropriate health decision' (28).

2.4. TECHNIQUES OF MEASUREMENT OF ADHERENCE

Adherence to ART is crucial and the aim is to prevent virus replication, resistance, and promote the health and survival of the HIV infected patient on ART. However, despite the multiple techniques of measurement of adherence, there is no gold standard technique to accurately evaluate children and adolescent's adherence in practice. Therefore, the reported rates of

adherence level may vary according to the method of assessment (26) and result in the difficulty to generalize findings across studies on HIV infected adolescent's adherence to ART.

There are direct and indirect techniques for adherence measurement (11). The direct methods involve the biological assay of the active drug, its metabolites and other markers in body fluid (29).

The indirect methods are self reporting and care givers report (11, 29), clinician assessment (11, 30), medical chart review, clinical attendance, pill count or medication return (26), pharmacy refill record (11), the electronic drug monitoring (MEMS) (11), behavioral observation (as directly observed therapy) (11), resistance testing (11) and unannounced pill count (26).

All of these methods have limitations in validity, reliability and feasibility (31). However, it seems that MEMS and unannounced pill count could be the gold standard technique of measuring accurately the medication adherence (26, 31).

The assessment of the rate of prescription refills can give an indication of adherence, but does not ensure that the child is ingesting the medication. Two studies have concluded that the prescription refill method could be a reliable method of measuring adherence among HIV infected adults (25) and adolescents (13) on ART. The assessment of the clinical response (virological and immunological response) is also an indirect method, because other factors besides adherence to ART can have an impact on the immunological status. In addition, a virological failure is not always caused by non- adherence to ART (32).

Self-reporting questionnaires are generally efficient means of assessing adherence and although such methods have been reported to overestimate the adherence by 30%, their accuracy may be affected by the wording of the questions (32).

At Baylor COE, the pill count is the technique used by pharmaceutical officers to measure adherence to ART over the previous month, as medication is given out on a monthly basis. Adherence to ART is considered perfect when the pill count estimate is superior and equal to 95% of ARV's taken by the child (4).

CHAPTER 3: METHODS

3.1 DEFINITION OF KEY TERMS

3.1.1 Adherence:

Adherence to the medication is a shared agreement between the care provider and the patient that involves the process of taking the right dose of the medication at the same time, following food restriction, and not skipping doses as the result of irregularity in routines (6).

Pill count is the technique used by pharmaceutical officer at COE to assess adherence to ART over the previous month, as medication is given out on a monthly basis.

The percentage of adherence is calculated as follow: (Appendix A) (33)

The numerator equals: the Total number of pills provided at previous visit – number of pills remaining.

The denominator equals: the number of pills instructed to take daily x number of days since last visit.

The percentage of adherence is obtained by multiplying the ratio by 100.

Adherence to ART is considered perfect when the pill count estimate is superior and equal to 95% of ARV's taken by the child (4).

3.1.2 The CD4+ lymphocyte count.

The CD4+ lymphocyte count is the number of white blood cells (WBC) or lymphocytes that bear the marker, CD4. It is a biological marker that is used to monitor the disease progression and adherence to ART as well. For children below 5 years, the percentage of CD4 lymphocytes is used. A successful adherence to ART in children results in an increase by 25 to 50 cells per blood micro liters in a year (34).

3.1.3 Viral load assay: is another biological marker to monitor disease progression and adherence to ART as well. It measures the quantity of the HIV virus ribonucleic acid (RNA) in the plasma or blood. The viral load can be expressed in logarithms (log). A drop of 1 log of viral load means that the level of RNA virus has dropped by 90 %. A successful adherence on ART results in a drop of 10 log (less than 400 copies of virus RNA in 1 millimeter of blood). This is also called the undetectable level of RNA virus. Generally, a successful adherence to ART among HIV infected children on ART results in an undetectable level after 6 months on medication (34)**.**

3.1.4 An adolescent: According to United Nations, adolescence (10 to 22 years) is the period of transition from the childhood to adulthood (35). This transition, according to the same source, is characterized by biological, cognitive, social and psychological changes. The psychological changes mostly result in the development of a sense of identity and self awareness that leads adolescents to interact more with their peers than with the family environment or while living with the family the adolescents try to develop their own identity (35).

3.2 STUDY QUESTION

What are the factors associated with adherence for adolescents on ART in Gaborone, Botswana?

3.3 NULL HYPOTHESIS

There is no difference in the distribution of factors or predictors between adherent and non adherent adolescents on ART in Gaborone, Botswana.

3.4 THE STUDY AIM

The main purpose of this study is to investigate the barriers to ART adherence among HIV infected adolescents and to explore their association with non adherence.

3.5 SPECIFIC OBJECTIVES

1. To determine the prevalence of adolescent adherence to ART.

2. To determine the main barriers associated with non adherence among HIV infected adolescents on ART.

3. To determine the association between barriers and non adherence among HIV infected adolescents on ART.

3.6 STUDY DESIGN

This study was a cross-sectional analytical study. The study design has been chosen based on the specific objectives. The descriptive component of the study was used to determine the prevalence (which is a rate) of adherence among the HIV infected adolescents on ART. The analytical part on the other hand was to identify barriers of adherence to ART and to answer the null hypothesis of the study.

3.7 STUDY SETTING

This study was conducted at COE in Gaborone, a comprehensive HIV treatment care outpatient centre based in Princess Marina Hospital (PMH), the unique referral hospital of the capital city Gaborone, in Botswana. The Center, which is the product of a public private partnership between the Baylor College of Medicine, one of the United States premier medical school, the Princess

Marina Hospital (where the investigator works at the time of the study) and the Government of Botswana, was officially opened in 2003 to provide a comprehensive HIV/AIDS care and treatment in clinical research and health professional training. Currently the Center offers many services that include the provision of the ART (which is ensured by the pharmaceutical officers from Princess Marina Hospital), the treatment adherence counseling and support, the monitoring of side effects of ART, the screening for HIV for children and their parents and a holistic care of HIV affected families (health education on HIV prevention, psychological support to optimize the elimination of stigma).

3.8 STUDY POPULATION

The study was targeting all HIV infected children aged between 13 and 18 years enrolled with the COE. The children of this age group were chosen because studies show that adolescent adherence to ART is suboptimal and that adolescents are faced with multiple challenges (emotional and physical changes) that would result in behavior changes and could impact on the adherence to the medication (3,13,14 and 20). In August 2010, when the study was conducted, the total number of children aged between 13-18 years enrolled in the ARV National Program at the COE was 400.

3.8.1 Inclusion criteria

All children who were eligible for the study were aged between 13 to 18 years and have been on ART for a period longer than 6 months. They also had their assent and consent forms completed to take part in the study (Appendix B) (36).

3.8.2 Exclusion criteria

All children aged between 13 to 18 years who were on ART for a period less than 6 months were not eligible for the study. For pediatric patients who start ART treatment, it usually takes 6 months for the viral load to reach the undetectable level (34).

3.9 SAMPLING

The sampling method used in this study is purposive sampling. Purposive/convenience sampling method was adopted by the principal investigator due to the difficulty in locating the care givers at the COE in order to get their consent to participate in the study. At Baylor COE, for the majority of the time, adolescents come alone to the center for their medical checkup or for prescription refills. Therefore, adolescents who had assent and had their care giver's consent were enrolled in the study. The sample size for this study was determined using the Raosoft software calculator for sample size (www.raosoft.com/samplesize) (37). A sample size of 197 participants with confidence interval of 95 % and a margin error of 5% was obtained.

3.10 SOURCE OF DATA

In this study, both primary and secondary data were used. For the primary data collection, a self administrated and structured questionnaire was used. The Questionnaire was adapted from the AIDS Clinical Trials Group (ACTG) (Appendix C and E8) (38). The questionnaire was divided into three parts and sought to give information on potential barriers to adherence. The followings information areas were covered: Family and friend network support, patient related factors (psycho-socio factors) and drug special instruction. For the secondary data collection, the electronic medical record (EMR) and the integrated patient management system (IPMS) were

used to retrieve patient socio-demographic data (such as: age, sex, relationship with care givers), clinical (such as the ART regimen, viral load and CD4 count) and pharmacy data (such as pill count and adherence percentage).

3.11 DATA COLLECTION PROCESS

The data for the study was collected in two phases:

Phase I

The first phase consisted of the collection of data by the use of the self administrated structured questionnaire (Appendix C1).The structured and self administrated questionnaire was answered by all adolescents who were eligible for the study. The questionnaires were answered either in presence of the peer educator, the pharmaceutical officers or the main investigator. In all circumstances, the participants were taken apart when answering the questionnaire to maintain independence and confidentiality amongst the responses. The peer educator, pharmaceutical officers were trained in the questionnaire and were able to assist the adolescents when necessary. Both the peer educator and pharmaceuticals officers were routinely reminded the purpose of the study to maintain consistency when explaining concepts to the adolescents participating in the study questionnaire.

All questionnaires answered had adolescent center registration numbers written on the top and were filed and kept in the dispensary. The questionnaires were collected later by the main investigator in case when the questionnaire was answered in his absence.

Phase II

The second step consisted of the collection of data from the medical record by using a data collection sheet (Appendix D).

All eligible adolescents who answered the questionnaire had their medical record reviewed to retrieve all socio-demographic, clinical and pharmacy data. All electronic medical records were retrieved by using the centre registration number of each participating adolescent to call their respective file either from EMR and the IPMS. Because the study is cross–sectional in nature, the CD4 cell count and the viral load measure were retrieved using same dates. The percentage of adherence was obtained from the last visit record.

Data were retrieved and captured between April and June 2011. All records were kept by the main investigator in a locker at the dispensary.

3.12 PILOT STUDY.

A pilot study was done to assess the questionnaires (Setswana and English versions) for accuracy and specificity before they can be used in the study. The Setswana translation of the questionnaire was validated by the Nurse in charge of the clinical research at the COE to cater for participants with difficulties in reading and understanding English language.

The piloting was done during five working days on the 2nd, 4th 16th, 18th and 19th November 2010 at COE.

During these 5 days, the questionnaires were distributed to 28 adolescents aged between 13 to 18 years and were asked to answer both versions of the questionnaire while waiting to be called for either a medical checkup or refilling for medication in the dispensary.

The questionnaires were answered in the presence of the main investigator who was recording the time spent by each adolescent to answer the questionnaires. The adolescent was asked to fill only the age and gender on the space provided on the questionnaires. At the end of the session, the adolescent was to give feedback on the followings: clarity, understanding, language used and ambiguity on any questions he found difficult to understand.

After each session, the questionnaires were reviewed by the main investigator. All changes that were done on the Setswana version of the questionnaire were always validated by the COE Nurse in charge of the clinical research. The changes made in the English version were validated by an adolescent who is a peer educator, bilingual, HIV infected and works at the Gaborone Adolescent Teen Club based at COE.

