FACTORS ASSOCIATED WITH VIRAL NON-SUPPRESSION AMONG HIV POSITIVE ADOLESCENTS IN CHULAIMBO HOSPITAL, KISUMU COUNTY, KENYA, 2018

BY

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MOI UNIVERSITY

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DECLARATION

Declaration by the Candidate

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DEDICATION

I dedicate this work to my dear husband Michael, and to my children Grace and Immanuel.

Your moral and emotional support gave me motivation and strength during the study.

ABSTRACT

Background: Kisumu County's HIV prevalence of 19.9% is about three times higher than the national average. In 2015, 52% of new HIV infections reported in the County were among adolescents. Globally, HIV viral suppression rates among adolescents are low. Kenya has adopted the 90-90-90 targets by joint United AIDS (UNAIDS), one of which is to have 90% of all people receiving anti-retroviral therapy (ART) virally suppressed by 2020.

Objectives: The objective of study was to estimate prevalence of viral non-suppression (VNS) and identify factors associated with VNS among HIV positive adolescents on ART at Chulaimbo Sub-County Hospital.

Methods: This was a cross-sectional study among HIV positive adolescents (10-19 years) on ART for >6 months. They must have had a routine viral load (VL) test done in ≤ 6 months with valid laboratory results. Study sample was randomly selected from laboratory VL register. A VL of ≥1000 RNA copies/ml was considered non-suppressed. Using a pre-tested structured questionnaire, disclosure status and socio-demographic data were obtained; adherence to ART was measured by pill counts and abstraction for clinical data was done from medical records. Data analysis was done using Epi info version 7 and STATA software. To identify factors associated with VNS, we conducted bivariate analysis for crude odds ratio (cOR) and stratified logistic regression to control for confounding and check for effect modification by computing adjusted OR (AOR).

Results: Out of 398 adolescents on ART, 212 had been tested for routine VL ≤ 6 months with valid VL results. Two hundred adolescents were randomly selected and interviewed; 103 (51.5%) were female; younger adolescents (10-14 years old) were 102 (51%) and 98 (49%) adolescents were 15-19 years old. The median duration on ART was 7.6 years (range 0.8-12.4years). One hundred and forty-two (71%) adolescents were on first line regimen and 58 (29%) on second line regimen; 110 (55%) had good (≥ 95%) adherence to ART. Seventy-one (35.5%) adolescents had VL result of ≥1000 RNA copies/ml. The odds of VNS were higher among those who had poor adherence to ART and there was effect modification with increasing age; older adolescents (AOR 13.93, 95% CI 3.20-60.74) compared to younger adolescents (AOR 4.41, 95% CI 1.18-16.54), and in males (AOR 22.33, 95% CI 4.35-114.63) compared to females (AOR 3.92, 95% CI 1.09-14.04). Being on first line regimen was negatively associated with VNS for males (AOR 0.06, 95% CI 0.00-0.87) and older adolescents (AOR 0.02, 95% CI 0.00-0.20).

Conclusion: The proportion of VNS was more than three times higher than the acceptable based on the 90% viral suppression target. Adolescents on second line regimens and those who are non- adherent to ART have higher odds of VNS, the odds being higher in males and older adolescents.

Recommendations: County ART program should reinforce targeted interventions to motivate adherence in HIV infected males and older adolescents towards attaining the 90% target and improve the treatment outcomes.

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ACKNOWLEDGEMENT

I acknowledge my thesis Supervisors Prof. Fabian Esamai, Professor of Child Health and Paediatrics, School of Medicine-Moi University, Eldoret, Kenya and Mr Tura Galgalo, Public Health Specialist, Division of Global Health Protection, US Centers for Disease Control and Prevention (CDC), Kenya who walked with me through the journey, from concept development to writing thesis report. Their knowledge, expertise, skills and experience in scientific research and communication helped to address my questions in research methods, project implementation and write-up.

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Above all, I thank God who has been gracious to me during this period, giving me good health, strength and determination to endure even when it was not easy.

CHAPTER ONE

INTRODUCTION

1.1 Background

The Public Health and clinical goal in HIV epidemic management is to ensure that the PLHIV know their status, are linked up with care and treatment, and attain sustained viral suppression (VS) (UNAIDS, 2014; WHO, 2016). In the Kenya AIDS Strategic Framework 2014-2019, the Ministry of Health has committed to meeting the Joint United Nations Program on HIV/AIDS (UNAIDS) 90-90-90 targets which seek to: have 90% of people living with HIV know their status, enroll 90% of people testing HIV positive on sustained antiretroviral therapy and to achieve 90% viral load suppression (<1000copies/ ml plasma) for those receiving ART (NASCOP, 2014). The UNAIDS targets are set to be achieved by the year 2020 in the scale-up of HIV response in low- and middle-income countries (LMIC), and are geared towards ending the epidemic by 2030 (UNAIDS, 2014). Globally, by end of 2017, 75% of PLHIV knew their status, 79% of PLHIV who knew their status were accessing ART and 81% of people on treatment had suppressed viral loads (UNAIDS, 2017).

Routine VL tests have been reported as the most reliable way of monitoring PLHIV enrolled on ART to determine if the treatment is able to suppress viral replication (Doherty, 2015) .Regular VL monitoring is important for identification of patients who may need a more intensive adherence support program, early detection of treatment failures, and helps to reduce the chances for development of drug resistance and unnecessary consecutive switch to more expensive ART regimen options (AIDSinfo, 2018; Bulage *et al*., 2017; McHugh *et al*., 2017; Mutevedzi *et al*., 2011; WHO, 2016).

Adolescence is a transitional phase of growth and development between childhood and adulthood. The drastic biological and psychosocial developmental changes that occur during adolescence influence the health-related behaviors and affect a spectrum of diseases, most especially chronic illnesses (WHO, 2014). The adolescents' life is characterized by a need for self-directing freedom and independence, search for identity, concern with appearance/self-image, need to fit in with peers, active lifestyle and all these compete with their solid thinking processes and risk-taking behaviors. As a result, it becomes challenging to attain and sustain adolescents' focus on maintaining good health practices, particularly when strict adherence to treatment is required as in the case of chronic illnesses like HIV/AIDS (AIDSinfo, 2011).

Older adolescents, transiting into adulthood, have been identified as a high-risk group for poor adherence to and defaulting ART (Nglazi *et al*., 2012).In a randomized clinical trial of HIV-infected adults initiating ART in three clinics in Kenya, it was found that patients who received short message services (SMS) support had significantly improved ART adherence and rates of VS compared with the control individuals (Lester *et al*., 2010).

1.2 Statement of the Problem

In 2014, HIV/AIDS was reported as the second leading cause of death globally among adolescents, after road injury (WHO, 2014). The same study estimated that the number of HIV related deaths is rising among the adolescents more so in the African region, at a time when HIV-related deaths are decreasing in other population groups (WHO, 2014). Adolescents have been reported to have a higher prevalence of non-suppression than adults (Bulage *et al*., 2017; Jobanputra *et al*., 2015; Salou *et al*., 2016). Non-suppressed viral load is the main cause of AIDS related deaths (Mutevedzi *et al*., 2011).

In 2017, it was estimated that 81% of all PLHIV on ART globally were virally suppressed (19% not suppressed) while in Kenya, 84% of PLHIV and on treatment were virally suppressed (16% not suppressed); the number of AIDS-related deaths globally was estimated at 940,000, with Eastern and Southern Africa region accounting for 380,000 (40%) and 28,000 in Kenya (AIDSinfo, 2017; UNAIDS, 2017). In 2017, an estimated 122,301 people were living with HIV PLHIV in Kisumu County, of which 9,211 (7.5%) were adolescents. AIDS-related deaths were estimated at 2,048 in the County, 157 (8 %) of these from adolescents (NACC, 2018).

1.3 Justification

Suppression of HIV replication and restoration of infected person's immunity are the main goals of antiretroviral therapy (ART) as it prevents AIDS-related morbidity and mortality, helps PLHIV stay healthier and reduces chances of HIV transmission to other people (Poerksen *et al*., 2009; UNAIDS, 2014). Challenges with adolescents/young adults remaining in care and achieving long-term viral suppression have been reported globally and types of interventions needed and implementation of relevant programs demand additional considerations in regards to populations most affected and the determinants (Hightow-Weidman *et al*., 2011; Sitapati *et al*., 2012; WHO, 2014; Zanoni & Mayer, 2014).

HIV prevalence in Kisumu County is estimated at 16.3%, which is 3.9 times higher than the national prevalence of 4.8%. Adolescents accounted for 884/4,012 (22%) of new HIV infections that were reported in the County in 2017 (NACC, 2018). In the same year, 13,851/ 99,321(14 %) routine VL tests done in the County yielded a result of ≥1000 copies/ml, with the proportion of VNS among adolescents at 30.1% (1,935/6,427) (NASCOP, 2017).

Among the five facilities in the County with highest number of VL samples submitted, Chulaimbo Sub-County hospital had the highest proportion for overall viral non-suppression (18.3%).

This study sought to estimate the prevalence of VNS and factors associated with HIV viral non-suppression among adolescents receiving HIV care services at Chulaimbo Sub-County Hospital, Kisumu Count.

1.4 Research Questions

1. What is the prevalence of viral non-suppression (VNS) among adolescents living with HIV (ALHIV) on ART at Chulaimbo Sub-County Hospital?
2. What are the factors associated with VNS among HIV positive adolescents on ART at Chulaimbo Sub-County Hospital?

1.5 Objectives

1.5.1 Broad objective

To estimate the prevalence and factors associated with VNS among adolescents living with HIV (ALHIV) enrolled on ART at Chulaimbo Sub-County Hospital, Kisumu County (CSCH).

