**UNIVERSITY OF NAIROBI**

# ADHERENCE TO ANTIRETROVIRAL THERAPY AMONG HIV INFECTED ADOLESCENTS AT KANGUNDO DISTRICT HOSPITAL

DISSERTATION SUBMITTED IN PARTIAL FULFILLMENT OF THE REQUIREMENTS OF THE UNIVERSITY OF NAIROBI FOR AWARD OF THE DEGREE OF MASTER OF MEDICINE IN PAEDIATRICS AND CHILD HEALTH

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## DECLARATION

I declare that this dissertation is my original work and has not been presented for the award of a degree in any other university.

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## DEDICATION

This dissertation in dedicated to my loving husband and children for their encouragement and support during my studies.

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God bless you all.

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## LIST OF ABBREVIATIONS

| | |
|---|---|
| AIDS | Acquired Immune-Deficiency Syndrome. |
| ADR | Adverse Drug Reactions. |
| ART | Antiretroviral Therapy |
| AYA | Adolescents and Young Adults |
| CCC | Comprehensive Care Clinic. |
| CDC | Center for Disease Control |
| CD4 | Cluster of Differentiation 4 |
| FGD | Focus Discussion Group |
| HAART | Highly Active Antiretroviral Therapy |
| HIV | Human Immune-deficiency Virus |
| KAIS | Kenya AIDS Indicator Survey |
| KDH | Kangundo District Hospital |
| LTFU | Loss To Follow Up |
| NASCOP | National AIDS and STI Control Programme. |
| NACC | National AIDS Control Council |
| PLWHIV | People Living With HIV/AIDS. |
| STI | Sexually Transmitted Infection |
| UNAIDS | Joint United Nations Programme on HIV/AIDS |
| WHO | World Health Organization. |
| RAL | Raltegravir |
| EFV | Efavirenz |

| | |
|---|---|
| ENF | Enfuvirtide |
| ETR | Etravirine |
| NVP | Nevirapine |
| FTC | Emtricitabine |
| 3TC | Lamivudine |
| ABC | Abacavir |
| TDF | Tenofovir |
| DDI | Didanosine |
| AZT | Zidovudine |
| d4T | Stavudine |
| ATV/r | Atazanavir/Ritonavir |
| MVC | Maraviroc |
| LPV/r | Lopinavir/Ritonavir |
| DRV/r | Darunavir/Ritonavir |
| NNRTI | Non-nucleoside Reverse Transcriptase Inhibitors |
| PI | Protease Inhibitors |

## ABSTRACT

**Background**: World Health Organization (WHO) defines adolescents as those aged 10–19 years. They represent 25% of the population in sub-Saharan Africa. Eighty-two percent of the estimated 2.1 million adolescents aged 10–19 years living with human immunodeficiency virus (HIV) in 2012 were in sub-Saharan Africa. Adherence to antiretroviral therapy (ART) is vital to HIV-infected adolescents for survival and quality of life. However, this age group faces many challenges to remain adherent.

According to the Kenya National surveillance of acquired HIV drug resistance in 2013; only 67% of adolescents had viral suppression which reflects poor adherence. It is important to define adherence rates in different groups of adolescents and in the proposed study we explore adherence in those residing in rural areas.

**Objectives:** The primary objective was to determine the level of optimal ART adherence among HIV infected adolescents on ART at the Kangundo District Hospital (KDH). The secondary objective was to describe the factors associated with adherence in the same population of adolescents.

**Methods:** This was a retrospective study with a cross-sectional qualitative component. HIV infected adolescents aged 10 to 19 years who had been on ART and in care at KDH for at least six months were eligible. Disclosure status was determined from the caregiver and, adolescents who fulfilled the inclusion criteria were enrolled in to the study after informed written consent from caregiver and assent from the adolescent. Recent ART adherence was determined by 3, 7 and 30 days recall. Long term adherence was determined as follows: adherence to pharmacy refill with data abstracted from pharmacy database, and adherence to clinic appointments with data abstracted from hospital records for six months prior to the interview date.

Factors associated with adherence to ART were sought including socio-demographic factors, clinical factors, drug related and health system related factors. Focus group discussions were held with HIV infected adolescents in care and who were aware of their HIV status to determine to a greater depth the factors impacting adherence

**Results**: A total of 98 adolescents aged between 10 to 19 years were enrolled into the study with a median (interquartile range (IQR)) age of 14.0 (13.-16.) years. Majority (76.2%) were in their teenage years (13-19 years) and none of the respondents was married. Most (78.6%) were in, or had completed primary school while a few (17.3%) were in secondary school or had already completed secondary school education. Most of the participants (91.8%) were on first line ARV regimen with a median (IQR) duration on ART 6.3 (4.4-8.1) years. At the time of initiation of ART, 11.2%, 35.7% and 53.1% of the study participants were at Stage one, two and three/four of HIV/AIDS respectively as described in the WHO guidelines. Majority 65.3% of the participants had disclosure of their HIV status while the rest (34.7%) had not.

The short term 3, 7 and 30 days optimal adherence, measured by self-report was poor with 76%, 55% and 69% being adherent respectively. Similarly the long term adherence over preceding 6 months as determined from hospital records was poor with only 66.3% being adherent to clinician's appointment and 64.3% optimally adhering to drug refill appointments.

From the univariate analysis several factor were shown to influence adherence negatively including: being in boarding school (*OR* 8.47, 95% *CI* 2.37-30.26, *P*=0.001), feeling tired of taking drugs daily (*OR* 0.13, 95% *CI* 0.05-0.37, *P* <0.001), reporting that dosing at specific times interfered with other daily activities (*OR* 0.27, 95% *CI* 0.10-0.71, *P*=0.006), non-disclosure of HIV status especially for adolescents aged >14 years (*OR* 8.5, 95% *CI* 1.57-46.08, *P* 0.009) and inconvenient appointment dates (*OR* 3.17, 95% *CI* 1,25-8.03, *P* 0.03). Clinicians' behavior perceived as good/excellent (*OR* 4.79, 95% *CI* 1.28-17.91, *P* 0.032), similarly pharmacists' behavior (*OR* 5.42, 95% *CI* 1.25-23.39, *P* 0.022) and adequate health education on HIV infection (*OR* 4.44, 95% *CI* 1.31-15.01, *P* 0.021) were associated with better adherence.

Multivariable analysis revealed that adolescents who were in day school were more likely to be adherent compared to those who were in boarding school (adjusted odds ratio (aOR) 7.99, 95% CI 2.85 – 22.41, p<0.001). Appointments fitting with daily activities was associated with about four-fold increment in the likelihood of adherence to ART (aOR (95% CI) 4.22 (1.51-11.83), p=0.006).

FGDs with adolescents' revealed that good social support, disclosure about HIV status to the adolescents, to other family members and at least one person in school were perceived to improve adherence. Health providers' behavior and attitude towards adolescents were also perceived to influence adherence with most adolescents reporting missed doses due to disappointments and dissatisfaction with the services provided at the clinic.

**Conclusion:** We concluded that adherence to ART among this cohort of adolescents in a rural set up was poor as shown by the self- report, clinicians' appointments and pharmacy refill appointments'. Poor adherence was significantly associated with age above 15 years, non-disclosure of HIV status, being in boarding school, feeling tired of taking drugs daily and dosing times interfering with other daily activities. Similarly, hostile health providers attitude, inadequate time spend by clinician addressing the adolescents needs, long waiting times, lack of privacy at the hospital and inconvenient timings of appointments were perceived as barriers to adherence. Stigmatization arising from the location of the CCC shows a need to re-design the service to protect confidentiality of adolescents living with HIV.

**Recommendations:** Our findings suggest need for strengthening of interventions to assist adolescents' in adhering to their medication including: Early disclosure, continuous psychosocial support, involvement of family and school "buddy" in adolescent care especially those in boarding schools. There is need to tailor the health services to be adolescent friendly at the level health provider, timing of appointments and privacy.

## CHAPTER 1. INTRODUCTION

The Human Immunodefiency Virus (HIV) is a human retrovirus which belongs to a large family of ribonucleic acid (RNA) lentiviruses that are associated with diseases that cause immunosuppression.[1, 2] There are two types of HIV, HIV-1 and HIV-2. HIV-1 is the most common subtype worldwide while HIV-2 is mostly found in West Africa with highest prevalence in Guinea-Bissau and Senegal.[3]

The hallmark of HIV infection is the progressive destruction and depletion of CD4 T-cells leading to onset of acquired immunodeficiency syndrome (AIDS). AIDS results during the advanced stages of HIV infection when the remaining CD4 T-cells are unable to do immune surveillance and prevent opportunistic infections (immune system failure).[2] It is a chronic potentially life-threatening condition.[2]

An estimated 35.3 million people were living with HIV globally in 2012, with over two million being adolescents aged 10 to 19 years, 82% of these adolescents were in Sub-Saharan Africa.[4]
Antiretroviral therapy (ART), the use of pharmacologic agents that have inhibitory effects on HIV replication has had remarkable expansion over the years, worldwide and also in Kenya particularly for the adult population. Around 9.7 million people living with HIV had access to ART in low- and middle-income countries.[4] In Kenya, 78.5% of adults eligible for ART were initiated to therapy by 2013, however, ART coverage in children still remains low at 43.3 % (figure 1).[5,6]

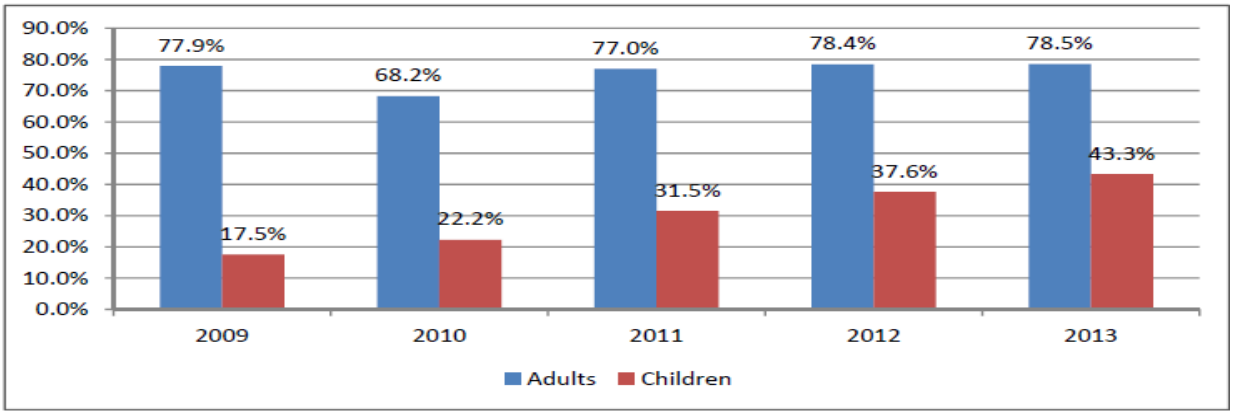


**Figure 2.1. Percentage of Children and Adults Eligible for Antiretroviral Therapy who are on Antiretroviral Therapy in Kenya.[6]**

For ART therapy to be successful, particularly for viral suppression, perfect adherence to treatment is critical and adherence has been shown to be a powerful predictor of survival for individuals living with HIV and AIDS.[7] It has been shown that 95% adherence to ART regimens is optimal[8] and that, 10% increase in the level of adherence results in a 21% reduction in disease progression.[9] Conversely, a 10% decrease in adherence was associated with doubling of the HIV RNA level, suggesting that small differences in adherence can result in major differences in biological control.[10] Non-adherence to therapy is a significant problem, particularly since the disease process is chronic and therapeutic regimens are employed for prolonged periods.[11] This is especially so in adolescents who face developmental, behavioral and cognitive challenges to remain adherent. A meta-analysis that utilized studies from all over the world on ART adherence in adolescents showed varying results. In Africa and Asia, 70% of adolescents were adherent while in Europe and North America 50- 60% adolescents were adherent.[12] In Kenya, according to the NASCOP 2013 surveillance of acquired HIV drug resistance survey, the viral suppression rate in adolescents was 67% suggesting poor adherence.[13]

Many factors have been shown to affect adherence, either negatively or positively. Before measures are implemented to improve adherence, it is essential to identify the main factors that contribute to inability of the clients to take their medications as expected.[14] The proposed study seeks to determine the level of adherence and describe the factors associated with adherence in adolescents on ART receiving care in a rural Hospital in Eastern Kenya.

# CHAPTER 2. BACKGROUND AND LITERATURE REVIEW

## 2.1. Epidemiology of Human Immunodeficiency Virus Infection

Globally, the HIV/AIDS epidemic continues to expand with an estimated 35.3 million people living with HIV in 2012.[3] Over two million are adolescents aged 10–19 years, and five million are young people aged 15–24. Of the 2.1 million adolescents aged 10 – 19 years living with HIV, 82% were in Sub-Saharan Africa.[3] There has been a notable decline in both number of new infections and number of AIDS related deaths.[3] This is due to the dramatic expansion in the availability and accessibility of Antiretroviral therapy especially in resource limited settings . There was 30% decline in AIDS related deaths between 2005 and 2012 (in 2012, 1.6 million people died from AIDS compared to 2.3 million in 2005 worldwide).[3]

Kenya has also noted an encouraging decline in the HIV prevalence from 1995 to 2003 (10.5% in 1995 to 6.7 % in 2003). [5, 6] The prevalence has however stabilized over the last decade due to the scale up of antiretroviral therapy and reduction in the number of new infection, currently the prevalence is 6% among people aged 15–49 years; 5.6 % male and 7.6 % females. Of the 1.6 million people living with HIV, 12 % are children below 15 years. [5, 6]

Of concern is that Adolescents and Young Adults (AYA) represented 40 % of new HIV infections globally and, in contrast to the overall decrease in AIDS related deaths between 2005 and 2012, the AIDS related deaths in adolescents aged 10 – 19 years more than doubled in Sub-Saharan Africa.[12]

## 2.2. The Natural History of Human Immunodeficiency Virus in Children and Adolescents

HIV infection during infancy and early childhood has been shown to have rapid disease course presenting with failure to thrive, severe bacterial and viral infections , AIDS defining illnesses like Pneumocystis Pneumonia, HIV encephalopathy and refractory candidiasis.[15] A bimodal disease pattern has been demonstrated in those infants infected through mother to child transmission (vertical transmission) in studies locally and globally. Infants infected in utero and perinatally

progress quickly into AIDS and die before 2 years of age (rapid progressors) and those infected through breast milk survive beyond 2 years and progress more slowly to AIDS and death.[16, 17]

In addition to vertical transmission, HIV in adolescents is due to sexual transmission (horizontal transmission), adolescents and young adults are more vulnerable to this mode of transmission in Sub-Saharan Africa and its noteworthy that horizontal HIV transmission rates are still rising among adolescents.[18] These adolescents show a progression similar to that seen in adults with 10% having rapid progress to AIDS in 2 to 3 years following infection (rapid progressors), 60 – 80% progressing to AIDS in 8 – 10 years ( typical progressors ) and about 10% will not develop AIDS even after 10 years (slow progressors).[19]

### 2.3. Treatment of Human Immunodeficiency Virus Infection

The World Health Organization recommends a combination of three or more antiretroviral (ARV) drugs to achieve viral suppression. There are six distinct classes of antiretroviral drugs; nucleoside and nucleotide reverse transcriptase inhibitors, the non-nucleoside reverse transcriptase inhibitors (NNRTIs), the protease inhibitors (PIs), the fusion inhibitors (FIs), the CCR5 co-receptor antagonists and the intergrase inhibitors.

In the 2013 guideline for treatment of HIV, WHO recommended earlier initiation of ART, the antiretroviral regimens and dosing schedules recommended for adults are also recommended for adolescents heavier than 35 kg.[24] The same guidelines have been adopted in the 2014 Kenyan guidelines on ART by the Ministry Of Health, the two tables below outline in details when to start treatment in children, adolescents and adults (Table 2.1 and 2.2).[25]

**Table 2.1. Kenya Guidelines: When to Start Antiretroviral Therapy in Adolescents and Adults[25]**

| Population | Recommendation |
|---|---|
| When to start ART in adolescents ≥15 years and adults | •All HIV-infected adolescents and adults with CD4 count <500 cells/mm3 irrespective of WHO stage<br>•All HIV-infected pregnant women irrespective of CD4 count, WHO stage or gestation age<br>•All HIV-infected breastfeeding women irrespective of CD4 count, WHO stage<br>•All HIV-infected spouses and sexual partners in sero-discordant relationships irrespective of their WHO stage or CD4 cell count<br>•All HIV-infected adolescents and adults with WHO stage 3 and 4 disease irrespective of CD4 count<br>•All Hepatitis B Virus/HIV co-infected persons irrespective of CD4 count<br>•All TB/HIV co-infected persons irrespective of CD4 count |

**Table 2.2. Kenya Guidelines: When to Start Antiretroviral Therapy in Children[25]**

| Population | Recommendation |
|---|---|
| When to start ART in children less than 15 years | •ART should be initiated in all HIV-infected children aged 10 years and below, regardless of WHO stage or CD4 count %.<br>•ART should be initiated in all HIV infected children above 10 years of age with CD4 cell count ≤500 cells/mm3, Regardless of WHO stage.<br>•All HIV-infected children above 10 years with WHO stage 3 and 4 disease, Hepatitis B Virus/HIV, TB/HIV co-infection should be initiated on ART irrespective of CD4 count.<br>•In circumstances where DNA PCR testing is not readily available ART should be initiated in any child younger than 18 months of age who meets criteria for presumptive diagnosis of severe HIV disease, confirmatory DNA PCR testing should be done as soon as possible. |

Three decades into the HIV/AIDS pandemic there is growing number of adolescents living with the virus. Since 2004, there has been scale up in pediatric ART access resulting in significant decline in the mortality rates in HIV infected children[20] unlike before, when HIV infected infants in Africa had 50% risk of dying before 2 years.[21] The improved access and availability of ART has resulted in a

rise in the life expectancy of children living with HIV and majority of these children, diagnosed and initiated on treatment early will grow in to adolescence and adulthood.[22] The use of anti retroviral drugs has transformed HIV in these adolescent into a chronic disease.[22]. In addition, a large number of children in Sub-Saharan Africa who got infected perinatally are presenting to health care institutions for the first time during adolescence.[23]

Patients on long-term ART with undetectable HIV in plasma still harbor replication competent virus as the proliferating CD4 lymphocytes and follicular dendrite cells in lymphoid tissues, and macrophages throughout the body remain as reservoirs of infection.[26, 27] Therefore, even after years of viral suppression with antiretroviral drugs, there is a rebound of detectable peripheral blood viremia within 2 weeks of stopping therapy.[28] For this reason, with the available antiretroviral drugs, treatment is life long, this is a challenge during adolescence, a phase that has been associated with deviations from expected or prescribed behaviour.[29] It makes it necessary for us to study adherence in this growing population and the factors that influence their adherence to ART in order to help health care providers and institutions to put measures in place to curb non-adherence.