At the 5th and last day of the piloting, it appeared that all teenagers of the study could use the English version of the questionnaire. Therefore the English version of the questionnaire was adopted with the advantage that would prevent any bias that could result from the use of both versions of the questionnaire.

3.13 ETHICS (Appendix E)

The study (the protocol and the data collection tool) was approved by the Post graduate committee of the Faculty of Health Sciences (Appendix E1), the Health Research and Development Division at the Ministry of Health in Botswana (Appendix E2), the Human Research Ethics Committee of the University of the Witwatersrand in South Africa (Appendix E4) and the Institutional Review Board for Human Subject Research for Baylor College of Medicine in Houston, Texas (Appendix E5). The permission to conduct the study at COE was later granted by the administration of the Center (Appendix E7).

All staff (permanent and volunteer) including the main investigator that participated in the study were required by the administration of the Center to have the GMP (Good Medical Practice) certificate on "Protecting Human Research Participants". All information was treated with utmost confidentiality. The answered questionnaires were attached to the informed and consent signed forms and were identified by the center registration number of the adolescent. The same registration number was used to retrieve information from the adolescent medical record. The principal investigator was the only person to keep all files.

The study was voluntary. The informed consent form (Appendix B) was given to all adolescents aged from 13 to 18 years enrolled in the National ART Program. Only those adolescents who did assent to participate in the study and with their care givers who consented to participate in the study were considered for enrolment. According to the legislation in Botswana, any child aged of 10 years has to assent and to get parental consent as well in order to participate in any research (social science and medical).

3.14 DATA ANALYSIS

This was a cross sectional analytical study using quantitative data. Data were initially captured on a excel spreadsheet and then analyzed in the SPSS. First, descriptive statistic (means, median, proportion and frequency) was carried out to explore the socio-demographic, the adherence rate and the clinical characteristics of the participants. Adherence was estimated by pharmacy pill count. The dichotomous value (≥95% or <95%) was used to determine the proportion of adolescent characterized as adherent or non adherent. Adolescents were characterized as adherent to their medication, if they had taken more than 95% of ARVs prescribed in the month prior the next visit. Non adherent were those who had taken less than 95% of ARV prescribed in

the month prior the next visit. The Chi-square test or the Fisher's exact test was used for categorical variables and the Student's t test was used for continuous variables to compare all exposure variables between the adherent and non- adherent adolescents and to analyze the association of different factors on adherence as well. A stepwise logistic regression was done to control the effects of confounding variables. Variables which showed a statistically significant association ($P<0.05$ and a prevalent odd ratio) in the bivariate analysis were included in the final model.

CHAPTER 4: RESULTS

This chapter highlights the findings of the study on barriers to adherence to ART among HIV infected adolescents. First, the characteristics of the study population were analyzed and then the association of factors with adherence assessed.

4.1 SOCIO-DEMOGRAPHIC AND CLINICAL CHARACTERISITCS

A total of 93 participants had given consent to participate in this study, but only 82 of were eligible for participation. The low answer rate (47%) resulted from low participation of the adolescents enrolled in the study. The major problem encountered during the study was the follow up to remind the teenagers to bring back signed informed consent forms in order to participate in the study. Most of the time the inform consent forms were left behind or brought in with no signature by the adolescents. The initial phase of the study began in August 2010 with the recruitment of eligible participants and ended in April 2011 covering an 8 months duration. During this phase, 500 informed consent forms (Setswana and English versions) were distributed. The forms were accessible to the adolescents at all sites in the center including the Adolescent Teen club monthly meeting site (usually with a gathering of more than 100 adolescents), and the consultation room attached to the dispensary of the centre. At each site, the purpose of the study was explained to the adolescent. A template was designed with the following information to trace the adolescents.

The following data was captured, name and surname of the patient, age, membership in the Teen Club, date to refill the prescription, and the telephone number (personnel or the care giver). The teens were reminded by telephonic message to bring the inform consent form the day before their appointment at the center. During the Teen Club meeting, arrangements were made to collect

the forms brought in by the teens. Lastly, the information on the template was used by the receptionist at the center to remind the adolescents to return the form to the dispensary when they arrive to the centre. This important step of the data collection could have been shortened with a better participation rate if the parents/caregivers/guardians had accompanied the adolescent to their consultation or prescription refilling. Most of the time, the adolescents attended the COE center alone.

Table 1 summarizes the socio-demographic and clinical characteristics of the study participants. Each variable is represented by the frequency (count) and the percentage. The study participants were aged between 13 to 18 years. The majority of the study subjects were 15 years old (32.9%) with a mean age of 15 years. More than half (57.3%) of the participants were female. The mean duration on ART medication for these participants was about 6.6 years and 59.8% of them had been on treatment for more than 6 years. The mean CD4 count measurement of the study participants was 914. 9 cells /mm^3. The majority of the care givers were females (89%) and 55.6% of them were the biological parents of the participants. About 63% of the care givers did know their HIV status. Most of the study participants (41.5%) had stage III HIV disease (WHO HIV disease classification). About 81.7% of the participants were immune competent (asymptomatic). Almost ninety four percent (93.9%) of the study participants had viral suppression and presented with a viral load of less than 400 copies /ml. The majority of the non-adherent participants of the study were 14 (30%), 15 (35%) and 16 (25%) years of age respectively.

Table 1 Socio–demographic and clinical characteristics of study participants

VARIABLE	N (%)
Age	
13-15	53 (64.6)
16-18	29 (35.4)
Sex	
Female	47 (57.3)
Male	35 (42.7)
Caregivers sex	
Female	73 (89)
Male	8 (9.8)
Duration on ART	
< 6 years	33 (40.2)
≥ 6 years	49 (59.8)
Relationship with care givers	
biological parents	45 (54.9)
non biological parents	36 (43.9)
Caregivers HIV status known	
Yes	52 (63.4)
No	29 (35.4)
Viral load	
≥ 400 RNA copies/ml	5 (6.1)

≤ 400 RNA copies/ml	77 (93.9)
WHO disease stage	
stage 1	12 (14.6)
stage 2	11 (13.4)
stage 3	34 (41.5)
stage 4	25 (30.5)
CD4 count mean	914.88 cell/mm3
CD4 WHO classification	
stage 1 (immune- competent)	67 (81.7)
stage 2 (mild immune-compromised)	10 (12.2)
Stage 3 (moderate immune-compromised)	3 (3.7)
Stage 4 (moderate immune-compromised)	2 (2.4)

4.2 Prevalence of ART adherence of the study participants

The prevalence of adherence was estimated by the ratio of the study participants who were adherent to their medication over the total number of the study participants.

As shown in Table 2, the proportion of participants who were adherent to their medication at the time of the study was n/N (75.6%), where n is the number of adherent participants and N is the total number of participants.

Table 2 Prevalence of adherence of the study participants

Adherence status	**N (%)**
Non- adherent	20 (24.4)
Adherent	62 (75.6)
Total	82 (100)

4.3 Association of non-adherence with socio -demographic measures

The results of the association between the socio-demographic variables and non-adherence among the participating adolescents are shown in the Table 3.

The p-value and odd ratio were calculated to determine the statistical significance and the strength of the relationship between the exposure variables and adherence to HAART (outcome variable) respectively. A p-value of less than 0.05% was considered to be statistically significant, while an odd ratio (OR) of 1 was used as a reference point to determine the strength of the association between the variables and the adherence. The p-values are reported together with respective confidence intervals.

In this study, gender was found to be significantly associated with the adherence among adolescents (p= 0.020). The study showed that males were nearly 70 % less likely to adhere to their ART medication compared to their female counterparts [OR=0.30, (95% CI: 0.10 – 0.85)].

The study further showed that adolescents whose care givers were female were 2.2 times more likely not to adhere to their ART medication compared to adolescents whose care givers were male [p= 0.441, 0R= 2.29, 95% CI (0.26 – 19.9)]. Similarly, adolescents aged between 13 to 15 were found to be 1.37 more likely not to adhere to their treatment than those who are aged

between 16 to 18 [p= 0.461, OR= 1.37, 95%CI: 0.46 – 4.078)]. However, this association was not statistically significant at the 5% level of precision.

Table 3 Univariate analysis: Socio-demographical variables and adherence.

Variables		Adherence (%)				
	N	**Non adherent**	**Adherent**	**OR**	**P value**	
Age						
13-15	53	14(70.0%)	39(62.9%)	**1.37**	0.564	
16-18	29	6(30.0%)	23(37.1%)			
Sex						
Female	47	7(35.0%)	40(64.5%)	0.29	**0.020**	
Male	35	13(65.1%)	22(35.5%)			
Caregivers sex						
Female	73	18(94.7%)	55(88.7%)	**2.29**	0.441	
Male	8	1(5.3%)	7(11.3%)			
Duration on ART						
< 6 years	33	7(35.0%)	26(41.9%)	0.74	0.582	
≥ 6 years	49	13(65.0%)	36(58.1%)			
Relationship with care Care givers						
biological parents	45	10(52.6%)	35 (56.5%)	0.85	0.769	
non biological parents	36	9(47.4%)	27 (43.5%)			

Caregivers HIV status known)						
No	29	6(31.6%)	23(37.1%)	0.78	0.661	
Yes	52	13(68.4%)	39 (62.9%)			

4.4 Association between clinical variables and adherence

The student t test was performed on the mean CD4 count and adherence. There was no significant difference between the mean CD4 count of adherent and non adherent study participants [t=-0.62, p=0, 533]. This study showed that there was association between the viral load and non- adherence. Adolescents who had not achieved a viral load suppression (viral load of less than 400 copies/ml) were nearly 2.2 times more likely to be non-adherent to their medication compared with adolescents whose viral load was suppressed [p= 0.402, OR= 2.18, 95%CI (0.33 – 14.11)]. However, this association was not statistically significant.

4.5 Association of adherence with predictors of non adherence

The association of a total of nineteen (19) factors that have been identified as barriers to good adherence among adolescents on ART (14, 28 and 39) had been analyzed. The result showed that four (4) factors were associated with non-adherence. However, only one (1) out of the four factors showed statistically significant association with non-adherence among the participants in this study.

4.5.1 Association between family and friend network support

This study found that adolescents who did not talk to their parents/care givers about the disease and pills were 1.14 times more likely to be non-adherent to their ART medication than their counterparts who did [p=0.824, OR=1.14, 95% CI (0.35 – 3.69)]. However, this study did not find any association of non-adherence with either the family assistance [(P=0.730, OR=0.75, 95%CI (0.146 – 3.862)] or friends assistance [(p=0.279, OR=0.56, 95%CI (0.20–1.59)] in reminding adolescents to take their medication.