1.5.2 Specific objectives

1. To estimate the prevalence of VNS among ALHIV who are on ART at CSCH
2. To identify factors associated with VNS among ALHIV who are on ART at CSCH

Conceptual Framework:

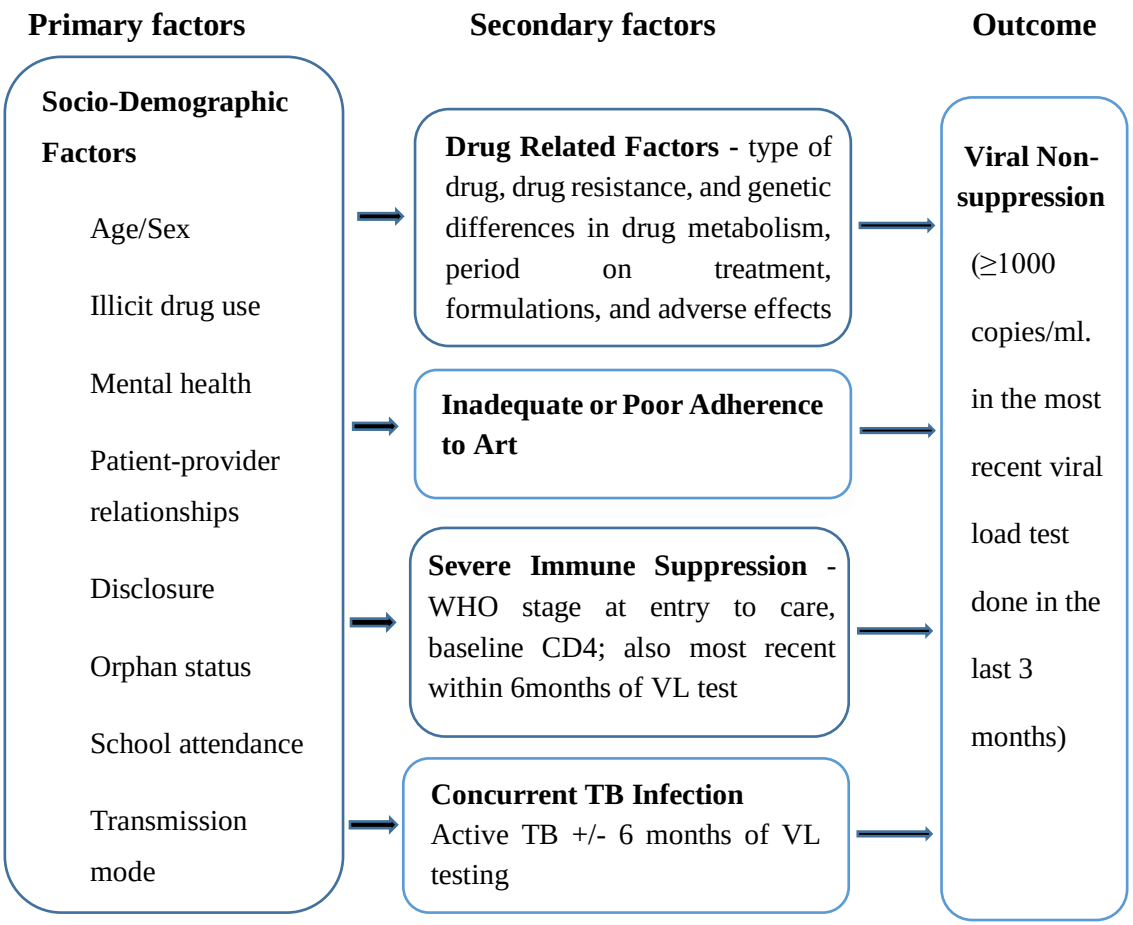

Figure 1.1: Conceptual framework of factors associated with virological non-suppression among adolescents

CHAPTER TWO

LITERATURE REVIEW

2.1 Introduction

Non-suppressed viral load has been reported as the leading cause of AIDS-related deaths while achieving viral suppression helps HIV positive people to have healthy, productive lives and reduces chances of HIV transmission to others (Mutevedzi *et al*., 2011). Globally, children and adolescents have been reported to have worse outcomes in terms of lower viral suppression rates, higher virological failure rates, and poor adherence compared to adults (Jean B Nachega *et al*., 2009; Jean B Nachega, Mills, & Schechter, 2010 Jean B. Nachega *et al*., 2012; Nglazi *et al*., 2012, Thompson et al., 2010) coupled with late entry and poor retention in HIV care (Cherutich *et al*., 2016).

HIV positive adolescents can be categorized into two; those who got the virus through mother to child transmission (MTCT) and those who acquired HIV during their teens mostly through sexual transmission. Adolescents who acquired HIV at infancy or peri-natally may clinically respond differently to treatment from adolescents infected later in life. This is because they may have had ART exposure since earlier in life with inadequate therapy regimens that often times result in incomplete viral suppression and development of viral resistance. After initiation of ART, appropriate support is highly recommended to ensure sustained optimal adherence that helps in achieving sustained viral suppression (AIDSinfo, 2011). Some adolescents are vulnerable to poor treatment outcomes and poor health which may be due to individual and environmental factors, marginalization, exploitation and lack of parental support as is common with orphan status (WHO, 2014).

2.2 HIV Global Burden and Treatment Access

HIV/ AIDS is a significant global health and development challenge that causes devastating effects on the health of infected individuals, impacts entire households, communities, as well as destabilizing the development and economic growth of affected nations (UNAIDS, 2016b, 2016c).

In 2015, about 36.7 million people who were living with HIV and about 2.1 million people were newly infected in the same year. This included 150,000 children, 56 000 from eastern and southern Africa (UNAIDS, 2016a). The steady scale up and improvement of services in the prevention of mother-to-child transmission (PMTCT) of HIV has reduced the annual number of new infections among children globally by 66% since 2010 (HIV/AIDS, 2016). The eastern southern Africa region PMTCT coverage in 2015 was 90% compared to 61% in 2010 (UNAIDS, 2016c).

By June 2016, 18.2 million PLHIV were enrolled on ART globally, up from 15.8 million in June 2015 (UNAIDS, 2016a). In East and Southern Africa,10.3 million PLHIV were accessing ART which accounted for 54% of PLHIV in the region (UNAIDS, 2016c).

2.3 HIV Burden in Kenya

Kenya, being one of the four HIV 'high burden' countries in Africa, has about 1.5 million PLHIV (UNAIDS, 2016b). There are an estimated 71,034 new HIV infections among adults and about 6,613 new infections among children aged < 2 years annually. The epidemic is geographically diverse, with 10 out of 47 Counties accounting for 65% prevalence (NASCOP - Kenya, 2016).

The high burden of HIV/AIDS burden in Kenya accounts for 29 % of annual adult deaths, 15 % of deaths among children under the age of five and 20% of maternal mortality. There were 28,000 AIDS-related deaths in 2017 and 53,000 new HIV infections in the same year (MOH, 2016).

Kenya has the second largest HIV treatment program in Africa after South Africa, with over 900,000 PLHIV enrolled on treatment by 2015. This includes 826,000 adults and 71,500 children (UNAIDS, 2016b). As recommended by WHO, Kenya has adopted routine viral load (VL) testing at six months and 12 months after initiation of treatment and every 12 months thereafter to monitor ART response (Doherty, 2015). The threshold for viral suppression is 1000 copies/ml. If after being on ART for six months the VL load result is <1000 copies/ml the patient viral load is considered suppressed and a second VL is done at 12 months, then annually going forward if the suppression is maintained.

Patients on the first line treatment with non-suppressed VL are supposed to receive intensive adherence counseling/assessment and a repeat VL done in three months. If not suppressed at repeat testing, treatment failure is then considered and patient switched to second-line ART as indicated on national VL testing algorithm (NASCOP-Kenya, 2016) (Appendix 5).

The HIV treatment cascade (Figure 2.1) illustrates the various steps in the HIV treatment continuum and how each of these steps leads to the ultimate goal of treatment, achievement of viral suppression and retention.

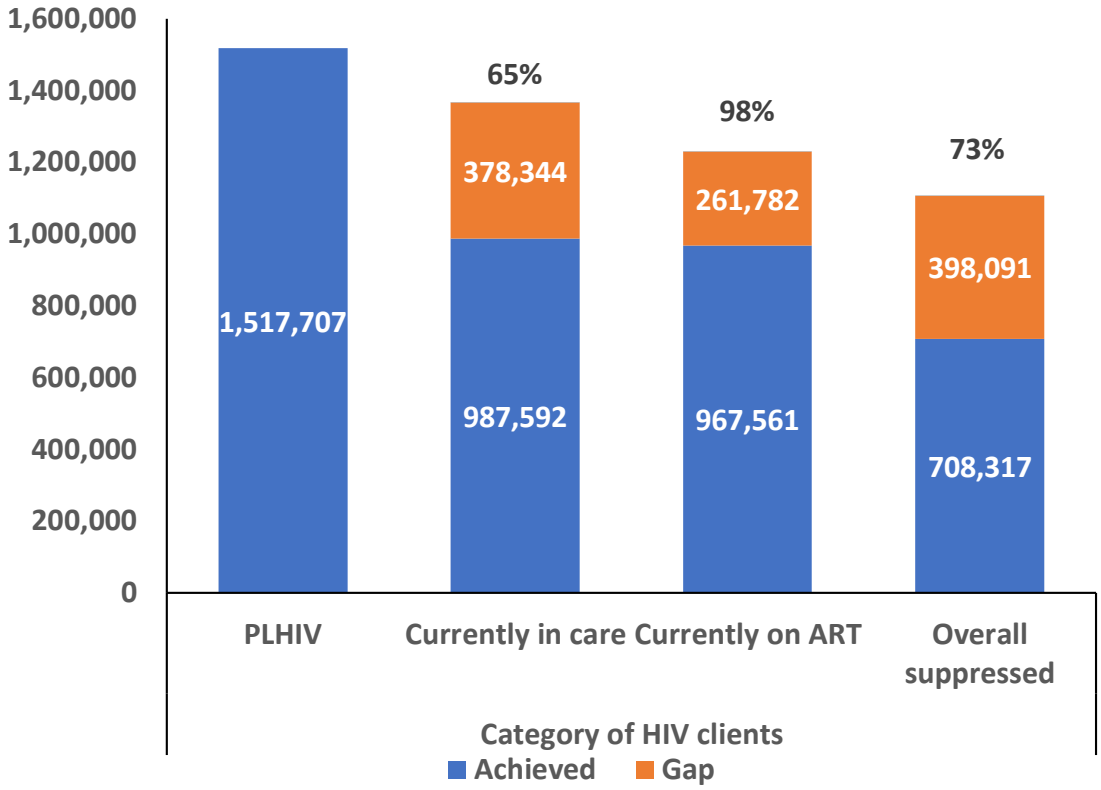

Figure 2.1: HIV treatment cascade for People Living with HIV (PLHIV) in Kenya, December 2016

2.4 Review of Past Studies on Predictors of HIV Viral Non-suppression

2.4.1 Poor adherence to treatment

For an HIV infected person to achieve and maintain an undetectable viral load, adherence to ART must be nearly perfect, between 90-95%, making it one of the most complicated and demanding medicine regimes prescribed (Hickson & Warren, 2016).

