FACTORS INFLUENCING ADHERENCE TO ANTIRETROVIRAL THERAPY AMONG HIV INFECTED AND HIV EXPOSED CHILDREN AT NAIVASHA DISTRICT HOSPITAL

A dissertation submitted in partial fulfilment of the requirements for the award of the degree of Master of Pharmacy in Clinical Pharmacy, School of Pharmacy, University of Nairobi

by

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DECLARATION

I hereby declare that this dissertation is my original work and has not been presented to any other academic institution for evaluation for research and examination.

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DEDICATION

I dedicate this work to my loving wife Lynda Namusonge Wangia who has inspired me to dream big, conquer all odds and achieve greatness in every sphere of life.

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ACRONYMS AND ABBREVIATIONS

AIDS	Acquired Immune Deficiency Syndrome
ART	Anti-retroviral Therapy
ARV	Anti- retroviral
CCC	Comprehensive Care Clinic
CWC	Child Welfare Clinic
DAART	Directly Administered Anti-retroviral Therapy
HAART	Highly Active Anti-retroviral Therapy
HIV	Human Immunodeficiency Virus
MHC	Major histocompatibility complex
MEMS	Medication event monitoring systems
MSH	Management Sciences for Health
NNRTI	Non-Nucleoside Reverse Transcriptase Inhibitor
PMTCT	Prevention of Mother to Child Transmission
UNAIDS	Joint United Nations Programme on HIV/AIDS
WHO	World Health Organization

DEFINITION OF TERMS

Adherence: Adherence to ART is taking all ARV pills in the correctly prescribed doses at the right time and in the right way observing any dietary restriction.

Age: This refers to the number of years that an individual has lived since date of birth.

AIDS: This refers to a progressive immune deficiency caused by infection of CD4+ T cells with the human immune deficiency virus (HIV).

Caregiver reported adherence: This will be calculated as follows:

$$\frac{\text{Number of doses reported as taken over 2 weeks}}{\text{Number of doses required to be taken over 2 weeks}} \times 100$$

CD4+: This refers to an antigen marker of helper/inducer T cell that recognizes antigens bound in class II MHC proteins.

Co-infection: Presence of two or more infections in a patient simultaneously.

MHC proteins: Major histocompatibility complex molecules found on every nucleated cell of the body whose function is to display fragments of proteins from within the cell to T cells; healthy cells will be ignored, while cells containing foreign proteins will be attacked by the immune system.

Optimal adherence: Proportion of those who take their medication $\geq$ 95% of the time.

Pharmacy pill count adherence: This was calculated as follows:

$$\frac{\text{Number of doses dispensed over 1 month period}}{\text{Number of doses prescribed for the 1 month}} \times 100$$

Poor adherence: Adherence rates < 95% by pharmacy pill counts over the 1 month period prior to clinic visit or reported adherence of < 95% in the 2 weeks prior to clinic visit.

Prevalence: This refers to the number of affected persons present in the population at a specific time divided by the number of persons in the population at that time.

Primary caregiver: The parent or the legal guardian of the child.

Sub-optimal adherence: Proportion of those who take their medication <95% of the time

Viral load: Levels of virus found in the blood per 10 millilitres (mls).

ABSTRACT

Background: Although non-adherence to prescribed therapies is widespread, it is particularly problematic with antiretroviral therapy for human immunodeficiency virus infection. Very high levels of adherence (≥95%) are required for antiretroviral therapy to be effective. There is limited information available in Kenya on adherence to antiretroviral therapy and its predictors in children.

Methodology: The study design was a cross-sectional study that used structured questionnaires to interview 129 study participants. Pharmacy pill count records for each participant were abstracted from the dispensing database software. Caregivers of children in this target groups were interviewed to determine their child's adherence to their antiretroviral drugs as well as factors influencing the same. The data was then analysed using SPSS version 13.0 software.

Results: The mean age of participants was 20 months while the median age was 15 months (inter-quartile range 6 - 33 months). The pharmacy pill count method yielded a mean adherence rate of 93.9%. However, only 48.1% of the participants had optimal levels of adherence (≥95%). There was a significant difference in adherence between the PMTCT regimen (94.7%) and the HAART regimen (93.4%), ($P = 0.045$). Treatment for co-infection was the single most significant factor influencing adherence ($P < 0.005$).

Conclusion: Adherence to antiretroviral therapy by children on antiretroviral therapy in Naivasha district hospital was low, with more than half of them reporting sub-optimal adherence. Treatment for co-infections and regimen simplicity were found to be the major factors positively influencing adherence among this study population of paediatrics.

CHAPTER ONE: INTRODUCTION

1.1 BACKGROUND

1.1.1 Human Immunodeficiency Virus/Acquired Immune Deficiency Syndrome

Acquired immune deficiency syndrome (AIDS) is the result of progression of HIV infection. HIV is a retrovirus that infects mainly helper T lymphocytes (CD4 lymphocytes), monocytes and macrophages. Without treatment, HIV infection causes generalized immune incompetence and progression to AIDS [1].

HIV is found in many body fluids including blood, semen, saliva, vaginal secretions, and breast milk. HIV infection can be transmitted by unprotected sexual contact, inoculation with infected blood or blood products, sharing or use of contaminated needles and vertical transmission from mother to child [2].

Perinatal transmission accounts for over 90% of prepubertal AIDS cases and almost all new paediatric HIV infections. Perinatal transmission may occur in utero, at the time of delivery, or via breast feeding. Indirect evidence suggests that about 30% of perinatal infections occur prior to birth [1].

1.1.2 The Global Picture of HIV/AIDS Pandemic

The impact of HIV worldwide will be felt for decades to come. Promising developments have been seen in recent years in global efforts to address the AIDS epidemic, including increased access to effective treatment and prevention programmes [3]. However, the number of people living with HIV continues to grow, as does the number of deaths due to AIDS. Approximately 39.5 million people worldwide were living with HIV in 2006 [4]. In 2007, new data showed

global HIV prevalence and the number of new infection had fallen, in part as a result of the impact of HIV programmes [5]. In 2007, 33.2 million people were estimated to be living with HIV, 2.5 million people became newly infected and 2.1 million people died of AIDS worldwide. In low and middle income countries 3 million people were receiving ARV treatment by end of 2007 [5], [6].

Sub-Saharan Africa remained the most affected region in the global AIDS epidemic [4], [5], [7]. More than two thirds (68%) of all people who are HIV positive lived in Sub-Saharan Africa where more than three quarters (76%) of all AIDS deaths in 2007 occurred [5]. It was estimated that 1.7 million people were newly infected with HIV in 2007, bringing to 22.5 million the total number of people living with the virus in Sub-Saharan Africa [5]. About 2.1 million people in Sub-Saharan Africa were receiving ART by end of 2007 [6]. Unlike other regions the majority of people living with HIV in Sub-Saharan Africa (61%) were women [5].

In Kenya, the national HIV estimates for the year 2006 were: males HIV positive were 320, 000, females 614,000; people HIV positive in urban areas were 400, 000, in rural areas 534,000, adults 50 and above 55,000 and children 0-14 years old 102,000 [8]. These figures illustrate the magnitude of the task to provide prevention, care and treatment, and support services for all who need them.

These estimates show that: 1.5 million pregnant women need counselling and testing each year to determine their HIV status, 68,000 need treatment to prevent mother-to child transmission of HIV, 23,000 children need ART and 200,000 need co-trimoxazole prophylaxis. 430,000 adults need ART; 2.4 million orphans need care and support from their extended families and

communities [9]. However, levels of adherence to ART below 95% have been associated with poor virological and immunological response [10], [11]. Adherence concerns have been one reason expressed by opponents of antiretroviral therapy in developing countries or resource poor settings [12], [13]. This strongly indicates the need to come up with strategies to maximize long-term ART adherence to ensure success as Kenya scales up ART programmes countrywide.

1.1.3 The Global Impact of HIV on children

Of 40.3 million people living with HIV, Children below 15 years constitute 2.3 million. Children constitute 700,000 of the 4.9 million of new global HIV/AIDS infections and 570,000 of 3.1 million HIV/AIDS deaths annually. The burden of paediatric HIV-1 infection globally is highest in sub-Saharan Africa, with over 2 million children infected currently. By the end of 2006 there were 14 million orphans due to HIV-AIDS [14]. It has been estimated that at a global level, 660,000 children require antiretroviral therapy, the majority (91%) of whom reside in sub-Saharan Africa. However, presently, less than 10% of all antiretroviral treatment occurs in children [15].

Kenya is home to an estimated 150,000 children who are infected with HIV/AIDS with an estimated 34,000 new paediatric infections in 2004 alone. Statistics suggest that 30,000 to 40,000 of these children require ART. Yet only 7,800 were on treatment by the end of 2006 [14].

CHAPTER TWO: LITERATURE REVIEW

2.1 OVERVIEW

2.1.1 Definition of adherence

Medication adherence refers to the extent to which an individuals' medication-taking behaviour coincides with medical advice [16]. Dracup and Melais [17] defined adherence as "the extent to which an individual chooses behaviours that coincide with a clinical prescription achieved through negotiation between the health professional and the patient." In the context of HAART this involves the introduction of multiple, strictly timed doses of several drugs into the patient's daily routine of life.