4.5.2 Association of non-adherence with patient related factors

Failure to collect ARTs from the pharmacy by either the adolescent or care giver/parents appeared to be the only factor to be significantly associated with non adherence. These results showed that adolescents who did miss a dose because their pills were not collected at the pharmacy either by themselves or by their care givers were 77 % less likely to adhere to their ART medication than those who did not miss a dose because they had their medication collected [p= 0.019, OR= 0.23, 95%CI (0.064 – 0.837)].

There was association between non-adherence and the perception of the treatment outcome. However, the association was not statistically significant. This study has found that adolescents who did not believe that the treatment could make them healthy people were 1.26 times more likely to be non-adherent to their medication than those who did believe in the treatment [p=0.788, OR=1.26, 95%CI (0.22 – 7.09)].

There was no association between the remaining factors with non-adherence among participants in this study. Those factors were: Self efficacy with the medication [p=0.851, OR= 0.80, 95%CI (0.085 – 7.675)], mood disorder [p=0.559, OR=0.679, 95%CI (0.184 – 2.50)], the failure to maintain adherence to treatment because pills are a reminder of the disease [p=0.198, OR=0.44, 95%CI (0.127 – 1.55)], forgetting to take pills at the prescribed time [p=0.142, OR=0.46, 95%CI (0.163 – 1.310)], the difficulty of integrating the regimen in the daily schedule or routine [p=0.129, OR=0.288, 95%CI (0.053 – 1.560)], the failure to maintain adherence to treatment during sickness [p=0.131, OR=0.382, 95%CI (0.10 -1.37)], the failure to maintain adherence when adolescents do not have the pills on their person [p=0.254, OR= 0.51, 95%CI (0.16 – 1.63)], sigma [p=0.240, OR=0.504, 95%CI (0.15 – 1.61)], the failure to maintain adherence to treatment during sleeping time [p=0.052, OR= 0.35, 95%CI (0.12 – 1.02)], the failure to

maintain adherence to treatment because of feeling healthy [p=0.320, OR 0.50, 95%CI (0.13 – 1.96)], the failure to maintain adherence because of being busy with other issues (p= 0.204, OR=0.49, 95%CI (0.10 – 1.48), the failure to maintain adherence because of missing one daily dose [p= 0.244, OR= 0.39, 95% CI (0.81 – 1.95)].

4.5.3 Association of non-adherence with medication factors.

Association between adherence and toxicity was found in this study, but that association was not statistically significant at the 5% precision level. The results indicated that adolescents who did not feel fine after taking their medication were 1.26 times more likely be non-adherent to their medication than those who did [p=0.788, OR=1.26, 95%CI (0.22 – 7.09)]. Other factors related to medication, such as the refusal to take the medication because it may result in changes in the body, were not associated with non-adherence [p=0.076, OR= 0.276, 95%CI (0.062 – 1.22)].

Table 4 Bivariable analysis with dominant predictors of non adherence.

Predictors to adherence	**N**	**Adherence (%)**		**P value (Chi square)**	**OR**
		Non adherent	**Adherent**		
Family support Network					
Do you and your parents /caregivers talk about the disease and the pills?					
No	19	5(25.0%)	14(22.6%)	0.824	**1.14**
Yes	63	15(75%)	48(77.4%)		
Perception (Outcome expectancy)					
Do you believe the pills you are taking are going to make you a healthy person?					
No	7	2 (10%)	5 (8.1%)	0.788	**1.26**
Yes	75	18(90%)	57 (91.9)		
Drug toxicity					
Do you feel fine after you have taken your pills?					
No	7	2 (10%)	5 (8.1%)	0.788	**1.26**
Yes	75	18(90%)	57 (91.9)		
Patient related factor					
have you ever missed a dose because yourself, parents or care givers did not collect the pills at the pharmacy					
No	69	13(68.4%)	56(90.3)	**0.019**	**0.23**
Yes	12	6(31.6%)	6(9.7%)		

CHAPTER 5

DISCUSSION, CONCLUSION AND RECOMMENDATIONS

5.0 INTRODUCTION

The main objective of this study was to determine the adherence prevalence among the HIV infected adolescents on ART at COE in Gaborone, Botswana. The factors associated to non adherence among the study participants has also been assessed. This study is among the first its kind to identify non-adherence factors in the comprehensive HIV treatment and care management centre in Gaborone.

5.1 DISCUSSION

The study has shown a high level of adherence of the study participants to their medication. Although relatively few studies have shown similarly high rates of adherence among HIV infected adolescents on ART (6 and 20), a lower rate of adherence among HIV infected adolescents has been reported in other studies (3,5,7,9,13-15). In 2009, a review of studies on HIV antiretroviral adherence and intervention among HIV–infected youth (13–24 years) reported an overall rate of adherence ranging from 28.3% to 69.8% (5). The latest study done in South Africa, in 2010, among adolescents aged between 11 and 19 reported a lower adherence rate of 20.7%, 14.3% and 6.6% respectively when the adherence was measured respectively at 6, 12 and 24 months after the commencement of HAART using the pharmacy refill technique (13). A number of reasons could probably explain the high rate of adherence reported in this study at the COE in Gaborone:

Firstly, the high rate of adherence could be attributed to the method of assessment of the adherence level used in the study: pharmacy pill count. It is difficult to estimate and to compare accurately ART adherence rates among adolescents across studies. This is probably due to the fact that there is still no standardized method for the measurement of adherence. In 2008, the result of a systematic review of the rate of adherence to ART among children less than 15 years old had reported a significant difference in the proportion of adherence based on the methods of measurement used: 73% self report, 50% pill count and 26 % MEMS (39). These results indicate an over-estimation of adherence level using the self-reporting and pill count techniques. MEMS, is considered today as the gold standard technique for accurate measurement of medication adherence (26, 31).

Although viral load suppression is not a perfect indicator of adherence (11), the methodology chosen to measure adherence is always validated by showing a statistically significant association between full adherence and the virological outcome at a pre-defined precision level (15 and 28). This study found association between adherence and viral suppression, but that association was not statistically significant at the 5% precision level [p= 0.402, OR= 2.18, 95%CI (0.33 – 14.11)].

The aim of this study was not to validate the pharmacy pill count methodology used to measure the adherence level. The pill count technique is the standard and preferred technique used at the Baylor Centre of excellence. In 2006, study done on pediatric antiretroviral adherence at COE has found that the care giver self-reporting to be unreliable (16). That study found out that care givers who reported perfect adherence were still to bring large amount of unused pills.

The high adherence level (75.6%) reported in this study could also be attributed to the fact that all adolescents who participated in this study share some characteristics which favor good

adherence to HAART. Firstly, they were all disclosed at the time of the study. The disclosure is a process viewed today to be an important support mechanism for adherence as a child gets mature and starts questioning the medication (19). In addition to that, all the study participants do attend the same adolescent clinic and the same Teen Club as well. Those two facilities, the adolescent clinic and Teen Club, provide a supportive environment that equips adolescents with appropriate skills to enable them to face challenges of adolescence (such as transitional changes to adulthood and risky health behavior such as non-adherence).

Analysis of the predictors of adherence, in this study revealed that two (2) main factors did influence adolescence non-adherence to ART: the socio – demographic factor and the structural barrier related to the patient. Female adolescents in this study have been found to be more likely to adhere to their treatment than male adolescents. Although, a number of studies have shown inconsistent findings with regard to association between gender and adherence (5), a study done in Togo, Lome, found that female adolescents were less likely to adhere to their medication than males (7). However, other study findings have consistently shown a higher seroprevalence of 73% and 72.7% among female adolescents than male adolescents (3, 13). Female early sexual debut and the social issues such as gender-power imbalance are in general, contributing factors (3) as evidence by this study where 57.3% of participants were females.

Similar findings with regard to failure to collect medication have been observed among HIV infected youths (12 – 24 years) in USA (14). The problem associated with the collection of the refill medication at the dispensary is a structural barrier that is known to impact on adolescent medication adherence (3). In this study, based on the investigator experience at the COE dispensary, changes were made in the formulation of this relevant barrier that shares the responsibility evenly between the care giver and the adolescent (see table 4). However, this study

did not examine the readiness of the adolescent to ensure equity in the responsibility for the collection of the refill medication. Therefore, further research is required here.

This study has identified other factors associated with non-adherence. Since the association was not statistically significant a logistic regression model could not be performed to depict the dominant barriers among them. They were socio-demographic and psychological factors: the perception (outcome expectancy) on the treatment outcome, the good communication/relationship between the care givers and the adolescent about the disease and pills, the side effects or toxicity related to the medication. Those factors (facilitators and barriers) have all been shown to impact positively (outcome expectancy, good relationship between the care giver/parent and the adolescent) and negatively (toxicity related to the medication) on adolescent adherence to ART (3 and 14).

This study had some limitations. First, the sample size was small hence difficult to generalize the findings. The full adherence level that has been assessed by the pharmacy pill count methodology did not show a statistically significant association with the viral load. In addition to that, four factors out of the six factors depicted by this study were not significantly associated with non-adherence.

A second limitation in this study was the study population characteristics which were not representative of the country's adolescent population. Adolescents from other facilities are not exposed to the same care and skills provided to the ones attending COE. Therefore it will be difficult to generalize the findings of this study to rest of the country.

Lastly, this study did not look at cultural, adolescent and health provider relationship issues that could impact on adolescent adherence to ART. Those are very important factors to look in to.

5.2 CONCLUSION

The study investigating factors associated with non-adherence among HIV adolescents on ART is the first to be conducted at COE comprehensive HIV treatment and care management centre in Gaborone.

The study has found that a high proportion (75.6%) of HIV infected adolescents aged 13 to 18 years that are attending the center are adherent to their ART medication.

The study has also found that male gender and the failure of collection of medication by adolescent or their caregivers were the main factors that showed association with non adherence to ART among adolescents. This underscores the fact that intervention to improve adherence among adolescents on HAART should focus on male adolescents and improved counseling on the hazards of poor adherence to treatment among patients and caregivers.

5.3 RECOMMENDATIONS

The findings of this study require further research in the followings:

-The need to develop and implement a validated technique for the measurement of adolescents' adherence to ART. This study used the standardized pill count technique comparatively to many studies that use the self reporting and pharmacy refill technique that have been found to be validated.

-The need to focus more on male adolescents and to explore factors that could improve their ability to adhere to ART.

-The need to assess the readiness of adolescent in the sharing of responsibility with the caregiver regarding the collection of refill medication without compromising the adolescent health.