Full benefits of ART, both at individual and population level will largely depend on strict adherence to the prescribed medication, the medical advice and follow-up plans. To avoid treatment failure and the need to switch patients to 2nd or 3rd line ART, it is necessary to have an adherence support strategy in place before ART initiation, anticipating common and individual barriers to good adherence (NASCOP-Kenya, 2016). Factors that influence adherence behavior are many, of which may be categorized as characteristics of the adolescent, the caregiver and/or family, the

treatment regimen, and societal or cultural practices and beliefs (Buchanan *et al*., 2012; Haberer & Mellins, 2009 Olds *et al*., 2015). With the expansion of treatment programs in resource-limited settings, optimal adherence to ART is proving to be exceedingly important and challenging to achieve as well (Haberer & Mellins, 2009).

According to studies done in South Africa, adolescents were less adherent to ART, had lower rates of viral suppression and immunologic recovery, and higher rates of virologic rebound after initial suppression in comparison to adults (Evans *et al*., 2013; Jean B Nachega *et al*., 2009). There is an urgent need to determine specific barriers to adherence for children and adolescents and to develop appropriate interventions (Bain-Brickley et al., 2011).

Some of the reported barriers to adherence among adolescents are; level of disclosure, inability to understand the disease or treatment, patient's developmental stage and emotional state, refusal to swallow the medicine, stigmatization, discrimination, low self-esteem and depression (WHO, 2014; Yang *et al*., 2018). Other factors include defiance related to a troublesome caregiver-child relationship, inadequate structures at school to support adherence, and lack of support systems for the adolescent (Bikaako-Kajura *et al*., 2006; Sm & Medicine, 2015).

Caregiver barriers to adherence include frequently changing or multiple simultaneous caregivers, elderly, or illiterate caregiver, depression, alcohol and other drug use and living far from the health facility. An absent or sick caregiver, having a poor understanding of HIV management due to inadequate counselling, being economically unstable, lack of affection between caregiver and child and lack of support systems for the caregiver may also be possible barriers (Bernays *et al*., 2014).

2.4.2 Late entry into care

Timely entry of HIV-infected adolescents into HIV medical care and retention is essential for prevention of HIV-related morbidity and mortality through timely ART initiation, monitoring and management of disease progression and treatment failure, and provision of medications and any other necessary form of supportive care (NASCOP-Kenya, 2016)

The WHO 'test and treat' guidelines launched in 2015 recommend ART initiation for all PLHIV, regardless of WHO clinical stage, CD4 count, age, pregnancy status, or comorbidities/co-infections. Once a diagnosis of HIV infection is confirmed, ART should be initiated preferably within a period less than two weeks, after patient readiness has been determined (WHO, 2016). However, it is necessary to ensure a patient is retained in care for the lifelong treatment.

The retention measures used and desired visit frequency, vary in different jurisdictions (Thompson *et al*., 2010). According to recent studies, late entry and poor retention in care negatively influence the virological outcomes most especially for younger people and those of a lower socio-economic status (Bulage *et al*., 2017; Feller *et al*., 2013; Yehia *et al*., 2015).

The true proportion of children who acquire HIV have a 50% chance to die before the age of two years if no treatment is given but with early entry in care and treatment and by observing clinic appointments this has been averted or reduced (Newell *et al*., 2004). In a Cohort study for children on ART across several African countries, only 18% died and half the children who were started on ART during infancy were still retained in care at 24 months (McNairy *et al*., 2013).

2.4.3 Concurrent tuberculosis infection

People living with HIV who are co-infected with tuberculosis (TB) have lower treatment success rates and significantly lower cure rates compared to TB patients who are not HIV positive. HIV co-infected TB (HIV/TB) patients have been shown to have significantly increased the likelihood of dying from TB disease and have multiple disease-specific and treatment-related factors that greatly affect their treatment outcomes (Daniel & Alausa, 2006; Luetkemeyer *et al.*, 2010). In a study done in Uganda 2014/15, having active TB was found to increase the odds of viral non-suppression (Bulage *et al*., 2017).

In Kenya, screening for TB is routinely done using the Intensive case finding tool (ICF) and PLHIV who are 12 months or older and negative for TB are put on Isoniazid preventive therapy (IPT) (NTLP-K, 2013). All PLHIV receive lifelong Cotrimoxazole Preventive therapy (CPT) unless they have an allergy to sulfa drugs or develop toxicity from CPT, which helps in preventing specific opportunistic infections (OIs) and reducing the risk for common bacterial infections, sepsis, diarrheal illness and malaria (NASCOP-Kenya, 2016; NTLP-K, 2013).

2.4.4 Drug-Related factors

Different patients will respond differently to the various types of regimen used. Some study findings have indicated disparities in virological outcomes based on the drug type a patient has been on. For instance, the relative risk of virologic failure for patients taking boosted protease inhibitors (PIs) in a cohort study was found to be approximately five times more than those on non- nucleoside reverse transcriptase inhibitor (NNRTI)(Martin *et al*., 2008). A study conducted in Uganda found second/third line ART regimens to be protective against non-suppression compared to first line.

However, drug-related factors are largely tied to poor adherence to ART (Bulage *et al*., 2017).

Effective ART consists of a minimum of three agents from at least two different classes of ARVs. The first few months of treatment may be the hardest to maintain optimal adherence, given that the patient is not yet used to taking their medications daily and they are not familiar with common side effects (NASCOP-Kenya, 2016). The main reason for sub-optimal adherence to ART has been reported as forgetfulness, followed by social barriers and ART-related factors, followed by social barriers and ART-related factors (Buchanan *et al*., 2012). Drug toxicity, complexity of the treatment and drug formulations, number, and type of medication prescribed have been shown, with some exceptions, to be negatively associated with adherence (Byabene *et al*., 2017; Cambiano *et al*., 2010).

With the availability of better-tolerated, simplified regimens, such as generic fixed-dose single-tablet regimens that are currently in wide clinical use for adults, access to ART has improved (Bulage *et al*., 2017).

HIV drug resistance has been associated with VNS even in Kenya. A cross-sectional study that was conducted to determine treatment failure and drug resistance mutations among adults receiving first-line and second-line treatment in Nairobi, Kenya, found 41% of adult patients failing first-line had drug resistance mutations and 30% among patients failing second-line, six patients had NNRTI resistance (Koigi *et al*.,2014).

CHAPTER THREE

METHODOLOGY

3.1 Study Area

The study was conducted in Kenya, a country that is situated in East Africa and its capital city is Nairobi. The Indian Ocean and Somalia borders Kenya in the East, Ethiopia and Sudan in the North, Uganda in the east and Tanzania in the South. The country covers an area of 582,646 square kilometers and has an estimated population of 44 million people which includes 10 million adolescents (KNBS, 2012). The HIV prevalence in Kenya is 4.8%. There are 47 Counties in Kenya among them Kisumu, which is one of the three HIV hyper-endemic Counties in the Country, with HIV prevalence of 16.3% (NACC, 2018). Homa Bay County borders Kisumu County to the South, Nandi County to the North East, Kericho County to the East, Vihiga County to the North West and Siaya County to the West. It covers a total land area of 2,009.5 km^2 and 567 km^2 is covered by water (Kisumu CIDP, 2013).

3.2 Study Site

The study site was Chulaimbo Sub-County Hospital (CSCH) formerly Chulaimbo Sub-District hospital. It is a level IV health facility located in Kisumu west sub-county, Kisumu County (Figure 3.1). The facility serves a catchment population of about 24,394 and offers both outpatient and inpatient services that include HIV medical care. There is a youth-friendly clinic in the outpatient department that offers ART services to adolescents and young adults living with HIV among other services. By the end of July 2017, there were 398 adolescents enrolled on ART in the facility.