2.1.2 Importance of adherence to HAART

Adherence to HAART is one of the potentially modifiable factors that determine outcomes for patients with HIV. The consequences of poor adherence include sub-therapeutic drug blood concentrations. This leads to poor virological control, a higher viral load and selection of viral strains that are resistant to ART which then leads to progression of HIV disease [18]. Additionally, the transmission of drug-resistant HIV has been well documented [19]. Therefore, accurately measuring adherence to ART plays a central role in efforts to improve it.

Sub-therapeutic antiretroviral drug levels resulting from poor adherence may enhance development of drug resistance to one or more drugs in a given regimen, and possible cross-resistance to other drugs in the same class. Consequently, sub-optimal adherence limits the

effectiveness of future drug regimens for patients who contract or develop drug-resistant viral strains of HIV.

Adherence is a complex health behaviour that is influenced by the regimen prescribed, patient and caregiver factors and characteristics of healthcare providers. A study done on the association of these characteristics with adherence to HAART among children revealed that medication adherence among HIV-infected children is lower than required for optimal viral suppression. Recommendations made were that responsibilities for medication related tasks should be clarified among family members, regimen knowledge should be emphasized and caregivers should avoid assigning treatment responsibility to a child prematurely [20].

2.1.3 Efficacy of antiretroviral therapy in children

The benefits of ART in the management of HIV disease in children are well established. Studies have shown that large and sustained CD4 cell count gains are possible regardless of baseline CD4 cell count so long as patients are adherent to ART [21], [22], [23], [24].

This leads to a reduction in morbidity, mortality and improves the well being of the patients. In a recent study by Wamalwa et al, Non Nucleotide Reverse Transcriptase Inhibitors (NNRTI) based first line first line antiretroviral therapy was shown to be highly efficacious in HIV-1 infected Kenyan children [22].

Comparable results were obtained in Thailand. In this study Puthanakit et al, showed a remarkable virological response in a prospective cohort of treatment-naïve children with advanced stage HIV infection [25].

2.1.4 Factors that may lead to poor drug adherence

In general, there is a limited availability of paediatric formulations of ARVs and also some of these drugs are unpalatable. There are also fears of drug toxicities and their side effects [26]. The younger children depend on caregivers to take their medication [27]. Therefore ART for children is often highly demanding because it involves introducing multiple, strictly timed doses of several drugs into the caregiver and child's daily life [28], [29]. This leads to an interruption of the child's normal activities, especially as the child grows older. All these factors may result in repeated potentially unpleasant child-caregiver encounters. In addition, the adult issues of accurately identifying varied pills and liquids, integrating multiple medications into daily activities, as well as maintaining privacy [30].

In most cases, children living with HIV disease and their families are often confronted with stressors like poverty and limited resources for caregiver and child support. These can present significant barriers to maintaining full adherence [27]. Most of these children are orphaned or live with sick parents. Such family disruptions may lead to lack of consistency of the caregiver with the child being tossed from one caregiver to another. Stigma and discrimination are primary concerns of caregivers who often choose not to disclose information about the child's HIV status to family members or others [31]. Also, some caregivers choose not to disclose to their child their HIV status until adolescence, potentially impeding their cooperation with treatment [27]. All these impair the family's ability to manage the child's illness, including the proper administration of medications.

Some cultural practices have been identified as barriers to adherence. Some patients may view HIV/AIDS as a curse which can only be overcome by divine intervention. For example, a study by Wanyama et al on adults in Kampala-Uganda showed that patients' belief in spiritual healing led patients to be non-adherent [32]. The family's beliefs concerning the treatment of HIV are important because the family members are usually the decision makers regarding the child's treatment.

2.2 PROBLEM STATEMENT

To achieve effective treatment and realize the benefits of treatment, strict adherence to treatment instructions are very critical. Sticking to the treatment instructions for a long term illness poses a great challenge to the patients [33]. Just having medicine available cannot solve the HIV and AIDS problems. Worldwide, regardless of the illness or treatment many people do not take their medications correctly. A significant proportion of all hospital admissions are due to drug non-adherence. In a survey in U.S.A by Stone (2000) [34], 21 % of AIDS patients who were on ARV drugs had missed a dose in 24 hours while 34 % had skipped a dose in 3 days.

Kenya has made tremendous strides in scaling up ART. However, anecdotal evidence is suggesting certain problems that contribute to defaulter rate, for instance it is said that some men use their partners ARVs irrespective of their status. A few patients may sell all or part of their ARVs for profit [35]. There is a possibility that defaulter rate is high among the youth and children under care of elderly. In Kenya, adherence is high but still reported to be sub optimal [4], [8].

In children, there are many barriers that make adherence to HAART difficult. These barriers include: lack of liquid formulations of some ARV drugs, high volume, poor availability, high pill burden, frequent daily dosing requirements, dietary restrictions and drug toxicities. Stigma issues like disclosure to family, friends and school also play an important role. Adherence also depends on caregivers. Poor treatment in the child will often lead to risk of virologic failure with high hospitalization rates, increased morbidity and mortality rates, development of drug resistance and an increase in the medication cost to the government which is providing the drugs at no fee to the patient.

A study in Mombasa Kenya showed that ART adherence rate among patients under directly administered antiretroviral therapy (DAART) program was greater than 95% compared to sub optimal rates (< 95%) for patients who were not under DAART program [36]. Antiretroviral drugs were being dispensed across the country including in all Provincial General Hospitals, District Hospitals, Sub-District Hospitals, Health Centres and Mission Hospitals in Kenya [37]. However, DAART program was not being implemented in other parts of the country including Naivasha district hospital, the site of the study. Therefore, this study aimed at determining factors that influence adherence to ART among HIV exposed and infected children in this setting.

2.3 JUSTIFICATION

It has been proven that HAART is effective in suppressing human immunodeficiency virus (HIV) replication, decreasing morbidity and mortality associated with HIV and improving the quality of life in adults as well as children infected with HIV. However, drugs don't work in

patients who don't take them. In the management of HIV infection it is now well established that optimal adherence to HAART is critical to successful outcomes of patients receiving therapy [38].

Important factors that influence adherence to HAART such as regimen related complexities, patient/family related issues and factors related to healthcare delivery system makes adherence to HAART challenging. Although numerous interventions to improve adherence have been investigated in developed as well as developing countries, majority of work in this area is focused on adherence in adults and data in children is limited [39]

Therefore, in order to facilitate adherence and improve outcome of HAART in the paediatric population, it is necessary to have a deep understanding of the factors influencing adherence and interventions that can improve adherence in children [38].

2.4 RESEARCH QUESTIONS

This study provided valuable information on prevalence and factors that influence adherence to HAART among HIV exposed and infected children at Naivasha district hospital. This information was found useful for further research in this area. It also provided key insights useful in planning effective intervention strategies for maximizing long-term adherence to HAART and successful treatment of HIV and AIDS.

The following research questions guided our study:

What are the adherence rates of HIV exposed and HIV infected children on PMTCT and HAART ARVs?

How does the type of drug formulation and ART regimen influence adherence to PMTCT and/or HAART among HIV exposed and HIV infected children?

How does treatment for a co-infection affect adherence to ART among HIV infected children on HAART?

What challenges do caregivers face in ensuring optimal adherence to PMTCT and/or HAART in their children?

How does the caregiver's knowledge of their child's ARV drugs influence the child's adherence to PMTCT and/or HAART?

2.5 OBJECTIVE

2.5.1 General objective

To find out the factors that influence adherence to HAART among HIV-infected and HIV exposed children at Naivasha District Hospital.

2.5.2 Specific objectives

To measure the adherence rates among children on HAART and PMTCT antiretroviral therapy at Naivasha district hospital.

To determine whether the type of drug formulation and ART regimen influences adherence rates among HIV exposed and HIV infected children.

To find out whether treatment for co-infections affects adherence to ART among HIV infected children on HAART.

To find out the challenges faced by caregivers in ensuring adherence.

To assess the caregivers' knowledge of their child's ARV drugs.