### 2.4. Characteristics of Adolescents

The World Health organization defines adolescents as those aged 10 to 19 years. Adolescence is a period of challenge, with Significant physical, cognitive, emotional and social changes .It is characterized by rebellious behavior, risk of peer influence both negatively and positively, fluctuations in self-esteem as well as incomplete physiological and biological development of the impulse control in the frontal cortex.[30] The pubertal changes in the limbic system (ventral striatum and amygdale) lead to increase in peer influence. The concrete thinking, impulsiveness, feeling of invulnerability and susceptibility to peer influence impacts adherence to ART negatively. Characteristics of adolescents are summarized in Table 3 below.

**Table 2.3. Stages of Development in Adolescents[31]**

| CATEGORY OF CHANGE | EARLY (10–15 years) | MIDDLE (14–17 years) | LATE (16–19 years) |
|---|---|---|---|
| **Sexual development** | Secondary sexual Characteristics appear | Advanced secondary sexual characteristics | Physically mature |
| **Growth spurt** | Rapid growth reaches a peak | Growth slows down; Reaches about 95% of adult size | |
| **Cognition** (ability to get knowledge through different ways of thinking) | Thinks in concrete terms (i.e. the "here and now")<br>Does not understand how actions affect future | Thinking is more abstract (theoretical) but goes back to concrete thinking when under stress<br>Better understands long term results of own actions | Abstract thinking now established<br>Plans for the future<br>Understands how current choices and decisions have an effect on the future |
| **Psychological and social** | Worries about rapid physical growth and body image<br>Has frequent mood changes | Has established body image<br>Thinks about fantasies /impossible dreams<br>Feels very powerful<br>May experiment with sex, drugs, friends, risks | Plans and follows long term goals<br>Has established sense of identity (who he or she is) |
| **Family** | Still defining comfort with independence/ dependence | Has conflicts with authority figures | Is moving from a child-parent/guardian relationship to more adult-adult relationships |
| **Peers** | Peers very important for development<br>Has intense friendships with same sex<br>Has contact with opposite sex in groups | Has strong peer friendships that help affirm self-image<br>Peer groups define right and wrong | Decisions/values less influenced by peers and more influenced by individual friendships<br>Selection of partner based on individual choice rather than on what others think |
| **Sexuality** | Focus is on self exploration and evaluation | Has preoccupation with romantic fantasy<br>Tests how he or she can attract others<br>Sexual drives emerging | Forms stable relationships<br>Has mutual and balanced sexual relations<br>Is more able to manage close and long-term sexual relationships<br>Plans for the future |

## 2.5. Defining Adherence to Antiretroviral Therapy

According to WHO 2003, adherence is the extent to which a client's behavior matches the prescribed care regimen as agreed upon through a shared decision making process between the client and the health care provider. This includes; right frequency, right dose and right time, observing dietary restrictions and attending all scheduled clinic visits. The ability to keep these instructions is defined as 100% adherence. Adherence of 95% and above has been accepted as optimal adherence, with lesser adherence level showing decreasing viral suppression.[8]

However, the level of adherence needed also depends on regimen used; Bengsberg D. et al in 2005 showed that less than 95% adherence was adequate for patients on Non-Nucleoside reverse transcriptase inhibitors. Table 4 below summarizes the results in Bengsbergs' study, after a median follow up of 9.1 months most people on NNRTI therapy had a viral load below 400copies/ml even with adherence level as low as 54%.[32]

**Table 2.4. Less than 95% of NNRTI Therapy is Adequate to Achieve Viral Suppression.[32]**

| Adherence by Pill Count, % | Level of Viral Suppression with NNRTI Group, % | Level of Suppression in the PI Group, % |
|---|---|---|
| 94 to 100 | 90 | 65 |
| 74 to 93 | 60 | 60 |
| 54 to 73 | 75 | 30 |
| 0 to 53 | 30 | 12 |

## 2.6. Adherence of Adolescents to Antiretroviral Therapy

The successful clinical, immunological and virological outcomes of ART are dependent on at least 95% adherence to the regimen.[8] Studies both locally and worldwide have shown varying but suboptimal adherence levels to ART by adolescents[39, 41] while other studies showed poor adherence in adolescents compared to adults and also children[33,34]

For example, a study done by Nachega et al in 2009 in South Africa showed that adolescents adherence to ART was lower than that of adults as measured by pharmacy refill. South African

adolescents' adherence was 20.7% at 6 months, 14.3% at 12 months, 6.6% at 24 months compared to adult's adherence of 40.5%, 27.9%, and 20.6% at each time point, respectively.[33]

Gross R. et al carried out a cross-sectional study among 262 adolescents aged 10 – 19 years, who had been on ART and aware of their status in two clinics in Zimbabwe. Adherence was determined by self reports and 61% of these adolescents were adherent .These adherent adolescents had these factors in common: most were living with family, majority were comfortable talking with their health-care provider, were confident in their ability to take medication and satisfied about their care.[39]

In Kenya, Gatuguta et al in 2009 carried out a study on adherence among 158 adolescents aged 10 – 19 years in Kenyatta National Hospital who had been on ART for at least 6 months prior to the study. Data was obtained by structured questionnaires, focus group discussions, assessed appointment keeping for six months prior to the interview and also drug refill records abstracted from pharmacy database. Good adherence was defined as 95% or more of the prescribed medication. Overall, 93.7% of the adolescents had good self-reported adherence, 96.8% kept their scheduled clinic appointment and 95.6% refilled their drugs on time. Commonest reasons given for missing doses by the adolescents included forgetting to take medication, being away from home and a school schedule that did not allow them time to take medications. Stigma and lack of social support were identified as significant barriers to adherence in these adolescents in both the qualitative and quantitative methods. Promoters of adherence were extensive counseling before treatment initiation as well as during treatment, peer counseling and support groups.[40]

In the United States of America (USA), a review of 21 articles that reported on ART adherence among HIV-infected youth showed suboptimal adherence rates ranging from 28.3 to 69.8%.[34] Similarly adherence has been shown to decrease as children grow into adolescence[35] and is much less in older adolescents, with adolescents above 15 years of age having a greater risk of non-adherence compared to younger adolescents.[36]

In another study in USA, Lindsey JC et al followed-up a cohort of 120 adolescents (11 to 22 years) on ART for 3 years. Of the 120 adolescents 44(37%) remained in the study for 3 years, only 24% of these were able to reach and maintain an undetectable viral load. The main variable associated with this poor response to ART was lack of adherence to therapy.[37]

In 2008, LF Filch et al carried out a cross-sectional study in Brazil among 102 adolescents 10- 19 years who had been on ART for at least 2 months. Adherence was determined by self report for the 3 days prior to the interview and viral load done before the interview was used to validate results. Adherence was defined as taking 95% and above of the prescribed ART, 94% of the adolescents in this study were adherent. Factors associated with non-adherence in this study were: adolescent not concerned about treatment, failure to carry required dose while away from home, lack of education by the health –care provider.[38]

Level of adherence to ART in adolescents varies in different parts of the world. In a systematic review and meta-analysis by Sung-Hee Kim et al in 2014, which included studies from all continents, overall adherence was 62% but varied from region to region. In Africa and Asia 83% of HIV infected adolescents and young adults receiving ART were adherent to therapy, with 53%, 62% and 63% adherence levels for North America, Europe and South America respectively. Adherence in these studies was measured using viral suppression (98% of the studies), self-report, Pharmacy refills and some used multiple methods. The difference in adherence levels was attributed to many factors including differences between focused and generalized epidemics, access to health care and funding.[12]

**Table 2.5. Adherence to Antiretroviral Therapy in Adolescents**

| Author/Year | Location | Number and age of patients | Definition of adherence | Measure of adherence | Percentage adherence |
|---|---|---|---|---|---|
| Gatuguta et al , 2009.[40] | Kenyatta National Hospital, Nairobi | 158<br>10 – 19 years | ≥ 95% | Pharmacy refill record ,clinic appointment & self report | 93.7 |
| Nyasulu P. et al, 2010 2011.[41] | Botswana | 82<br>13 – 18 years | >95% | Pill count<br><br>Viral load | 75.6<br><br>94 |
| Gross R. et al, 2014.[39] | Zimbabwe | 262<br>10 – 19 years | ≥ 95% | Self reports | 61 |
| L. F. Filho et al, 2008.[38] | Brazil | 102<br>10 – 19 years | ≥ 95 | Self report | 94 |

## 2.7. Effects of Poor Adherence to Antiretroviral Drugs

While the ultimate goal of ART is to reduce HIV-related morbidity and mortality, the primary aim is full and durable viral suppression. Poor adherence is the driving cause of treatment failure, HIV drug resistance, disease progression and HIV transmission. Full viral suppression, only achievable with good adherence helps to maintain maximum immune function and minimizes the development of drug-resistant virus selected by ongoing replication in the presence of antiretroviral drugs. Various studies have shown that for most patients, near-perfect (>95%) adherence is necessary to achieve full and durable viral suppression.[8, 10]

### *2.7.1. Adherence and Antiretroviral Drug Resistance*

HIV-1 has a high mutation rate with nearly one nucleotide mutation per replication cycle.[42] This ability to rapidly generate new variants allows HIV-1 to evade the immune system and develop ARV drug resistance. Drug resistance can either be acquired through drug selection pressure (acquired resistance), or transmitted from person to person (transmitted resistance). Naturally occurring drug-resistant viruses are rare since development of drug resistance requires the

concurrence of two factors: antiretroviral drug exposure and ongoing viral replication. Friedland & Williams suggested that the relationship between adherence and the development of resistance to antiretroviral drugs may be 'bell-shaped' in which high and low levels of adherence have a little risk of antiretroviral drug resistance, and intermediate adherence levels have the highest risk for development of ARV drug resistance. His study further showed that missing one out of five ART doses lead to ART resistance.[43] Similar findings were demonstrated by Seth et al, his study showed that the highest risk of virological failure and development of new drug resistance occurred in the 70–90% adherence range, with lower risks of new resistance at both higher and lower adherence levels. He also noted that self reported adherence longitudinally correlated well with incidence of HIV drug resistance.[44]

In Kenya, a study looking at treatment failure and antiretroviral drug resistance (ADR) in adults, fifteen years and above showed that poor adherence was related with development of antiretroviral drug resistance. They studied 232 adults on first–line ART, 57 (24.6%) of these patient had virological failure. Of these patients identified as having virological failure, 52.7% had at least one detectable HIV-1 resistance associated mutation, giving an overall antiretroviral drug resistance prevalence of 12.5%. Of note is that younger age was associated with poor adherence with those aged 15 – 34 years having higher prevalence of ADR compared to those aged ≥35 years (frequency 19% and 10% respectively, $p < 0.001$).[45] The genetic barrier to resistance and potency (antiviral activity) of an antiretroviral determine in large part how susceptible that antiretroviral is to development of HIV-1 resistance (figure 2.2).

The level of non-adherence that lead to drug resistance are different for NNRTI and PI based regimens, very little drug pressure is required to create a selective advantage for NNRTI resistance and levels of adherence as low as 2% are enough to select for NNRTI resistance virus.[47] However, adherence falling below 85% is required to select for unboosted PI resistant virus, the level that selects for boosted PI resistant virus is unclear.[48]

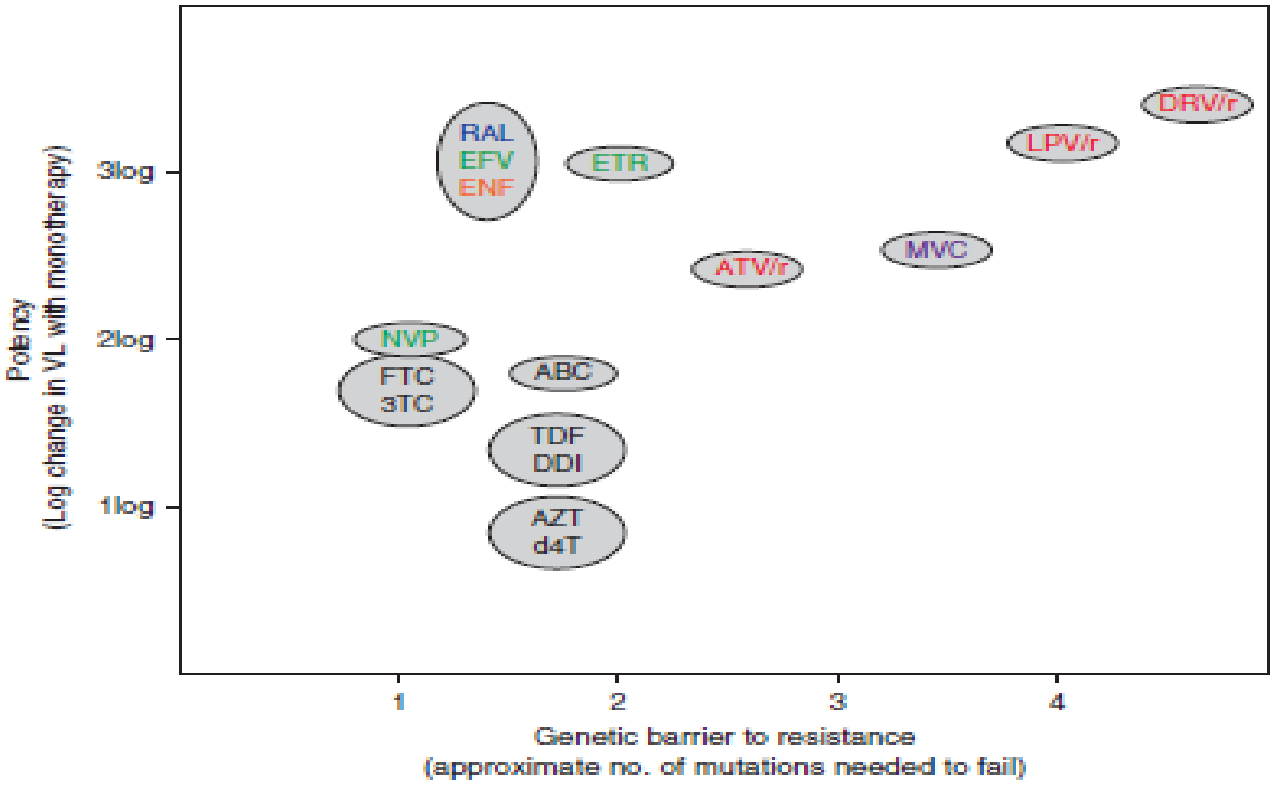


**Figure 2.1. Genetic Barriers and Potencies of Commonly used Antiretrovirals**[46]

*2.7.2. Adherence and Treatment Failure*

"Treatment failure is defined by a persistently detectable viral load exceeding 1000 Copies/ml (that is, two consecutive viral load measurements within a three-month interval, with adherence support between measurements) after at least six months of using ARV drugs." WHO provides three criteria for defining treatment failure, including clinical (progression to new AIDS-defining illness), immunologic (falling CD4) and virology failure (failure of viral suppression or rebound of plasma HIV-1 RNA).[24] The three types of treatment failure may happen alone or together, but generally, virologic failure happens first, followed by immunologic failure, and then clinical progression and may happen months to years apart. Viral load is recommended as the preferred monitoring approach to diagnose and confirm ARV treatment failure, where it cannot be done routinely, CD4 count and clinical monitoring should be used to diagnose treatment failure.[24] Viral load should be undetectable within 24 weeks of starting treatment, for some this occurs within 3 to 6 months.

Seth et al in 2003 recruited and followed up a cohort of 195 patients on ART at the Johns Hopkins outpatient centre. The results showed that missing 11 – 30% of ART doses after achieving viral suppression, and recently missing a scheduled clinic visit was associated with a great risk of viral rebound and significant risk of resistance.[44]

Mathieu et al in Cameroon analyzed a subset of 194 patients whose 6-month viral load and pharmacy refill charts were available, 38% of the pharmacy refill non-adherent patients demonstrated virological treatment failure while 95% of pharmacy refill adherent patients presented with virological suppression. Self reported adherence in this study did not predict virological suppression.[49]

## 2.8. Factors Affecting Adherence to Antiretroviral Therapy

Chesney in 2007 stated that, "Before measures are implemented to improve adherence, it is essential to identify the main factors that contribute to inability of the clients to take their medications as expected."[14] JR. Ickovics & SC Meads categorized factors that influence adherence to antiretroviral therapy into five main groups as illustrated in figure 2.2. These factors included client factors, treatment regimen factors, disease characteristic, client-provider relationships and clinical settings/ systems of care related factors.[51]

### *2.8.1. Disease Characteristics and Adherence*

Based on studies looking at chronic diseases, degree of symptoms and opportunistic infections adversely affect adherence.[8] On the contrary, another study showed that severe opportunistic infections increased adherence, as such clients may perceive their illness to be severe and adhere better to their treatment.[11]

### *2.8.2. Client Factors and Adherence*

Patient's factors include socio-demographic characteristics such as gender, ethnicity, educational level, unemployment and behavior, psychosocial factors such as active drug or alcohol use, degree of social support, disclosure, social stability, depression and other psychiatric illnesses. Studies

have shown that male sex, black race, older age, higher level of education and literacy were associated with better adherence while depression, active drug or alcohol consumption results to poor adherence.[11, 52, 55] Disclosure status is a major determinant of adherence in adolescents, a study done in Uganda reported that 75% of adolescents who knew their status reported perfect adherence to medication, while only 20% of those who had not been disclosed to reported similar adherence. Additional studies in Uganda and Kenya also showed similar results. [54] With fewer medication regimens available to sub-Saharan Africa, it is vital to encourage disclosure with the subsequent increase in adherence, as this knowledge could help prolong the lives of those infected.