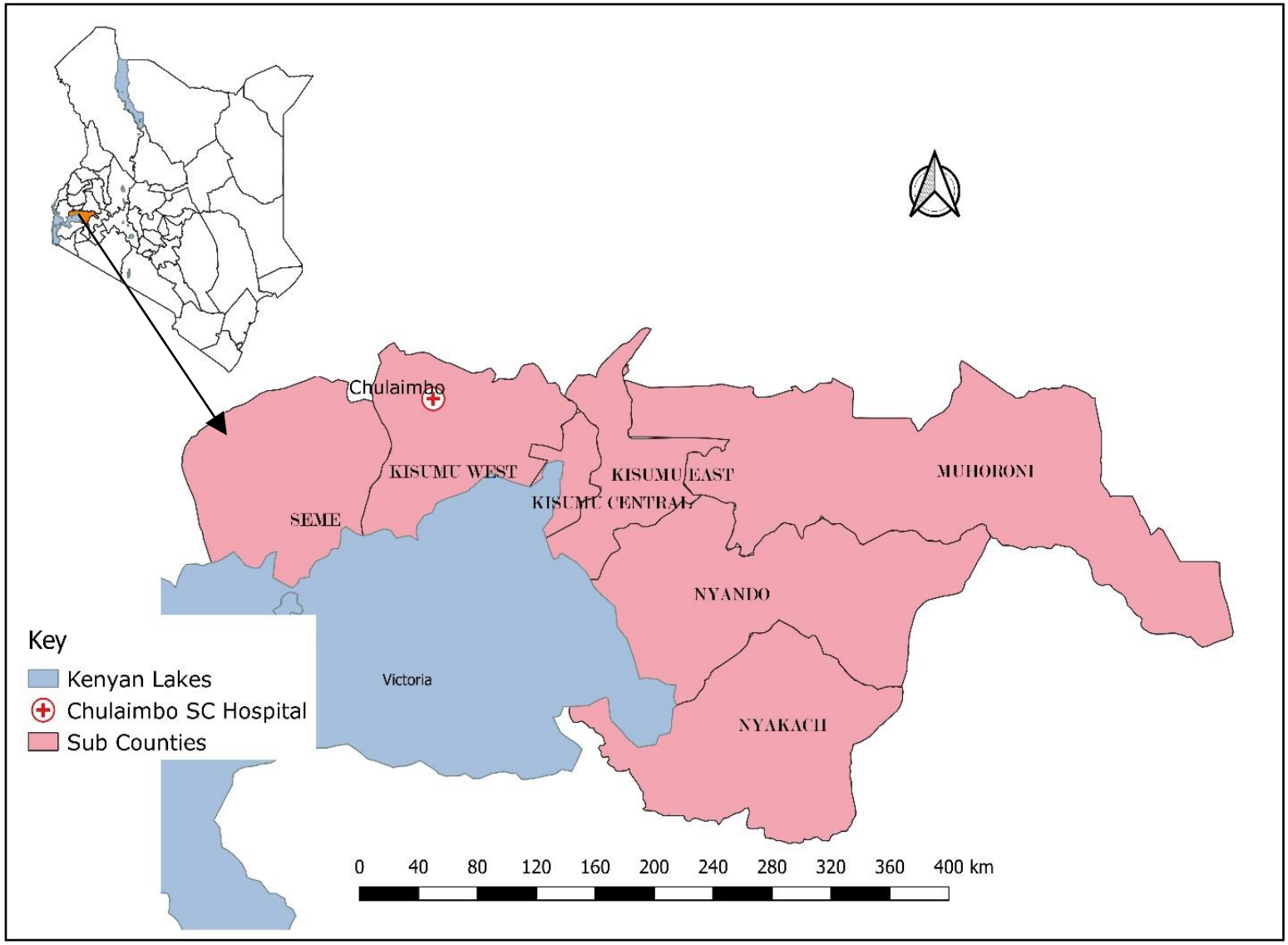

Figure 3.1: Location of Chulaimbo Sub-County Hospital, Kisumu County, Kenya

3.3 Study Design

This was a hospital-based cross-sectional study involving questionnaire administration and abstraction of medical data.

3.4 Study Period

The study was conducted from July 2018 through September 2018.

3.5 Study Population

The study population was adolescents (10 to 19 years old) living with HIV who had been on ART at Chulaimbo Sub-County Hospital for a period not less than six months. We randomly selected a study sample from this population.

3.5.1 Inclusion criteria

A study participant had to be an adolescent living with HIV (ALHIV) who had been on ART for a period > 6 months, had a routine viral load test done within the last six months with valid laboratory results, with no cognitive impairment or too sickly by clinician's judgment and had attended ART clinic at Chulaimbo hospital in the last six months (to ensure availability of necessary records).

3.5.2 Exclusion criteria

Any ALHIV on ART at CSCH with no viral load test done in the last six months and adolescents who had transferred out or died.

3.6 Sample Size Determination

Sample size determination for analysis of VL non-suppression is dependent on the number of events per variable (EPV) which is the number of virally non-suppressed adolescents per risk factor. According to Peduzzi *et al*. , roughly, 10 EPVs are required for binary logistic regression analysis (Peduzzi *et al*., 1996).

The required sample size was given by the formula below;

$$n = \frac{10 \times EPVs}{p}$$

where p was the desired prevalence of viral non-suppression. Since p was unknown, 50% was used to calculate sample size envisioning a maximum of eight risk factors (EPVs).

The minimum sample size required was $n = (10 \times 8)/0.5 = 160$. After accounting for a 10% non-response rate, the desired sample size obtained was 176 adolescents.

3.7 Sampling Procedure

The principal investigator (PI) selected study participants from the VL tracking log at the hospital's laboratory. The log had a record of patients referred for VL test and indicated the clinic number, age, date sample was collected and results. Study participants were determined through simple random probability sampling. The PI identified all ALHIV on ART who were eligible to prepare the sampling frame. Random selection of numbers was done using MS Excel table of random numbers to identify the sampling units.

The research assistant nurse retrieved telephone numbers for selected adolescents and called each of them to remind them about the next appointment a day before their scheduled visit to minimize missed appointments.

3.7.1 Replacement of Selected Study Participants

The clinician assessed the adolescents' fitness to participate and a replacement was done if they appeared too sickly or suffered serious cognitive impairment by clinical judgement.

In the event a selected adolescent declined participation or failure to honor the appointment, two missed scheduled appointments, the above constituted non-compliance and therefore necessitated replacement. This was done by conducting simple random sampling of the remaining eligible adolescents on the sampling frame.

3.8 Data Collection

The study involved research assistants (RAs) who included a clinician (clinical officer with BSc in public health), nurse (Diploma, Kenya registered nurse) and a data clerk (Diploma in health records). These were staff who routinely serve the clients visiting the youth clinic and were adequately trained on good research practice and ethics and trained on data collection tools and procedures by the principal investigator. This was to ensure consistency and minimize errors and biases. Data collection involved interviews using a structured questionnaire and abstraction from medical records which included VL register, TB register and patient files. The study team pre-tested questionnaire in the same facility to identify any gaps and amended the tool before rolling out the study. It also helped to estimate the average time spent to administer the questionnaire to each participant. The participants in the questionnaire pre-test were not included in the final study.

On arrival at the reception, the data clerk who was a research assistant issued study participants a card bearing their unique study identification (ID) numbers and asked them to give it to the clinician in the consultation room.

The clinician stuck a pre-designed code on the study ID card to indicate if the participant is well enough to participate in the study. The clinician referred back the participant with the coded ID card to the data clerk at the reception, who then coordinated the flow of participants to the private interview room where the consenting

and administration of a structured questionnaire took place by the principal investigator/nurse.

In case of more than one participant waiting at any given time, the data clerk directed them to a waiting bay, and if they were not able to wait, they were requested to come the following day or any day of the week convenient for them. Failure to come on the second appointment the selected participant was replaced (Figure 3.2).

After sharing the study details with study participants, voluntary consenting was done followed by administration of the questionnaire by the principal investigator/nurse who was blinded to the virological status of the patient. The interviewer obtained disclosure status from the caregiver for minors. Data collected included socio-demographics, physical pill counts, drug-related factors, health-care related factors and clinical data abstraction from the medical records.

All data collection tools for a specific study participant bore their unique identifier and were attached together. The data clerk at the reception kept a record of all study participants on a daily basis with their respective clinic identification numbers.

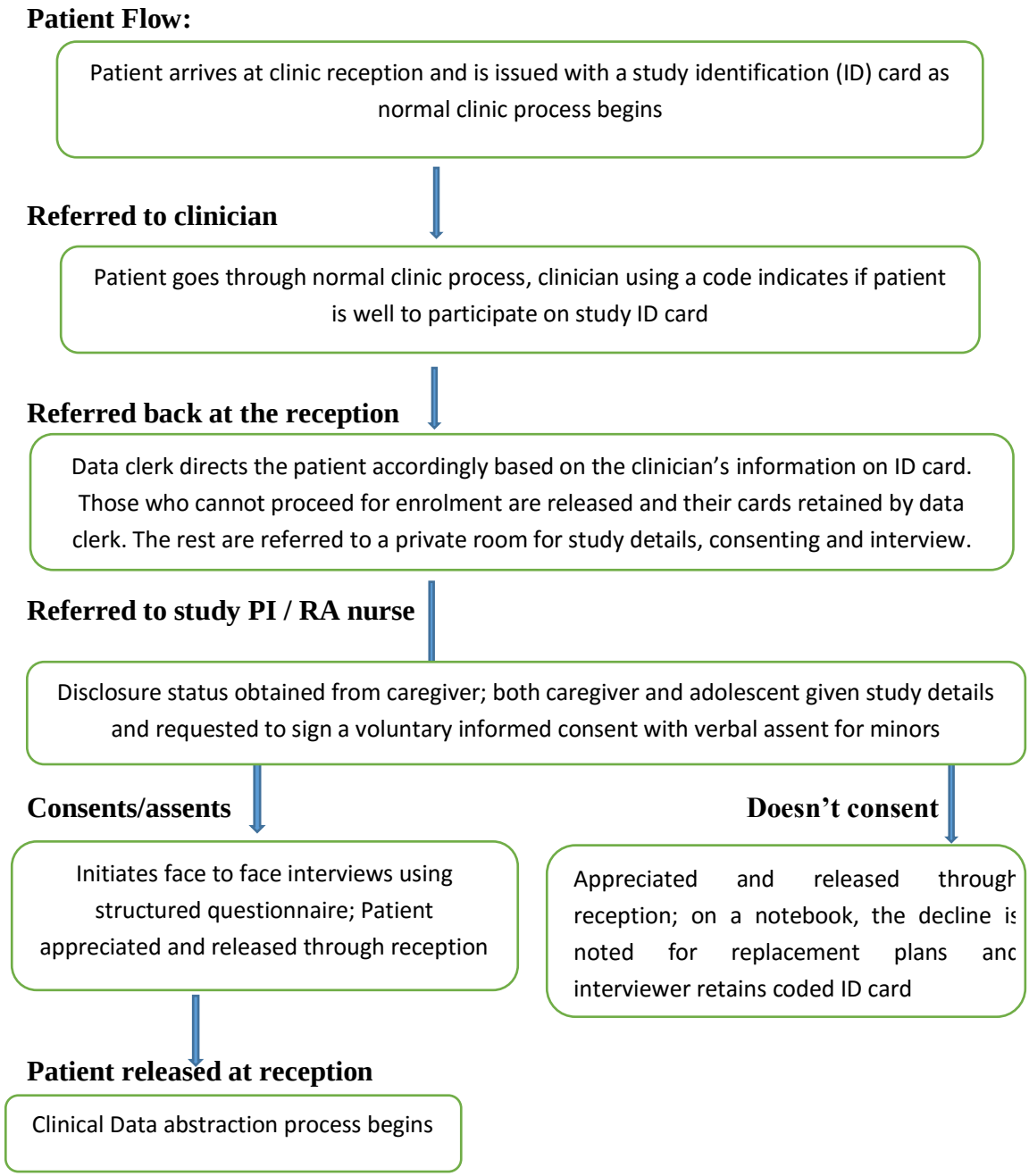

Figure 3.2: Data collection flow chart

3.8.1 Measures of study variables

3.8.1.1 Viral suppression

Determined by the most recent VL test done ≤6 months before starting the study as indicated in the VL log. Those with VL results < 1000 copies/ml were considered to be

virally suppressed whereas those with VL results ≥1000 copies/ml were considered virally non-suppressed.