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APPENDIXES

APPENDIX A: ADHERENCE PERCENTAGE CALCULATION

Calculating Adherence Percentage

Formula for calculating adherence percentage:

Total number of pills provided at previous visit – number of pills remaining

---------- X 100

Number of pills instructed to take daily x number of days since last visit

Table for determining adherence percentage:

(Assuming monthly visits with a window of 7 days; 1 pill daily; 33 pills dispensed)

Adherence Percentage

# of Pills Remaining	#of days Since						
0	27	28	29	30	31	32	33
1							100
2						100	97
3					100	97	94
4				100	97	94	91
5			100	97	94	91	89
6			97	94	91	89	85
7			94	91	89	85	82
8			91	89	85	82	79

APPENDIX B: **INFORMED CONSENT FORM**

APPENDIX B1: INFORMED CONSENT FORM (English version)

TITLE OF THE PROJECT: Barriers to anti-retroviral therapy adherence among human immunodeficiency virus –infected adolescents (13-18 years) in Gaborone (Botswana).

This informed consent form is for parents or guardians of adolescent girls and boys who are participating in the research titled: barriers to anti-retroviral therapy adherence among human immunodeficiency virus –infected adolescents (13-18 years old) in Gaborone (Botswana). The research will be done at Botswana Baylor Center of Excellence in Gaborone by Maimouna N'Diaye, a pharmacist, working at Princess Marina Hospital Pharmacy in Gaborone.

Information Sheet

Introduction

I am Maimouna N'diaye and am studying for a Masters degree in public health at the University of the Witwatersrand (Wits) in Johannesburg (South Africa). I work as a pharmacist in the pharmacy at Princess Marina Hospital.

I am requesting that you permit your child to participate in the study I am doing. The study has two objectives. The first one is to determine the level of adherence of the ART medication of adolescent's boys and girls who are getting their treatment at Baylor Center of Excellence. The second objective is to determine the factors leading to non adherence to ART. The purpose of this research is to have a better understanding of the barriers to good adherence among adolescents who are on ART. I am hoping that the findings of this study will lead to

prevent treatment failure as well as to ensure better treatment outcomes through increased rate of survival.

Part of my study will require me to ask some questions to adolescent boys and girls about their knowledge and beliefs about their medication, reasons and factors that prevent them not to adhere to their medication.

In Botswana and in Botswana Baylor Center of Excellence (COE), before any research on children could be carried out, the parents /guardians are asked for their permission. If you do agree to participate, then I will ask for the consent of the boys and girls as well. Both of you have to agree independently before the study begins. Your consent and the child assent are both necessary for your child participation in the study.

I am planning to interview adolescents aged 13 to 18 years old who have been on ART (between August and February) for 6 months and above. There are two reasons for this; Studies done in other African countries have shown that adolescents of the same ages are not fully adherent to their ARV medications. The second reason is to determine whether there is any difference between both groups in terms of length of the treatment and adherence to ART.

Participation

You should understand that participation in this study is strictly voluntary. Your child may decide at any time during the interview not to give an answer to a question or to decide to no longer participate in the study. You should know that any decision to withdraw for the study will not affect at all any services that you and your child are getting from the center.

If you and your child participate in the study, the questions will be asked to your child either in English or Setswana. You and your child will not be compensated for participating in the study (interview).

Protocol

The interview will take place in an isolated room or in the garden outside the center and no one else but the interviewers, myself and a nurse specialized in clinical research at Baylor COE, will be present unless your child asks for someone else to be there. If your child does not wish to answer any question he or she may say so and we will move on to the next question.

The interview may take a minimum of 30 minutes to a maximum of 1 hour.

Benefits of participation

There will be no immediate and direct benefit to your child or to you for participating in this study. However, the findings in the study may help identify some of the potential barriers to good adherence of adolescent to ART in Gaborone (Botswana) and to help future generation to achieve a better treatment outcome.

Risks, discomforts and inconveniences

The risks, discomforts, and inconveniences of the child participating in this study are minimal. No drug will be involved in this study. Your child will be inconvenienced one time when they are interviewed. The presence of the interviewer, a Motswana nurse who is specialized in clinical research and is fluent in both Setswana and English, will be a support in counseling for any discomfort (trauma) and inconvenience that may occur while your child will be answering the questionnaire.

Confidentiality

Your child's identity will be kept confidential. To maintain anonymity no patient identifiers will be used. We will create our own unique numbers that will not associate the record to your child. Completed questionnaires will be coded and the results will be kept in a secure office

under lock and a key. The findings of the study will be made available to the Ministry of Health in Botswana and for any presentation or publication of data and your child's complete confidentiality will be maintained.

Your child's participation is entirely voluntary and your refusal or withdrawal will not cause any penalty or alteration in your and your child medical care at the Center.

Inquiries.

For information related to research study, please contact:

Maimouna N'Diaye

Princess Marina Hospital Pharmacy

Phone: 267 744 00 421.

This research has been approved by the following institutions:

The University of the Witwatersrand Human Research Ethics Committee. If you need any information about the right of the participants or any concerns about the ethical conduct of the research you may contact the Committee through the Human Research Ethics Committee Secretary: Ms Anisa Keshav, Tel 00 27 11 717 1234; Email: anisa.keshav@wits.ac.za or the Chairman: Professor Peter Cleaton Jones Tel: 00 27 11 717 2301.

The Ministry of Health in Botswana (Health Research and Development Division). If you need any information about the right of the participants or any concerns about the ethical conduct of the research you may contact P. Khulumani Tel 267 3914467; E-mail: pkhulumani@gov.bw or Mary Kasule Tel: 267 3632466; E-mail: marykasule@gmail.com.

The Institutional Review Board for Human Subject Research of Baylor College of Medecine in Houston, Texas. If you need any information about the right of the participants or any concerns

about the ethical conduct of the research you may contact the BCM IRB (Study H-27353) Tel: (00 1)713 798 6970; Email: irb@bcm.tmc.edu.

TITLE OF THE PROJECT: Barriers to anti-retroviral therapy adherence among human immunodeficiency virus –infected adolescents (13-18 years old) in Gaborone (Botswana).

Consent by parent/guardian

I…… acknowledge the foregoing information. I have had the opportunity to ask questions about it and any questions that I have asked have been answered to my satisfaction. I consent voluntarily for my child to participate in this study and I understand that I have the right to withdraw my child from the study at any time without in anyway affecting our care at this Centre. I know that Research and Ethics Committee of Wits University in South Africa and Botswana Ministry of Health has approved this study. I am fully aware that the results obtained at the end of this study will be used for scientific purposes and may be published. I agree to this, provided the confidentiality of my child is guaranteed.

Print Name of Parent or Guardian _____

Signature of Parent of Guardian_____

Date _____

Day/month/year

Assent by the child/adolescent

My parents/guardians know about the study and want me to participate in the study if I want to. I understood the study as explained to me by the pharmacist/nurse and I know that I can withdraw from the study anytime I want to and without informing anybody. I also understood that the pharmacist and the nurse could talk about the study with only my parents/guardians, but will not talk about it with anyone else who is not working on the study unless I and my parents/guardians say it is OK. I know that I can call the pharmacist any time I have any questions.

Print Name of child _____

Date _____

Day/month/year _____

Statement by the researcher

I provide verbal information regarding this study and I agree to answer any future questions pertaining to this study to the best of my ability. The approved research protocol will be respected.

…….. …….. …….

Signature Place Date

APPENDIX B2: INFORMED CONSENT FORM (Setswana Version)

Fomo ya tumalano ya gore molwetse o dumela go nna bontlha bongwe jwa patlisiso e

Fomo e, e e supang gore molwetse o dumela go nna bontlha bongwe jwa patlisiso e, e tshwanetswe go tladiwa ke motsadi kgotsa motlhokomedi wa mosetsana kgotsa mosimane wa dingwaga tse di fa gare ga lesome le metso e le meraro le lesome le metso e le mene (13-18 years). Patlisiso e, e lopa go itse mabaka a a kganelang balwetse ba ba fa gare ga dingwaga tse di lesome le metso e le meraro le lesome le metso e le mene (13-18 years) go tsaya sentle dipilisi tse di ritibatsang bolwetse ja AIDS . Patlisiso e, e tlaa tshwarelwa ko Botswana Baylor Center of Excellence mo Gaborone mme e tlaa bo e dirwa ke mme Maimouna N'Diaye, modiredi wa sepatela sa Princess Marina mo Gaborone yo o dirang mo lephateng la kabo ya dipilisi.

Tse o tshwanetseng wa di itse ka patlisiso e

Tshimologo

Leina lame ke Maimouna N'Diaye. Ke ithutela dithuto tse di kgolwane tsa Masters ko Unibesithing ya Witwatersrand ko Africa Borwa. Ke bereka ko sepateleng sa Princess Marina mo lephateng la kabo ya dipilisi.

Ke kopa gore ngwana wa gago a tsenelele patlisiso ka ga tse di kganelang balwetse go dirisa dipilisi tsa bolwetse jwa AIDS sentle. Patlisiso e, e maikaelelo mabedi. Maikaelelo a yone a ntlha ke go bona gore bana ba ba tsayang dipilisi tsa AIDS ko Baylor Center of Excellence ba di dirisa go le kana kang. Maikaelelo a bobedi ke go batlisisa gore ke mabaka afe a a kganelang bana ba go dirisa dipilisi tse sentle. Maikaelelo a patlisiso e ke go leka go tlhaloganya mabaka a a itsang bana go tsaya dipilisi tsa bone ka mokgwa o o siameng. Re eletsa gore re tle re kgone go itse gore re ka emisa go sa berekeng sentle ga dipilisi tse jang le gore re tle re bone gore re ka thusa batho jang gore kalafi ya bone e bereke sentle mme matshelo a bone a tokafale.

Mo patlisisong e, go tlaa tlhokega gore ke botse banana ba ba fa gare ga dingwaga tse di lesome le metso e le meraro le lesome le metso e le mene (13-18 years) dipotso dingwe mabapi le se ba se itseng ka tiriso ya dipilisi ga mmogo le gore ditumelo tsa bone ke eng ka dipilisi tsa bolwetse jwa AIDS le gore ke mabaka afe a a ba kganelang go tsaya dipilisi tsa bone sentle.

Mo lefatsheng la Botswana, ga mmogo le ko kokelong ya Botswana Baylor Center of Excellence (COE), pele ga motho a ka dira patlisiso epe e e amanang le ngwana, o tshwanelwa ke go kopa tetla mo motsading wa ngwana kgotsa motlhokomedi wa ngwana. Fa wena o le motsadi o dumela gore ngwana a tsenelela patlisiso e, ke tlaa kopa tetla le mo ngwaneng pele ga ke ka simolola patlisiso. Ngwana ga mmogo le motsadi, ba tshwanetse go dumela gore ke ka dira patlisiso e pele ga ke ka simolola go botsolotsa monana/ngwana dipotso.