### *2.8.3. Medication Factors and Adherence*

These include: Dosage, taste, formulations, pill burden, medication fatigue, inadequate knowledge to medication regime, difficult side effects, poor fit between drug dosing and patient's life style and eating habits. Studies have shown that lack of knowledge about ART, high pill burden, side effects and inconvenient dosing were associated with lower the adherence level, however, dosing schedules and food restrictions appeared to have more influence on adherence than pill burden.[52, 55] Adolescents identified lack of education by healthcare giver on how to take antiretroviral drugs and school schedule that did not allow them time to take medications as impediments to good adherence.[38, 40]

### *2.8.4. Client-Provider Relationship and Adherence*

Supportive relationship between the client and healthcare provider helps the client overcome some barriers to adherence. Trust and confidence in the provider has been shown to increase the levels of ART adherence, good relationship improved the adherence.[52, 55] Perception of the provider competence, quality and clarity of communication, compassion shown by the provider and involvement of the client in the treatment decisions have been identified as motivators of ART adherence. A friendly, supportive and non judgmental attitude of the health care providers, convenient appointment scheduling and confidentiality contribute to better adherence.[5]

### *2.8.5. Health Systems and Adherence*

Accessibility of health care facilities, waiting time, opening time, availability of counseling services for PLWHIV plays a major role in influencing the degree of adherence to the prescribed ART regimen.[55, 57]

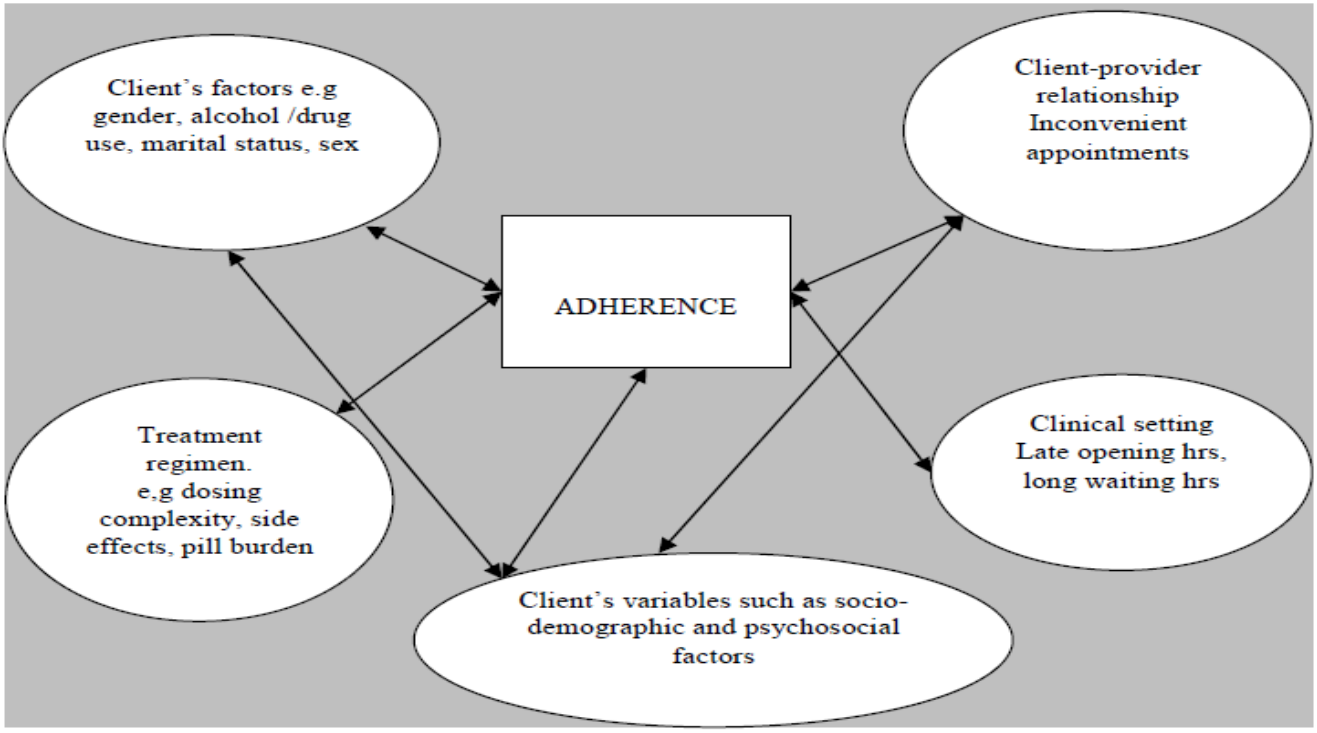


**Figure 2.2. Interrelationships of Key Factors Influencing Antiretroviral Adherence.[51]**

## 2.9. Assessing Adherence

There are different methods for assessing adherence and the level of adherence is specific not only to places and patient groups but also to the method of adherence measurement used. They include direct methods such as biologic markers and body fluid assays, or indirect methods such as self-report or interview administered questionnaires, pill counts, pharmacy records, appointment keeping records, Medication Event Monitoring (MEMs), and viral load monitoring.[58] There are no gold standard methods for measuring adherence and a combination of these methods can be used.

Patient self-reports is the most widely used given its ease of implementation, affordability and less staff needed. Studies have also indicated that self-reports emphasizes the active role of patients and caregivers in their own care, correlates well with both viral load and clinical outcomes hence suggested as strong predictor of adherence.[10,59] However, self-reports have low sensitivity, tend to overestimate adherence due to recall bias[60] and hence needs validation with a more objective method of assessing adherence as treatment failures have been shown, even with high levels of self-reported adherence.[61]

Pill count and appointment keeping adherence have been recommended by WHO as predictors of HIV drug resistance.[62] Manual pill count is cheap and an easy way to determine adherence. However, it is limited because of intense need for staff and possibility of pill sharing and dumping. Appointment keeping is easily abstracted from patient's record but it does not directly predict adherence to medication.

Pharmacy refill is an objective method of assessing adherence used in clinical care. It has been validated as a measure of ART adherence related to viral load but use in predicting patient outcome has not been well demonstrated. [63, 64] However, in a study in Cameroon in 2009, pharmacy-refill adherence was a good predictor of virologic outcome at 6 months. Results showed that 38% of the pharmacy non-adherent patients demonstrated virological treatment failure while 95% of pharmacy adherent patients presented with virological suppression.[49]

Use of Medication Event Monitoring/computerized medication caps and monitoring of surrogate markers are reliable and less prone to respondent bias. However, these need advanced technology, high cost, and complex logistics and therefore not widely applicable in sub-Saharan Africa.[65]

## 2.10. Conceptual Framework

Several interacting elements may influence adherence to ART including health system and health care provider factors, disease related factors, drug related factors and patient related factors. In our study, we set out to investigate socio-demographic, drug related, health system related and clinical factors influencing adherence. The conceptual framework of the factors associated with adherence is shown below in figure 2.3.

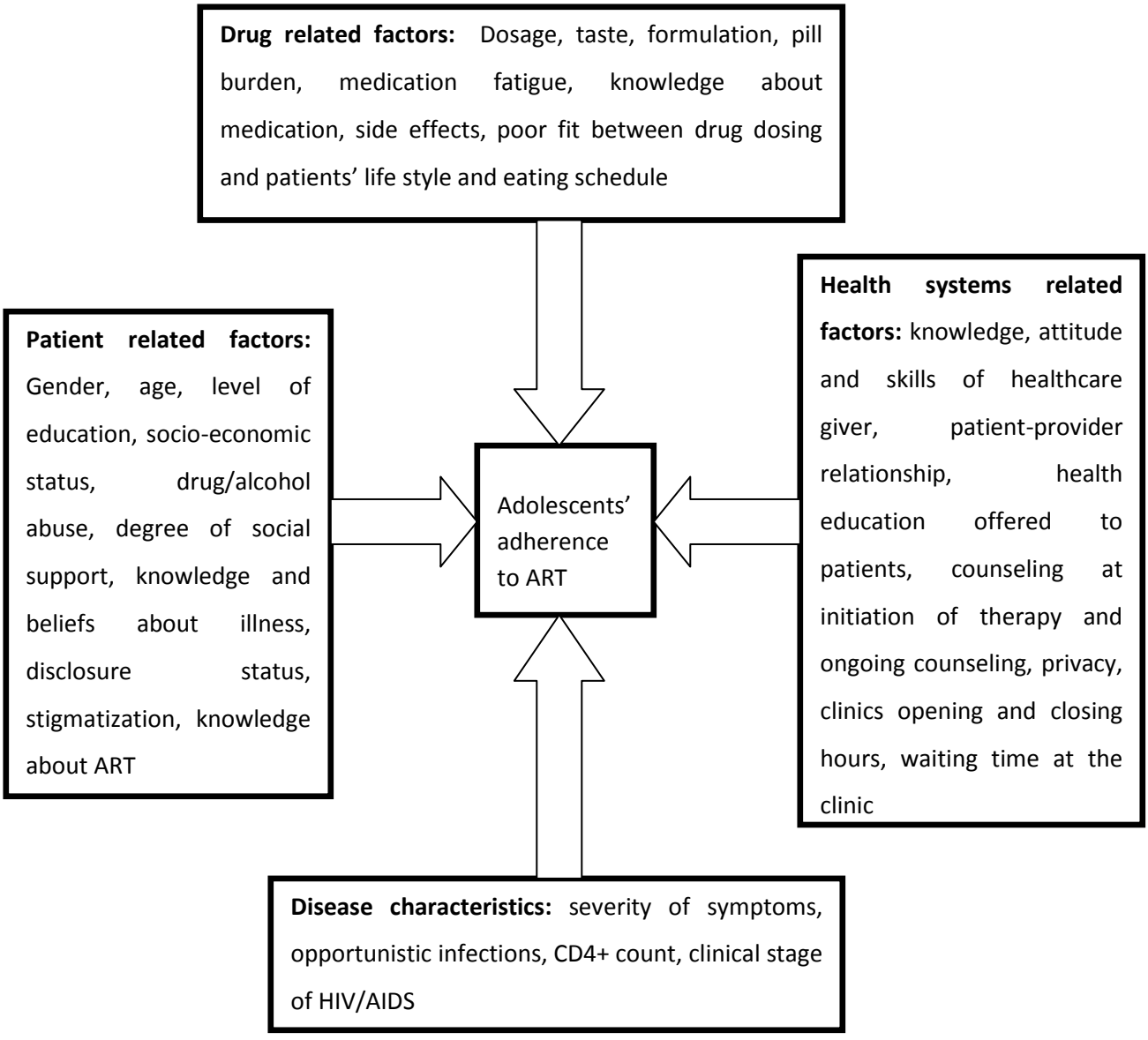


**Figure 2.3. Factors Influencing Adolescents Adherence to ART**

## 2.11. Study Justification

HIV is lifelong and without treatment it may kill. Available treatment is only effective if high adherence level is maintained and continued for life. Adolescence is a phase associated with deviation from expected or prescribed behavior, have incomplete physiological and biological development of impulse control in the frontal cortex,[29,30] these make them more likely to have poor adherence to ART.

Adolescents and Young Adults (AYA) represented 40 % of new HIV infections globally and, in contrast to the overall decrease in AIDS related deaths between 2005 and 2012, the AIDS related deaths in adolescents aged 10 – 19 years more than doubled in Sub-Saharan Africa.[12] Poor adherence is a major factor contributing to the high mortality rate in adolescents. Existing evidence has shown that adherence to ART is poor among adolescents compared to adults and children [33,34] and decreases as children grow into adolescents.[35] Poor ART adherence increases the likelihood of ART drug resistance, HIV disease progression, death and lack of future therapeutic options, adolescents remains healthy and are able to achieve optimal growth and development.

There is limited data on level and factors associated with adherence to ART among adolescents especially in our rural areas. In the past a lot has been done in terms of diagnosis and initiation of treatment, poor adherence threatens to reverse the expected gains as good outcome with ART can only be realised with high level of adherence. It is therefore paramount for health care providers to invest more in enhancing adherence in HIV positive adolescent. Studies among the adolescents will go along way in helping to understand their unique challenges and guide in designing policies aimed at tackling the specific challenges. This study sought to determine the level of, and factors associated with adherence to ART in HIV infected adolescents in care at the Kangundo District Hospital (KDH).

## 2.12. Study Utility

The study will provide valuable information on pertinent factors that affect adherence to ART in adolescents and hence guide clinicians in putting measures in place to help improve adherence in adolescents at the KDH, and Kenya as a whole. The study will also identify priority areas requiring urgent action, guiding clinicians and policy makers to prioritise when laying down strategies to curb non-adherence.

# CHAPTER 3. RESEARCH QUESTIONS AND STUDY OBJECTIVES

## 3.1. Research Question

What is the level of optimal adherence to antiretroviral therapy and what factors impact adherence among HIV infected adolescents in care at the Kangundo District Hospital?

## 3.2. Study Objectives

***Primary Objective***

To determine the level of optimal adherence to antiretroviral therapy among HIV infected adolescents in care at the Kangundo District Hospital.

***Secondary Objective***

To describe the factors associated with optimal adherence among HIV infected adolescents in care at the Kangundo District Hospital. Factors of interest included socio-demographic, clinical factors, drug related facors, health system related factors and disclosure of HIV status.

# CHAPTER 4. METHODOLOGY

## 4.1. Study Design

We conducted a retrospective cohort study with a cross-sectional qualitative component. The retrospective cohort design was used to evaluate the level of adherence and factors associated with adherence among the adolescents at KDH. The cross-sectional qualitative component in form of focus group discussions, was used to further elucidate the factors associated with adherence.

## 4.2. Study Setting

The study was conducted at KDH, a level four Hospital in Kangundo sub-county in Machakos county. The Hospital lies in the lower Eastern part of Kenya approximately 60 kilometres East of Nairobi. It serves approximately 250,000 people most of them being from the Kamba ethnic group, their main occupation is small scale farming and livestock keeping. 56% of the population lives below poverty level with 25% to 35% of the population being unemployed. Kangundo District Hospital provides inpatient and outpatient services to both children and adults. It's daily patient turnover is 200, with 100 of these being children.

Kangundo level 4 Hospital's HIV clinic was started in 2005. At present it has 3500 patients ever enrolled into care. Out of these, 150 are adolescents aged 10 – 19 years. The personnel in the clinic include a medical officer who heads the HIV clinic, other medical officers and clinical officers who work in the clinic on a rotational basis, a nurse, a pharmacist, a health records officer, 2 lay counsellors and 3 peer educators. The clinic runs from monday to Friday, 8am to 5pm and all services are provided free of charge. Paediatric and adolescent clinic runs every Thursday 8am to 5pm.

The structures in the clinic includes a records room where patients files are kept, a counselling room where the nurse and one peer educator do counseling including adherence counselling to new and existing patients and take anthropometric measurements before sending them to either of the two consultation rooms for review by the clinician. After review, the patient is sent to pharmacy to collect medications after which they go back to the records room to obtain the next

appointment date. Approximately 20-30 patients are reviewed each day. The clinic has a defaulter tracing mechanism. Patients who miss their clinic appointment are entered in the defaulter tracing register. They are then contacted by phone the following day, if they do not turn up to the clinic, they are contacted by phone again after 1 week and then monthly for at least 3 months.

**Study period**: November to December 2015

### 4.3. Study Population

***Inclusion criteria***

All HIV infected adolescents, 10 to 19 years of age in care at the Kangundo District Hospital and who had been on antiretroviral therapy for six months and above were enrolled into the study after informed consent from caregiver and assent from adolescents.

***Exclusion criteria***

We excluded adolescents in care at the Kangundo District Hospital who had never been initiated on antiretroviral therapy.

***Study outcomes and Definitions***

**Adherence**: It is the extent to which clients' behavior coincides with the prescribed healthcare regimen as agreed upon through a shared decision making process between the client and a health care provider (WHO 2003).

**Adolescents:** Those aged between 10 to 19 years inclusive.[24]

**Factors:** One of the several things that influence something or anything that affects how a patient takes or adheres to the ART regimen.

**Non-adherence:** It is a client's failure to follow the collaborative process of more than 95% of prescribed treatment regimen.

**Opportunistic infections:** Infections in an immune-compromised individual caused by pathogens that usually do not cause disease in a healthy immune system.

**Virologic Failure:** Plasma viral load above 1000 copies/ml based on two consecutive viral load measurements after 3 months, with adherence support.[24]

**Immunological Failure:** defined depending on age: for adults and adolescents CD4 count falls to the baseline (or below) or persistent CD4 levels below 100 cells/mm3, for children younger than 5

years persistent CD4 levels below 200 cells/mm3 or <10%, older than 5 years persistent CD4 levels below 100 cells/mm3.[24]

**Clinical Failure**: Defined depending on age: For adults and adolescents defined as new or recurrent clinical event indicating severe immunodeficiency (WHO clinical stage 4 condition) after 6 months of effective treatment, for children defined as new or recurrent clinical event indicating advanced or severe immunodefiency (WHO clinical stage 3 and 4 clinical condition with exception of TB) after 6 months of effective treatment.[24]

**Self Report:** Method of measuring adherence where the patient voluntarily reports to the healthcare provider the number of doses of antiretroviral drugs missed over a given period. For the purpose of this study this period will be 3, 7 and 30 days.

**HIV infection**: For this study, HIV infected person was the one in whom blood test had been done and identified the HIV virus in him or her, as documented in their hospital medical record.

**Optimal short Term Adherence to ART**: Taking 95% or more of the prescribed doses over a period of 3, 7 and 30 days

**Poor short Term Adherence**: Taking less than 95% of the prescribed doses over a period of 3, 7 and 30 days

This will be calculated as follows:

$$\frac{\text{Number of doses reported as taken over a specified period}}{\text{Number of doses required to be taken over a specified period}} \times 100$$

**Clinician's appointment Keeping**: A patient was classified as having missed an appointment if they were more than 3 days late to their expected appointment. Rescheduled visit were not considered as missed if the client attended the clinic at the rescheduled date. The number of clinic visits attended and those missed over a period of 6 months were determined. Good adherence was considered as honoring 95% and above of the appointments.

Adherence to clinic appointment was calculated as follows:

Clinic appointments attended in 6 months x 100

The appointments prescribed in 6 months.