3.8.1.2 Drug (ARVs) related factors

Data collected using a structured questionnaire; included the current line of treatment($1^{st}/2^{nd}$), drug combinations, dose frequency, date of treatment line switch (where applicable), time on treatment in years categorised as: ≤ 2 years and 2-5 years,6-10 years and 10+ years. Clinical data were abstracted from medical records.

3.8.1.3 Adherence

We measured adherence to treatment by pill counts. The nurse asked the patients to bring all their remaining pills to the clinic during their visit. The number of pills that should be remaining were calculated based on the previous prescription date and amount prescribed, and compared to how many pills are actually remaining. We assumed excess pills to be missed doses and the following table used to calculate adherence.

Table 3.1: Adherence Rating based on Pill Counts

Missed doses per month		**% of medications taken**	**Adherence rating**
For once-daily regimen	For BD regimen		
1 dose	1-3 doses	≥ 95%	Good
2- 4 doses	4-8 doses	85-94%	Inadequate
≥ 5 doses	≥ 9 doses	< 85%	Poor

3.8.1.4 Immuno suppression

We abstracted baseline CD4 count and WHO clinical stage. If baseline CD4 count and WHO stage at ART initiation date were not available, the ones taken closest to ART initiation date were used (within +/- 6 months). If none is recorded within that period it was considered as missing. The most recent WHO clinical stage taken +/- 6 months of

the last VL test was abstracted to monitor response to treatment. There was uniformity in the source of Laboratory data in regards to the laboratory that did the test to ensure validity. CD4 count was categorized into ≤350 cells/mm^3 and >350cells/mm^3.

3.8.1.5 TB/HIV Co-infection status

Reported active TB in the last six months from client's medical records

3.8.1.6 Social-demographics

The data was obtained through interview. A structured questionnaire was administered to the study participants (and/or caregiver for minors who had not undergone disclosure).

3.8.2 Variables

i) Clinical and Laboratory data

a) Baseline CD4 count

b) Most recent routine VL results

c) Baseline and most recent WHO clinical stage: The World Health Organization (WHO) has developed case definitions for HIV surveillance and the system uses standardized clinical parameters that categorizes HIV patients into one of four hierarchical clinical stages ranging from stage 1 (asymptomatic) to stage 4 (AIDS). A Patient is assigned to a particular stage when they demonstrate at least one clinical condition in that stage's criteria (WHO, 2005).

ii) Social-demographics

Data included age, sex, educational background, type of school being attended if any (boarding/ day), proximity to the health facility, relationship to caregiver, availability of parents, household income.

iii) Drug-related factors

Daily dosage per day, line of anti-retroviral regimen in use

iv) Adherence- measured by Pill counts

v) Health care factors- These included relationship with health care worker (HCW), convenience of appointment days and times, availability of all necessary services e.g. counselling and consultations

3.9 Data Management

The collected data in hard copies per day was kept secure in a lockable cabinet in a room with limited access. It was entered on MS Excel for cleaning prior to analysis.

3.10 Data Analysis

Anonymized data was analyzed using Epi info version 7 (CDC, Atlanta, GA, USA) and STATA version 12 (Stata Corp., College Station, Texas, USA) software, in a password secured laptop. Descriptive analysis (univariate) included measures of central tendency and dispersion for continuous variables, e.g. age, and frequencies and proportions for categorical variables including period on treatment, sex, line of treatment etc.

In bivariate analysis, factors associated with VNS were assessed using crude Odds Ratio (cOR) and those with a p-value of 0.2 were included in the multivariate model.

Independent factors associated with VNS were identified using logistic regression to obtain the adjusted OR at 95% confidence interval at a P-value of $\alpha=0.05$. Stratified logistic regression was conducted for age and sex to control for confounding and check for effect modification.

The obtained results were presented in tables.

3.11 Ethical Requirements

Ethical approval was obtained from the Institutional Research and Ethics Committee, Moi University, Eldoret, Kenya (Appendix 6).

Clearance was sought from the County Department of health, Chulaimbo hospital administration (Appendix 8) as well as the partner supporting the facility, Academic Model Providing Access to Healthcare -AMPATH (Appendix 7).

3.11.1 Informed consent

The nurse/principal investigator received the study participants warmly and slowly explained to them study information. Caregivers were required to accompany un-emancipated minors.

The study team shared with them detailed study information including, purpose and justification of study, the role of the participant and their level of involvement in the study, potential benefits and risks associated with participation in the study. Use of unique identifiers for confidentiality, the approval procedures by the ethical committee and measures in place to minimize risks was discussed.

Participation was voluntary, and participants were free to withdraw from the study at any stage, without being reprimanded. For adolescents ≥ 18 years of age, the consent was given by the participant. The un-emancipated minors were requested to provide verbal assent while their respective caregivers gave voluntary written consent. In the case of emancipated minors, the adolescent gave the informed voluntary consent (Appendix 1a/1b).

The participants were given principal investigator's contacts in case of any concerns or inquiries.

3.12 Management of Adverse or Unexpected Events

In this study, there were no foreseeable adverse effects given that there were no interventions, but there was potential for breach of confidentiality for which the principal investigator would take responsibility. However, we minimized this by use of study assistants who were selected from practicing health care workers serving at the youth-friendly clinic, who were trained on data collection and understood the value of confidentiality and research ethics.

3.13 Dissemination, Notification, and Reporting of Results

Results from this study were summarized in a report that will be disseminated to Chulaimbo Sub-County hospital, through County AIDS and STI coordinator (CASCO) Kisumu County, NASCOP, and abstract submitted to a scientific conference. The manuscript will be published in peer review journals.

3.14 Expected Benefits

With the dissemination of results, the County health team will be able to strategize on how to support the study population and to reinforce measures put in place to help attain the 3rd 90 (90% viral suppression rate) hence improving treatment outcomes for adolescents. Improved treatment outcomes and wellness translate to reduced mortality and reduction in further transmission of HIV. The findings obtained from this study will guide the County ART program and hospital management in planning and prioritization of HIV response activities.

CHAPTER FOUR

RESULTS

This chapter presents the results of the study as obtained from the analysis of collected data with the aim of achieving the two objectives of the study. A description of the sociodemographic and clinical characteristics of the study sample serves as the introduction to the main results followed by results for the proportion of non-suppression in various sub-categories of the study sample. The associations between VNS and clinical as well as socio-demographic characteristic are presented. Lastly, the chapter closes with the identification of factors associated with VNS in bivariate and multivariate analysis.

4.1 Socio-demographic Characteristics

We enrolled 200 adolescents on ART at the youth clinic, Chulaimbo sub-County hospital Kisumu, from June through August 2018. We interviewed 161 (80.5%) who had completed the disclosure process and for the 39 (19.5%) who had not completed disclosure, we got part of the information from the caregiver. The median age was 14 years (range 10-19) and 103 (51.5%) of the study participants were female. The median distance to the health facility from home was 19Km (range 1.9-169) with 124 (62%) patients living within a distance of less than 20 km from the hospital. The monthly median household income was $80 (range $20 -$350). Those currently in school were 195 (97.5%) of which 25 (13%) were in boarding schools. The highest level of education attained at the time of the study was primary education for 134 (67%) of the participants and secondary education for 62 (31%) adolescents (Table 4.1).

Table 4.1: Socio-demographic characteristics of HIV Positive Adolescents on Anti-retroviral Treatment at Chulaimbo hospital, Kisumu County, 2018

Variable	Characteristic	Frequency	%
Age	Median 14 years (10-19)		
	10-14years	102	51
	15-19years	98	49
Sex	Female	103	51.5
	Male	97	48.5
Education level	Primary	134	67
	Secondary	62	31
	Tertiary	3	1.5
	Never gone to school	1	0.5
In school/college	Yes	195	97.5
	No	5	2.5
Type of school	Boarding school	25	13
	Day school	170	87
Availability of parents	Both parents alive	78	39
	Orphan	50	25
	Mother alive	49	24.5
	Father alive	23	11.5
Main caregiver	Mother	100	50
	Father	45	22.5
	Grand parent	28	14
	Other relative	27	13.5

4.2 Clinical Characteristics

The study participants were enrolled in HIV care at a median age of 5 years (range 1-18) with a baseline median CD4 count of 754 cells/mm^3 (range 30-2728), 135 (79%) having >350cells/mm^3. The baseline WHO clinical stage for the study population was as follows; 60 (30%) in stage I, 70 (35%) in stage II, 55 (27.5%) in stage III and five (2.5%) in stage IV and data was missing for 10 participants. The most recent WHO clinical stage was stage I for 53 (26.5%) adolescents, stage II for 61 (30.5%), stage III for 54 (27%), four adolescents (2%) in stage IV and it was not recorded for 28 adolescents.

One adolescent was reported as having active TB. Seventy-one (35.5%) adolescents had most recent viral load result as ≥1000 RNA copies/ml (Table 4.2).