2.6 CONCEPTUAL FRAMEWORK

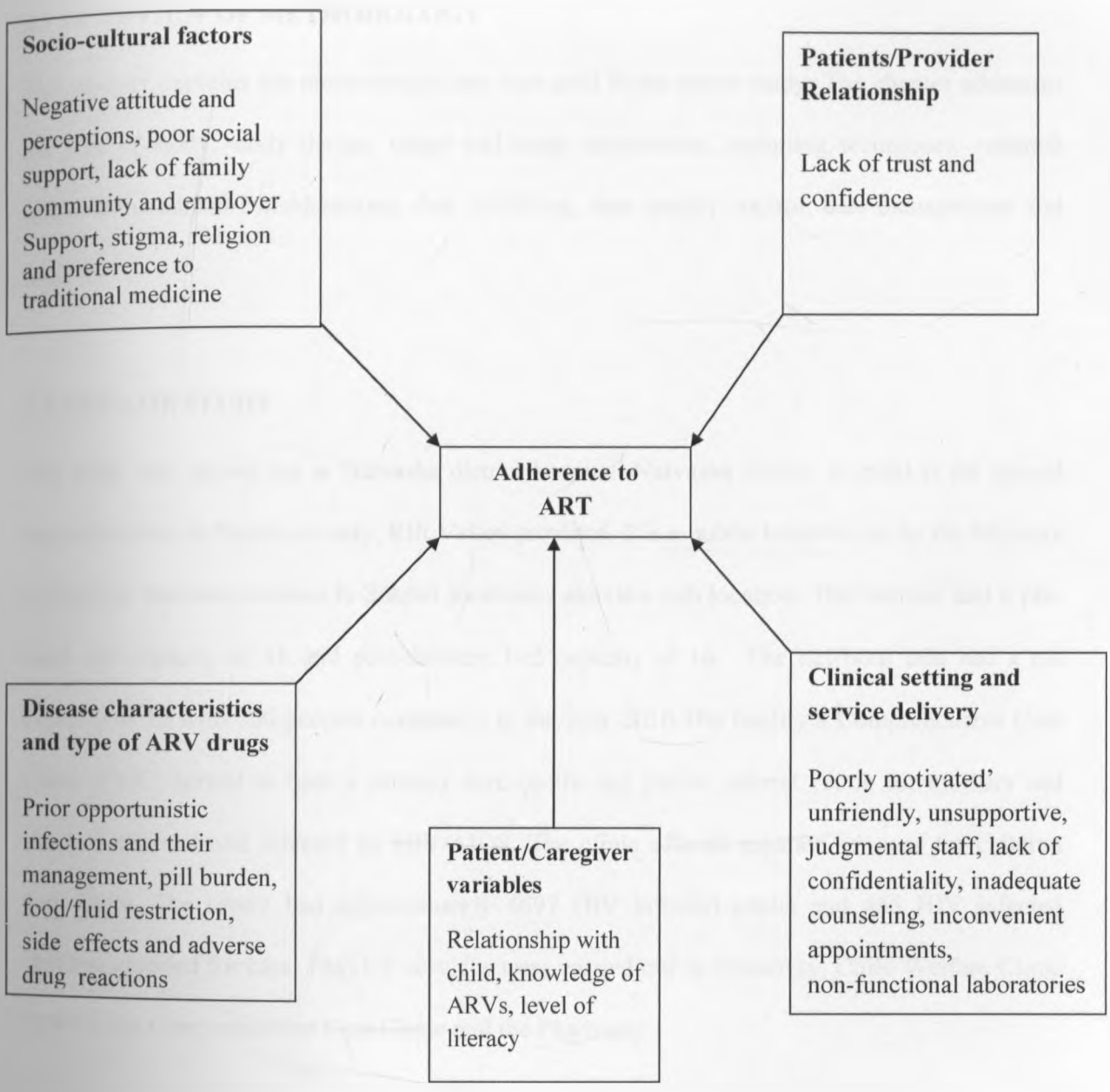

Figure 1: Problem Analysis Diagram of Possible Factors Influencing Adherence to ART

Adopted from Chesney *et al.* (2000)[40], Kgatlwane *et al.* (2005)[41], Nakiyemba *et al.* (2005)[42]

CHAPTER THREE: METHODOLOGY

3.1 OVERVIEW OF METHODOLOGY

This chapter explains the methodology that was used in the entire study. The chapter addresses the area of study, study design, target and study populations, sampling techniques, research instruments, ethical considerations, data collection, data quality control, data management and analysis.

3.2 AREA OF STUDY

The study was carried out at Naivasha district hospital. Naivasha district hospital is the second largest hospital in Nakuru county, Rift Valley province. It is a public hospital run by the Ministry of Medical Services, located in Sokoni location, Lakeview sub location. The hospital had a pre-natal bed capacity of 16 and post-delivery bed capacity of 16. The newborn unit had a cot capacity of 15 with 200 percent occupancy in the year 2010.The facility's Comprehensive Care Clinic (CCC) served as both a primary care centre and public referral centre for mothers and children affected and infected by HIV/AIDS. The clinic offered separate services for children and adults. The centre had approximately 4697 HIV infected adults and 466 HIV infected children enrolled for care. PMTCT services were carried out in Maternity, Child Welfare Clinic (CWC), the Comprehensive Care Clinic and the Pharmacy.

3.3 STUDY DESIGN

A cross-sectional study design was used. The study design provided information about the presence and strength of associations between variables, permitting the generation and testing of hypotheses about such associations. Both primary and secondary data was collected.

Primary data was collected through interviewing study participants and through observation. Secondary data was collected through reviewing medical records of the study participants after getting authority from the health facility's administrator and consent from study participants.

3.4 TARGET POPULATION

The target groups were HIV infected or exposed children aged between 0 – 59 months who were enrolled on antiretroviral therapy either for PMTCT or HAART at the comprehensive care clinic at Naivasha District Hospital.

3.4.1 Inclusion criteria

HIV infected children between 18-59 months enrolled on HAART and attending the comprehensive care centre clinic at Naivasha District Hospital.

HIV exposed children less than 18 months on ARVs for PMTCT enrolled in the comprehensive care clinic at Naivasha District Hospital.

HIV infected children for whom the caregivers had signed the consent form.

3.4.2 Exclusion criteria

HIV infected and exposed children between the ages of 0 – 59 months who had not been put on antiretroviral therapy.

HIV infected and exposed children for whom the caregivers did not consent to participate in the study

3.5 ETHICAL CONSIDERATIONS

3.5.1 Approval to carry out the study

Permission to carry out the study was obtained from the Ethics and Research Committee at Kenyatta National Hospital. (Appendix 6)

3.5.2 Informed consent

Consent from the caregivers of the children who met the inclusion criteria was sought and the consent forms signed by the caregivers before inclusion into the study. (Appendix 1)

3.5.3 Confidentiality

The caregivers were interviewed in private and all the information obtained was handled with utmost confidentiality. Serial numbers were used instead of the child's name to protect the child's identity.

The data collecting material was kept under lock and key during the entire study time. During data analysis only the study number was used and as such the identity of the child was concealed.

3.5.4 Risks involved

There were no risks with regard to the patients who were involved in the study

3.5.5 Benefits from the study

Caregivers with children who were found to be non-adherent were counselled on the importance of adherence and advised on strategies they can employ to improve their child's adherence.

Once the study results were analysed, the findings were communicated to the clinicians at Naivasha District Hospital to contribute in improving the quality of care of the HIV infected and/or HIV exposed children.

3.6 SAMPLING PROCEDURE/SAMPLE SIZE CALCULATION

Rates of adherence to Antiretroviral Therapy in children

Studies on adherence to ART in populations of children with HIV infection have reported sub-optimal adherence rates ranging from 58 to 89% depending on definitions of adherence, modes of assessment and duration of treatment assessed [11], [28], [43]. Self report has generally been shown to overestimate adherence. Lower adherence rates are obtained when more objective measures like pharmacy pill count and Medication event monitoring systems (MEMS) are used [28], [44]. Farley et al in a study on children compared MEMS, pharmacy pill counts and self report methods and found adherence rates of 81.4%, 92%, and 100% respectively [43]. For the purpose of this study, the average prevalence rates of adherence by MEMS, self report and pharmacy pill count were used.

The convenient sampling method was used and caregivers of the children who met the inclusion criteria were interviewed consecutively as they were routinely seen in the CCC at Naivasha District Hospital.

The sample size was calculated using Fischer's formula:

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

$$\mathbf{n = \frac{1.96^2 \times P(1-P)}{d^2}}$$

Where:

n is the sample size

Z is 1.96 which is the normal deviate corresponding to a confidence interval of 95%

P is 0.91 which is the estimated average prevalence rate of adherence to ART among children as reported by caregivers (self report), by MEMS and by pharmacy pill count be used.

d is 5% degree of precision/accuracy.

Thus:

$$p = \frac{(1+0.92+0.81)}{3} = 0.91$$

$d = 0.05$

$$n = \frac{1.96^2 \times 0.91(1-0.91)}{0.05^2}$$

$n = 125.85 \sim 126$

3.7 DATA COLLECTION METHOD

Caregivers were interviewed using standardized questionnaires at the Naivasha District Hospital CCC. (Appendix 2)

3.8 INSTRUMENTS OF DATA COLLECTION

3.8.1 Self-reported adherence

Caregiver reported adherence was assessed by use of a face-to-face structured interview with the caregiver. The interviewer began by reading a statement acknowledging that most people have difficulty taking all their HIV medication. The child's ARV regimen was then clarified. The caregiver was asked if the child had missed any doses of antiretroviral medicine in the three days and two weeks prior to the clinic visit. If a child was found to have missed any doses, further details were be obtained as to the exact drugs involved, the number of doses missed and the reason for missed doses.

3.8.2 Pharmacy pill count records

All patients who attend the CCC at Naivasha District Hospital refill their prescriptions from the main pharmacy on specified dates. This pharmacy used a dispensing software known as the Management Sciences for Health – Antiretroviral (MSH-ART) dispensing tool to monitor adherence. This tool showed the patient's demographic data, current regimen, dates when drugs were dispensed, drug formulation, quantities of doses dispensed, and the expected date for prescription refill. Drugs were dispensed for 30 days supply. For the liquid formulations, liquid estimation was done by the use of a syringe.