**Pharmacy Refill**: It measures if a client picks up the prescribed antiretroviral drugs. For this study, patient was considered to have missed a refill appointment if drugs were not collected on or before the date the previous supply is finished. Adherence was calculated as ARV refills picked up divided by ARV refills prescribed for a period of 6 months.[64] Good adherence was considered as honoring 95% and above of the appointments.

Number of refills appointments attended over 6 months x 100

Number of refills appointments prescribed for the 6 months

### 4.4. Sample Size and Sampling

Kangundo District Hospital has approximately 150 adolescents ever initiated on ART with approximately 126 in active care. All adolescents were eligible if they met the inclusion criteria and efforts were made to interview all the adolescents on ART. The precision of the study was calculated.

$$n = \frac{Z^2 P(1-P)}{d^2}$$

Where:

**n =** sample size of **98**

**z** = is the standard normal deviation of **1.96**(corresponds to **95%** Confidence Interval).

**d =** degree of precision

**P =** estimated proportion of adolescents adherent to ART (**67%** from NASCOP surveillance on ART resistance 2013)

**d = 0.09**

Thus, 98 study subjects gave a degree of precision of 0.09

### 4.5. Study Tools

A Structured investigator-administered questionnaire was used to obtain the quantitative data and focus discussion groups for qualitative data.

### 4.6. Study Procedure

The structured investigator-administered questionnaire was pre-tested among HIV infected adolescents who were on antiretroviral therapy at the KDH prior to the actual study period. Pre-testing was done on 10% of the proposed sample size, after the pre-test, the questionnaire and the interview process was refined accordingly in readiness for the survey. Research assistants include nurses and peer counselors working at the HIV clinic. The lead investigator trained them on good research practices, study objectives and the actual study tool. Good research practices included confidentiality, integrity, clear and accurate documentation of responses. Great emphasis was put on training the research assistants on use of our study tool, the questionnaire, to get the intended information.

Adolescents were recruited from the comprehensive care clinic. Lead investigator or the research assistant approached the adolescent and their caregiver during their routine visit to the clinic, explained the purpose and method of the study, subsequently allowed the caregiver to give voluntary informed consent and assent by the adolescent. Those who were not accompanied by caregivers were requested to bring their caregivers along at a date convenient for them. A pre-designed consent form was availed to the caregiver; which described the purpose of the study, procedure to be followed and potential benefits and risks of participating in the study. Any questions regarding the study from the caregiver and /or adolescent were answered before signing of the consent. Consenting was voluntary and free of coercion. The investigator also countersigned the consent forms. Records were kept regarding reasons for non-participation of eligible participants.

Following recruitment, the study subjects were taken to one of the consultation room and a questionnaire administered to them. The following data was collected:

a) Socio-demographic details; Age, sex, relation with caregiver (biological parents, relatives or others), level of education of the adolescent, distance travelled to access care, monthly income of the household.
b) Adherence was determined by self reports, refill records and clinician's appointment keeping. Self reports were obtained during face to face interviews and any missed doses in 3, 7, 30 days prior to the interview date were recorded. Reasons for missed doses were sought.
c) Drug related factors: Including frequency of doses, taste, formulations, pill burden, medication fatigue and knowledge about the medication they are taking, difficult side effects and poor fit between the drug dosing and patient's life style and eating habits.
d) Health system related factors: Waiting time, relationship with health care provider, friendliness, health education and counseling before initiation of ART and throughout treatment, inconvenient appointments and availability of antiretroviral drugs in the clinic.

After the face to face interviews, we abstracted data from the Hospital database on the pharmacy refill appointment records of the interviewed adolescents and also clinician appointment records. Both were assessed retrospectively for a period of 6 months prior to the interview date. Adherence on drug refill and clinician's appointment were calculated from data abstracted. Clinical data of these adolescents was also abstracted including; date of enrollment in to care, CD4+ count at initiation, duration on ART, WHO HIV stage at initiation of ART, current regimen –1$^{st}$ line or 2$^{nd}$ line? If on 2$^{nd}$ line, when was the switch done and why it was done, most recent CD4+ count, history of opportunistic infections over the 6 months prior to interview.

*Focus Group Discussions*

To further elucidate factors associated with adherence to ART, FGDs were held with the adolescents. The inclusion criteria in to the FDGs were willingness to participate and disclosure of HIV status. Participants were consecutively recruited in to the FDGs. The focus discussion groups were held in four groups each made of 5 - 8 participants: ages 10 to 14 years, boys and girls separately and ages 15 to 19 years, boys and girls separately. Each session lasted 1 to 1.5 hours, prior to the discussion and in order to put the participants at ease, they were engaged in small talk

and had snacks. This created a warm and friendly environment. The study and its objectives were explained, adolescents were requested to write nicknames on cards which were placed in front of each participant for easy reference by other respondents during the discussions.

The lead investigator was the moderator with an assistant who took notes, including facial expressions and gestures on paper and helped to tape the conversation. Discussions were conducted in Kamba, Kiswahili and English with adolescent often mixing all languages. Discussions were guided by the themes that were set by the investigator which included: effect of disclosure of the HIV status on adherence, family and social factors, drug related factors and health system related factors influencing adherence. Immediately after the group discussions, there was a debriefing session with the research assistant to reconstruct the contents while the session was still fresh in their minds. Within two weeks of the FGDs, the audio tapes and hand written notes were transcribed and translated verbatim into English.

### 4.7. Data Management and Analysis

Data from the interviewer administered questionnaire was entered into Microsoft Access database, cleaned, coded then both the data analysis and statistical analysis was conducted using STATA statistical software version 13. The prevalence of optimal adherence was calculated as a percentage: those adolescents with adherence of 95% and above divided by all the adolescents interviewed. Descriptive statistics for socio-demographic and clinical characteristics were obtained to characterize the study respondents. Quantitative variables were summarized using means, medians and standard deviations. Chi-square test was done for grouped variables, the analysis of variance for parametric data and Man whitney test to compare medians for non-parametric data. The main outcome variable was coded as optimal for those with adherence of 95% and above and poor for those with adherence of less than 95%. univariable and multivariable analyses were performed to determine correlates of adherence and to assess the relationship between the independent variable and the outcome variable. The results were then presented in tables, Charts and graphs. Raw qualitative data was translated and transcribed verbatim into English. The data was rearranged, similar themes were grouped together according to the appropriate framework to

which they related. The transcripts were then entered into Microsoft word and analysed manually based on the prior set themes.

***Control of Errors and Biases***

Short period of study frame was used while assessing adherence by self report to reduce risks of recall bias. Pre-tested questionnaire was used to reduce insensitive measure of bias and ensure that the questionnaire was able to capture necessary data for the different variables. Lead investigator assessed the filled questionnaires daily and had double data entry to ensure its validity.

***Data Dissemination***

The information from these analyzes will disseminated to KDH Medical team, Ministry of Health, NASCOP and the Department of Paediatrics and Child Health, University of Nairobi. It shall be presented to the wider scientific community through publications in conference presentations (Kenya Paediatric Association) and peer-reviewed journals.

## 4.8. Ethical Considerations

Approval was obtained from the Kenyatta National Hospital / University of Nairobi Ethics Research committee, Machakos County Health Committee and the Kangundo District Hospital management.

Informed written consent from caregiver and assent from adolescents were also obtained prior to the study, voluntarily and without coercion. Strict confidentiality was upheld throughout the study period, participants were assigned study identification numbers and no personal identification data was recorded. Participants in the study accrued benefits such as receiving education regarding HIV/AIDS, advantages of good adherence and ways to overcome some of the factors affecting adherence negatively. No costs were incurred by the participants upon participation

The information obtained from this study was availed to the stakeholders of the Kangundo HIV clinic to help in designing measures appropriate to improve adherence in the adolescents in care.

# CHAPTER 5. RESULTS

## 5.1. Baseline Characteristics of Respondents

### *5.1.1. Sociodemographic Characteristics of the Adolescents*

A total of 110 adolescents were approached to participate in the study. Of these 8 did not meet the inclusion criteria, 3 caregivers did not consent and one adolescent did not assent. A final number of 98 adolescents were recruited, 46 (46.9%) females and 52 (53%) males were enrolled into the study during the period of November to December 2015. Median (interquartile range (IQR)) age was 14.0 (13.0-16.3) years with 23 (23.5%) aged 10 to 12 years while 40.8% and 35.7% were in the range of thirteen to fifteen years and more than fifteen years respectively . Majority (76.2%) were in their teenage years (13-19 years). None of the respondents was married and most (78.6%) were in, or had completed, primary school. A few 17 (17.3%) were in secondary school or had already completed secondary school education. The median (IQR) household monthly income was KSh. 5,000 (3,375 – 10,000) and a substantial proportion of the respondents hailed from families whose household income was less than KSh. 10,000 per month (Table 5.1). The median (IQR) distance from the study participants' place of residence to Kangundo Hospital was 6.0 (3.0 - 12.0) kilometres.

### 5.1.2. *Clinical and Follow-up Characteristics*

The clinic visits for the study participants were scheduled at three months' intervals for majority. Most of the participants were on first line ARV regimen (91.8%). The median (IQR) duration on ART 6.3 (4.4-8.1) years. At the time of initiation of ART, 11.2%, 35.7% and 53.1% of the study participants were at Stage one, two and three / four of HIV/AIDS as described in the WHO guidelines. Enquiries on the disclosure status revealed that 65.3% of the participants had disclosure of their HIV status while the rest (34.7%) had not. Further, 24.5% of the respondents reported that they always had a caregiver accompanying them to the consultation room during the appointments at the CCC (Table 5.2).

**Table 5.1. Sociodemographic Characteristics of the Adolescents (N=98)**

| Characteristic | Frequency | % |
|---|---|---|
| **Gender** | | |
| Female | 46 | 46.9 |
| Male | 52 | 53.1 |
| **Age (years)** | | |
| 10 - 12 | 23 | 23.5 |
| 13-14 | 40 | 40.8 |
| 15 - 19 | 35 | 35.7 |
| **Education** | | |
| Tertiary | 4 | 4.1 |
| Secondary | 17 | 17.3 |
| Primary | 77 | 78.6 |
| **Monthly HH income (KSh.)** | | |
| <2500 | 11 | 11.2 |
| 2500-5000 | 35 | 35.7 |
| 5000-10000 | 21 | 21.4 |
| >10,000 | 15 | 15.3 |
| No response | 16 | 16.3 |
| **Type of school** | | |
| Boarding | 14 | 14.3 |
| Day | 79 | 80.6 |
| Not in school | 5 | 5.1 |
| **Biological parents alive** | | |
| None alive | 32 | 32.7 |
| Father only | 25 | 25.5 |
| Mother only | 19 | 19.4 |
| Both parents alive | 22 | 22.4 |
| **Caregiver relationship to adolescent** | | |
| Mother | 35 | 35.7 |
| Father | 13 | 13.3 |
| Grandparent | 27 | 27.6 |
| Other relatives* | 21 | 21.4 |
| No blood relation | 2 | 2.1 |

* *Uncle, aunt, sister, brother*

**Table 5.2. Clinical and Follow-up Characteristics of the Adolescents ( N=98)**

| Characteristic | Frequency | % |
|---|---|---|
| **Duration on ART (years)** | | |
| <2 | 16 | 16.3 |
| 2-5 | 13 | 13.3 |
| >5-10 | 62 | 63.3 |
| >10 | 7 | 7.1 |
| **Type of ARV regimen** | | |
| 1st line | 93 | 94.9 |
| 2nd line | 5 | 5.1 |
| **ART regimen** | | |
| NVP based | 71 | 72.4 |
| EFV based | 22 | 22.4 |
| LPV/r based | 5 | 5.1 |
| **Clinical Stage at initiation of ART** | | |
| Stage one | 11 | 11.2 |
| Stage two | 35 | 35.7 |
| Stage three | 49 | 50.0 |
| Stage four | 3 | 3.1 |
| **Disclosure** | | |
| *All* | | |
| Done | 64 | 65.3 |
| Not done | 34 | 34.7 |
| *Age group 10-14 years* | | |
| Done | 24 | 46.2 |
| Not done | 28 | 53.8 |
| *Age group 15-19 years* | | |
| Done | 40 | 87.0 |
| Not done | 6 | 13.0 |
| **Main caregiver in room** | | |
| *Age group 10-14 years (n=52)* | | |
| Always | 19 | 36.5 |
| Sometimes | 17 | 32.7 |
| Never | 16 | 30.8 |
| *Age group 15-19 years(n=46)* | | |
| Always | 5 | 10.9 |
| Sometimes | 8 | 17.4 |
| Never | 33 | 71.7 |
| *All adolescents* | | |
| Always | 24 | 24.5 |
| Sometimes | 25 | 25.5 |
| Never | 49 | 50.0 |

## 5.2. Adolescents' Adherence to Antiretroviral Therapy

5.2.1. *Short Term Antiretroviral Therapy Adherence by Self Report (3, 7 and 30 Days' Periods)*

Adherence to ART was assessed by patients self report on three, seven and thirty days' periods preceding the interview date. Overall, 74 (76%) of the respondents had optimal adherence for the three days having taken at least 95% of the prescribed doses (Table 5.3). Those who had missed a single dose were 13.3% while 4.1% of the participants were found to have missed two doses for the three days'. Fifty four (55%) of the adolescents were optimally adherent for the 7 days preceding interview, of those who were non-adherent, 13.3% had missed one dose while 10.2% had missed 2 doses.

Of the adolescents interviewed 68 (69.4%) had optimal adherence to ART for the thirty days period prior to the day of the interview. The proportion of respondents who had missed no dose was 46%. Additionally, those who had missed one, two and three doses were 9.2%, 10.2% and 4.1% respectively. Three respondents (3%) had missed all the doses prescribed for the entire period under investigation. The corresponding adherence levels are listed in Table 5.3.

**Table 5.3. Short-term Self- reported Antiretroviral Therapy Adherence among Adolescents, over the Preceding 30 days (N=98).**

| No. of doses missed | Preceding 3 days | | Preceding 7 days | | Preceding 30 days | |
|---|---|---|---|---|---|---|
| | % Adherence | Number of Adolescents (%) | % Adherence | Number of Adolescents (%) | % Adherence | Number of Adolescents (%) |
| 0 | [100] | 74(76) | 100 | 54(55) | 100 | 45 (46) |
| 1 | [83] | 13(13) | 93 | 13(13) | 98 | 9(9) |
| 2 | [67] | 4(4) | 86 | 10(10) | 97 | 10(10) |
| 3 | [50] | 2(2) | 79 | 2(2) | 95 | 4(4) |
| 4 | [33] | 2(2) | 71 | 9(9) | 93 | 4(4) |
| 5 | 0 | 0(0) | 64 | 1(1) | 92 | 1(1) |
| 6 | [0] | 3(3) | 57 | 1(1) | 90 | 5(5) |
| 7 | | | 50 | 1(1) | 88 | 1(1) |
| 8 | | | 43 | 2(1) | 87 | 3(3) |
| 11 | | | 29 | 1(1) | 82 | 1(1) |
| 13 | | | 0 | 4(4) | 78 | 1(1) |
| 14 | | | | | 77 | 5(5) |
| 17 | | | | | 72 | 1(1) |
| 18 | | | | | 70 | 1(1) |
| 19 | | | | | 68 | 1(1) |
| 20 | | | | | 67 | 1(1) |
| 21 | | | | | 65 | 1(1) |
| 28 | | | | | 53 | 1(1) |
| 60 | | | | | 0 | 3(3) |

Figure 5.1 provides further details on the levels of adherence among the study participants for preceding 30 days. Hundred per cent adherence was observed in 45.9% of the respondents, 38.9% had adherence of 90 -<100% and 10.2% had adherence of 80 – 90%. Those who reported very poor adherence of < 80% were 15.2% of the interviewed adolescents.

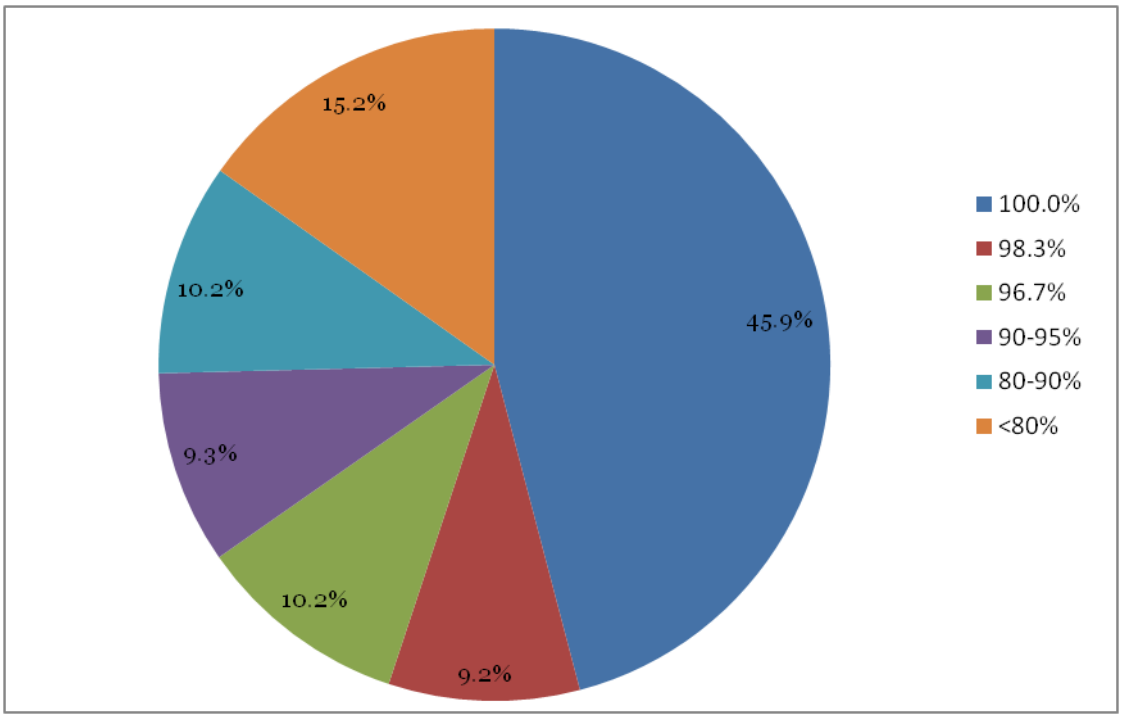


**Figure 5.1. Levels of self-reported adherence among adolescent over the preceding 30 days**

We then classified level of self reported adherence into two categories: Optimal adherence (for those who had taken 95% and above of the prescribed doses) and poor adherence (for those who had taken < 95% of the prescribed doses). Using this categorization for the preceding 30 days, 68 (69.4%) of the adolescents reported high adherence to their ART (Table 5.4).