4.2.1 Treatment history

The adolescents in this study had a median duration on ART of 7.6 years (range 0.8-12.4); 142 (71 %) were on first line ART regimen and 58 (29%) on second line. One hundred and ten (55%) had ≥ 95% adherence to ART (Table 4.2). The median number of daily pills was 4 (1-10) which included both anti-retroviral drugs and any other drugs the participants were on e.g. Cotrimoxazole, TB medication, Isoniazid preventive therapy.

Table 4.2: Clinical Characteristics of HIV Positive Adolescents on Anti-retroviral Treatment at Chulaimbo hospital, Kisumu County, 2018

Variable	Characteristic	Frequency	%
Most recent Viral load:			
	<1000 RNA copies/ml	129	64.5
	≥1000 RNA copies/ml	71	35.5
Disclosure:			
	Complete	161	80.5
	Incomplete	39	19.5
Baseline WHO stage*	I and II	130	68
	III and IV	60	32
Baseline CD4 count*	>350/ mm3	135	79
	≤350/ mm3	35	21
Most recent WHO stage*	I and II	114	66
	III and IV	58	34
Line of treatment:			
	1st line	142	71
	2nd line	58	29
Adherence:			
	Good (≥ 95%)	110	55
	Inadequate (85-94%)	31	15.5
	Poor (<85%)	59	29.5
Duration on treatment:			
	10+ years	51	25.5
	6-10 years	85	42.5
	2-5 years	60	30
	< 2 years	4	2
Daily dosage of pills:			
	Once per day	51	25.5
	Twice per day	149	74.5

*** Incomplete records (<200 records)**

4.2.2 Proportion of Adolescents on ART with Viral Non-Suppression

Adolescents on ART for less than two years had the highest proportion of VNS, at 3/4 (75%) while those on ART for 10+ years were 12/51 (24%). Viral non-suppression among those with ≥ 95% adherence to treatment were 19/110 (17%) and 38/59(64%) for adolescents with <85% adherence (Table 4.3).

Table 4.3: Proportion of Viral Non-suppression among HIV Positive Adolescents on Anti-retroviral Treatment at Chulaimbo Sub-County hospital, Kisumu County, 2018 (N-200)

Variable	Characteristic	VNS freq*	%	VS fre**	%
Sex:	Female	42	**41**	61	59
	Male	29	30	68	70
Age:	10-14yrs	34	33	68	67
	15-19yrs	37	**38**	61	62
Highest education level:	Primary	46	34	88	66
	Secondary	23	37	39	63
	Tertiary	2	67	1	33
	No schooling	0	0	1	100
Currently in school	Yes	69	35	126	65
	No	2	40	3	60
Type of school	Boarding school	9	36	16	64
	Day school	60	35	110	65
Main care giver:	Father	14	31	31	69
	Mother	38	38	62	62
	Grandparent	11	39	17	61
	Other relatives	8	30	19	70
Disclosure:	Complete	59	37	102	63
	Incomplete	12	31	27	69
Baseline WHO stage***	I and II	46	35	84	65
	III and IV	21	35	39	65
Baseline CD4 count***	>350/ mm3	42	31	93	69
	≤350/ mm3	18	51	17	49
Recent WHO stage***	I and II	40	35	74	65
	III and IV	21	36	37	64
Active TB	Yes	0	0	1	100
	No	71	36	128	64
Line of treatment:	1st line	38	27	104	73
	2nd line	33	**57**	25	43
Adherence:	Good (≥ 95%)	19	17	91	83
	Inadequate (85-94%)	14	**45**	17	55
	Poor (<85%)	38	**64**	21	36
Duration on treatment:	10+ years	12	24	39	76
	6-10 years	35	41	50	59
	2-5 years	21	35	39	65
	< 2 years	3	**75**	1	25
Daily dosage of pills	Once per day	19	37	32	63
	Twice per day	52	35	97	65

***viral non-suppression frequency: ** viral suppression frequency, ***Incomplete records**

4.3 Factors Associated with VNS

At bivariate analysis, poor and inadequate adherence, baseline CD4 count, line of regimen and duration on treatment had significant association with VNS (Table 4. 4).

Table 4.4: Factors associated with Viral Non-suppression among HIV positive Adolescents on Anti-retroviral Treatment in Chulaimbo hospital, Kisumu County, 2018 (N=200)

Variable	Category	VNS	VS	cOR	95% CI	P-value
Sex	Female	42	61	1.61	0.90-2.90	0.109
	Male	29	68	1		
Age	15-19yrs	37	61	1.21	0.68-2.17	0.584
	10-14yrs	34	68	1		
Highest education level	Primary	46	88	0.26	0.02-2.96	0.278
	secondary	23	39	0.29	0.00-6.07	0.33
	Tertiary	2	1	1		
Type of school	Boarding	9	16	1.031	0.43-2.47	0.945
	Day school	60	110	1		
Main care giver	Father	14	31	1.07	0.38-3.03	0.895
	Mother	38	62	1.45	0.58-4.72	0.453
	Grandparent	11	17	1.54	0.50-5.76	0.424
	Other relatives	8	19	1		
Disclosure	Incomplete	12	27	0.77	0.36-1.63	0.492
	Complete	59	102	1		
Baseline WHO stage	I and II	46	35	1.02	0.54-1.93	0.959
	III and IV	21	35	1		
Baseline CD4 count	≤350/ mm3	18	17	2.34	**1.10-4.99**	**0.025**
	>350/ mm3	42	93	1		
Recent WHO stage	I and II	40	74	0.95	0.49-1.84	0.885
	III and IV	21	37	1		
Line of treatment	1st line	38	104	0.28	**0.15-0.52**	**0.000**
	2nd line	33	25	1		
Adherence	Poor	38	21	8.67	**4.19-17.93**	**0.000**
	Inadequate	14	17	3.94	**1.66-9.35**	**0.002**
	Good	19	91	1		
Duration on treatment	< 2 years	3	1	9.75	0.93-102.63	0.058
	2-5 years	21	39	1.75	0.76-4.04	0.19
	6-10 years	35	50	2.27	**1.04-4.95**	**0.038**
	10+ years	12	39	1		
Daily dosage of pills	Once per day	19	31	0.9	0.47-1.75	0.762
	Twice per day	52	97	1		

We subjected all variables with a P-value of <0.2 at bivariate level to logistic regression. These were; baseline CD4 count, line of regimen, adherence, duration on treatment, sex, main caregiver and daily dosage of pills (Table 4.5).

Table 4.5: Independent Factors associated with VNS among HIV positive adolescents on anti-retroviral treatment in Chulaimbo Hospital, Kisumu County, 2018

Variable	Category	VNS	VS	AOR	95% CI	P-value
Sex	Female	42	61	1.57	0.65-3.83	0.318
	Male	29	68	1		
Main care giver	Father	14	31	0.83	0.21-3.24	0.789
	Mother	38	62	1.27	0.38-4.22	0.695
	Grandparent	11	17	1.5	0.32-6.90	0.603
	Other relatives	8	19	1		
Baseline CD4	≤350/ mm3	18	17	1.85	0.65-5.32	0.251
	>350/ mm3	42	93	1		
Line of treatment	1st line	38	104	0.02	**0.00-0.14**	**0.000**
	2nd line	33	25	1		
Adherence	Poor	38	21	7.88	**2.99-20.76**	**0.000**
	Inadequate	14	17	6.44	**1.97-21.02**	**0.002**
	Good	19	91	1		
Duration on ART	< 2 years	3	1	1		
	2-5 years	21	39	0.81	0.21-3.23	0.766
	6-10 years	35	50	2.12	0.80-5.68	0.132
	10+ years	12	39	1		
Daily dosage	Once per day	19	31	1.14	0.44-2.96	0.789
	Twice per day	52	97	1		

Age stratified logistic regression indicated that age was an effect modifier. In bivariate analysis the crude OR indicated higher odds for VNS among adolescents on first line of treatment regimen (OR= 0.28, 95% CI 0.15-0.52), but in stratified analysis a strong association was found with adolescents aged 15-19 years old on first line regimen (AOR=0.02, 95% CI 0.00-0.20) and no association was found with adolescents aged 10-14 years on first line regimen (Table 4.6).

Table 4.6: Age stratified Logistic Regression for Independent Factors associated with Viral Non-suppression among HIV Adolescents at Chulaimbo Hosital, Kisumu County, 2018

Independent factors		VNS	VS	15-19 years			10-14 years		
				AOR	95% CI		AOR	95% CI	
Adherence									
	Inadequate (85%-94%)	**14**	**17**	**5.51**	**1.34**	**22.59**	**2.99**	**0.67**	**13.22**
	Poor (<85%)	**38**	**21**	**9.14**	**2.69**	**31.07**	**5.99**	**1.7**	**21.07**
	Good (≥ 95%)	**19**	**91**	**1**					
Duration On ART*									
	<2 years	**3**	**1**	**1**					
	2-5 years	**21**	**39**	**1.09**	**0.29**	**4.1**	**1.41**	**0.13**	**15.21**
	6-10 years	**35**	**50**	**2.05**	**0.58**	**7.23**	**3.71**	**0.4**	**34.03**
	10+ years	**12**	**39**	**1**			**1**		
Regimen line									
	First line	**38**	**104**	**0.31**	**0.03**	**0.29**	**1**		
	second line	**33**	**25**	**1**			**1**		

***Antiretroviral treatment**

In sex stratified logistic regression, sex was found to be both a confounder and effect modifier. (Table 4.7). The pooled odds of having VNS for adolescents with poor adherence was cOR=8.67, 95% CI 4.19- 17.93) while in sex stratified analysis, males with poor adherence to ART had higher odds of VNS (AOR =22.33, 95% CI 4.35-114.63) compared to females with poor adherence (AOR=3.92, 95% CI 1.09-14.04). Being female on first line regimen was not associated with VNS while being male on first line regimen had strong association (AOR=0.06, 95% CI 0.00-0.87).