For those whose refill data was found missing in the MSH-ART dispensing software, data was retrieved from the hard copy of the prescription on which the pharmacist also records information on returned doses. The hard copies were usually stored in the pharmacy. Prescription medication refill data was abstracted from the above pharmacy records and recorded in a pharmacy data abstraction form.

(Appendix 3)

3.9 DATA MANAGEMENT

3.9.1 Data processing and analysis

The data collected was transferred from the data collection form into a Microsoft access database and routinely checked for accuracy and completeness. On completion of data entry, data cleaning was done to correct any mistakes that may have occurred during entry. Any errors and omissions found were duly rectified. The data was then analysed using SPSS version 13.0 software. The level of significance was set at 0.05 and p values less than or equal to 0.05 were considered statistically significant.

3.9.2 Data quality control

The data collection form was be piloted before use by randomly interviewing 14 caregivers of HIV infected and 6 caregivers of HIV exposed children at the Kenyatta National Hospital CCC. The data collection tool was found to be satisfactory and no changes were made to it.

CHAPTER FOUR: RESULTS

4.1 Overview of Results

This chapter presents results of quantitative findings. The section covers the following findings: Basic information on HIV exposed and infected children at Naivasha District Hospital, a summary of age distribution of study participants, information on the various ARV regimens that study participants were on and their proportions, adherence to ARVs among study participants and factors influencing the adherence to ARVs.

4.2 Basic characteristics of HIV Exposed and Infected Children at Naivasha District Hospital

Between June 2012 and July 2012, 178 caregivers of children attending the CCC and MCH clinics for HAART or PMTCT services respectively were approached for consent to be interviewed by the investigator. Out of these, 143 met the selection criteria and 129 consented to be interviewed.

Slightly more than half of the study participants were males accounting for 53.5% of the population. The study participants with both parents alive represented the largest proportion at 81.4% while those with both parents deceased were 3.9%. The proportion of study participants who had their biological mother as their caregiver was 107 (83%). while 9 (7%) had their biological father as their caregiver.

The baseline characteristics of the patients included in the study are described in Table 1 below

Table 1: Basic information for Study Participants at Naivasha District Hospital

Characteristic	Number (N)	Percentage (%)
Gender		
Female	60	46.5
Male	69	53.5
Parental status		
Both parents alive	105	81.4
Father Deceased	15	11.6
Both parents deceased	5	3.9
Mother deceased	4	3.1
Relationship between caregiver and child		
Biological mother	107	83
Biological father	9	7
Grandparent	6	4.6
Aunt	3	2.3
Guardian	3	2.3
Sibling	1	0.8
Total	**129**	**100**

4.3 Summary of Age Distribution of Study Participants

The criteria for selection included age between 0 – 59 months. The total number of participants was 129 with a mean age of 20 months, a standard deviation of 16 months, a median age of 15 months and an inter-quartile range from 6 to 33 months. The minimum age was 1 month and the maximum was 58 months. This age distribution is shown in Figure 2 below:

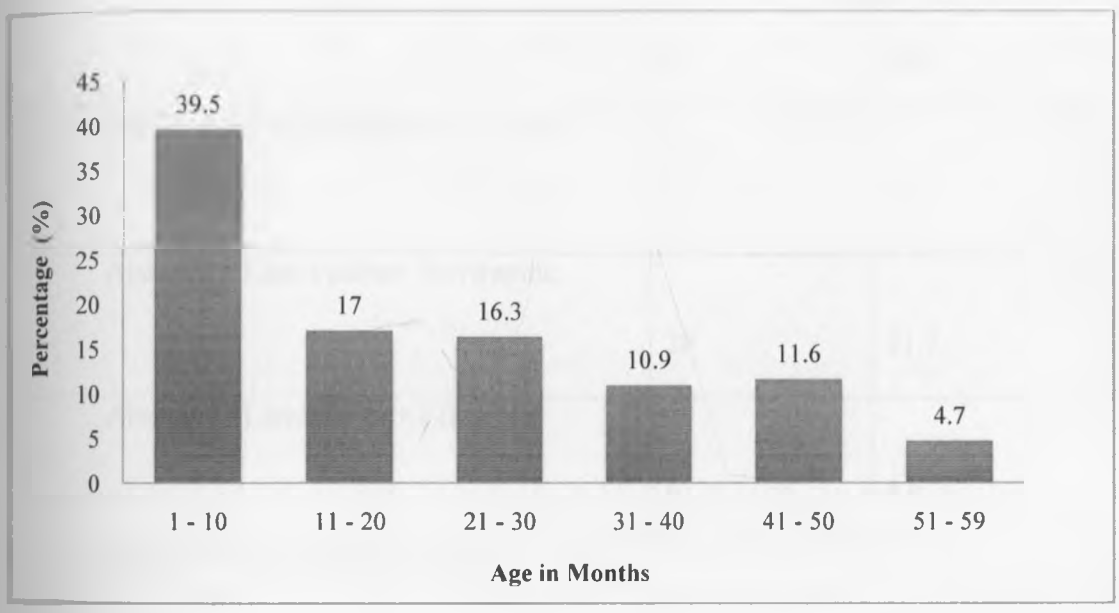

Figure 2: Percentage Age Distribution of Study Participants

4.4 ARV Regimen Characteristics

4.4.1 Information on Study Participants' Paediatric ARV Regimen

All the 129 study participants in the study were currently on antiretroviral therapy either for PMTCT or HAART. Those on PMTCT regimen of Nevirapine alone were 52 (40.3%) while 77

(59.7%) were on HAART regimen. Among those on the HAART regime, *Zidovudine+Lamivudine+Nevirapine* accounted for the largest percentage (31%).

This is illustrated in table 2 below:

Table 2: Study Participants and Paediatric ARV Regimen at Naivasha District Hospital

ARV regimen	**Number (N)**	**Percentage (%)**
Nevirapine (PMTCT)	52	40.3
Zidovudine+Lamivudine+ Nevirapine	40	31.0
Abacavir+ Lamivudine+ Nevirapine	28	21.7
Abacavir+ Lamivudine+ Efavirenz	6	4.6
Abacavir+ Lamivudine+Kaletra	2	1.6
Zidovudine+ Lamivudine+Efavirenz	1	0.8
Total	129	100

4.4.2 Child refusal to take medicine.

Among the study population, 27.6% reported refusal to take medicine as shown in figure 3 below.

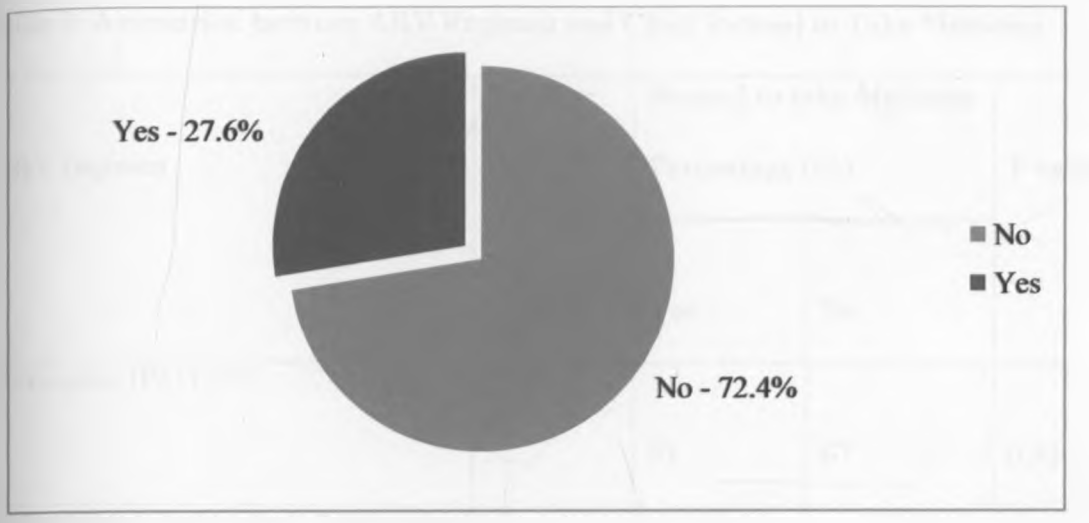

Figure 3: Refusal to take ARV by children at Naivasha District Hospital

There was no statistically significant association between refusal to take medicine among the participating children and any of the specific regimens as shown in table 3 below (P = 0.526).

Table 3: Association between ARV Regimen and Child Refusal to Take Medicine

ARV regimen	**Number (N)**	**Refusal to take Medicine Percentage (%)**		**P value**
		Yes	**No**	
Nevirapine (PMTCT)	52	33	67	0.526
Zidovudine+Lamivudine+ Nevirapine	40	23	77	
Abacavir+ Lamivudine+ Nevirapine	28	21	79	
Other regimens	9	33	67	
Total	129	27.6	72.4	

4.5 Adherence to ARV Medication

Adherence was measured by various methods. These were:

4.5.1 Caregiver Self-Report Method

According to caregiver self-reports 124 (96%) study participants had optimal levels of adherence (≥95%). The number of participants who reported missing at least one dose of ARV medication in the last 3 days was 25 (19.5%). This was higher than those who reported missing a dose of ARVs in the last 2 weeks who were 15 (11.7%).