**Table 5.4. Classification of based on 30 days self-reported adherence (N=98)**

| Classification | frequency | % |
|---|---|---|
| Adherent | 68 | 69.4 |
| Non-adherent | 30 | 30.6 |

*Reasons for Missing Doses*

Adolescents who had missed doses of ARV drugs volunteered a number of reasons as outlined in figure 5.2 with some giving more than one reason. Forgetfulness was the commonest reason (70.2%) followed by fear that someone would find out they were on ART (17.5%) and lack of food to take along with the medications (11.3%). Other reasons included running out of drugs (8.8%), dosage schedule being too complex (7.0%) and side effects (7.0%) among others (Figure 5.2).

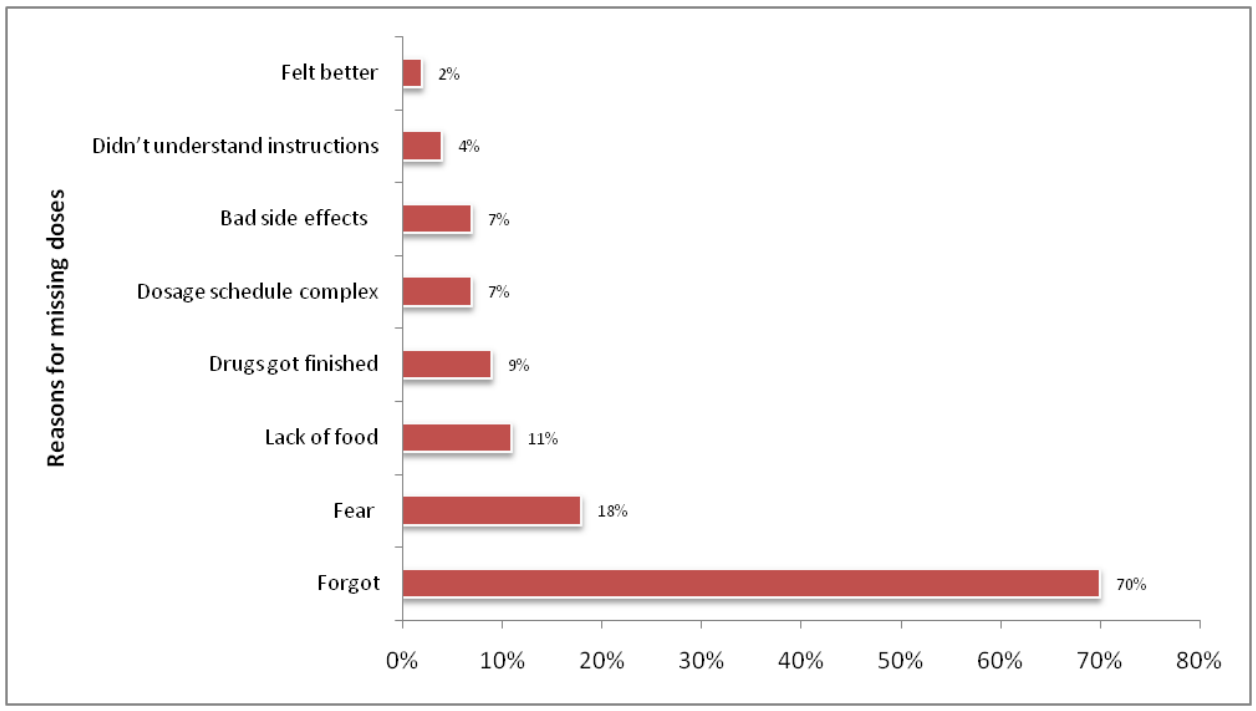


**Figure 5.2. Reasons given by Adolescents for Missing Doses (N=57)**

5.2.3. *Long Term (6 Months) Adherence to Pharmacy Refill and Clinicians' Appointments*

*a) Adherence to Pharmacy Refill Appointments*

Analysis of data abstracted from the hospital pharmacy's records showed that 63 (64.3%) of the adolescents had optimal adherence to their pharmacy refill appointments and 35 (35.7%) delayed in collecting their drugs from the pharmacy in the 6 months preceding the current survey. The number of days the client had delayed on picking the medications ranged from one to 180 with the median being 13 days (IQR 6-20). Of those who had delayed in collecting drugs from the pharmacy, 31.4% had delayed by seven days or less while 28.6% and 25.7% delayed for a period of 8 to 14 days and 15 to 21 days respectively. The rest (14.3%) had delayed picking the ARVs by more than three weeks. The number of appointments for refill in the 6 months preceding the current survey amongst the study participants ranged from one to four (Table 5.5). Of the 35 participants who had missed pharmacy appointments, 71.4% had done it once.

The most common remedial actions taken on noting a client's failure to honor a pharmacy appointment was telephoning or sending a message to the caregiver via a mobile phone (74.3%).

The most frequently reported reasons offered for failure to honor refill appointments was forgetting (45.2%), not wanting to go to the clinic and/or taking medications (32.7%), being in school/tuition during holidays (26.0%) and caregiver not being available to take the client to the clinic (15.4%)

**Table 5.5. Adherence to Pharmacy Refill Appointments and Reasons for Missed Appointments.**

| Characteristic | Frequency | % |
|---|---|---|
| **Client delayed in collecting drugs in the last 6 months (n=98)** | | |
| Yes | 35 | 35.7 |
| No | 63 | 64.3 |
| **Days delayed in picking drugs (n=35)** | | |
| ≤7 days | 11 | 31.4 |
| 8-14 days | 10 | 28.6 |
| 15-21 days | 9 | 25.7 |
| >21 days | 5 | 14.3 |
| **No. of pharmacy appointments in the last 6 months (n=98)** | | |
| 1 | 4 | 4.1 |
| 2 | 48 | 49.0 |
| 3 | 45 | 45.9 |
| 4 | 1 | 1.0 |
| **No. of appointments delayed (n=35)** | | |
| 1 | 25 | 71.4 |
| 2 | 10 | 28.6 |
| **Action taken by health workers on delaying in collecting drugs (n=35)** | | |
| None | 8 | 22.9 |
| Telephone call or SMS to caregiver | 26 | 74.3 |
| Home visit | 1 | 2.9 |

5.2.4. *Adherence to Clinician's Appointment*

Sixty five (66.3%) of the 98 study participants had optimal adherence to the clinicians' appointment while 33 (33.7%) missed at least one scheduled clinician appointments in the 6 months preceding the survey. The visits scheduled during the period under consideration ranged from one to four as shown in Table 5.6. No clinician appointments were scheduled for two participants while 43.9% and 48.0% of the participants had two and three clinician's visits schedules for the six months' period preceding the study. Further, 66.7% and 33.3% of the respondents had missed their clinicians' appointment by more than three days once and twice respectively in the six-month period preceding the survey. The action taken most frequently by the

health providers on missing an appointment was phoning or text messaging the caregiver (75.9%). On the other hand, forgetting an appointment, travelling and unavailability of a caregiver to take the child to the clinic were reported as reasons for failing to honor appointments by 30.3%, 24.2% and 15.2% of the study participants respectively (Table 5.6).

**Table 5.6. Adherence to Clinician's Appointments and Reasons for Missed Appointments**

| Characteristic | Frequency | % |
|---|---|---|
| **Missed scheduled visit in the last 6 months by more than 3 days (n=98)** | | |
| Yes | 33 | 33.7 |
| No | 65 | 66.3 |
| **Clinician's visits scheduled in the last 6 months (n=98)** | | |
| 0 | 2 | 2.0 |
| 1 | 5 | 5.1 |
| 2 | 43 | 43.9 |
| 3 | 47 | 48.0 |
| 4 | 1 | 1.0 |
| **Appointments missed by >3days (n=33)** | | |
| 1 | 22 | 66.7 |
| 2 | 11 | 33.3 |
| **Action taken on missing appointment (n=33)** | | |
| None | 7 | 21.2 |
| Phone/SMS to caregiver | 25 | 75.8 |
| Home visit | 1 | 3.0 |
| **Reason for missing (n=33)** | | |
| Forgot appointment | 10 | 30.3 |
| Travelled | 8 | 24.2 |
| Caregiver not available to take child to clinic | 5 | 15.2 |
| No reason/Child refused to go to clinic | 3 | 9.1 |
| School | 2 | 6.1 |
| Lack of transport money | 1 | 3.0 |
| Lost the blue card for appointment | 1 | 3.0 |

Adolescents who had more frequent pharmacy refill appointments (3 to 4 appointments over 6 months) were less likely to miss appointments compared to those who had more widely spaced pharmacy appointments ( 1 to 2 in 6 months) [OR=0.475 (95% CI 0.245-0.92, p=0.026).

Optimal adherence to clinicians' appointments did not differ between those adolescents seen by the clinician frequently (3 to 4 appointments over 6 months) and those seen less frequently (1 to 2 appointments in 6 months), Table 5.7.

**Table 5.7. Comparison of the scheduled and missed or delayed appointments**

| Appointments | | Adherence to appointments | | OR (95% CI) | P-value |
|---|---|---|---|---|---|
| **No. scheduled** | **No. appointments** | **Honoured (Freq, %)** | **Missed (Freq, %)** | | |
| **Pharmacy** | | | | | |
| One or two | 100 | 75(75.0) | 25(25.0) | 0.48(0.25-0.92) | 0.026 |
| Three or Four | 139 | 120(86.3) | 19(13.7) | Ref | |
| Total* | 239 | 195(81.6) | 44(18.4) | | |
| **Clinician's** | | | | | |
| One or two | 91 | 70 (76.9) | 21(23.1) | 1.65 (0.91-3.00) | 0.099 |
| Three or Four | 145 | 97(66.9) | 48(33.1) | Ref | |
| Total* | 236 | 167(70.8) | 69(29.2) | | |

**Total number of appointments over the 6 months period*

Further analyses (Mc-Nemans paired testing) revealed statistically significant differences between pharmacy refill adherence and self -reported adherence (p=0.006). Adherence levels were also significantly different when comparisons were conducted between the self -reported adherence and adherence to clinician's appointment (Table 5.8).

**Table 5.8. Comparison of self-reported adherence against hospital records of adherence to appointments (N=98)**

| Appointment | Total no. of appointments. | Self -reported adherence | | OR (95% CI) | P value |
|---|---|---|---|---|---|
| | | **Adherent** | **Non-adherent** | | |
| **Pharmacy refill adherent** | | | | | |
| Yes | 35 | 18(51) | 17(49) | 0.00(0.00- | 0.006 |
| No | 63 | 50(79) | 13(21) | Reference | |
| **Clinic appointment adherent** | | | | | |
| Yes | 65 | 52(80.0) | 13(20.0) | 4.25(1.70- | 0.001 |
| No | 33 | 16(48.5) | 17(51.5) | Reference | |

The overall optimal adherence based on self reports, and records on pharmacy refill and clinician's appointment were 69%, 64% and 66% respectively (Figure 5.3).

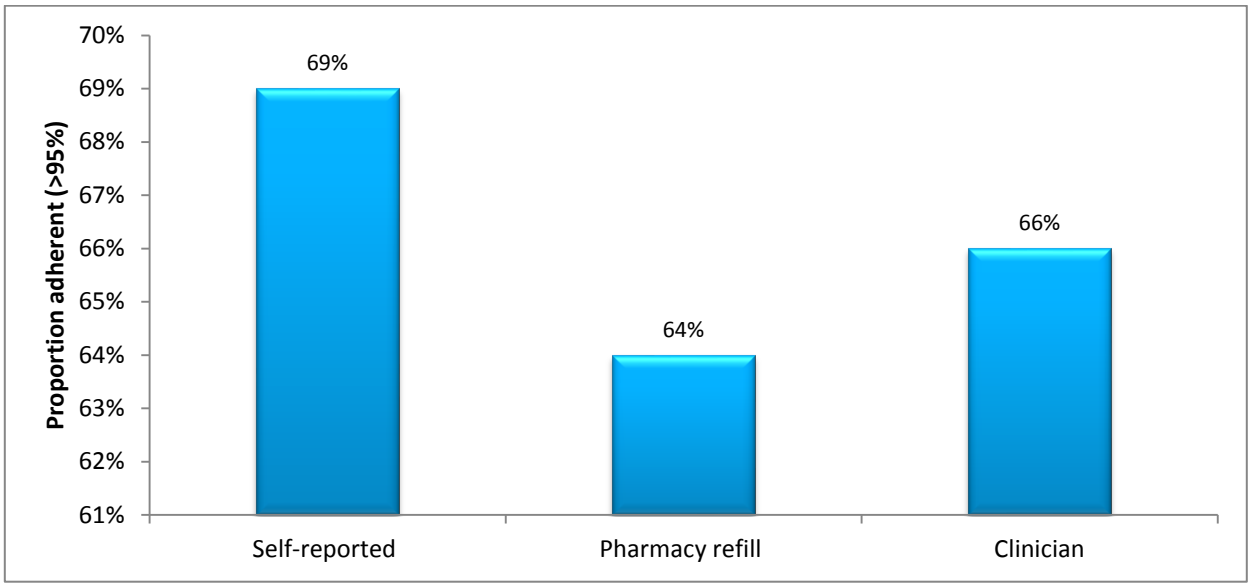


**Figure 5.3. Corresponding adherences among adolescents**

## 5.3. Factors Associated with Self-reported Adherence to antiretroviral therapy

5.3.1. *Association between Self-reported Adherence and Sociodemographic factors*

Selected sociodemographic variables were assessed for association with ART adherence and the key findings are outlined in Table 5.9. Age was associated with optimal adherence to ART with younger adolescents (10-14 years) having about three-fold increased likelihood of adhering to ART when assessed against their older counterparts of 15-19 years (OR (95% CI) 3.23 (1.31-7.97), p=0.009) There was no significant difference in the levels of adherence between male and female respondents (p=0.635). Although lower adherence levels were observed among respondents who had completed, or were still in primary school as compared to those who were in secondary school or in post-secondary institutions or had attained either of the two levels , this relationship failed to reach statistical significance (respectively, 67.5% versus 76.2%, p=0.595).

5.3.2. *Association between Self-reported Adherence and Clinical and Follow-up Characteristics*

The last available median (IQR) CD4+ count for the adherent and non-adherent study participants was 593.5(361.8-969.3) and 629.0(350.5-986.3) cells/µL. The results from Mann-Whitney U test showed that the median CD4+ count did not differ between the groups at last available CD4+ ( adherent CD4+ 593.5, non-adherent group 629, p = 0.986). The median duration (IQR) on ART was similar between adherent adolescents 69.5 (50.5-93.0) and non-adherent adolescents 83.5 (57.3-106.8), p=0.125.

In general, disclosure was not associated with adherence (p=0.233) and all the other variables assessed including WHO clinical stage at initiation, type of ARV regimen and having caregiver accompanying adolescents to consultation rooms failed to show any significant association with adherence to ART as shown in Table 5.9.

5.3.3. *Association between Self-reported Adherence and Drug- Related Factors*

There was no significant difference in the responses given by the optimally adherent and non-adherent group of respondents on being asked if the dose, taste and formulation of ARVs made it difficult to take the medications (p=0.335). Similarly, adherence to ART was no different among the respondents who opined that the pills taken per day were *'too many'* as compared to their

colleagues who reported that the pills were '*appropriate*' (p=0.613). On the other hand, significantly fewer respondents who felt tired of taking medication were classified as optimally adherent to ART when compared to those who were not tired of medication (48.9% versus 88.2% respectively, OR o.13, 95% CI 0.05-0.36, p<0.001).

Further, respondents who reported that taking medications at specified times affected their day's schedule of activities were 73% less likely to be adherent to ART when assessed against those who reported the contrary (OR 0.27, 95% CI 0.10-0.71, p=0.006). Experiencing side effects at the time of the study as well as the rating of the severity were not predictive of adherence status of the respondent (Table 5.9).