Go na le mabaka a le mabedi a a dirang gore ke eletse go botsolotsa bana ba dingwaga tse di fa gare ga lesome le metso e meraro go ya ko go ba ba lesome le bohera bobedi dipotso ba ba neng ba dirisa dipilisi tsa mogare wa AIDS go simolola ka kgwedi ya August (2009) go fitlha ka kgwedi ya February (2010). Lebaka la ntlha ke gore dipatlisiso tse di dirilweng mo mafatsheng a mangwe a Aferika mo baneng ba ba dingwaga tse di fa gare ga lesome le metso e meraro go ya ko go ba ba lesome le bohera bobedi di supile gore bana ba dingwaga tse ga ba tseye dipilisi tsa bone ka fa mokgweng. Lebaka la bobedi ke gore ke eletsa go itse gore ngwana o na le nako e kana kang a dirisa dipilisi go na le seabe mo go sa diriseng dipilisi sentle.

Go tsenelela patlisiso e

Motho ga a patikiwe go tsenelela patlisiso e. Patlisiso e, e tsenelelwa ka go ithaopa. Monana/ngwana o kgona go gana go araba potso nngwe le nngwe ka nako nngwe le nngwe fa potsolotso e ntse e tsweletse kgotsa a emise go tsaya karolo mo patlisisong e ka nako nngwe le nngwe e a batlang go dira jalo. Motsadi o tshwanetse go itse gore le fa ngwana wa gagwe a

ipolelela gore ga a sa batla go tsaya karolo mo patlisisong e, seo gase kake sa ama thuso e ngwana kgotsa motsadi wa gagwe a e bonang mo go ba Botswana Baylor Center of Excellence.

Fa wena le ngwana wa gago le tsaya karolo mo patlisisong e, le tlaa botswa dipotso ka Setswana kgotsa ka Sekgoa. Ga gona tuelo epe e ngwana kgotsa motsadi a tlaa e fiwang a e neelelwa go tsaya karolo mo patlisisong e.

Tsamaiso

Baylor Center of Excellence. Mo nakong ya potsolotso, go tlaa bo go na le babotsa dipotso, nna (mmatlisisi), mooki yo o nang le kitso ee faphegileng ya patlisiso go tswa Baylor Center of Excellence. Le gale fa ngwana wa gago a tlhokana le gore go nne le mongwe gape, seo se ka rulaganngwa. Mo nakong ya potsolotso, fa ngwana wa gago a sena keletso ya go araba potso nngwe, o ka re itsise mme ka jalo re ka fetela ko potsong e e latelang. Potsolotso e tlaa tsaya nako ya metsotso e le masome a mararo go ya go oura.

Mosola wa go tsaya karolo mo patlisisong e

Bomosola jwa go tsaya karolo mo patlisisong e ga bo nke bo bonale ka pela mo motsading kgotsa mo ngwaneng. Mme le gale, patlisiso e, e ka nna ya re thusa go itse gore tse di kgoreletsang banana ba tikologo ya Gaborone mo Botswana go dirisa dipilisi sentle ke eng. Ka jalo kitso e, e ka re thusa gore re itse gore mo nakong e e tlang re ka thusa banana jang go dirisa dipilisi sentle gore botsogo ja bone bo tokafale.

Dikgobalo kgotsa borai jwa go tsaya karolo mo patlisisong e

Ga gona dikgoballo dipe kgotsa borai bope le fa e le bosula bope jo bo kalokalo jo bo ka dirafalelang monana yo o tsenelelang patlisiso e. Ga gona tiriso ya dipilisi dipe mo patlisisong e. Kgoreletso fela e e ka diragalelang monana yo o tsayang karolo mo patlisisong e ke tiriso ya nako ya gagwe jaaka a tlaa bo a botsolotswa dipotso. Jaaka ke setse ke kaile, go tlaa bo go na le mooki wa kitso ee faphegileng mo go tsa dipatlisiso yo o tswang mo Baylor Center of Excellence yo e tlaa bong e le ene a botsolotsang banana dipotso ka Setswana kgotsa Sekgoa. Mooki yo ka a itse Setswana, o tlaa kgona gore ere fa a bona monana a sa phuthologa kgotsa a utlwile botlhoko, a buisane nae go ritibatsa maikutlo a gagwe kgotsa go mo gomotsa.

Bosephiri jwa patlisiso

Ga go nke go dirisiwe maina a monana ope mo patlisisong e. Ga gona maina ape a batsaya karolo a a tlaa dirisiwang mo patlisisong e go dira gore go tlhoke ope yo o ka itseng gore banana ba ba tsereng karolo mo patlisisong e ke bomang le gore karabo ya gore e filwe ke monana ofe. Re tlaa naya batsaya karolo dinomoro tse di tlaa re thusang go farologanya dikarabo tsa bone mme re sa dirise maina ape. Dipampiri tsa dipotsolotso tse di nang le dikarabo, le tsone di tlaa fiwa dinomoro mme di tlaa bewa mo tlong ya sephiri e e nnang e lotletswe ka nako tsotlhe. Maduo a patlisiso e, a tlaa neelwa ba Lephata la Botsogo mo Botswana mme a ka nna a dirisiwa

gape mo diphuthegong tse di buisanyang ka tsa botsogo kgotsa a kwalwa mo dibukeng tse go kwalang ka tsa botsogo mme ga gona maina ape a banana a tlaa dirisiwang gope.

Go tsaya karolo ga motsadi kgotsa ga monana ke go ithaopa, jalo he, motsadi kgotsa monana, o ka nna a ikgogela morago ka nako nngwe le nngwe mme seo ga se nke se ame dithuso tse ba ntseng ba di bona mo Baylor Center of excellence.

Setlhogo: Patlisiso ka ga tse di kganelang tiriso sentle ya kalafi ya mogare wa AIDS mo bananeng ba dingwaga tse di lesome le boraro go fitlha lesome le bone mo Gaborone, Botswana

Tumalano ya motsadi kgotsa motlhokomedi wa ngwana

Nna ke le _____ ke dumela gore ke badile mokwalo o. Ke nnile le sebaka sa go botsa dipotso ka patlisiso e, mme dipotso tsotlhe tse ke di boditseng di arabilwe mo go nkgotsofaditseng. Ke dumalana gore ngwanake o ka tsaya karolo mo patlisisong e. Ke tlhaloganya gore ngwanake o ka nna a ikgogela morago mo patlisisong e kgotsa mo go arabeng dipotso tsa patlisiso e nako nngwe le nngwe e a e batlang, le gore se, ga se nke se ame thuso e a e bonang mo go ba Baylor Center of Excellence. Ke na le kitso ya gore komiti ya ditshwanelo tsa batho mo dipatlisisong ya Unibesithi ya Wits ko Aferika Borwa le ba Lephata la Botsogo mo Botswana ba letleletse gore patlisiso e e ka dirwa. Ke na le boitemogelo jwa gore maduo a patlisiso e a tlaa dirisiwa go oketsa maranyane a tsa botsogo mabapi le tiriso ya dipilisi tsa bolwetse ja AIDS le gore maduo ao a ka nna a kwalwa mo dibukeng. Se ke dumelana le sone ka kutlwisiso ya gore leina la ga ngwanake ga le nke le dirisiwe gope.

Leina la motsadi kgotsa motlhokomedi wa ngwana _____

Monwana wa motsadi kgotsa motlhokomedi wa ngwana _____

Letsatsi_____Kgwedi_____Ngwaga_____

Tumalano ya monana/ngwana

Batsadi bame kgotsa motlhokomedi wame, ba/o itse ka patlisiso e, mme ba/o dumalana gore ke ka tsaya karolo mo go yone fa ke batla. Ke tlhaloganya se se tlhokegang mo patlisisong e jaaka ke tlhaloseditswe ke mmatlisisi. Ke tlhaloganya gore ga ke patikege go tsaya karolo mo patlisisong e le gore ke ka nna ka ikgogela morago nako nngwe le nngwe e ke batlang go sa tlhokege gore ke itsise mmatlisisi mabaka. Ke tlhaloganya gore mmatlisisi o ka bua ka patlisiso ya gagwe le batsadi bame kgotsa motlhokomedi wame fela eseng le ope gape yo o seng bontlhabongwe jwa patlisiso e. Go bua le ope yoo seng bontlha bongwe jwa patlisiso e, mmatlisisi o tshwanelwa ke go kopa tetla ya batsadi bame. Gape ke tlhaloganya gore ke ka leletsa mmatlisisi nako nngwe le nngwe fa ke na le potso.

Leinala ngwana:_____

Monwana wa ngwana: _____

Letsatsi: _____ Kgwedi _____ Ngwaga _____

Kitsiso go tswa mmatlisising

Ke ikemisetsa go itsise ba tsaya karolo ka tsotlhe tse ba tlhokanang le go di itse ka patlisiso e le go araba dipotso tsotlhe tse ba nang natso mo nakong e e tlang ka patlisiso e. Gape ke ikemisitsa go sala morago melao e ke e filweng ke ba ba fang tetla ya go dirisa dipatlisiso mo sechabeng.

Leina la Mmatlisisi_____

Monwana _____ Lefelo _____ Letsatsi_____

Fa o batla go itse sengwe ka patlisiso e, o ka itshwaraganya le:

Maimouna N'Diaye

Princess Marina Hospital Pharmacy

Mogala: 267 744 00 421

Patlisiso e e letleletswe ke ba lephata la melawana ya badira dipatlisiso mo sechabeng ba Unibesithi ya Wits ko Aferika Borwa. Fa o tlhokana le go itse ka ditshwanelo tsa batsaya karolo kgotsa o na le mathata mangwe ka boitshwaro jwa mmatlisisi mo nakong ya patlisiso e, o ka itshwaraganya le mokwaledi wa lephata la melawana ya badira dipatlisiso mo sechabeng kwa Unibesithi ya Wits ko Aferika Borwa, Mme Anisa Keshav ko mogaleng wa 002711-7171234. Gape Mme Keshav o ka kwalelwa ko atereseng ya anisa.keshav@wits.ac.za. Go ka leletswa gape modula-setilo wa lephata ebong Professor Peter Cleaton Jones yo mogala wa gagwe eleng: 002711-7172301. Lephata la Botsogo mo Botswana (Lekalana la Botsogo la Dipatlisiso le Ditlhabololo). Fa o batla kitso ka ga ditshwanelo tsa batsaya karolo kana matshwenyego ka ga tsamaiso ya patlisiso o ka nna wa itshwaraganya le P. Khulumani, Mogala 267 3914467; E-mail pkhulumani@gov.bw kana Mary Kasule, Mogala 267 3632466; E-mail marykasule@gmail.com.