Table 4: Caregiver Reported Adherence

	Frequency (N)	**Percentage (%)**
Missed medication in the last 2 weeks		
No	113	88.3
Yes	15	11.7
Missed medication in the last 3 days		
No	103	80.5
Yes	25	19.5
Total	129	100

4.5.2 Pharmacy Pill Count Method

According to pharmacy pill count records, 62 (48.1%) of the study participants had optimal levels of adherence ≥95%. The pharmacy pill count method yielded an overall mean adherence over 6 months of 93.9% and 94.5% over 1 month (P = 0.176).

Table 5: Pharmacy Pill Count Mean Adherence

	Number (N)	Mean	Standard Deviation	Minimum	Maximum	P value
Mean adherence over 6 months	129	93.9%	3.44	82.2%	100%	0.176
Mean adherence over 1 month	129	94.5%	5.54	78.3%	100%	

4.6 Factors influencing Overall Mean Adherence to ARVs (Pharmacy Pill Count)

4.6.1 ARV Formulation

The participants were either on syrup or tablet formulations. The difference in mean adherence between participants on exclusive syrup formulations (93.3%) and those on exclusive tablet formulations (93.5%) was not statistically significant, P value of 0.167. This is shown in table 6 below.

Table 6: Factors influencing Adherence at 6 months (ARV Formulation)

	Mean adherence at 6 months	**Difference (95% CI)**	**P value**
ARV Formulation			
Syrup	94.3%	-0.8% (-2.03 to 0.35)	0.167
Tablet	93.5%		

4.6.2 PMTCT Regimen versus HAART Regimen

As illustrated in table 3 above, 40.3% of the study participants were on PMTCT regimen of Nevirapine alone while the rest (59.7%) were on HAART regimen. There was a statistically significant difference in adherence between the PMTCT regimen (94.7%) and the HAART regimen (93.4%), P = 0.045. This is illustrated in figure 4 and table 7 below.

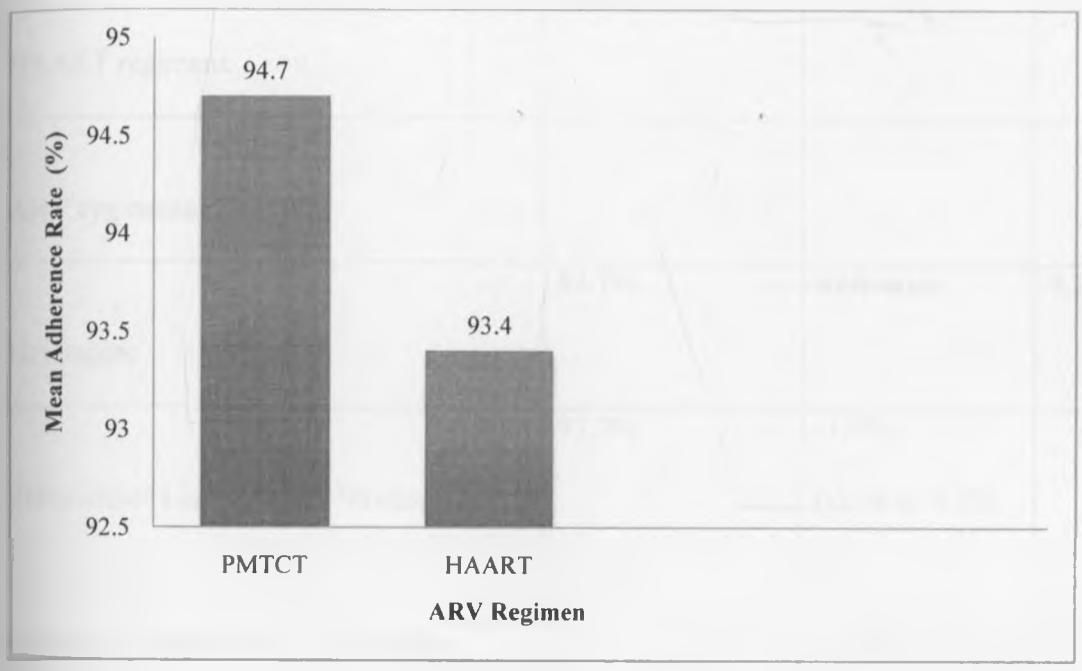

Figure 4: ARV Regimen versus Mean Adherence Rate

Table 7: Factors influencing Overall Mean Adherence over 6 months (ARV Regimen)

	Mean adherence over 6 months	Difference (95% CI)	P value
PMTCT and HAART regimen			
Nevirapine (PMTCT)	94.7%	-1.3% (-2.22 to -0.03)	0.045
HAART regimens	93.4%		
ARV regimens			
Nevirapine	94.7%	Reference	0.290
Zidovudine+Lamivudine+ Nevirapine	93.7%	-1.0% (-2.48 to 0.53)	
Abacavir+ Lamivudine+ Nevirapine	93.2%	1.5% (-0.096 to 2.97)	
Abacavir+ Lamivudine+ Efavirenz	92.4%	2.3% (-0.72 to 5.23)	
Abacavir+ Lamivudine+Kaletra	94.8%	N/A	
Zidovudine+ Lamivudine+Efavirenz	91.9%	N/A	

4.6.3 Patient Factors and Overall Mean Adherence

Linear regression shows that for every unit change in the age of the child on ARVs there was a slight and non-significant (-0.02%) change in percentage overall adherence (P = 0.19). This is shown in Table 8 below.

Table 8: Age in Months and Overall Mean Adherence over 6 Months

	Coefficient	Standard error	T	P	95% Confidence Interval	
Age in months	-0.02	0.02	-1.31	0.19	-0.06	0.01
Constant	94.43	0.49	193.56	0.00	93.47	95.40

There was a slight and non-significant increase in percentage overall adherence of 1.49% (P = 0.1) among children with both parents alive compared to those with at least one parent deceased as shown in Table 9 below.

Table 9: Other Patient Factors and Overall Mean Adherence over 6 Months

	Mean adherence over 6 months	**Difference (95% CI)**	**P value**
Gender			
Female	94.04%	0.19% (-1.01 to 1.4)	0.75
Male	93.84%		
Guardian			
Biological parent	94.07%	-1.40% (-3.72 to 0.93)	0.219
Other relationship	92.68%		
Parental status			
Both parents alive	94.21%	1.49% (-0.3 to 3.28)	0.100
At least one parent deceased	92.72%		

4.6.4 Co-infection Treatment and Overall Mean Adherence over 6 Months

A total of 21 (16.3%) of the patients were being treated for co-infections. The mean age of patients on treatment for co-infection was 26.3 months (SD 15.5). Patients not receiving co-infection treatment were slightly younger with a mean age of 19.1 months (SD15.9) but the age difference between the two groups was not statistically significant (P = 0.065).

There was a statistically significant difference in the mean adherence over 6 months between patients receiving treatment for co-infections and those not receiving treatment for co-infections. Figure 5 below shows that the mean adherence over 6 months for patients not receiving treatment for a co-infection was 3.03% (P = 0.004) lower than those being treated for a co-infection.

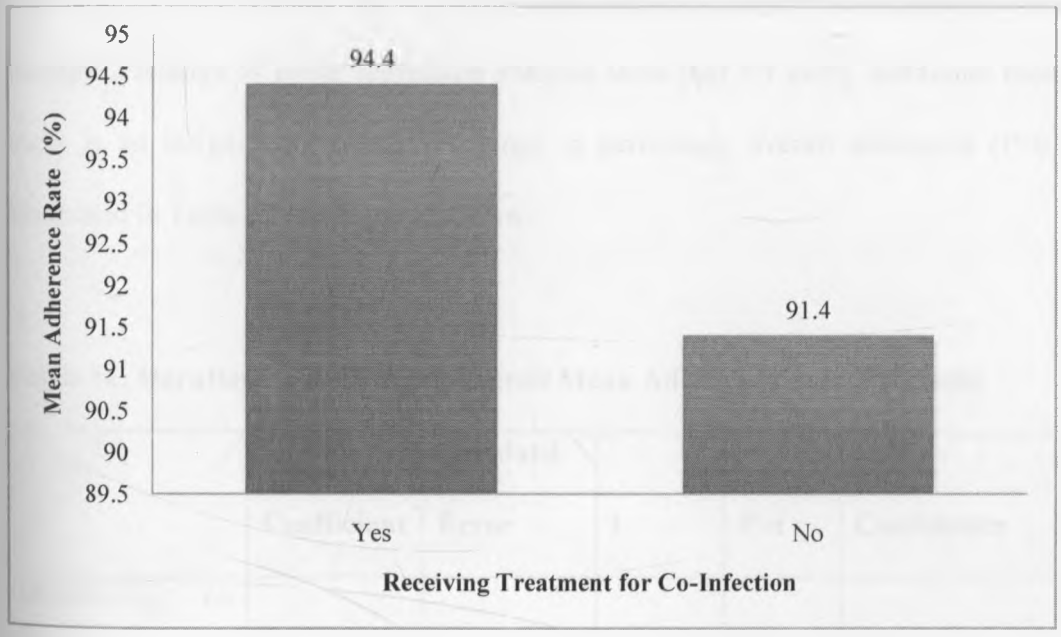

Figure 5: Co-infection Treatment versus Mean Adherence Rate

4.6.5 Duration of ARV treatment and Age ARV started versus Overall Mean Adherence

The median age at which ARVs were started among the study population was 12.7 months while the median duration the participants had been on ARVs was 11.2 months.