**Table 5.9. Association between Patient Factors and Self-reported Adherence**

| Factor | Total N (%) | Respondents status | | OR (95 CI) | P-value |
|---|---|---|---|---|---|
| | | Adherent (Freq, %) | Non-adherent (Freq, %) | | |
| **SOCIODEMOGRAPHIC FACT ORS** | | | | | |
| **Age (years) (n=98)** | | | | | |
| 10 - 14 | 52(53) | 42(81) | 10(19) | 3.23 (1.31-7.97) | **0.009** |
| 15 - 19 | 46(47) | 26(57) | 20(44) | | |
| **Sex (n=98)** | | | | | |
| Female | 46(47) | 33(71.7) | 13(32.7) | 1.23(0.52-2.98) | 0.635 |
| Male | 52(53) | 35(67.3) | 17(32.7) | | |
| **Education (n=94)** | | | | | |
| (Post-) secondary | 17(18) | 16(76.2) | 5(23.8) | 1.54(0.51-4.68) | 0.595 |
| Primary | 77(82) | 52(67.5) | 25(32.5) | | |
| **Type of school(n=93)** | | | | | |
| Day | 79(85) | 61(77.2) | 18(22.8) | 8.47(2.37-30.26) | **0.001** |
| Boarding | 14(15) | 4^(28.6) | 10(71.4) | | |
| **Parents (n=98)** | | | | | |
| Both alive | 22(22) | 13(59.1) | 9(40.9) | 0.55(0.21-1.48) | 0.234 |
| One alive/Orphan | 76(73) | 55(72.4) | 21(27.6) | | |
| **Mum (n=98)** | | | | | |
| Alive | 41(42) | 26(63.4) | 15(36.6) | 0.62(0.26-1.47) | 0.277 |
| Dead | 57(58) | 42(73.7) | 15(26.3) | | |
| **Relationship with main caregiver (n=96)** | | | | | |
| Parent | 48(50) | 34(71) | 14(29) | 1.21(0.51-2.88) | 0.660 |
| Other relative** | 48(50) | 32(67) | 16(33) | | |

| | | | | | |
|---|---|---|---|---|---|
| **CLINICAL FACTORS** | | | | | |
| **Disclosure status (n=98)** | | | | | |
| Done | 64(65) | 47(73.4) | 17(26.6) | 1.71(0.71-4.15) | 0.233 |
| Not done | 34(35) | 21(61.8) | 13(38.2) | | |
| **Clinical Stage at initiation of ART (n=98)** | | | | | |
| Stage one/two | 46(47) | 32(69.6) | 14(30.4) | 1.02(0.43-2.40) | 0.999 |
| Stage three/four | 52(53) | 36(69.2) | 16(30.8) | | |
| **Duration on ART (n=98)** | | | | | |
| <5 years | 23(23) | 14(61) | 9(39) | 0.61(0.23-1.61) | 0.311 |
| ≥5 years | 75(77) | 54(72) | 21(28) | | |
| **Type of ARV regimen (n=98)** | | | | | |
| 1st Line | 93(95) | 65(70.0) | 28(30.0) | 1.56(0.25-9.85) | 0.639 |
| 2ndLine | 5(5) | 3^(60.0) | 2^(40.0) | | |
| **Frequency of being with main caregiver in the clinician's room (n=98)** | | | | | |
| Always | 24(24) | 19(79.2) | 5(20.8) | 1.94(0.65-5.81) | 0.311 |
| Sometimes/Never | 74(76) | 49(66.2) | 25(33.8) | | |
| **DRUG RELATED FACTORS** | | | | | |
| **Dose, taste & formulation make it hard to take medication (n=91)** | | | | | |
| Yes | 78(86) | 54(69.2) | 24(30.8) | 0.41(0.08-1.99) | 0.335 |
| No | 13(14) | 11(84.6) | 2(15.4) | | |
| **Opinion of the pills you take per day (n=98)** | | | | | |
| Too many | 42(43) | 28(66.7) | 14(33.3) | 0.80(0.34-1.90) | 0.613 |
| Appropriate | 56(57) | 40(71.4) | 16(28.6) | | |
| **Feel tired of taking medication (n=98)** | | | | | |
| Yes£ | 47(48) | 23(48.9) | 24(51.1) | 0.128(0.05-0.36) | **<0.001** |
| No§ | 51(52) | 45(88.2) | 6(11.8) | | |
| **Taking medication at specified time affect my day's schedule of activities (n=98)** | | | | | |
| Yes | 55(56) | 32(58.2) | 23(41.8) | 0.27(0.10-0.71) | **0.006** |
| No | 43(44) | 36(83.7) | 7(16.3) | | |
| **Currently experiencing side effects (n=92)** | | | | | |
| Yes | 28(30) | 21(75.0) | 7(25.0) | 1.68(0.62-4.56) | 0.303 |
| No | 64(70) | 41(64.1) | 23(35.9) | | |
| **Rating of severity of side effects (n=28)** | | | | | |
| (Very) severe | 13(46) | 10(76.9) | 3^(23.1) | 1.21(0.22-6.80) | 0.999 |
| Mild | 15(54) | 11(73.3) | 4^(26.7) | | |

**Grandparent, *Aunt, uncle, sister, brother, non-blood relatives: ^Fischer's Exact correction applied*

****odds ratio* †*95% confidence interval* £Median (IQR) age *15 (13-16) years* §Median (IQR) age *13(13-17) years*

5.3.4**.** *Association between Self-reported Adherence and Health System Related factors*

The median (IQR) distance from the place of residence to the hospitals was statistically not different for those with optimal adherence and the non-adherent group of respondents 8.0 (3.0-12.0) and 5.0 (3.0-8.0) km respectively, p=0.161). Those who reported the clinician's behaviour as excellent/good were about 4.7 times more adherent than those who were of a divergent opinion (73.3 % vs.36.4% respectively, OR=4.793 (95% CI 1.283-17.908), p=0.032).

A higher proportion of adherence was observed in the group who rated the time spent by the doctor addressing their needs as adequate or very adequate when appraised against the group of respondents whose rating was poor (71.4% compared to 33.3% respectively). Nevertheless, the association did not reach statistical significance (p=0.072). Respondents who reported that privacy and confidentiality during examination as either excellent or good were more likely to be optimally adherent compared with those who reported on the contrary though the association was not significant statistically (respectively, 73.4% versus 50.0%, OR 2.762 (0.966-7.894), p=0.052). Compared to respondents who reported the pharmacist's behavior as average or poor, those who were of the opinion that the behavior was either excellent or good had a 5.4-fold likelihood of being optimally adherent to ART (OR 5.42 (95% CI 1.25-23.39), p=0.022).

Provision of health education that was rated as either excellent or good was found to increase the likelihood of adherence by 4.4 times as shown in table 5.10 below (OR 4.44, (95% CI 1.31-15.01), p=0.021). Higher levels of adherence were found in respondents who rated the waiting time during appointments as appropriate (73.1%) when assessed against their counterparts who felt that the waiting time was long or extremely long (52.6%). This association, however, was not significant (OR 2.44, (95% CI 0.87-6.84), p=0.084). Appointment always fitting with daily activities of the respondents resulted in 3.1-fold increment in the likelihood of being adherent (OR 3.17, (95% CI 1.25-8.03), p=0.013). There was no significant difference in the proportions of adherence between the respondents who rated the education/information given about the drugs as either good or excellent compared to those who reported on the contrary (p=0.656). Other health

system related factors including nursing care as well as counseling failed to show any significant association with adherence to ART among the adolescents (Table 5.10).

**Table 5.10. Association between Self-reported Adherence and Health System Factors**

| Factor | Total | Respondents status | | OR (95 CI) | P-value |
|---|---|---|---|---|---|
| | | Adherent Freq (%) | Non-adherent Freq (%) | | |
| **Education/information given about the drugs (n=98)** | | | | | |
| Excellent/Good | 62 | 44(71.0) | 18(29.0) | 1.22(0.51-2.96) | 0.656 |
| Average/Poor | 36 | 24(66.7) | 12(33.3) | | |
| **Clinician's behaviour (n=97)** | | | | | |
| Excellent/Good | 86 | 63(73.3) | 23(26.7) | 4.79(1.28-17.91) | **0.032** |
| Average/Poor | 11 | 4*(36.4) | 7(63.6) | | |
| **Time spent by doctor addressing client's needs (n=97)** | | | | | |
| (Very) Adequate | 91 | 65(71.4) | 26(28.6) | 5.00(0.86-28.98) | 0.072 |
| (Very) Inadequate | 6 | 2*(33.3) | 4*(66.7) | | |
| **Privacy/confidentiality during examination (n=97)** | | | | | |
| Excellent/Good | 79 | 58(73.4) | 21(26.6) | 2.76(0.97-7.89) | **0.052** |
| Average/Poor | 18 | 9(50.0) | 9(50.0) | | |
| **Pharmacist's behavior (n=98)** | | | | | |
| Excellent/Good | 89 | 65(73.0) | 24(27.0) | 5.42(1.25-23.39) | **0.022** |
| Average/Poor | 9 | 3(33.3) | 6(66.7) | | |
| **Nursing care (promptness in meeting needs, enquiries about discomfort, etc) (n=97)** | | | | | |
| Excellent/Good | 92 | 64(69.6) | 28(30.4) | 1.52(0.24-9.63) | 0.647 |
| Average/Poor | 5 | 3*(60.0) | 2*(40.0) | | |
| **Provision of health education (n=96)** | | | | | |
| Excellent/Good | 83 | 61(73.5) | 22(26.5) | 4.44(1.31-15.01) | **0.021** |
| Average/Poor | 13 | 5(38.5) | 8(61.5) | | |
| **Waiting time during appointments (n=96)** | | | | | |
| Appropriate | 78 | 57(73.1) | 21(26.9) | 2.44(0.87-6.84) | 0.084 |
| (Extremely) Long | 19 | 10(52.6) | 9(47.4) | | |
| **Appointment fitting with daily activities (n=95)** | | | | | |
| Yes, always | 66 | 51(77.3) | 15(22.7) | 3.17(1.25-8.03) | **0.013** |
| Sometimes/Rarely | 29 | 15(51.7) | 14(48.3) | | |
| **Counseling offered at initiation of therapy (n=55)** | | | | | |
| Excellent/Good | 40 | 30(75.0) | 10(25.0) | 1.50(0.41-5.45) | 0.735 |
| Average/Poor | 15 | 10(66.7) | 5(33.3) | | |
| **On-going counseling (n=96)** | | | | | |
| Excellent/Good | 82 | 58(70.7) | 24(29.3) | 1.81(0.57-5.79) | 0.311 |
| Average/Poor | 14 | 8(57.1) | 6(42.9) | | |

**Fishers exact correction applied wherever frequency was less than 5*

**Preamble: Selection of Variables for Adjusted Analysis**

Following univariate analysis, the following factors were considered for multivariate model: age (years), disclosure, type of School, tired of medication, specified dosing times of medication affecting one schedule of daily activities, clinician's behavior, pharmacist's behavior, health education and appointment to clinic fitting with daily activities.

Age was deemed a priori to be associated with disclosure of HIV status, duration on ART and being tired of taking medication. We compared median ages against each of these factors and found that age and disclosure were associated (p<0.001). The duration on ART was not different in the younger teens when compared with their older counterparts (p=0.230). Additionally, there was no difference in median ages of the teens who were tired of medication compared to those who were not tired (p=0.483). Where there was association between age and a factor, we took care not to put both in the same multivariate model to retain a statistically sound model.

**Table 5.11. Evaluation for association between age and other patient factors**

| | Non-disclosure | Disclosed | P-value |
|---|---|---|---|
| | **Freq (%)** | **Freq (%)** | |
| **Age** | | | |
| Median (IQR) age (years) | 13(11-14) | 16(13-17) | <0.001 |
| 10 - 14 years | 24 (46) | 28(54) | <0.001 |
| 15 - 19 years | 40(87) | 6(13) | |
| All | 64(65) | 34(35) | |
| | **Median** | **IQR** | **P-value** |
| **Disclosure** | | | |
| Disclosed | 13 years | 11-14 years | <0.001 |
| Not disclosed | 16 years | 13-17 years | |
| **Duration on ART** | | | |
| 15-19 years | 75 months | 50-102 months | 0.230 |
| < 15 years | 76 months | 59 - 93 months | |
| **Tired of medication** | | | |
| Tired | 15 years | 13 - 16 years | 0.483 |
| Not tired | 13 years | 13 - 17 years | |

Among adolescents aged 14 years and above, significantly higher adherence was observed in those who knew their HIV diagnosis (71%) compared to those who did not know (22%), ( OR 8.50, (95%

CI 1.6-46.1), p=0.009). Among adolescent younger than 14 years, adherence was similar between those who knew their HIV diagnosis (81%) and those who did not know (76%, P=0.992)

**Table 5.12. Association between Self-reported Adherence of Different Ages and Disclosure**

| Characteristic | Total | Respondents status | | OR (95 CI) | P-value |
|---|---|---|---|---|---|
| | | Adherent Frequency (%) | Non-adherent Frequency (%) | | |
| **Disclosure for respondents ages ≥14 years (n=57)** | | | | | |
| Done | 48 | 34(70.8) | 14(29.2) | 8.50(1.57-46.08) | 0.009 |
| Not done | 9 | 2(22.2) | 7(77.8) | | |
| **Disclosure for respondents ages<14 years (n=41)** | | | | | |
| Done | 16 | 13(81.3) | 3(18.8) | 1.368(0.29-6.48) | 0.992 |
| Not done | 25 | 19(76.0) | 6(24.0) | | |

5.3.5. *Multivariate Analysis to determine factors Independently Associated with Self-reported Adherence*

Adolescents who were in day school were more likely to have optimal adherence compared to those who were in boarding school (adjusted odds ratio (aOR) 12.56, 95% CI 3.47 – 1.04, p<0.001). Other variable including age, being tired of taking medication, as well as medications affecting an individual's schedule of activities were not associated with adherence to ART as shown in Table 5.13a.

**Table 5.13a. Multivariate Analysis Evaluation between Patient-Specific Factors and Self-reported Adherence (N=93)**

| Variable | aOR* | 95% CI§ | | P-value |
|---|---|---|---|---|
| | | Lower | Upper | |
| Age | 0.96 | 0.89 | 1.04 | 0.327 |
| Boarding School (Ref: Boarding) | 12.56 | 3.47 | 45.42 | <0.001 |
| Tired of medication (Ref: No) | 0.54 | 0.18 | 1.69 | 0.293 |
| Medication affects my schedule of activities (Ref: | 0.54 | 0.17 | 1.73 | 0.297 |

** Adjusted odds ratio §Confidence interval*

Again, in this model, adolescents who were in day school were more likely to be optimally adherent compared to those who were in boarding school (adjusted odds ratio (aOR) 7.99, 95% CI

2.85 – 22.41, p<0.001). Other variables that were evaluated in the regression failed to show significant associations with ART adherence (Table 5.13b).

**Table 5.13b. Multivariate Analysis Evaluation between Patient-Specific Factors and Self-reported Adherence (N=93)**

| Variable | aOR* | 95% CI§ | | P-value |
|---|---|---|---|---|
| | | Lower | Upper | |
| Disclosure (Ref: Not done) | 1.08 | 0.44 | 2.65 | 0.870 |
| Boarding school (Ref: Boarding) | 7.99 | 2.85 | 22.41 | <0.001 |
| Tired of medication (Ref: No) | 0.49 | 0.16 | 1.48 | 0.204 |
| Medication affects my schedule of activities (Ref: No) | 0.46 | 0.15 | 1.43 | 0.180 |

** Adjusted odds ratio §Confidence interval*

Evaluation between health systems factors and self-reported adherence revealed that appointment fitting with daily activities was associated with about four-fold increment in the likelihood of adherence to ART (aOR (95% CI) 4.22 (1.51-11.83), p=0.006). The rest of the variables were not associated with self-reported adherence (table 5.13c).

**Table 5.13c. Multivariate analysis Evaluation between health systems factors and self-reported adherence (N=95)**

| Variable | aOR* | 95% CI§ | | P-value |
|---|---|---|---|---|
| | | Lower | Upper | |
| Privacy/confidentiality during examination | 1.90 | 0.47 | 7.72 | 0.367 |
| Clinician's behavior (Ref: Average/Poor) | 1.07 | 0.25 | 4.66 | 0.928 |
| Pharmacist's behavior (Ref: Average/Poor) | 0.80 | 0.15 | 4.15 | 0.788 |
| Health education (Ref: Average/Poor) | 0.55 | 0.17 | 1.77 | 0.318 |
| Appointment fits with daily activities (Ref: Sometimes/Rarely) | 4.22 | 1.51 | 11.83 | 0.006 |

** Adjusted odds ratio §Confidence interval*

## 5.4. Focus Discussion Groups with HIV infected Adolescents

We conducted four different Focus Group Discussions (FGDs) between 18th and 22nd December 2015. The inclusion criteria into the FGDs were willingness to participate and disclosure of HIV status. Eligible adolescents were consecutively recruited for the FGDs. The four FGDs were composed of: group A 8 females aged 15-19 years, group B 5 females aged 10-14 years, group C 8 male 15-19 years and group D 8 males 10-14 years.

Prior to the FGDs and in order to put the participants at ease, they were engaged in small talk and had snacks. This created a warm and friendly environment. Each adolescent chose a nickname for the purpose of the FGD and wrote it on a card. The nickname was then placed in front of each participant for easy reference by other respondents during the discussions and only nicknames were used in the documentation of the discussions. This enabled us to protect identity of the participants.

The lead investigator was the moderator with an assistant who took notes, including facial expressions and gestures on paper and helped to tape the conversations. Discussions were conducted in Kikamba, Kiswahili and English with adolescent often mixing all languages. Discussions were guided by the themes that were set by the investigator which included: effect of disclosure of the HIV status on adherence, family and social factors, drug related factors and health system related factors influencing adherence. Immediately after the group discussions, there was a debriefing session with the research assistant to reconstruct the contents while the session was still fresh in the mind.

Within two weeks of the FGDs, the audio tapes and hand written notes were transcribed and translated verbatim into English. The data was rearranged; similar themes were grouped together according to the appropriate framework to which they related. The transcripts were then entered into Microsoft word and analysed manually based on the prior set themes.

**Theme 1: Effect of Disclosure of the HIV Status on Adherence to Antiretroviral Therapy.**

Overall, disclosure of HIV diagnosis had a positive influence on adherence to ART with most adolescents reporting that since disclosure they took their medication much better. Even those who reported to have stopped taking medication upon disclosure, after some counseling they started taking their drugs much better. Knowing their HIV status made them understand the need to adhere, aware that treatment was for life and they understood that poor adherence lead to recurrent infections.

**Suz group A:** *"Nai muwau muno yila nathimiwe…..kuthekatheka .Nathimwa nanywie dawa isu kwa kavinda na yila noonie niendeeye nesa naekana nasyo. Naseng'aa nitindaa ninywite indawa no nivoaa. Nataviiw'e ovaa clinic ati niwaite ukimwi, natavua nambiia kunywa dawa nesa nundu naeleiwe naile kuinywa maisha."*

*I was very sick when I was tested…..giggling. After taking drugs for some time and getting better I stopped because I wondered why I never got cured. I was told about my HIV status in this clinic, since then I take my drugs well because I understood that I needed them for life*.

**Shaks group A***: "Vile sikuwa najua dawa ni za nini, nilikuwa nachukua hizo dawa narusha na ninakunywa maji tupu, after kuambiwa nikaelewa lazima nizitumie, na sasa nakunywa vizuri"*

*Smiling, giggling…….Before I knew what the drugs were for, i used to take the drugs and throw them away and drink only the water, after knowing my status I take my drugs well*.

**Dol group D**: *"Neewie woo natavua kila niwaite. Yila ndeesi kila niwaite, nawangaa muno nundu ndyanyuusa ndawa nesa, lakini yu namanya neethia ni lasima ninywe, ninyusaa nesa na ndiwangaa muno."*

*I was unhappy after knowing my status. Before I knew what I was suffering from, I got sick more often because I did not take my drugs well. After knowing I take my drugs well and I rarely get sick.*

**Theme 2: Family and Social Factors affecting Adherence to Antiretroviral therapy**

The discussion brought out several family and social factors that had a negative influence on adherence to ART. Among them were stigma at home and at school, lack of food at home, family instability, poor social support at home and school.

A few reported that good support at home and at school had a positive influence on adherence. Some lived with relatives who knew their status and played a good role reminding them to take their drugs, while others had disclosed their status to either a teacher, school nurse or matron and, they supported them in taking their ART at school.