Lekalana la Barulanyi ba Tshekatsheko ya Batho ba ba Tsayang Karolo mo Dipatlisisong ya Baylor College of Medicine mo Houston, Texas. Fa o batla kitso ka ga ditshwanelo tsa batsaya karolo kana matshwenyego ka ga tsamaiso ya patlisiso o ka nna wa itshwaraganya le BCm IRB (Study H-27353) Mogala (001) 713 798 6970; E-mail: irb@bcm.tcm.edu.

APPENDIX C: QUESTIONNAIRES

APPENDIX C1: QUESTIONNAIRE ON BARRIERS TO NON ADHERENCE

This section addresses different factors that could influence adherence

1. **Family and friend network support.**

Do family members help you remember to take your medication?

1. Yes
2. No

Do you and your caregiver talk about the disease and the medication?

1. Yes
2. No

2. Patient related factors.

Are you able to take the medicine as you have been told?

1. Yes
2. No

The drugs you are taking are they going to make you a healthy person?

1. Yes
2. No

Do you feel ok after you have taken your medication?

1. Yes
2. No

You haven’t taken your medicines because you feel that you do not need them any longer because you feel you are healthy

1. Yes
2. No

You haven’t taken your medicines because you felt depressed or overwhelmed

1. Yes
2. No

You haven’t taken your medicines because the medicine reminds you about the disease

1. Yes
2. No

You haven’t taken your medicines because you felt sick or ill

1. Yes
2. No

You haven’t taken your medicines because you were busy with other things

1. Yes
2. No

You haven’t taken your medicines because you fell asleep or slept through dose time

1. Yes
2. No

You haven’t taken your medicines because you wish to make change in day routine

1. Yes
2. No

You haven’t taken your medicines because you did not have the medication with you.

1. Yes
2. No

You haven’t taken your medicines because your care giver did not collect your medicine at the pharmacy

1. Yes
2. No

You haven’t taken your medicines because you have simply forgot

1. Yes
2. No

You haven’t taken your medicines because you were afraid of the changes in the way your body looks (such as deposits and weight gain)

1. Yes
2. No

3. Factors related to drug special instructions

Do you ever forget to take your medication?

1. Yes
2. No

Do you ever decide not to take your medication because you have missed a dose?

1. Yes
2. No

Do you have any problem of anyone beside your caregiver knowing that you are taking these medicines?

1.Yes

2. No

APPENDIX C2: QUESTIONNAIRE ON BARRIERS TO NON ADHERENCE

(Setswana version)

Potsoloso ka tse di thibelang go sala morago melawana ya tiriso ya dipilisi tsa bolwetse j wa AIDS

1. Thotloetso ya balelwapa le ditsala

   A ba lelwapa ba go gakolola go tsaya dipilisi?

   Ee

   Nyaa

   Wena le motlhokomedi wa gago a letle le bue ka bolwetse jo, le ka melemo ya gago?

   Ee

   Nyaa

2. Tse di amanang le molwetse

   A o tsaya dipilisi jaaka o laetswe?

   Ee

   Nyaa

   Fa o lebile, a dipilisi tse o di tsayang di tsile go go fa botsogo?

   Ee

   Nyaa

   A o ikutlwa o siame o sena go nwa melemo?

   Ee

   Nyaa

Ga o a dirise dipilisi tsa gago ka gore, o ikutlwa o tsogile sentle

Ee

Nyaa

Ga o a dirisa dipilisi tsa gago ka gore, o ne o ikutlwa o sa tsoga mo moweng

Ee

Nyaa

Ga o a dirisa dipilisi tsa gago ka gore,di go gakolola gore o na le bolwetse

Ee

Nyaa

Ga o a dirisa dipilisi tsa gago ka gore ga o a tsoga

Ee

Nyaa

Ga o a dirisa dipilisi tsa gago ka gore,o a bo o sena nako?

Ee

Nyaa

Ga o a dirisa dipilisi tsa gago ka gore,o ne wa tshwarwa ke boroko go feta nako ya tsone

Ee

Nyaa

Ga o a dirisa dipilisi tsa gago ka gore,o eletsa o ka ikhutsa go di nwa

Ee

Nyaa

Ga o a dirisa dipilisi tsa gago ka gore,o a bo o sa di tshola

Ee

Nyaa

Ga o a dirisa dipilisi tsa gago ka gore, motlhokomedi wa gago one a satla go di go tseela.

Ee

Nyaa

Ga o a dirisa dipilisi tsa gago ka gore,o lebetse

Ee

Nyaa

Ga o a dirisa dipilisi tsa gago ka gore,o bona selebego sa mme le wa gago se fetogile (sekai, gongwe o a nona).

Ee

Nyaa

3 Tse di amanang le ditaelo tse di faphegileng tsa tiriso ya dipilisi

A o atle o lebale go nwa dipilisi?

Ee

Nyaa

A o atle o tlogele go nwa Melemo ha nako ya teng e fetile?

Ee

Nyaa

A o nale bothata jula gore mongwe ko ntle ga motlhkomedi wag ago o ka itse gore o nula melemo?

Ee

Nyaa

APPENDIX D: DATA COLLECTION SHEET

DATA SHEET:

CM number: ……

SECTION 1: SOCIO-DEMOGRAPHIC DATA

AGE OF THE CHILD 1. 13-15 years 2. 16-18 years
SEX OF THE CHILD 1. boy 2. girl
SEX OF CARE GIVERS 1.male 2.female
LEVEL OF EDUCATION OF THE CARE GIVER 1. primary 2.secondary 3.tertaire
IIS THE HIV STATUS OF THE CARE GIVERS KNOWN 1. yes 2. no

CARE GIVER OCCUPATION 1. not employed 2. working private sector 3.working with the government 4. others
IS THE CARE GIVER 1.The biological parent 2.The non biological parent 3.others
AGE OF DISCLOSURE OF THE CHILD 1. 6 – 9 years 2. 10 – 14 years
DOES THE CARE GIVER USE OF DRUG OR RELATED ABUSIVE SUBSTANCE 1.yes 2. no
IS CHILD AWARED OF CAREGIVERS MENTAL STATUS/ANTIDEPRESSIVE MEDICATION 1.yes 2.no

SECTION 2. CLINICAL DATA

THE ART REGIMEN THE CHILD IS TAKING

1.first

2.second

3.third

CD4 COUNT

1. >500 cells/μL
2. 499 -350cells/ μL
3. 349 – 200 cells/ μL
4. < 200 cells/ / μL

VIRAL LOAD

1. < 400 copies/ml
2. > 400 copies/ml

CDC DISEASE STAGE

1. Stage I
2. Stage II
3. Stage III
4. Stage IV

SECTION 3. PHARMACY DATA

MEASURE OF ADHERENCE (PILL COUNT)

1. Less than 95%
2. More than 95%

APPENDIX E. ETHICS AND APPROVALS

APPENDIX E 1: Approval from the Post graduate committee of the Faculty of Health Sciences. University of the Witwatersrand in South Africa

Faculty of Health Sciences
Medical School, 7 York Road, Parktown, 2193
Fax: (011) 717-2119
Tel: (011) 717-2745

Reference: Ms Tania Van Leeve
E-mail: tania.vanleeve@wits.ac.za
08 December 2009
Person No: 0709719V
PAG

Ms M Ndiaye
Maimouna Ndiaye
C/O Dr Kone Zoumana
BIFM P.O. Box 185BR, Fairgrounds Office Park
Gaborone
0000
Botswana

Dear Ms Ndiaye

Master of Public Health (Health Measurement): Approval of Title

We have pleasure in advising that your proposal entitled "*Barriers to Anti-Retroviral therapy adherence among Human Immunodeficiency Virus-infected adolescents (13-18 years old in Botswana*" has been approved. Please note that any amendments to this title have to be endorsed by the Faculty's higher degrees committee and formally approved.

Yours sincerely

Mrs Sandra Benn
Faculty Registrar
Faculty of Health Sciences

APPENDIX E 2: Approval from the Health Research and Development Division at the Ministry of Health in Botswana

Telephone: (267) 363200
FAX (267) 353100
TELEGRAMS: RABONGAKA
TELEX: 2818 CARE BD

MINISTRY OF HEALTH
PRIVATE BAG 0038
GABORONE

REPUBLIC OF BOTSWANA

REF NO: PPME-13/18/1 Vol V (242)

17 February 2010

PERMANENT SECRETARY
MINISTRY OF HEALTH
RESEARCH UNIT
17 FEB 2010
P/BAG 0038
GABORONE
REPUBLIC OF BOTSWANA

Health Research and Development Division

Notification of IRB Review: New application

Ms Maimouna Ndiaye
C/O Dr Kone Zoumana
BIFM
Private Bag BR 185
Gaborone

Protocol Title:	A STUDY OF THE BARRIERS TO ANTI-RETROVIRAL THERAPY ADHERENCE AMONG HUMAN IMMUNODEFICIENCY VIRUS - INFECTED ADOLESCENTS (13-18 YEARS) IN GABORONE
HRU Protocol Number:	HRU 00593
Sponsor:	N/A
HRU Review Date:	16 February 2010
HRU Expiration Date:	15 February 2011
HRU Review Type:	HRU reviewed
HRU Review Determination:	Approved
Risk Determination:	Minimal risk

Dear Sir

Thank you for submitting a new application for the above referenced study. This approval includes the following:

1. Application Form
2. Proposal
3. Consent forms
4. Data collection tools

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. Copies should also be submitted to all other relevant authorities.

If you have any questions please do not hesitate to contact Mr. P. Khulumani at pkhulumani@gov.bw, Tel +267-3914467 or Mary Kasule at mkasule@gov.bw or marykasule@gmail.com Tel: +267-3632466

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. 9A 10 or Ministry of Health website: www.moh.gov.bw or can be requested via e-mail from Mr. Kgomotso Motlhanka, e-mail address: kgmmotlhanka@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 summarize the proposed change and the rationale for it in the amendment form available from the Health Research Division Office (HRDD), Office No. 9A 11 or Ministry of Health website: www.moh.gov.bw or can be requested via e- mail from Mr. Kgomotso Motlhanka, e-mail address: kgmmotlhanka@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.

Do not hesitate to contact us if you have any questions. Thank you for your cooperation and your commitment to the protection of human subjects in research.