Table 10: Age ARV started and Duration on ARV drugs

	Median	Minimum	Maximum
Age ARV started (months)	12.7	14 days	57.5 months
Duration on ARV (months)	11.2	8 days	50.3 months

4.6.5.1 Overall Mean Adherence over 6 Months versus Duration on ARV

Duration on ARV therapy did not show a statistically significant association with adherence to therapy. Findings of linear regression analysis show that for every additional month on ARVs there is an insignificant (-0.03%) change in percentage overall adherence (P=0.23). This is illustrated in Table 11 and Figure 6 below.

Table 11: Duration on ARVs and Overall Mean Adherence over 6 Months

	Coefficient	Standard Error	t	P>t	[95% Confidence	Interval]
Duration on ARVs (months)	-0.03	0.03	-1.22	0.23	-0.08	0.02
Constant	94.4	0.49	191.7	0	93.4	95.4

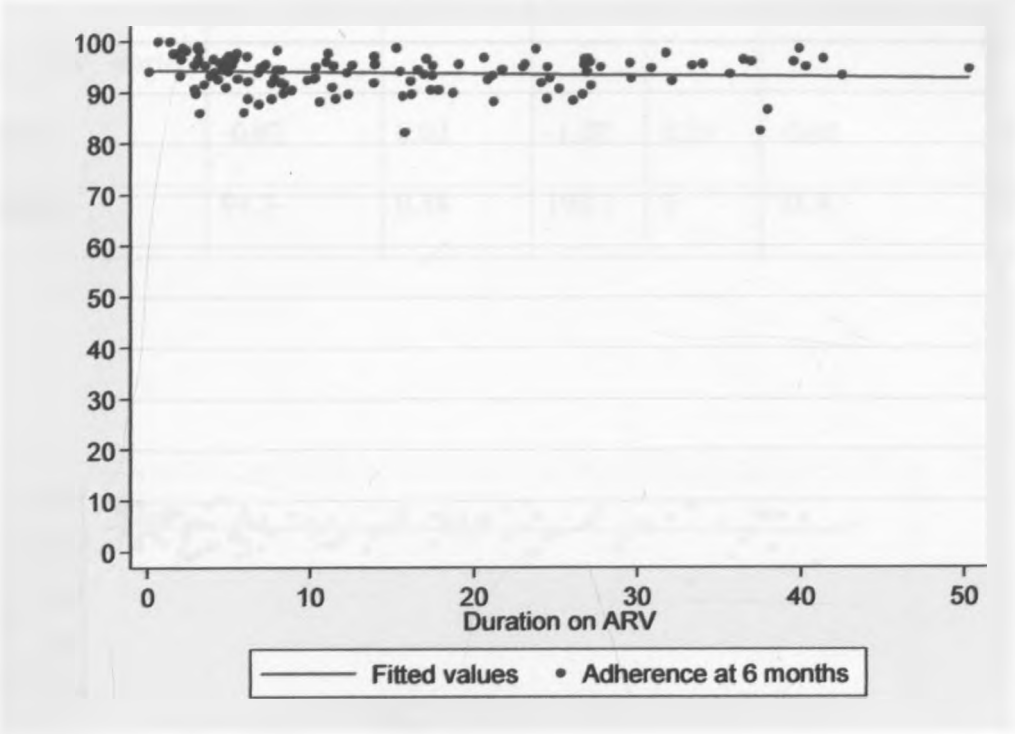

Figure 6: Linear Regression of Duration on ARVs vs. Overall Mean Adherence (%)

4.6.5.2 Overall Mean Adherence versus Age ARV started

Linear regression shows that for every unit change in the age at which ARVs were started there was a slight and non-significant (-0.02%) change in percentage overall adherence (P=0.29). This is shown in Table 12 and Figure 7 below.

Table 12: Age ARVs started and Overall Mean Adherence

	Coeffecient	Standard Error	t	P>t	[95% Confidence	Interval]
Age ARV started (months)	-0.02	0.02	-1.07	0.29	-0.06	0.02
Constant	94.3	0.48	198.1	0	93.4	95.3

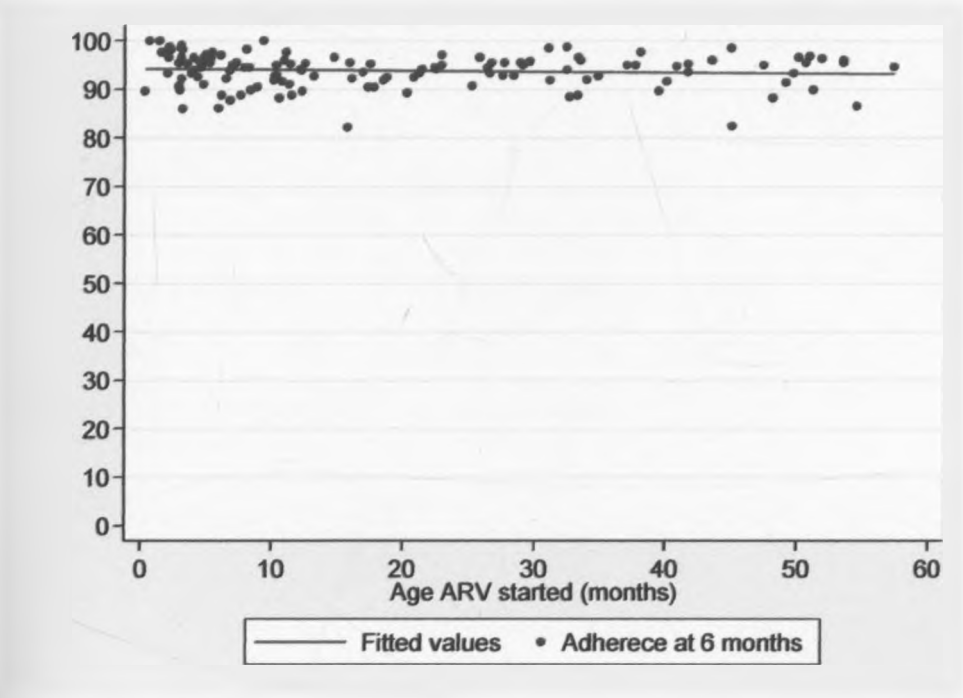

Figure 7: Linear Regression of Age ARVs started vs. Overall Adherence (%)

4.6.6 Multivariable Adjusted Analysis

Results of the multivariable linear regression analysis are presented in Table 13 below. After adjusting for other patient factors such as age, gender and treatment factors including ARV regimen and ARV formulation, treatment for co-infection was still significantly associated with overall ARV adherence ($P < 0.001$). The average adherence among patients not being treated for co-infection was 3.9% lower (95% CI -6.1 to -1.8%) than the adherence among patients on co-infection treatment.

Table 13: Adjusted Analysis of Factors influencing Mean Adherence over 6 Months

	Coefficient	Standard Error	t	P	95% Confidence Interval	
Age (months)	-0.01	0.03	-0.21	0.8	-0.07	0.06
Gender	-0.5	0.6	-0.9	0.4	-1.8	0.7
Rx co-infection	-3.9	1.1	-3.6	0.00	-6.1	-1.8
ARV regimen						
Abacavir, Lamivudine, Kaletra	0.6	3.0	0.2	0.84	-5.38	6.57
Abacavir, Lamivudine, Nevirapine	-2.4	1.8	-1.3	0.2	-5.95	1.23
Nevirapine	-1.5	2.3	-0.7	0.5	-6.0	3.0
Zidovudine, Lamivudine, Efavirenz	-0.4	3.7	-0.1	0.9	-7.7	6.9
Zidovudine, Lamivudine, Nevirapine	-2.0	1.7	-1.2	0.2	-5.5	1.4
ARV formulation	-0.4	1.3	-0.3	0.8	-2.9	2.1
Constant	97.4	2.5	38.9	0.0	92.4	102.4

CHAPTER FIVE: DISCUSSION

Our study aimed to find out the factors influencing adherence to HAART among HIV exposed and infected children aged between 0 to 59 months at Naivasha District Hospital. This is a particularly vulnerable group of paediatrics with regard to HIV care and treatment. This is especially so because adherence to HAART among this population is highly dependent on external factors beyond their control such as the caregiver's attitude and knowledge of their child's treatment.