**Llyn group A:** *Sometimes Dad chases us out of the house and I am unable to take my drugs, I think people with complete families are able to take drugs well*.

**Suz group A**: *"Antie atindaa angulitye nituiia unywa matalwa aa niki no nivoaa, muvaka mavinda maingi ndyiwua nanoa nimakulyo asu make muvaka ngalea kunywa nikana ndakambone ndinywa."*

*My aunt keeps asking me why I take medications every day and why I never get cured, making me not take my drugs and so that she does not see me*.

**Tats group A**: *"Shule mimi nilikuwa najipea drug holidays, kwa dorm ni ngumu kunywa madawa vizuri, unapata marafiki wako wamekaa kwa bed yako, ama karibu na saduku yako kwenye unaweka madawa, so unajiambia, ngai wacha nijipee drug holiday. Lakini kwa sasa hii si shida kwani mimi hushiriki katika mikutano ya kitaifa ya HIV na counseling pia imenisaidia "*

*I used to give myself drug holidays because of stigma, I was afraid that school mates will see me take drugs. In the Dormitory it's hard to take your drugs well, sometimes my friends are sitting on your bed or near your box where you keep your drugs, so I decide to take a drug holiday. I have however overcome this since I have been counseled and take part in national HIV conferences.*

**Moty and Robi group D:** *"Oyu kwi sikukuu kwi aeni aingi musyi, uikwatwa ni stigma nauikia andu makwona*."*Now during the festive season, there are visitors at home, you get stigma and fear them seeing you taking drugs*.

**Shats group c:** *My Dad always reminds me. "Don't forget to take your medication, I am also taking mine."*

Agatha: *The deputy head teacher was told about my status and reminds me to take drugs while at school.*

**Theme 3: Drug Related Factors affecting Adherence to Antiretroviral Therapy**

Several aspects of the drugs negatively affected adherence in these adolescents. These included Pill burden, colour and smell of some pills, bottles used to package drugs being reported as noisy, the big size of some pills and the unpleasant effect like nausea. Most adolescents reported the blue tablets and the noisy bottles as most discouraging. However most adolescents admitted that taking drugs kept them healthy, had fewer hospital visits and this encouraged them to adhere to treatment.

**Vics group D**: *"Yila wi muwau uendaa sivitali na uinewa dawa ingi ukethia mbeke ni mbingi, mivai mingi, saa isu uikw'a ngoo uyithia ndwisa kuinywa, ndinyuva kunywa ila nanewe sya kila niwaite oyu."*

*When you are sick you go to the hospital, you get more drugs, this makes it very difficult to take, all the types, all the pills. So I decide to take the drugs prescribed for the current illnesses.*

**Llyn group A:** *"Package ya hizi dawa kwa mikebe ni mbaya sana, zinapiga kelele mingi na kama huko kwa Dorm inabidi tu husikuchue kwa sababu kila mtu atajua."*

*The bottles/tins that contain these tablets are very bad, they make lots of noise, so if you are in the dormitory, you can't take them otherwise everybody will know you are taking the drugs.*

**Suz group A**: *"Hiyo dawa ya blue unifanya nisikie ni kama niko na ulcer, wakati mwingine nakosa kuinywa."*

*The blue tablet makes me feel like I have an ulcer, so sometimes I just don't take the drugs.*

**Kivuva group C**: *The drugs are nauseating, sometimes I vomit and decide not to take the them. Taking the drugs however encourages me because I am less sick.*

**Theme 4: Health System Factors Affecting Adherence to Antiretroviral therapy**

The health system at Kangundo was perceived by some to be an impediment in adhering to treatment among these adolescents. Some of the factors reported to be negatively affecting adherence included; the clinic location which is open to every person visiting the Hospital, hostility of some healthcare providers, the long waiting hours during clinic visits, lack of privacy during consultation, partiality during treatment by some healthcare providers and language barrier with doctors who do not speak Kikamba. The long distance they had to walk to access the clinic and lack

of drugs to treat opportunistic infections were also brought out as barriers of adherence to treatment.

Adolescents mentioned some factors they thought influenced adherence positively; individual counseling, psychosocial classes attended by every adolescent during their clinic visits, the informative posters displayed all over the clinic and some healthcare providers who were a constant source of encouragement to them.

**Jaris group C**: "Mavinda angi ndinengawe ndawa sianiie kuvika matuku ma clinic, na nundu nyie ni boarding school ndyikala ndeunywa ndawa muvaka matuku ma clinic kiingi sukulu sya vingwa. Vaa clinic kii withiaa ve open muno, andu ala angi mokite sivitali nimatwonaa vaa, na atui maithii matavitye andu."

*At times you are not given enough medication to last till your next appointment, and since I am in a boarding school, I miss medication till the next appointment which is usually during the holidays. The clinic is very open to other people visiting the Hospital, neighbours who see us here as they pass by go telling everyone.*

**Moty group C**: *"Ndakitali ingi ni nthuku mwa. Ta ala ma lab, matuneenasya nai, kututonyanga na kutwikalya vau. Nikyo kitumi twanewa tuthangu twa kuthimwa CD4, viral load tukitaa kwikya itheka na tuyinuka."*

*Some healthcare workers are bad. Like the ones in the lab, they talk to us badly, prick us many times na kutwikalya vau muno. That's why when we are send to do blood tests like CD4+/ viral load, we throw away the requests forms and go home*.

**Vics group D**: *"Saa ingi walika kwona daktari andu angi maivingua muomo uineena, itumaa ona ulwa ni kila ukuweetaa, no saa ingi ni kindu kya maana, uyisa kulilikana winukite…onthe vamye iiiiii……tavia isu ninthuku muno, na ingi ulikaa ukethia matakitali aingi vu nthini, mailye ta committee , na ndwisa kuneena andu asu onthe mevo!"*

*Sometimes people open the door while you are talking to the doctors, this disrupts what you are saying, sometimes you are telling him a very important thing, you forget and only remember on your way home….all join in …yes yes and this is bad, sometimes you get in to the consultation*

*room and find many "doctors," it just looks like a committee, you can't talk in presence of so many people!*

**Obi group C:** *"Andu aa maitueleawa, nundu nyie numaa vaasa, ngali syimwoo kwitu, saa ingindyuka namaau na navika mayambiia kundetya, ona kunuma…imutwe yii inuka nikana umanye kukaa tene. On the vamwe….Na yu makwia winuke, wooka unu usu mayambiiya kuutetya ingi, kwanza muno mayiukulya kila kinatumie utoka kiliniki matuku ala maku iyoo, uikita kuseng'a" These people don't understand us, i come from very far, when I get late at times because of lack of means of transport (which is not my fault) I am quarrelled, they even abuse us…… "go home so that you learn how to come early next time"…….all the participants join in……"they even send us back home after the quarrel and tell you to come back the following day because they are tired, mmmmmm if you come the following day, they quarrel you even more because you have come for clinic on a day that is not your appointment date yet they sent you away the previous day, you wonder"…….. all laughing.*

# CHAPTER 6. DISCUSSION, CONCLUSIONS AND RECOMMENDATIONS

## 6.1. Discussion

### 6.1.1. Adherence to Antiretroviral therapy among Adolescents

*Self reported Adherence*

In this study, level of optimal adherence and factors associated with adherence to ART among adolescents in care at the Kangundo District Hospital, Kenya were explored. Overall 69.4%, 55.1% and 77.5% were found to have optimal adherence in 30, 7 and 3 days respectively, having taken 95% and above of the prescribed doses for these durations. These result demonstrated poor adherence to ART among adolescents, comparable to results obtained elsewhere in the world.[12, 13, 39] A study in Zimbabwe looking at self reported adherence among adolescents showed an adherence level of 61%, slightly lower than the results obtained from our study.[39] These results are similar to the results obtained in the Kenya National surveillance of acquired HIV drug resistance in 2013, were only 67% of adolescents had viral suppression, reflecting poor adherence. Similarly, a meta-analysis by Sung-Kim et al in 2014 looking at the level of adherence to ART in adolescents globally, found the adherence level in Africa to be 80%.[12]

However, adherence in our study was markedly low compared to adherence among adolescents in Kenyatta National Hospital in a study done in 2009, were self reported adherence was 93.7%.[40] The great variation in these studies could be attributed to the fact that, Kenyatta is a highly researched HIV clinic with proper strategies in place to manage non adherence which may not be the case in the rural HIV clinic at Kangundo. In addition, adolescents in KNH reported extensive adherence counseling, good guality of care and good relationship with healthcare providers (93%) which are factors associated with good adherence.[52,55,56]

*Adherence to Pharmacy Refill Appointments*

Adherence to Pharmacy refill appointments was poor, with only 64.3% of adolescents refilling their drugs on time, findings similar to those of other studies elsewhere among adolescents, where pharmacy refill adherence was low.[33, 35] Adherence to pharmacy refill appointments has been validated as a good measure of ART adherence and predictor of virological failure[49, 63, in] our study

the findings predicts possible existing virological failure. Nachega et al in 2009 demonstrated poor pharmacy refill adherence among adolescents compared to adults in South Africa with only 20.7% of adolescents having 100% adherence at 6 months compared to 40.5% adults.[33] On the contrary, adolescents in care in KNH CCC had much higher pharmacy refill adherence level of 95.6% in a study by Gatuguta et al in 2009.[40] This variation can be explained by the fact that KNH CCC is in a research institution where a lot of emphasis has been put on patient care and monitoring.

*Adherence to Clinician's Appointments*

Adherence to clinicians' appointment was also low with only 66.3% of the adolescents keeping their clinicians' appointment. Although limited data were available in literature regarding the adherence to clinics' appointment in adolescents, WHO recommended it as a predictor of HIV drug resistance.[62] Unlike our findings, adolescents in KNH had high level of appointment keeping (96.8%)[40] which could be explained by the satisfaction of care offered at KNH to adolescents, contrary to what we gathered from KDH especially from the FGDs.

The refill appointments' and clinic appointments' adherence were both low, giving credence to the low self-reported adherence which has been associated with overestimation due to recall bias.[60]

### 6.1.2. Factors influencing Adherence to Antiretroviral Therapy

*Sociodemographic factors associated with Self Reported Adherence*

Being in boarding school was shown to negatively affect adherence, this could be explained by the fact that privacy in boarding school is almost non-existent and also lack of social support (Multivariate analysis P=0.002). During FGDs adolescents sited several challenges faced in boarding schools; stigma both perceived and experienced, schools did not accommondate their ART needs, difficult accessing their drugs from the dorms especially in the evening, lack of privacy to store and take their drugs. Although studies looking at the effect of being in a boarding school on adherence are limited, one study in Rwanda showed that lack of privacy to keep and take ART in boarding schools adversely affected adherence.[35] In this study lack of social support in boarding was a major impediment to ART adherence.[35]

Like in other studies where adherence has been shown to be much lower in older adolescents more than 15 years,[35] self reported adherence in our study was much higher in those aged 10 – 14 years compared to those aged 15 – 19 years, 81% and 57% respectively. Similarly, adherence to pharmacy refill appointments' was much lower for those aged > 15 years when compared to those aged 10-14 years. (48.8% and 57% respectively) This could be explained by the fact that older adolescents have the responsibility of administering their drugs unlike younger one who are likely to be helped by caregivers. Sex, mother being alive or dead, relationship with primary caregiver, level of education (primary versus secondary education) had no significant effect on adherence among our study participants. This is unlike other studies where being male, being more literate and adolescent living with family (reflecting social support) have been associated with better adherence in patients. [11, 39, 52, 55]

Disclosure status is a major determinant of adherence in adolescents'. For those aged >14 years, adherence was much higher among study participant in whom disclosure had been done ($p$=0.009). This is comparable to findings of a study done in Uganda where 75% of adolescents who knew their status reported perfect adherence to medication, compared 20% of those who did not know their status.[54] Disclosure increases the knowledge and understanding of HIV and AIDS, helps facilitate adolescent's adjustment to the illness, improves psychosocial well-being and adherence.[35], [53] Similar findings where found during the FDGs were adolescents' confessed that disclosure of their HIV status actually helped them understand why they were taking drugs and hence adhere more.

Of the adolescents interviewed those who always had their caregiver accompanying them to the consultation room had better adherence compared to those who did not, absence of caregiver during review could mean poor social support which has been identified as a barrier to adherence.[35], [40] Similarly, a study by Bikaako et al revealed that strong parental relationships were related to good adherence.[53]

*Drug related factors influencing Self Reported Adherence to Antiretroviral therapy.*

Poor adherence was shown among adolescents who reported being tired of taking their medication and those who reported that taking medication at specified times interfered with their other activities of the day. In other studies, adolescents identified lack of education by healthcare giver on how to take antiretroviral drugs and school schedule that did not allow them time to take medications as impediments to good adherence.[35, 38, 40] similar to the findings from FGDs where adolescents reported that being on medication for the prolonged period discouraged them and that they were unable to adhere to specified times for medication; schools did not allow them time to take their drugs and at home, other house chores prevented them from taking medication especially at specified times.

Although statistically insignificant, medication factors including dose frequency, side effects, unpleasant taste, pill burden and drug side effects were also shown to influence adherence These findings are similar to those of other studies were high pill burden, side effects and inconvenient dosing were associated with lower adherence level**.**[35, 52, 55] These findings were supported during FGDs where similar drugs factors negated adherence: "the blue tablet reported as unpalatable, the noisy bottles used to package the drugs, taste of drugs, their smell, too big tablets and the pill burden. Transition to the once daily fixed dose combination once adolescents' achieve appropriate weight and age without delay would be helpful in improving adherence.

*Health System related factors associated with Self Reported Adherence*

Several health system related factors were shown to influence adherence negatively both from the quantitative and qualitative methods, these included clinicians behavior, inadequacy of time spend by clinician addressing the needs of adolescents, lack of confidentiality at the clinic, pharmacists behavior, health education and inconvenience of appointments. These were factors echoed in the united Nations General Assembly Special Sessions on HIV and AIDS 2010, Kenyan country report.[56]

Similarly, studies have shown that trust and confidence in the provider, good relationship between patient and healthcare provider, friendly, supportive and non judgmental attitude of the

health care provider, convenient appointment scheduling and confidentiality improved adherence.[40],[52, 55, 56]

These were further reinforced as negatively affecting adherence during FGDS and also during FGDs conducted with adolescents at the KNH by Gatuguta et al.[40] Change in attitude of healthcare providers and a friendly approach would help boost adherence in this cohort of adolescents.

Long distance travelled to the health facility, nursing care, adequacy of counseling at initiation of therapy and ongoing counseling were also shown to influence adherence though insignificantly from the quantitative data. This could be explained by the fact that our study sample was small. On the contrary, from the qualitative methods these factors were brought out as majorly influencing adherence among these adolescents. Studies elsewhere have also shown that, accessibility of health care facilities, waiting time, opening time, availability of counseling services for PLWHIV plays a major role in influencing the degree of adherence to the prescribed ART regimen.[55, 57]

***Study strengths and Limitations***

Being a rural set up, we were able to interview almost the whole cohort of adolescents in this clinic therefore our findings are generalizable to adolescents in care in rural set ups.

During our study, only respondents who turned up for their appointment participated in the study, defaulters might have different views and which we were unable to obtain. In addition, required data were not available for all the adolescents interviewed since we relied on data from existing records.

## 6.2. Conclusions

We conclude that:

- The ART adherence among the adolescents in this rural set up was poor, with 69.4%, 66.3% and 64.3% being adherent by self report, clinician's appointment and drug refill appointments respectively.
- Poor adherence was significantly associated with age above 15 years, non-disclosure of HIV status, being in boarding school, feeling tired of taking drugs daily and dosing times interfering with other daily activities.
- Hostile health providers attitude, inadequate time spend by clinician addressing the adolescents needs, long waiting times, lack of privacy at the hospital, inconvenient timings of appointments and long distance to health facility were perceived as barriers to adherence.
- Qualitative's main themes that adolescents gave as helping them adhere to treatment included: disclosure of HIV status, good social support, disclosure about the adolescents' HIV status to other family members and to at least one person in school who encouraged them to take medications. Stigmatization arising from the location of the CCC shows a need to re-design the service to protect confidentiality of adolescents living with HIV.

## 6.3. Recommendations

Our findings suggest need for strengthening of interventions to assist adolescents' in adhering to their medication including:

- Early disclosure, continuous psychosocial support, involvement of family and school "buddy" in adolescent care especially those in boarding schools.
- There is need to tailor the health services to be adolescent friendly at the level health provider, timing of appointments and privacy.

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# 8. APPENDICES

## APPENDIX A: IMPLEMENTATION TIMETABLE

| ACTIVITY | TIME |
|---|---|
| Proposal writing and submission | Feb - May 2015 |
| Questionnaire pre-test | October 2015 |
| Data collection | November - December 2015 |
| Data analysis | January - February 2016 |
| Thesis writing | March – April 2016 |
| Thesis submission | May 2016 |
| Final thesis defence | August 2016 |

## APPENDIX B: STUDY BUDGET

| Category | Remarks | Units | Unit Cost (KShs) | Total (KShs) |
|---|---|---|---|---|
| Proposal Development | Printing drafts | 1000 pages | 5 | 5,000 |
| | Proposal Copies | 8 copies | 500 | 4,000 |
| Data Collection | Stationery Packs (Pens, Paper and Study Definitions) | 10 | 100 | 1,000 |
| | Training research assistants | 1 day | 1000 | 1, 000 |
| | Research assistants (2) | 2 assistants | 1000 X 2 | 24, 000 |
| Transport cost | For investigator<br>clients | 40 days<br>32 (FGDs) | 500<br>100 | 20,000<br>3,200 |
| Data Analysis | Statistician | 1 | | 20,000 |
| Thesis Write Up | Computer Services | | | 5,000 |
| | Printing drafts | 1000 pages | 5 | 5,000 |
| | Printing Thesis | 10 copies | 500 | 5,000 |
| Study dissemination | | | | 5,000 |
| Contingency funds | | | | 15,000 |
| **Total** | | | | **113,200** |

## APPENDIX C: INFORMED CONSENT FORM

**STUDY TITLE: LEVEL OF ADHERENCE TO ANTIRETROVIRAL THERAPY AMONG HIV INFECTED ADOLESCENTS AT KANGUNDO DISTRICT HOSPITAL**

**Lead Investigator**

Dr. Jane Mwongeli Kimanthi: MBChB

Paediatric Resident, University of Nairobi.