Table 4.7: Sex-stratified Logistic Regression for Independent Factors associated with Viral Non-suppression among HIV Positive Adolescents at Chulaimbo Hospital, Kisumu County, 2018

Independent factors	**VNS**	**VS**	**Female**			**Males**		
			AOR	95% CI		AOR	95% CI	
Adherence								
Inadequate (85%-94%)	14	17	**5.39**	**1.11**	**26.20**	**4.68**	**1.13**	**19.40**
Poor (<85%)	38	21	**5.63**	**1.81**	**17.54**	**13.81**	**3.49**	**54.67**
Good ≥ 95%)	19	91	1					
Duration On ART*								
<2 years	3	1	1.00			14.75	0.71	305.25
2-5 years	21	39	0.76	0.16	2.76	1.90	0.33	11.08
6-10 years	35	50	1.76	0.46	6.75	3.54	0.74	16.83
10 + years	12	39	1					
Regimen line								
First line	38	104	1.00			**0.64**	**0.06**	**0.67**
second line	33	25	1					

***Antiretroviral treatment**

CHAPTER FIVE

DISCUSSION

In this study, our aim was to estimate the prevalence of viral non-suppression among adolescents on antiretroviral treatment at Chulaimbo Sub-County hospital, and to identify factors associated with viral non-suppression among the study population, which included both socio-demographics and clinical factors. We found a viral non-suppression prevalence of 35.5% among the study population. This finding is similar to one of a recent cross-sectional study conducted in Kenya that reported a non-suppression prevalence of 36 % among adolescents 10 <20 years (Mwau *et al*., 2018).

Adolescents who had been on ART for <2 years were found to have the highest proportion of VNS while those on ART for 10+ years had the least. In a prospective cohort study conducted by Mujugira *et al*., the proportion of non-suppression decreased with increase in time on ART (Mujugira *et al*., 2016). A study conducted in Nairobi, Kenya found a 2.8 fold increase in virological failure in a universal test and treat (UTT) group compared to pre-UTT group (Kabogo *et al*., 2018). Earlier initiation on ART as guided by universal test and treat policy guidelines recently introduced may predispose adolescents to sub-optimal ART adherence due to inadequate time for psychological preparation and acceptance. In pre-UTT era, a person who turned HIV positive did not immediately qualify for ART unless the CD4 count was below cut-off. This provided the patient with ample time for better psychological preparation before initiation of treatment.

Females had a higher prevalence of VNS in our study than males. The finding contrasts that of a study which involved retrospective analysis of national viral load data in Kenya which reported males to have higher prevalence of VNS (Mwau *et al*., 2018).

This is possibly due to the vulnerabilities of adolescent girls originating from the unequal cultural and social status in the community and family set-up. The African adolescent girl has more responsibilities than the male which may be overwhelming sometimes, affecting adherence to ART.

Low baseline CD4 count at initiation of therapy was not associated with non-suppression. However, some past studies have reported a significant association between low baseline CD4 and VNS (Mwau *et al*., 2018; Pau & George, 2014). In a prospective study of HIV-1-infected persons who had a known heterosexual HIV-1-uninfected partner in Kenya and Uganda, failure to achieve viral suppression at 6 and 12 months after ART initiation was independently associated with lower levels of pretreatment CD4 count which may indicate late entry into care (Mujugira *et al*., 2016). However, nearly all HIV-infected women (97%), initiating ART were virally suppressed by 24 months, irrespective of baseline CD4 count (Mujugira *et al*., 2018). In a retrospective cohort study conducted in British Columbia, HIV patients initiated on ART with a CD4 count of >500cells /ul had better treatment outcomes than those with <500cells/ul. However, due to virological blips it was not possible to maintain the low prevalence of VNS in follow up (Lima *et al*., 2015).

Inadequate and poor adherence to ART was significantly associated with VNS. Compared to adolescents with good (optimal) adherence, those with poor adherence were nine times more likely to have viral non-suppression while those with inadequate adherence had six times higher odds.

Achieving adherence may especially not be easy in the early stages of ART initiation because the patient is adapting to the daily routine of taking drugs, may experience drugs side-effects and challenges with stigma and disclosure (NASCOP-Kenya, 2016).

About three quarters of study participants were on 1st line and the rest on 2nd line ART regimen. More than half of adolescents on 2nd line regimen and a quarter of adolescents on 1st line had VNS. Adolescents on 1st line regimen had less odds of VNS compared to those on 2nd line. In stratified analysis, being male or older adolescent (15-19 years) on first line regimen was protective of VNS. These finding contrasts findings in similar study where the second line has been reported as protective of non-suppression in comparison to first line (Bulage *et al*., 2017). However, similar to our findings, the same study reported higher prevalence of non-suppression among those on second line than those on first line. The poor virological outcomes for those on second line may point to non-adherence to ART as the possible cause given that the drugs are known to be superior to first line. It is possible that for most of the adolescents being switched from 1st to 2nd line, the reason of treatment failure is non-adherence which if not adequately addressed causes treatment failure even after regimen switch. The wide confidence intervals for non-adherence may mean the study was not adequately powered, and study may need to be repeated with a larger study sample for the kind of analysis to narrow the 95% CI interval.

5.1 Limitations

There were data quality issues (incompleteness) encountered during data abstraction. However, this was adjusted for in analysis by using the appropriate denominator for each variable.

CHAPTER SIX

CONCLUSION AND RECOMMENDATIONS

6.1 Conclusion

The prevalence of viral non-suppression among adolescents on ART at Chulaimbo Sub-County hospital, Kisumu was 35.5%, which translates to a viral suppression prevalence of 64.5%. This means the proportion of virally suppressed adolescents in the facility is below the expected 90% UNAIDS target.

An estimated 45% of adolescent on ART were not optimally adherent to the HIV medication. Adolescents with poor or inadequate adherence to ART and those on second line of treatment at Chulaimbo hospital have higher likelihood to be virally non-suppressed, more so among older adolescents (15-19 years) and among males.

6.2 Recommendations

The County and hospital ART program should consider reinforcing strategies of targeted interventions to motivate adherence, achieve and sustain viral suppression in HIV infected adolescents on ART, with emphasis on those on 2nd line of treatment, males and older adolescents (15-19years). Monitoring adherence on every visit may be necessary to help in early detection of non-adherence.

There is need for an analytical study that will focus on identifying factors associated with sub-optimal ART adherence among HIV positive adolescents, being that it was significantly associated with viral non-suppression.

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APPENDICES

Appendix 1a: Voluntary Informed Consent (English version)

Study Title: Factors Associated with Viral Non-Suppression among HIV Positive Adolescents in Chulaimbo Hospital, Kisumu County, Kenya, 2018

Principal Investigator: Beatrice King'ori

Introduction: The principal investigator of this study is a post-graduate student at the Moi University and we are kindly requesting for your participation in this study.

Viral suppression is the hallmark of antiretroviral therapy for everyone on treatment. When one is virally suppressed, it means the viruses are reduced to such a level that one can live a normal life without opportunistic infections. However, this is not always achieved. We are seeking to know those factors that influence viral non-suppression in adolescents.

Purpose of study: This study will be looking for factors that are associated with being virally non-suppressed while on anti-retroviral therapy. This is important because it will help us to know how to improve the number of adolescents who attain viral suppression and improve their health. Information from this study will assist in planning on HIV care and treatment services for adolescents.

Benefits of participation: The participant will have a chance to ask questions they may have regarding their management and these will be answered satisfactorily.

In addition, the data collected will help the health care workers at Chulaimbo Sub-County hospital to understand how best they can support adolescents on treatment to attain sustained viral suppression and hence better treatment outcomes.

Risks of participation: There are no known risks of you / your child taking part in this study. Refusal to participate will in no way jeopardize your treatment or that of your child.

Freedom of participation: Participation in this study will be voluntary. You are free to participate or withdraw from the study at any point.

Procedure: The study will be conducted using a questionnaire, and data will also be abstracted from the pharmacy, clinical and laboratory records.

Privacy and Confidentiality: The interviewer will keep all information about you confidential, your name will not be used during the study, and 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 have any questions about the research, you can contact principal investigator Beatrice King'ori on 0738 490 706, and if you have any concerns or complaints regarding the way the research has been conducted, you can contact:

Ethics Officer, Moi University
Moi Teaching & Referral Hospital building,
P.O. Box. 3-30100 Eldoret, Kenya.
Office line: 0787723677
Email: irecmtrh@gmail.com or contact@irec.or.ke; Website: irec.or.ke

Participant/ caregiver consent form

I, the undersigned have read/have been read for and fully understood the explanation given to me regarding this study. The investigators have answered all my questions satisfactorily. I hereby consentto my/ my child's participation in this study.

Signed……..Date……

Name.....

Witness sign……Date…….....

Name……..

Appendix 1b: Voluntary Informed Consent (Swahili version)

Anwani ya utafiti: Mambo yanayohusiana na kutofikia ukandamizaji wa virusi kwa vijana wanaotumia madawa ya kupambana na virusi vya ukimwi katika Hospitali ya Chulaimbo, Kisumu Kenya

Mtafiti mkuu: Beatrice King'ori

Utangulizi: Mtafiti mkuu katika huu utafiti anafanya shahanda la uzamili katika Chuo Kikuu cha Moi na tunasali kwa ushiriki wako/mtoto wako kwa huu utafiti.

Ukandamizaji wa virusi ndilo lengo kuu kwa kila mtu ambaye anatumia matibabu ya kupunguza makali ya ukimwi. Wakati virusi zimekandamizwa, inamaanisha zinapungua kwa kiwango kama ambacho mtu anaweza kuishi maisha ya kawaida bila maambukizi ya uwezekano. Hata hivyo, hii haipatikani kila wakati. Tunatafuta kujua mambo ambayo yanahusiana na virusi kutofikia ukandamizaji kwa vijana. **Madhumuni ya Utafiti**: Utafiti huu utapima sababu zinazohusiana na kuwa virusi hazikandamizwi wakati wa tiba ya kupambana na virusi vya ukimwi. Hii ni muhimu kwa sababu itatusaidia kujua jinsi ya kuboresha idadi ya vijana ambao wanapata ukandamizaji wa virusi na kuboresha afya zao. Taarifa kutoka kwa utafiti huu itasaidia katika mipango ya huduma na matibabu ya ukimwi kwa vijana.