Adherence was measured using caregiver reports and pharmacy pill count records. The caregiver report showed 96% of the study participants with optimal adherence ≥95% while the pharmacy pill count records classified only 48.1% as having optimal adherence. It is very likely that the pharmacy pill count records yielded more accurate results of adherence rates as compared to the caregiver reported adherence due to recall bias. This is because the caregivers did not recall clearly the exact number of doses missed in the past two weeks. This made it difficult to ascertain the child's actual adherence rate. On the other hand, pharmacy pill count records could be abstracted from as far back as 6 months prior to the current visit. These findings are consistent with Farley et al who noted the lack of reliability of caregiver self-report as a mode of assessing adherence to HAART [43].

The mean adherence by pharmacy pill count over 6 months was 93.9% and over 1 month was 94.5% both of which are sub-optimal but quite close to the optimum adherence of ≥95%. The difference in mean adherence over 1 month and 6 months was not significant -0.6% (95% CI, -1.38 to 0.26), P = 0.176. Therefore, the mean adherence at 6 months was used to reference the factors influencing adherence.

With regard to the ARV formulation as a factor influencing adherence we compared the children on tablet formulations with those exclusively on syrup formulations. We found that there was a slight difference of -0.8% (P = 0.167) in the adherence levels between those on syrups and tablets. This probably points to the fact that good adherence practices among caregivers of children on ARVs, as noted by Phelps et al [45], have a stronger bearing than ARV formulation on the child's subsequent adherence.

The study participants were put on various paediatric ARV regimens mainly for PMTCT or HAART. When compared we found that those on the PMTCT regimen had significantly higher adherence rate (94.7%) than those on HAART regimen (93.4%) P = 0.045. However, there was no significant difference in adherence among the participants on different HAART regimen. In addition, we found that there was no statistically significant association between refusal to take medicine among the participating children and any of the specific regimens (P = 0.526).

This suggests that the pill burden and regimen complexity in HAART regimen could contribute to lowering the adherence rates significantly as opposed to the single drug PMTCT regimen

of Nevirapine alone. These findings are in tandem with those of Staci M et al [20] who noted a correlation between regimen complexity and adherence to ARVs. Moreover, it is possible that the caregivers of children on PMTCT have a higher motivation to ensure their children adhere to the medication so as to prevent transmission of the virus. This hope is invariably lost for the caregivers whose children are on HAART.

With regard to patient factors we found that age, gender and parental status did not have a significant influence on the mean adherence over 6 months. We also compared the mean adherence over 6 months with the age at which the child was started on ARVs and found that the age at which ARVs were started did not show a significant association with adherence to ARVs ($P = 0.29$). A similar trend was observed between mean adherence over 6 months and duration that the child had been on ARVs. These findings suggest that in reference to adherence rates, patient factors are largely influenced and controlled by the caregiver among this study population.

Our study went on to explore the association between treatment for co-infections and adherence to ARVs among the study population. We found that the mean adherence over 6 months for patients not receiving treatment for a co-infection was 3.03% ($P = 0.004$) lower than those being treated for a co-infection. The implication of this finding is that patients with an active infection put on treatment for a co-infection seem to have a higher propensity to adhere to their ARV medication. This could be related to the need to treat the active infection and is probably driven by the knowledge that adherence to ARVs directly influences reduction of opportunistic infections. This association is alluded to by Turkova et al [46].

Results of a multivariable analysis showed that neither the patient factors (age, $P = 0.8$, gender, $P = 0.4$) nor ARV therapy factors (ARV formulation, $P = 0.8$ or ARV regimen) were significantly associated with the level of adherence in the adjusted analysis. However, treatment for co-infection was still significantly associated with overall mean adherence ($P < 0.001$).

CHAPTER SIX: STUDY LIMITATIONS, CONCLUSIONS & RECOMMENDATIONS

6.1 STUDY LIMITATIONS

There were several limitations in our study. To begin with, we found that because face-to-face interviews were quite subjective, the caregivers may have reported what they felt was socially acceptable to the clinician. This may have led to an over estimation of adherence levels by caregiver self-report method.

Also, the caregiver may not feel free to tell the clinician the truth about missed doses if they perceive that the consequences of reporting non-adherence may be punitive, including stopping of the medication.

Considering that some of the liquid formulation ARVs may have spilt during administration, the actual pharmacy adherence may have been lower than what we obtained. In addition, estimation of liquid formulations was a challenge and may not have been accurate due to inter-observer error.

In the pharmacy, patients were required to bring back all the remaining doses and sometimes they forgot or they may have left out excess doses intentionally therefore masking non-adherence.

While collecting information on reported adherence, some of the caregivers present may not have been the ones that routinely administered drugs to the child and this may have confounded the accuracy of information obtained.

6.2 CONCLUSIONS

It is a matter of great concern that only about half (48.1%) of the HIV exposed and infected children at Naivasha District Hospital reported optimal adherence (≥95%) to antiretroviral therapy by Pharmacy pill count method. Encouragingly though, the reported mean adherence rate of 93.9% is quite close to the optimal rates. This suggests that optimal rates of adherence may be achieved by further interventions, especially in the vulnerable group.

Treatment for co-infections and regimen complexity were found to be the major factors influencing adherence among this study population of paediatrics. Co-infection treatment was found to improve the adherence to antiretroviral therapy. Similarly, the simpler PMTCT regimen was found to have better adherence than the more complex HAART regimens.

Caregivers were largely able to control the negative influence of patient factors such as age, gender, parental status and duration on antiretrovirals on adherence. This may have been due to the practice at Naivasha district hospital of giving the caregivers adherence counseling and preparation prior to initiating antiretrovirals.

6.3 RECOMMENDATIONS

Intensified adherence counseling and preparation be given to caregivers of HIV exposed and infected children to prepare them prior to initiating ARVs. The role of a Clinical Pharmacist in providing individualized patient care and counseling to the caregiver is pertinent. This means establishing a rapport with the caregiver and child so as to partner with them in achieving optimal levels of adherence. In addition, carrying out demonstrations on medicine use advice using visual aids is especially useful for syrup and suspension formulations.

There is also a need to understand the individual patient needs and challenges and provide adherence counseling that is applicable to each unique situation.

Special focus needs to be put on the class of patients with complex paediatric ARV regimens that are a mix of various formulations such as a syrup, tablet, and capsule.

Also, closer emphasis needs to be placed on adherence of children on HAART and PMTCT who do not have active co-infections. This is a vulnerable group that according to our findings are more likely to be non-adherent to their ARVs.

Further research needs to be done to explore the association between caregiver characteristics and adherence to HAART among this study population

We also recommend that health sector policy makers and stakeholders establish structures to consistently monitor adherence to ARVs at paediatric comprehensive care clinics all across the country using pharmacy pill count method.

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APPENDICES

Appendix 1: CONSENT FORM

To be read in a language that the respondent is fluent in.

Title of the study: Factors influencing adherence to antiretroviral therapy among HIV infected and HIV exposed children at Naivasha District Hospital.

Institution: Department of Pharmaceutics and Pharmacy Practice, School of Pharmacy, University of Nairobi, P.O BOX 30197-00400, Nairobi.

Investigator: Dr Wangia Simon Waudo, P.O BOX 56192-00200, Nairobi.

Supervisors: Prof G. Muriuki, Department of Pharmacology and Pharmacognosy; Dr Shital Maru, Department of Pharmaceutics and Pharmacy Practice, Dr E.M. Mwangangi, Department of Pharmaceutics and Pharmacy Practice.

Ethical Approval: Kenyatta National Hospital/ University of Nairobi Ethical and Research Committee, P.O BOX 20723-00100, Nairobi. Tel 2726300/2716450 Ext 44102

Permission is requested from you to enroll in this medical research study. You should understand the following general principles which apply to all participants in a medical research:

i. Your agreement to participate in this study is voluntary.

ii. You may withdraw from the study at any time without necessarily giving a reason for your withdrawal.

iii. After you have read the explanation please feel free to ask any questions that will enable you to understand clearly the nature of the study.

Introduction: In this study am assessing the adherence to antiretroviral therapy among HIV exposed and infected children less than 5 years of age.

Purpose of the study: The purpose of the study is to find out the factors influencing adherence to antiretroviral therapy among HIV infected and HIV exposed children.

Procedure to be followed: With your permission, I will ask you some questions about your child's ARV medication use. I will also use your child's file to obtain some information on your child's HIV status and history of antiretroviral use. All information will be handled with confidentiality and will only be used for the purpose of this study.

Risks: There will be no risks involved in this study.

Benefits: You will be advised on how to improve your child's adherence and the findings will be useful in improving the quality of antiretroviral therapy among children less than 5 years of age.

Assurance of confidentiality: All information obtained from you will be kept in confidence. At no point will you or your child's name be mentioned or used during data handling or in any resulting publications. Codes will be used instead.

Contacts: In case you need to contact me, my academic department or the Kenyatta National Hospital/ University of Nairobi Ethics and Research Committee concerning this study please feel free to use the contacts provided above.

I now request you to sign the consent form attached.