Mobile phone number: 0721483528

**Supervisors**

Prof Elizabeth Maleche - Obimbo: MBChB, MMed (Paed), MPH (Epi), FPulm (Paed)

Professor, Department of Paediatrics and Child Health,

University of Nairobi.

Professor Dalton Wamalwa: MBChB, M.Med (Paeds), MPH (Epi)

Associate Professor in the Department of Paediatrics and Child Health

University of Nairobi.

Dr. Christine Gichuhi: MBChB, MMed (Paeds), MSc (Epi)

Lecturer, Department of Clinical Medicine and Therapeutics,

University of Nairobi.

**Introduction:** The human immunodeficiency virus infection continues to increase especially in adolescents. HIV infection causes progressive destruction and depletion of the CD4+ cells leading to the onset of AIDS when immune system failure occurs. With antiretroviral drugs, HIV has become a chronic manageable illness. Good adherence is important in the success of ART. Several factors have been shown to affect adherence to ART. This study seeks to determine the level and factors affecting adherence to ART in adolescents.

**Purpose of study:** Researchers from the University of Nairobi are conducting a study in adolescents (10- 19 years) in care at the KDH. The study will seek to know the level and factors associated with adherence to antiretroviral drugs. Adolescents will be interviewed with their

caregivers. You taking part in this study will help your health caregivers to provide the best care to you and also institute policies that will help take care of you and other adolescents on ART.

**Benefits:** No direct benefits or payments, however, the adolescent will have a chance to ask questions they may have regarding their management and these will be answered. In addition, the data collected will help the health care workers at KDH to put in place measures aimed at improving adherence.

**Risks:** There are no known risks of you and your child taking part in this study. Refusal to participate will in no way jeopardize the treatment of your child.

**Voluntariness:** Participation in this study will be fully voluntary. There will be no financial rewards to you for participating in the study. One is free to participate or withdraw from the study at any point.

**Procedure:** The study will be conducted using a questionnaire, focus group discussion and data will also be abstracted from the pharmacy database and clinic appointment records.

**Privacy and Confidentiality:** The interviewer will keep all the information about you confidential, your name will not be used during the study, questionnaires will be numbered instead. Only study personnel will have access to the data collected, and such data will be kept in a secure place.

**Problems or Questions:** If you ever have any questions about the study or about the use of the results you can contact the lead investigator, **Dr. Jane Kimanthi** by calling, **0721483528.**

If you have any questions on your rights as a research participant you can contact the **Kenyatta National Hospital Ethics and Research Committee (KNH- ESRC)** by calling **726300-9.** The KNH/UoN-ERC can also be contacted via email**: uonknh_erc@uonbi.ac.ke**

**Respondent's agreement**

I……Of…….....hereby consent to participate in the study entitled Level of adherence to antiretroviral therapy among HIV infected adolescents in care at the Kangundo District hospital. The nature of the study has been explained to me and I understand that my participation or refusal to participate will not in any way affect the course of my treatment at Kangundo District Hospital. I have been assured that no detriment to my health or care will ensue during the course of my participation in the study.

Signed……Date……

I confirm that I have fully explained to the participant the nature and scope of the study and the contents of this consent form in detail. I confirm that no coercion or remuneration, monetary or otherwise has been offered to the participant.

Interviewer…… signature……..Date ……

**SWAHILI VERSION OF CONSENT FORM**

**STUDY TITLE: KIWANGO CHA UZINGATIAJI WA TIBA ZA KUREFUSHA MAISHA MIONGONI MWA VIJANA WALIONA UKIMWI KATIKA HOSPITALI YA WILAYA YA KANGUNDO**

**Kuanzishwa:** Kiwango cha maambukizi ya virusi vya ukimwi kinaendelea kuongezeka kwa vijana. Maambukizi ya virusi vya ukimwi husababisha uharibifu na kupungua kwa seli za CD4+ na ukimwi wakati kinga za mwili zinaposhindwa kuzuia magonjwa. Madawa ya virusi vya ukimwi yameweza kuthibiti ukimwi, uzingatiaji mzuri wa madawa ni muhimu katika matibabu. Mambo kadhaa yameonyeshwa kuathiri uzingatiaji huu. Utafiti huu una madhumuni ya kuamua kiwango cha, na mambo yanayoathiri uzingatiaji wa madawa kwa vijana.

**Madhumuni ya Utafiti**: Watafiti hutoka chuo kikuu cha Nairobi wanafanya utafiti kwa vijana (miaka 10 hadi 19) wanaofuatiliwa kwa kliniki cha CCC katika Hospitali ya wilaya ya Kangundo. Utafiti huu una madhumuni ya kuamua kiwango na mambo yanayohusiana na uzingatiji wa dawa za kutibu ukimwi. Vijana na walezi wao watahojiwa. Kushiriki kwako katika utafiti huu utasaidia madaktari wako kutoa huduma bora kwako na pia kuanzisha sera ambazo zitasaidia kutunza vijana wengine wanaotumia madawa haya.

**Faida za Utafiti:** Hakuna faida kwa mtu binafsi, hata hivyo, vijana watapata fursa ya kuuliza na kujibiwa maswali kuhusu malezi wanayopata kutoka kwa kliniki. Aidha, takwimu zitakazokusanywa zitasaidia madaktari wenu kuweka mikakati ya kokomeza madhara ya kutozingatia matibabu.

**Madhara:** Hakuna hatari inayojulikana wewe kushiriki katika utafiti huu. Kutoshiriki katika utafiti huu hakutaathiri malezi unayopokea katika kliniki hii.

**Hiari ya kushiriki:** Kushiri kwa utafiti huu itakuwa ni kwa hiari yako. Hakutakuwa na zawadi za fedha kwa ajili ya kushiriki na kila mtu yuko huru kushiriki au kuondoka kutoka kwa utafiti huu wakati wowote.

**Utaratibu**: Utafiti utafanyika kwa kutumia dodoso, vikundi vya majadilianona, data kutoka kwa chumba cha madawa and uteuzi recodi.

**Siri ya Utafiti:**Taarifa zote kukuhusu zitawekwa siri na watafiti. Majina yako hayatatumika wakati wa utafiti, badala yake dodoso zitakuwa na nambari. Watafiti na wasaidizi ndio tu watakuwa na idhini ya kufikia takwimu hizi.

**Matatizo au maswali:** Iwapo utakuwa na maswali yoyote kuhusu utafiti au matumizi ya matokeo unaweza kuwasiliana na mpelelezi mkuu, **Daktari Jane Kimanthi**, nambari **0721483528.**

Kama una maswali yoyote juu ya haki zako kama mshiriki katika utafiti huu, unaweza kuwasiliana na Hospitali kuu ya Kenyatta na Kamati ya utafiti (KNH-ESRC) kwa nambari **726300-9**

**Idhini ya Muhojiwa**

Mimi……mleziwa…….nimekubali kwa hiari yangu kushiriki katika utafiti huu. Nimeelezewa na nimeelewa kuhusu utafiti huu, maswali yangu yamejibiwa na nikiwa na maswali ninaweza kupiga simu kwa Daktari Jane M. Kimanthi kwa nambari 0721483528.

Nimeelewa ya kwamba kushiriki au kutoshiriki kwangu hakutaathiri kwa njia yoyote matibabu yangu katika Kliniki hii. Nimepewa uhakika kwamba kushiri katika huu utafiti hakuna hathari kwa afya yangu au huduma ninayopokea katika Hospitali hii yaWilaya ya Kangundo.

Sahihi……Tarehe…….

Mimi nathibitisha kwamba nimeelezea kikamilifu upeo wa utafiti huu na yaliyomo katika fomu hii ya idhini.Nathibitisha kuwa sijashurutisha ama kupeana manufaa yoyote, fedha ama vingenevyo ndio muhonjiwa ashiriki kwa huu utafiti.

Mtafiti……sahihi……Tarehe……..

## APPENDIX D: STUDY QUESTIONNAIRE.

**STUDY TITLE: LEVEL OF ADHERENCE TO ANTIRETROVIRAL THERAPY AMONG HIV INFECTED ADOLESCENTS AT KANGUNDO DISTRICT HOSPITAL**

Questionnaire no…… Date……

INSTRUCTIONS**:** This questionnaire is to be carried out in an environment which ensures privacy and confidentiality.

**A. Disclosure**

Disclosure done ☐ Disclosure not done ☐

**B. Socio-Demographic Data**

1. Gender of the adolescent?

   Female = 1 Male = 2

2. What is your age in completed years? ……..

   Date of birth (date/month/year)……

3. What is your marital status?

   Married=1 Single = 2 Widowed = 3 Divorced/ Separated = 4 No answer = 5

   Others (specify) ……

4. What is your level of educational? Highest completed.

   Tertiary = 1 Secondary = 2 Primary = 3 Never gone to school = 4

5. What is your occupation?

   Employed = 1 Unemployed = 2 Primary school student = 3

   Secondary school student= 4 Others (specify)……

   Type of school: Day school = 1 Boarding school = 2

6. What is the average income per month of the participant's household (in Ksh)?.....

7. Are your biological parents alive?

   Both parents alive = 1 Mother alive = 2 father alive = 3

   None of the parent is alive =4

8. What is the relationship between you and your main caregiver?

   Mother = 1 father = 2 grandparent = 3 other blood relative = 4

   No blood relation =5

8 Do you always have your main caregiver in the room with you during clinic visits?

Always = 1 sometimes = 2 never = 3

9 What is the distance from your place of stay to the Kangundo District Hospital? In kilometers……..

10 Have you ever been treated differently by family members/friends because of the medication you are taking?

Yes = 1 No = 2

11 If your answer is yes to question 13 above, how?

Social support was withdrawn by family members ☐

Discriminated ☐

Isolated by family members/ friends at school ☐

Stigmatized ☐

Others (Specify)……..

**C. Determining Adherence**

1. Show me your medication, how many times do you take these drugs (ART) in a day?

   Once per day = 1 Twice per day = 2 Three times per day = 3

   Others (Specify……

2. How many pills do you take in a day? (24hrs)……

3. Many people find it hard to always take their medications as prescribed. Have you ever missed any of your prescribed medications:

   Yes = 1 No = 2

4. If yes to question 3 above, please fill in the table below.

| Duration | How many doses did you miss? | No of doses prescribed |
|---|---|---|
| In the last 3 days | | |
| In the last 7 days | | |
| In the last 30 days | | |

5. If you answered yes to question 3 above, what were the reasons for missing? Put a tick where applicable.

   Forgot …….. ☐
   Bad side effects…….. ☐
   Did not understand instructions…… ☐
   Felt better…… ☐
   The dosage schedule is too complex …… ☐
   Drugs got finished…… ☐
   Fear that someone will find out am taking the drugs … ☐
   Others Specify ……..

**D. Drug Related Factors and Adherence**

**Choose an appropriate response**

1. Do the dose, taste and formulation of your medication make it hard to take them?

   Yes = 1 No = 2 not sure = 3 no response = 4

2. What is your opinion of the number of pills you take per day?

   Too many = 1 appropriate = 2 Not sure = 3 no response =4

3. Do you feel tired/ fatigued of taking your medication?

   Yes = 1 No = 2 not sure = 3 No response = 4

4. In your opinion, how would you rate the education/information given to you about the drugs you are taking?

   Excellent = 1 Good = 2 Average = 3 Poor = 4 not educated =4

5. Does taking your medication at specified time affect your day's schedule of activities?

   Yes ☐ No ☐

6. Have you experienced any side effects as a result of using these drugs?

   Yes = 3 No = 2 No response = 3 Don't remember =4

7. If yes to the above, how would you rate the severity?

   Very severe = 1 severe = 2 mild = 3

8. How did this side effect affect your overall perception ART?

……

**E. Health System Related Factors Associated with Adherence**

**Choose an appropriate response**.

1. In your opinion, how would rate the clinician's behavior (friendly, caring, listening etc)?
   Excellent = 1 Good = 2 Average = 3 Poor = 4 Don't Know = 5
2. In your opinion, how would rate the time spent by the doctor addressing your needs (explaining about your health and your medication, is he/she patient & not in a hurry etc)?
   Very adequate = 1 Adequate = 2 Inadequate = 3 Very inadequate =4 Don't Know = 5
3. In your opinion, how would you rate privacy/confidentiality during examination at this clinic?
   Excellent = 1 Good = 2 Average = 3 Poor = 4 Don't Know = 5
4. In your opinion, how would rate the behavior of the pharmacist (polite, caring, attitude, supportive, time to talk, time to explain on the medications dispensed etc)?
   Excellent = 1 Good = 2 Average = 3 Poor = 4 Don't Know = 5
5. In your opinion, how would you rate the nursing care (promptness in meeting needs, enquiries about discomfort etc)?
   Excellent = 1 Good = 2 Average = 3 Poor = 4 Don't Know = 5
6. How would you rate the provision of health education at this clinic?
   Excellent = 1 Good = 2 Average = 3 Poor = 4 Don't Know = 5
7. How would rate the waiting time during your clinic appointment?
   Appropriate = 1 long = 2 extremely long = 3 don't know = 4
8. In your opinion, do your appointment dates and time fit with your daily activities?
   Yes = 1 sometimes = 2 rarely = 3 No = 4 don't know =5
9. How would you rate counseling offered at initiation of therapy?
   Excellent = 1 Good = 2 Average = 3 Poor = 4 Don't Know = 5
10. How would you rate the on-going counseling at the clinic?
    Excellent = 1 Good = 2 Average = 3 Poor = 4 Don't Know =

**TO BE ABSTRACTED FROM PATIENTS RECORDS**

**F. Clinical Data**

1. What was the client's date of enrollment in to the Comprehensive care clinic……..
2. How long has the client been on ART (in completed months) ……..
3. What was the disease stage at initiation of therapy?

   stage one = 1 stage two = 2 stage three = 3 stage four = 4
4. What is the current Regimen –1st line ☐ 2nd line ☐

   The specific drugs in the regimen……
5. Any history of regimen switch yes ☐ No ☐
6. What was the reason for regimen switch?

   Treatment failure = 1 adverse drug reaction = 2 Drug interaction = 3

   Others (specify)……..
7. What was the CD4+ count at initiation of treatment?.....
8. What is your most recent CD4+ count?.....

**G. Pharmacy Refill Records**

1. Has the client delayed in collecting his drugs from the pharmacy in the last 6 months?

   Yes = 1 No = 2
2. By how many days did the client delay to pick up his/her medication, this is from the last day when the previous dispensed drugs were finished?.....
3. Of the appointments given in the last 6 months, how many did the client delay in picking drugs?

   Number of appointments in the last 6 months ……

   Appointments for which the client delayed collecting drugs …….
4. If client delayed in collecting drugs, what action was taken?

   None = 1 telephone call or SMS to the caregiver = 2 home visit = 3
5. What reasons did the client give for the delayed refill?.....

**H. Clinic Appointment Records.**

1. In the last 6 months, did the client miss any of the scheduled clinic visits?

   Yes = 1 No = 2
2. In the last 6 months, how many clinic visits were scheduled for the client?.....
3. How many of these appointments did he miss (by more than 3 days)?.....

4. What action was taken for missing appointment?

   None = 1 phone call or SMS to care giver = 2 Home visit = 3

5. What reasons did the client give for delayed appointment?

## APPENDIX E: FOCUS GROUP DISCUSSION TOOL

**Study Title: Level of Adherence to Antiretroviral Therapy Among HIV Infected Adolescents at Kangundo District Hospital**

1) Introduction: Focus group discussion modulator introduces herself together with her assistant and then gives an opportunity to the adolescents to introduce themselves.

Many people find it hard to always remember to take their pills or medicines. For example: Some people get busy and forget to carry their pills with them, some people find it hard to take their pills according to all the instructions some decide to skip taking pills to avoid adverse effects, some feel better and stop taking medications and people in school may not find time to take them. Others do not want their friends and relatives to know, while our health care providers and hospitals influence our adherence in one way or the other. In our discussion we would like to talk about those factors; at home, in school and in our clinic that influence the way we take our medication.

2) How did disclosure about your HIV status affect your adherence to ART?
3) What are the Individual and Family/Social Factors Influencing your Adherence to ART?
4) What are the drug related factors that affect your adherence, negatively or positively?
5) What are the health system related factors that influence your adherence?
6) **Conclusion:** Thank you for accepting to participate in this discussion. The information you have given us will be handled confidentially and will help us to improve your care at the Kangundo HIV clinic and the care of the persons of your age who are not here.

## APPENDIX F: ETHICAL APPROVAL

18 SEP 2015


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Ref: KNH-ERC/A/392

18th September 2015

Dr. Jane Mwongeli Kimanthi
H58/67642/2013
Dept.of Paediatrics & Child Health
School of Medicine
University of Nairobi

Dear Dr. Kimanthi

**Research Proposal – Level of Adherence to Antiretroviral Therapy among HIV Infected adolescents at Kangundo District Hospital (P434/06/2015)**

This is to inform you that the KNH/UoN-Ethics & Research Committee (KNH/UoN-ERC) has reviewed and **approved** your above proposal. The approval periods are 18th September 2015 – 17th September 2016.

This approval is subject to compliance with the following requirements:

a) Only approved documents (informed consents, study instruments, advertising materials etc) will be used.
b) All changes (amendments, deviations, violations etc) are submitted for review and approval by KNH/UoN ERC before implementation.
c) Death and life threatening problems and serious adverse events (SAEs) or unexpected adverse events whether related or unrelated to the study must be reported to the KNH/UoN ERC within 72 hours of notification.
d) Any changes, anticipated or otherwise that may increase the risks or affect safety or welfare of study participants and others or affect the integrity of the research must be reported to KNH/UoN ERC within 72 hours.
e) Submission of a request for renewal of approval at least 60 days prior to expiry of the approval period. (*Attach a comprehensive progress report to support the renewal*).
f) Clearance for export of biological specimens must be obtained from KNH/UoN-Ethics & Research Committee for each batch of shipment.
g) Submission of an *executive summary* report within 90 days upon completion of the study. This information will form part of the data base that will be consulted in future when processing related research studies so as to minimize chances of study duplication and/or plagiarism.

For more details consult the KNH/UoN ERC website **http://www.erc.uonbi.ac.ke**

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Yours sincerely,

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