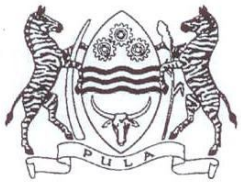
Yours sincerely

P. Khulumani
For Permanent Secretary

PERMANENT SECRETARY
MINISTRY OF HEALTH
RESEARCH UNIT
17 FEB 2010
P/BAG 0038
GABORONE
REPUBLIC OF BOTSWANA

APPENDIX E3: Approval Renewed from the Health Research and Development Division at the Ministry of Health in Botswana

Telephone: (267) 3632000
FAX (267) 353100
TELEGRAMS: RABONGAKA
TELEX: 2818 CARE BD



MINISTRY OF HEALTH
PRIVATE BAG 0038
GABORONE

REPUBLIC OF BOTSWANA

REFERENCE No: PPME: 13/18/1 Vol V (174) 17 February 2011

Principal Investigator: Ms Maimouna Ndiaye

Department/ Organization: Baylor Children's Center of Excellence

Protocol Title: **STUDY ON THE BARRIERS TO ANTI-RETROVIRAL THERAPY ADHERENCE AMONG HUMAN IMMUNODEFICIENCY VIRUS INFECTED ADOLESCENTS**

Review Type: Health Research and Development Committee

Review Date: 13 February 2011

Expiration Date: 16 February 2012

Attachments:

- Continuing review application form dated 7 February 2011.

This certifies that the continuing review request for the protocol above was reviewed under expedited review procedures and approved. The research qualifies for expedited review because:

____ the research poses minimal risk to participants

___X_ the study is still ongoing

Continuing Review

In order to continue work on this study (including data analysis) beyond the expiration date, the Health Research and Development Committee (HRDC) must reapprove the protocol after conducting a substantive, meaningful, continuing review. This means that you must submit a Continuing Report form as a request for continuing review. To best avoid a lapse, you should submit your request 3 months before the lapse date. Please use the forms supplied by our office available on our website: http://www.moh.gov.bw

As a courtesy, the HRDC 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.

Reporting

*O*ther 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
Do not hesitate to contact us if you have any questions.

Thank you for your cooperation and your commitment to the protection of human subjects in research.

Yours sincerely

P. Khulumani
For/Permanent Secretary

PERMANENT SECRETARY
MINISTRY OF HEALTH
RESEARCH UNIT
17 FEB 2011
P/BAG 0038
GABORONE
REPUBLIC OF BOTSWANA

APPENDIX E4: Approval from the Human Research Ethics Committee of the University of the Witwatersrand in South Africa

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG
Division of the Deputy Registrar (Research)

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)
R14/49 Ms Maimouna Ndiaye

CLEARANCE CERTIFICATE	**M10253**
PROJECT	A Study on teh Barriers to Antiretorviral Therapy Adherence among Human (13-18 Years) in Gaborone (Botswana)
INVESTIGATORS	Ms Maimouna Ndiaye.
DEPARTMENT	School of Public Health
DATE CONSIDERED	26/02/2010
DECISION OF THE COMMITTEE*	Approved unconditionally

Unless otherwise specified this ethical clearance is valid for 5 years and may be renewed upon application.

DATE 25/05/2010 **CHAIRPERSON** .....
(Professor PE Cleaton-Jones)

*Guidelines for written 'informed consent' attached where applicable
cc: Supervisor :

DECLARATION OF INVESTIGATOR(S)

To be completed in duplicate and **ONE COPY** returned to the Secretary at Room 10004, 10th Floor, Senate House, University.
I/We fully understand the conditions under which I am/we are authorized to carry out the abovementioned research and I/we guarantee to ensure compliance with these conditions. Should any departure to be contemplated from the research procedure as approved I/we undertake to resubmit the protocol to the Committee. **I agree to a completion of a yearly progress report.**

PLEASE QUOTE THE PROTOCOL NUMBER IN ALL ENQUIRIES...

APPENDIX E5: Approval from the Human Subject Research for Baylor College of Medicine in Houston,Texas

July 28, 2010

BCM
Baylor College of Medicine

Baylor College of Medicine
Office of Research
One Baylor Plaza, 600D
Houston, Texas 77030
Phone: (713) 798-6970
Fax: (713) 798-6990
Email: irb@bcm.tmc.edu

GORDON E SCHUTZE
BAYLOR COLLEGE OF MEDICINE
PEDIATRICS: RETROVIROLOGY

H-27353 - A STUDY OF THE BARRIERS TO ANTI-RETROVIRAL THERAPY ADHERENCE AMONG HUMAN IMMUNODEFICIENCY VIRUS-INFECTED ADOLESCENTS (13-19 YEARS) IN GABORONE

APPROVAL VALID FROM 7/28/2010 TO 7/19/2011

Dear Dr. SCHUTZE

The Institutional Review Board for Human Subject Research for Baylor College of Medicine and Affiliated Hospitals (BCM IRB) is pleased to inform you that the research protocol named above was approved.

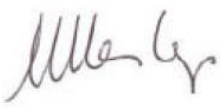
The study may not continue after the approval period without additional IRB review and approval for continuation. You will receive an email renewal reminder notice prior to study expiration; however, it is your responsibility to assure that this study is not conducted beyond the expiration date.

Please be aware that only IRB-approved informed consent forms may be used when written informed consent is required.

Any changes in study or informed consent procedure must receive review and approval prior to implementation unless the change is necessary for the safety of subjects. In addition, you must inform the IRB of adverse events encountered during the study or of any new and significant information that may impact a research participants' safety or willingness to continue in your study.

The BCM IRB is organized, operates, and is registered with the United States Office for Human Research Protections according to the regulations codified in the United States Code of Federal Regulations at 45 CFR 46 and 21 CFR 56. The BCM IRB operates under the BCM Federal Wide Assurance No. 00000286, as well as those of hospitals and institutions affiliated with the College.

Sincerely yours,



Association for the Accreditation of Human Research Protection Programs, Inc.
Full AAHRPP Accreditation

HELEN E HESLOP, M.D., M.B.,Ch.B.
Institutional Review Board for Baylor College of Medicine and Affiliated Hospitals

APPENDIX E6: Approval Renewed from the Human Subject Research for Baylor College of Medicine in Houston,Texas

May 31, 2011

BCM
Baylor College of Medicine

GORDON E SCHUTZE
BAYLOR COLLEGE OF MEDICINE
PEDIATRICS: RETROVIROLOGY

Baylor College of Medicine
Office of Research
One Baylor Plaza, 600D
Houston, Texas 77030
Phone: (713) 798-6970
Fax: (713) 798-6990
Email: irb@bcm.tmc.edu

H-27353 - A STUDY OF THE BARRIERS TO ANTI-RETROVIRAL THERAPY ADHERENCE AMONG HUMAN IMMUNODEFICIENCY VIRUS-INFECTED ADOLESCENTS (13-19 YEARS) IN GABORONE

APPROVAL VALID FROM 5/31/2011 TO 5/30/2012

Dear Dr. SCHUTZE

The Institutional Review Board for Human Subject Research for Baylor College of Medicine and Affiliated Hospitals (BCM IRB) is pleased to inform you that the research protocol named above was approved.

The study may not continue after the approval period without additional IRB review and approval for continuation. You will receive an email renewal reminder notice prior to study expiration; however, it is your responsibility to assure that this study is not conducted beyond the expiration date.

Please be aware that only IRB-approved informed consent forms may be used when written informed consent is required.

Any changes in study or informed consent procedure must receive review and approval prior to implementation unless the change is necessary for the safety of subjects. In addition, you must inform the IRB of adverse events encountered during the study or of any new and significant information that may impact a research participants' safety or willingness to continue in your study.

The BCM IRB is organized, operates, and is registered with the United States Office for Human Research Protections according to the regulations codified in the United States Code of Federal Regulations at 45 CFR 46 and 21 CFR 56. The BCM IRB operates under the BCM Federal Wide Assurance No. 00000286, as well as those of hospitals and institutions affiliated with the College.

Sincerely yours,

Danielle SoRelle

DANIELLE R SORELLE,
Institutional Review Board for Baylor College of Medicine and Affiliated Hospitals

Association for the Accreditation of Human Research Protection Programs, Inc.
Full AAHRPP Accreditation

APPENDIX E7: Approval from Botswana Baylor Children's Clinical Center of Excellence in Gaborone

BOTSWANA BAYLOR CHILDREN'S CLINICAL CENTRE OF EXCELLENCE

BCM
Baylor College of Medici

22 March 2010

Human Research Ethics Committee
University of the Witwatersrand
Johannesburg

Attention: Ms Anisa Keshav

Dear Sir/Madam

Ref: Ms Maimouna Ndiaye: a study on the Barriers to Antiretroviral Therapy Adherence among Human Immunodeficiency Virus Infected 13-18 year old Adolescents in Gaborone, Botswana

I wish to confirm that permission for the above named study to be conducted at this centre will be granted upon receipt of ethical approval for the same from relevant authorities.

Yours faithfully,

Gabriel M. Anabwani
Executive Director

Princess Marina Hospital • Hospital Way • Plot 1836
Private Bag BR129 • Gaborone • Botswana
Tel 3190083 • Fax 3190079

APPENDIX E8: ACTG BASELINE QUESTIONNAIRE

ACTG Adherence Baseline Questionnaire

Date: _____ Self Interviewer Both

Patient ID: _____ How Administered? ☐ 1 ☐ 2 ☐ 3

The answers you give on this form will be used to plan ways to help other people who must take pills on a difficult schedule. Please do the best you can to answer all the questions. If you do not wish to answer a question, please draw a line through it. If you do not know how to answer a question, ask your study nurse to help. Thank you for helping in this important study.

INSTRUCTIONS: Please answer the following questions by placing a circle around the appropriate number response.

A. How sure are you that:

Please circle one response for each question.

		Not at All Sure	Somewhat Sure	Very Sure	Extremely Sure
1.	You will be able to take all or most of the study medication as directed?	0	1	2	3
2.	The medication will have a positive effect on your health?	0	1	2	3
3.	If you do not take this medication exactly as instructed, the HIV in your body will become resistant to HIV medications?	0	1	2	3

B. **The following questions ask about your social support.**

Please circle one response for each question.

		Very Dissatisfied	Somewhat Dissatisfied	Somewhat Satisfied	Very Satisfied
1.	In general, how satisfied are you with the overall support you get from your friends and family members?	0	1	2	3

		Not At All	A Little	Somewhat	A Lot	Not Applicable
2.	To what extent do your friends or family members help you remember to take your medication?	0	1	2	3	4

C. People may miss taking their medications for various reasons. Here is a list of possible reasons why you may have missed taking any medications within the **past month**.

If you have **NOT** taken **any** medications within the **past month**, please check this box and skip to Section D. ☐ 1

In the past month, how often have you missed taking your medications because you:

Please circle one response for each question.