CONSENT FORM

FACTORS INFLUENCING ADHERENCE TO ANTIRETROVIRAL THERAPY AMONG HIV INFECTED AND HIV EXPOSED CHILDREN AT NAIVASHA DISTRICT HOSPITAL, KENYA

I _____the parent/guardian of _____ hereby consent to respond to questions on the questionnaire. I also give consent to the investigator to use my child's file to obtain information for his study. The nature of the study has been explained to me by Dr. Simon Waudo Wangia.

Date _____ Signature _____

I confirm that I have explained to the caregiver the nature and effect of the study.

Date _____ Signature _____

Appendix 2: QUESTIONNAIRE

Date of Interview: _____

Study No. _____

Relationship of the caregiver with the child:

Biological mother ☐

Biological father ☐

Sibling ☐

Other relative: Aunt ☐

Uncle ☐

Grandparent ☐

Cousin ☐

Foster parent/guardian ☐

Step-parent ☐

A) Information on the child

Date of birth: _____ Age:_____

Gender: male ☐ female ☐

Parental status of the child

Both parents alive ☐

Father deceased ☐

Mother deceased ☐

Both parents deceased ☐

B) The following questions are about antiretroviral drugs which are usually given to HIV infected persons.

1. Is the child currently on any ARV drugs? Yes ☐ No ☐

2. If yes when was the child started on ARV drugs? (dd/mm/yyyy) _____

3. Which ARV drugs is the child currently on and how have you been giving them to the child? (confirm from patient file)

S. No.	Drug name	Dose	Frequency	Dosage	Formulation

4. Does the child at times refuse to take his/her medicines? Yes ☐ No ☐

If **yes,** how do you ensure that the child takes the medicines?

Mix the drug with sweet things ☐

Promise the child a reward ☐

Give strong tasting foods immediately after giving drug ☐

Give with plenty of juice/milk or any other fluid ☐

Force the child through beating, shouting, or threatening ☐

Other

Specify _____

_____

5. Does the child experience any kind of problem immediately after taking the medicines?

Yes ☐ No ☐

If yes,

a) What kind of problem(s)? _____

_____

b) How do you deal with the problem?

_____

_____

C) Adherence information

Instructions to the study participant: Now I would ask questions on how your child has been taking the ARV medications in the past two weeks. Please be aware that everyone misses doses sometimes. Be assured that this information will neither change the way you receive ARV medications from the CCC nor your opportunity to participate in this study.

1. Has the child missed doses of medicine in the last two weeks? Yes ☐ No ☐
2. Has the child missed doses of medicine in the past 3 days? Yes ☐ No ☐

3. a) Last time the child missed a dose, did the missed dose include all the drugs or specific drug(s)?

Missed all three drugs ☐

Missed specific drug(s) ☐

N/A ☐

b) Specify the drugs missed and number of doses missed in the past 3 days.

Drugs Missed	**Number of doses missed**

c) Specify the drugs missed and number of doses missed in the past 2 weeks.

Drugs Missed	**Number of doses missed**

4. If any dose of antiretroviral drug was missed, what led to the dose(s) being missed?

Ran short of the specific drug	☐
Was away from home	☐
Forgot	☐
Was too busy	☐
Child vomits on taking the medicine	☐
Side effects of the medicine	☐
Fear that someone may find out child's HIV condition	☐
Medicine tastes bad, child spits out	☐
The health of the child improved	☐
Other	
Specify	

_____

_____

Appendix 3: PHARMACY DATA ABSTRACTION FORM

	Quantities of doses prescribed and dispensed					
Drugs	**1.**		**2**		**3.**	
	No. of doses dispensed	No. of doses prescribed	No. of doses dispensed	No. of doses prescribed	No. of doses dispensed	No. of doses prescribed
Month 1 (1st refill) Date……						
Mean adherence rate						
Month 2 (2nd refill) Date……						
Mean adherence rate						
Month 3 (3rd refill) Date……						
Mean adherence rate						

Month 4 (4^{th} refill) Date…….						
Mean adherence rate						
Month 5 (5^{th} refill) Date……						
Mean adherence Rate						
Month 6 (6^{th} refill) Date……						
Mean adherence rate over 6 months per drug						

a) Mean adherence rate over one month (month 1) ……%

b) Overall mean adherence rate over 6 months ……..%

Appendix 4: WORKPLAN

January 2012 to November 2012

Research Activity Description	**Time Period**										
	J	**F**	**M**	**A**	**M**	**J**	**J**	**A**	**S**	**O**	**N**
Proposal development under guidance of supervisors	X	X	X								
Submission to Ethic & Research Committee for approval				X							
Receive Approval letter from Ethics & Research Committee					X						
Data collection commences and continues						X	X				
Data entry and analysis								X			
Report writing and supervisors' corrections and guidance									X		
Submission of final dissertation of project is done										X	
Defense of study to the board of examiners and grading										X	X

Appendix 5: FINANCIAL BUDGET AND FUNDING INFORMATION

S.no.	Cost Item	Cost Units	No. of Days	Unit Cost (KES)	Costing	Total (KES)
1	**Preparations Phase**					
	a) Stationary (Notebooks, pens, printing of questionnaires	1	1	2000	1*1*2000	2000
	b) Transport	1 principal investigator	2	500	1*2*500	1000
	c) Communication	1 principal investigator	2	250	1*2*250	500
	d) Finalization of concept paper	1 principal investigator	1	2000	1*1*2000	2000
	i)	**Sub-total**				**5500**
2	**Implementation Phase: Situation Analysis Survey**					
	i) At the start of the program					
	a) Site visit for data verification (transport, communication, and out of pocket)	1 principal investigator	1	3000	1*1*3000	3000
	b) Project proposal development	1 principal investigator	3	1000	1*3*1000	3000
	c) Accommodation for principal investigators	1 principal investigator	30	1500	1*30*1500	45,000
	d) Incidentals for principle investigators	1 principal investigator	30	500	1*30*500	15,000
	e) Transport and communication	1 principal investigator	30	500	1*30*500	15,000
	f) Bio-statistician data analysis fee	1	30	500	1*30*500	10,000
	ii)	**Sub-total**				**91,000**
Total Cost						**96,500**

FUNDING INFORMATION

The study funding was from the Maternal Newborn and Child Health grant linked to Partnership for Innovative Medical Education in Kenya (PRIME-K). The project described was supported by Award Number 5R24TW008907 from the US National Institutes of Health. The content is solely the responsibility of the authors and does not necessarily represent the official views of the US National Institutes of Health. The Partnership for Innovative Medical Education in Kenya (PRIME-K) is made up of the University of Nairobi and two of its longstanding training partners; the University of Washington and the University of Maryland Baltimore. It was funded as part of a bigger proposal evaluating implementation of PMTCT services at the Naivasha District Hospital comprising of 9 multidisciplinary members. Through the Linked Grant 'Strengthening Maternal, Newborn and Child Research Training' the PRIME-K program provided opportunities for four teams of post-graduate students, each team being made up of between nine to eleven individuals from different disciplines, to carry out research within four public hospitals; Naivasha District Hospital, Garissa District Hospital, Coast General Hospital and Mbagathi District Hospital.

The main goal of PRIME-K is to strengthen and build the clinical and research capacity at the University of Nairobi and thereby improve human resource capacity for health and health outcomes in Kenya.

All the individuals awarded the seed grant funding underwent, throughout the research period, training in; implementation science and applied research, health metrics and evaluation and program leadership relevant to achieving Kenya's health development goals. Each team received approximately ten thousand U.S. dollars to carry out their studies.

Appendix 6: ETHICAL APPROVAL

UNIVERSITY OF NAIROBI
COLLEGE OF HEALTH SCIENCES
P O BOX 19676 Code 00202
Telegrams: varsity
(254 020) 2726300 Ext 44355

KNH/UON-ERC
Email: uonknh_erc@uonbi.ac.ke
Website: www.uonbi.ac.ke
Link: www.uonbi.ac.ke/activities/KNHUoN

KENYATTA NATIONAL HOSPITAL
P O BOX 20723 Code 00202
Tel: 726300-9
Fax: 725272
Telegrams: MEDSUP, Nairobi

Ref: KNH-ERC/A/190

22 June 2012

Dr Wangia Simon Waudo
Dept. of Pharmaceutics and Pharmacy Practice
School of Pharmacy
University of Nairobi

Dear Dr. Waudo

Research proposal: "Factors influencing Adherence to Antiretroviral Therapy among HIV infected and HIV exposed children at Naivasha District Hospital" (P220/04/2012)

This is to inform you that the KNH/UoN-Ethics & Research Committee (ERC) has reviewed and **approved** your above revised research proposal. The approval periods are 22nd June 2012 to 21st June 2013.

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 severe 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 **www.uonbi.ac.ke/activities/KNHUoN**

"Protect to Discover"

Yours sincerely,

PROF. A.N. GUANTAI
SECRETARY, KNH/UON-ERC

c.c.
The Deputy Director CS, KNH
The Principal, College of Health Sciences, UoN
The Dean, School of Pharmacy, UON
The HOD, Records, KNH
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Dr. Shital Maru Shah, Dept. of Pharmaceutics & Pharmacy Practice, UON