		Never	Rarely	Sometimes	Often
1.	Were away from home?	0	1	2	3
2.	Were busy with other things?	0	1	2	3
3.	Simply forgot?	0	1	2	3
4.	Had too many pills to take?	0	1	2	3
5.	Wanted to avoid side effects?	0	1	2	3
6.	Did not want others to notice you taking medication?	0	1	2	3
7.	Had a change in daily routine?	0	1	2	3
8.	Felt like the drug was toxic/harmful?	0	1	2	3

9. Fell asleep/slept through dose time?	0	1	2	3
10. Felt sick or ill?	0	1	2	3
11. Felt depressed/overwhelmed?	0	1	2	3
12. Had problem taking pills at specified times (with meals, on empty stomach, etc.)?	0	1	2	3
13. Ran out of pills?	0	1	2	3
14. Felt good?	0	1	2	3

D. When was the last time you missed taking any of your medications? Check one box.

- ☐ 5 Within the past week
- ☐ 4 1-2 weeks ago
- ☐ 3 2-4 weeks ago
- ☐ 2 1-3 months ago
- ☐ 1 More than 3 months ago
- ☐ 0 Never skip medications or not applicable

E. In the past week how often did you:

Please circle one response for each question.

		Never/ Rarely	Sometimes	Often	Mostly or Always
1.	Feel like you couldn't shake off the blues even with help from your family or friends?	0	1	2	3
2.	Have trouble keeping your mind on what you were doing?	0	1	2	3
3.	Feel that everything you did was an effort?	0	1	2	3
4.	Have trouble sleeping?	0	1	2	3
5.	Feel lonely?	0	1	2	3
6.	Feel sad?	0	1	2	3
7.	Feel like you just couldn't "get going"?	0	1	2	3

F. In the past month, how often have you:

Please circle one response for each question.

		Never	Almost Never	Sometimes	Fairly Often	Very Often
1.	Been upset because of something that happened unexpectedly?	0	1	2	3	4
2.	Felt unable to control the important things in in your life?	0	1	2	3	4
3.	Felt nervous and "stressed"?	0	1	2	3	4
4.	Felt confident in your ability to handle your personal problems?	0	1	2	3	4
5.	Felt that things were going your way?	0	1	2	3	4
6.	Found that you could not cope with all the things that you had to do?	0	1	2	3	4
7.	Been able to control irritations in your life?	0	1	2	3	4
8.	Felt that you were on top of things?	0	1	2	3	4
9.	Been angered because of things that happened that were outside of your control?	0	1	2	3	4
10.	Felt problems were piling up so high that you could not overcome them?	0	1	2	3	4

G. People have various health habits. The following questions ask about your alcohol and drug use, past and current.

1. **How often have you had a drink containing alcohol – a glass of beer, wine, a mixed drink, or any kind of alcoholic beverage – in the last 30 days?** Check one.

Daily	Nearly Every Day	3 or 4 Times A Week	Once or Twice A Week	2 or 3 Times A Month	Once A Month	Never
☐ 6	☐ 5	☐ 4	☐ 3	☐ 2	☐ 1	☐ 0

If Never, skip ahead to question #4.

2. **On days when you drank any alcoholic beverages in the last 30 days, how many drinks did you usually have altogether? By a drink we mean a can or glass of beer, a 4-ounce glass of wine, a 1-1/2 ounce shot of liquor, or a mixed drink with 1-1/2 ounces of liquor?** Check one.

1 or 2 Drinks Per Day	3 or 4 Drinks Per Day	5 or 6 Drinks Per Day	7 or 8 Drinks Per Day	9 - 11 Drinks Per Day	12 or more Drinks Per Day
☐ 0	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

3. **During the past 30 days, how often have you had 5 or more drinks of alcohol in a row, that is, within a couple of hours (e.g. 2-4 hours)?** Check one.

Daily	Nearly Every Day	3 or 4 Times A Week	Once or Twice A Week	2 or 3 Times A Month	Once A Month	Never
☐ 6	☐ 5	☐ 4	☐ 3	☐ 2	☐ 1	☐ 0

4. Please check "Yes" or "No" for each question.

a. ☐ 1 Yes ☐ 2 No **Have you ever used marijuana?**
If you used this drug, have you used it within the past 6 months?
☐ 1 Yes ☐ 2 No

b. ☐ 1 Yes ☐ 2 No **Have you ever used cocaine (powder, crack, or freebase)?**
If you used this drug, have you used it within the past 6 months?
☐ 1 Yes ☐ 2 No

c. ☐ 1 Yes ☐ 2 No **Have you ever used heroin?**
If you used this drug, have you used it within the past 6 months?
☐ 1 Yes ☐ 2 No

d. ☐ 1 Yes ☐ 2 No **Have you ever used amphetamines (speed)?**
If you used this drug, have you used it within the past 6 months?
☐ 1 Yes ☐ 2 No

5. **Are you <u>currently</u> in methadone treatment?** ☐ 1 Yes ☐ 2 No
If Yes, skip to Question H.

If No, have you <u>ever</u> been in methadone treatment? ☐ 1 Yes ☐ 2 No

H. These last questions ask about your background.

1. **What is the highest level of education you have completed?** (check one)

- ☐ 0 11th grade or less
- ☐ 1 High school graduate or GED
- ☐ 2 2 years of college / AA degree / Technical school training
- ☐ 3 College graduate (BA or BS)
- ☐ 4 Master's degree
- ☐ 5 Doctorate / medical degree / law degree

2. **What is (are) the most likely way(s) that you became infected with HIV?** (check "Yes" or "No" for each question.)

a. Sex with a man who was HIV+

☐ 1 Yes ☐ 2 No

b. Sex with a woman who was HIV+

☐ 1 Yes ☐ 2 No

c. Shared needles with a person who was HIV+

☐ 1 Yes ☐ 2 No

d. Blood transfusion or other medical procedure

☐ 1 Yes ☐ 2 No

e. Don't know

☐ 1 Yes ☐ 2 No

f. Other (needle stick at work, etc.)

☐ 1 Yes ☐ 2 No

Please specify: _____

3. **Do you work for pay outside the home?** ☐ 1 Yes ☐ 2 No

4. **Do you have any children?** ☐ 1 Yes ☐ 2 No

If Yes, how many live with you? ☐☐

I. The following questions ask about symptoms you might have had during the past four weeks. Please check the box that describes how much you have been bothered by each symptom.

		I DO NOT HAVE THIS SYMPTOM	I HAVE THIS SYMPTOM AND ...			
			It doesn't bother me	It bothers me a little	It bothers me a lot	It bothers me terribly
1.	Fatigue or loss of energy?	0	1	2	3	4
2.	Fevers, chills or sweats?	0	1	2	3	4
3.	Feeling dizzy or lightheaded?	0	1	2	3	4
4.	Pain, numbness or tingling in the hands or feet?	0	1	2	3	4
5.	Trouble remembering?	0	1	2	3	4
6.	Nausea or vomiting?	0	1	2	3	4
7.	Diarrhea or loose bowel movements?	0	1	2	3	4

8.	Felt sad, down or depressed?	0	1	2	3	4
9.	Felt nervous or anxious	0	1	2	3	4
10.	Difficulty falling or staying asleep?	0	1	2	3	4
11.	Skin problems, such as rash, dryness or itching?	0	1	2	3	4
12.	Cough or trouble catching your breath?	0	1	2	3	4
13.	Headache?	0	1	2	3	4
14.	Loss of appetite or a change in the taste of food?	0	1	2	3	4

15.	Bloating, pain or gas in your stomach?	0	1	2	3	4
16.	Muscle aches or joint pain?	0	1	2	3	4
17.	Problems with having sex, such as loss of interest or lack of satisfaction?	0	1	2	3	4
18.	Changes in the way your body looks, such as fat deposits or weight gain?	0	1	2	3	4
19.	Problems with weight loss or wasting?	0	1	2	3	4
20.	Hair loss or changes in the way your hair looks?	0	1	2	3	4

Thank you very much for completing these questions.
The information that you provided will help with the development of better drug regimens for all patients with HIV.

PLEASE NOTE: Section "I" on this questionnaire was developed by Amy Justice and Linda Rabaneck. To cite this 20-item symptom index, please contact Dr. Amy Justice at Amy.Justice@med.va.gov.

A STUDY ON THE BARRIERS TO ANTI – RETROVIRAL THERAPY ADHERENCE AMONG HUMAN IMMUNODEFIENCY VIRUS – INFECTED ADOLESCENTS IN GABORONE (BOTSWANA)

ABSTRACT

Introduction: Barriers associated with good adherence to Antiretroviral Therapy (ART) among human immunodeficiency virus (HIV) infected adolescents are multiple and complex. Those barriers contribute to low adherence levels putting infected adolescents at risk of developing resistance and decreasing their survival time. Patients care givers psychosocial and demographic variables, medication related factors and health care delivering factors are among the barriers that correlate with non adherence to antiretroviral drugs (ART's) among HIV infected adolescents. Those barriers vary across individuals within the same population of adolescents.

This study was conducted to determine the level of adherence among HIV infected adolescents on ART and to identify barriers associated with non adherence among this population attending the Botswana Baylor Children's Clinical Center of Excellence (COE) in Gaborone, Botswana.

Materials and methods: A cross sectional analytical study using quantitative data was performed. A structured, self administrated questionnaire adapted from the AIDS Clinical Trials Group (ACTG) was used to identify the barriers while the socio-demographic and clinical data were retrieved from study participants' medical records. The adherence level was estimated using the pharmacy pill count technique. The adolescents aged 13 to 18 years receiving ART for more than 6 months and attending the ART National Program at the time of the study and who did assent and had their care givers consent to participate in the study were included in the analysis.

Results: A high adherence level (75.6%) was reported among the study participants. Besides gender, no other socio-demographic and clinical variables showed association with non adherence. Male adolescents were found to be 70% less likely to adhere to their medication than their counterpart females [p= 0.020, OR=0.30, 95% CI (0.10 – 0.85)]. Furthermore adolescents who missed a dose because their pills were not collected from the pharmacy either by themselves or by their care givers were 77 % less likely to adhere to their ART medication than those who did not miss a dose because they had their medication collected [p= 0.019, OR= 0.23, 95%CI (0.064 – 0.837)].

Conclusion: A high proportion of HIV infected adolescents attending the Baylor Center of Excellence ART National Program were adherent to their medication. Despite the high level adherence to ART among this age group, interventions to improve adherence level should be designed with a focus on male adolescents and to reinforce counseling of care givers and adolescents about the hazards of poor adherence to treatment. Further research is however, needed to elucidate more about the two main barriers that were found to be significantly associated with non adherence among adolescents at Botswana Baylor Children's Clinical Center of Excellence: male-gender and medication collection from the pharmacy.

Key words: Barriers - Anti - Retroviral Therapy - Adhrence - Immunodefiency Virus Adolescent - Botswana