Faida za kushiriki:

Ukishiriki utakuwa na nafasi ya kuuliza maswali ambayo unaweza kuwa nayo kuhusu usimamizi wako/mtoto wako na haya yatashughulikiwa.

Aidha, data zilizokusanywa zitasaidia wafanyakazi wa huduma za afya katika hospitali ya Chulaimbo kuelewa jinsi wanavyoweza kusaidia vijana juu ya matibabu ilikupata upunguzaji wa virusi na hivyo matokeo bora ya matibabu.

Hatari za Kushiriki: Hakuna hatari inayojulikana ya wewe / mtoto wako kushiriki katika utafiti huu. Kukataa kushiriki hakuna njia yoyote ya kuhatarisha matibabu yako au ya mtoto wako.

Uhuru wa kushiriki: Ushiriki katika utafiti huu utakuwa kikamilifu kwa hiari. Wewe/mtoto wako ni huru kushiriki au kujiondoa kwenye utafiti wakati wowote.

Utaratibu: Uchunguzi utafanyika kwa kuuliza maswali machache kutumia dodoso, na data pia itanukuliliwa kutoka kwenye rekodi za dawa, kliniki na maabara.

Faragha na Usiri: Mchunguzi ataweka maelezo yote juu yako/mtoto wako ya siri, jina lako/ la mtoto wako halitatumiwa wakati wa utafiti na vijikartasi vya maswali vitatambulishwa na namba badala ya majina. Wachunguzi tu ndio watapata kuona taarifa zilizokusanywa, na taarifa hizo zitahifadhiwa mahali salama.

Matatizo au Maswali: Ikiwa una maswali yoyote kuhusu utafiti huu, unaweza kuwasiliana na mtafiti mkuu Beatrice King'ori mnamo 0738 490 706, na ikiwa una matatizo au malalamiko kuhusu jinsi utafiti umefanyika, unaweza kuwasiliana na afisa wa Maadili, Chuo Kikuu cha Moi kwa anwani hii:

Ethics Officer, Moi University
Moi Teaching & Referral Hospital building,
P.O. Box. 3-30100 Eldoret, Kenya.
Nambari ya simu ya ofisi: 0787723677

Barua pepe: irecmtrh@gmail.com au contact@irec.or.ke; Tovuti: irec.or.ke

Idhini ya mshiriki/Mlezi

Mimi,mwenye ishara iliyoko hapa chini,nimesoma/nimesomewa na kuelewa kikamilifu ufafanuzi uliotolewa kuhusu utafiti huu. Maswali yangu yote yamejibiwa kwa kuridhisha na wachunguzi. Ninakubali kushiriki kwangu/mtoto wangu katika utafiti huu.

Ishara ....Tarehe .....

Jina ....

Ishara ya shahidi ... .Tarehe ....

Jina ....

Appendix 2a: Assent Form (English version)

(*To be read aloud to the child*)

Principal Investigator: Beatrice King'ori

Introduction: We are conducting a study on '**Factors Associated with Viral Non-Suppression among HIV Positive Adolescents in Chulaimbo Hospital, Kisumu County, Kenya, 2018**' and the principal investigator of this study is a student at the Moi University. We are kindly requesting for your participation in this study.

Purpose of study: This study will be looking for factors that are associated with being virally non-suppressed while on anti-retroviral therapy. This is important because it will help us to know how to improve the number of adolescents who attain viral suppression and improve their health. Information from this study will assist in planning for better care and treatment services for adolescents.

Benefits of participation: The participant will have a chance to ask questions they may have regarding their management and these will be answered. In addition, the information collected will help the health care workers at Chulaimbo hospital to understand how best they can support adolescents on treatment to attain viral suppression and hence better treatment outcomes.

Risks of participation: There are no known risks of you taking part in this study. Refusal to participate will in no way affect your treatment in this hospital.

Freedom of participation: We have permission from your parent/guardian, but we also want to make it clear that you can choose to participate or not, and even if you choose to take part, you can also withdraw from the study at any point if you change your mind.

Procedure: We will ask you a few questions using a questionnaire, and other information will be obtained from your pharmacy, clinical and laboratory records.

Privacy and Confidentiality: We will keep all the information about you confidential, your name will not be used during the study, questionnaires will be numbered instead of using names. Only investigators will have access to the information collected, and the same will be kept in a secure place.

Do you have any questions or concerns?

(*Respond to any question or concerns the child may have*).

Just take five minutes to discuss with your parent/guardian and let me know your decision.

Will you agree to take part in this study?

(*If the response is "Yes" the child is enrolled for study and if the response is "No" the child is released together with the parent/guardian*)

Appendix 2b: Assent Form (Swahili version)

(*Soma kwa sauti mtoto akifuatilia*)

Mtafiti mkuu: Beatrice King'ori

Kuanzishwa: Tunafanya utafiti wa mambo yanayohusiana na kutofikia ukandamizaji wa virusi kwa vijana wanaotumia madawa ya kupunguza makali ya ukimwi katika hospitali ya Chulaimbo. Mtafiti mkuu anafanya shahanda la uzamili katika Chuo Kikuu cha Moi na tunakuomba kushiriki kwa huu utafiti.

Madhumuni ya Utafiti: Tunatafuta kujua mambo ambayo yanahusiana na kutofikia ukandamizaji wa virusi kwa vijana ambao wanatumia madawa ya kupunguza makali ya ukimwi.Hii ni muhimu kwa sababu itatusaidi akujua jinsi ya kuboresha idadi ya vijana ambao wanapata ukandamizaji wa virusi na kuboresha afya zao. Taarifa kutoka kwa utafiti huu itasaidia kupanga mipango ya huduma na matibabu kwa vijana.

Faida za kushiriki: Mshiriki atakuwa na nafasi ya kuuliza maswali ambayo anaweza kuwa nayo kuhusu usimamizi waona haya yatashughulikiwa. Aidha, data zilizokusanywa zitasaidia wafanyakazi wa huduma za afya katika hospitali ya Chulaimbo kuelewa jinsi wanavyoweza kusaidia vijana juu ya matibabu ili kupata upunguzaji wa virusi na hivyo matokeo bora ya matibabu.

Hatari zaKushiriki: Hakuna hatari inayojulikana ya wewe kushiriki katika utafiti huu. Kukataa kushiriki hakuna njia yoyote ya kuhatarisha matibabu yako katika hii hospitali.

Uhuru wa kushiriki: Tuko na ruhusa kutoka kwa mzazi /mlezi wako. Lakini tungetaka kuweka uwazi kwamba waweza ukaamua kushiriki au la, na pia ukiamua kushiriki unaweza kujiondoa kwenye utafiti wakati wowote ukibadili mawazo.

Utaratibu: Tutakuuliza maswali machache kwa kutumia dodoso, na mambo mengine yatanukuliwa kutoka kwenye rekodi zako za dawa, kliniki na maabara.

Faragha na Usiri: Tutaweka maelezo yote juu yako ya siri, jina lako halitatumiwa wakati wa utafiti na vijikartasi vya maswali vitatambulishwa na namba badala ya majina. Wachunguzi tu ndio watapata kuona taarifa zilizokusanywa, na taarifa hiyo itahifadhiwa mahali salama.

Je, uko na swali lolote?

(*Jibu maswali yote ambayo mtoto atauliza*)

Chukua dakika tano ujadiliane na mzazi/ mlezi wako kisha unijulishe ukikata kauli.

Je, utakubali kushiriki kwa huu utafiti?

(*Kama jibu ni "Ndio" muandikishe mtoto kwa utafiti na kama ni "La" muachilie pamoja na mzazi/mlezi wake*)

Appendix 3: Study Questionnaire

Study Title: Factors Associated with HIV Viral Non-Suppression among Adolescents on Anti-Retroviral Therapy, Chulaimbo County Hospital, Kisumu County, Kenya
Questionnaire No…… Date……

Instructions: This questionnaire is to be administered in an environment, which ensures privacy and confidentiality

A. Disclosure

Disclosure completed ☐ Disclosure not complete ☐

B. Socio-Demographic Data

1. Gender

   Female = 1 Male = 2

2. What is your age in years? ……..
3. Date of birth (date/month/year)…….
4. What is your marital status?

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

5. What is your highest completed level of education?

   Tertiary = 1 Secondary = 2 Primary = 3 Nursery=4 Never gone to school = 5

6. Employment history

   a) Employed = 1 c) Unemployed = 3

   b) Self- employed=2 d) In school/college=4

7. (For those in school) what type of school? Day school = 1 Boarding school = 2
8. What is the average income per month of the household (Ksh. /$)-----

9. Are your biological parents alive?

   Both parents alive = 1

   None of the parent is alive =2

   Mother alive = 3

   Father alive = 4

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

    Mother = 1 Grandparent = 3 Guardian (unrelated) =5

    Father = 2 Other relatives = 4

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

    Yes = 1 sometimes = 2 never = 3

12. What is the distance from your residence to Chulaimbo Hospital in Kms…?

13. Have you ever been treated differently by family members/friends because of the medication you are taking? Yes ☐ No ☐

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

    Withdrawal of Social support ☐ other ☐

    Discriminated ☐ Specify……..……

    Stigmatized ☐

    Isolated by family members/ friends at school ☐

C. Drug Related Factors

1. How many pills do you take in a day? (24hrs)……
2. 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 other = 4
3. What is your opinion of the number of pills you take per day?

Too many = 1 Appropriate = 2 Not sure = 3 No response =4

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

   Yes ☐ No ☐
5. Do you feel tired/ fatigued of taking your medication?

Yes = 1 No = 2 No response = 4

6. Have you experienced any side effects because 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. Have you ever missed taking your drugs in the last one month?

   Yes ☐ No ☐
9. Have you ever missed taking your drugs in the last one week (7 days)?

   Yes ☐ No ☐

10. If you answered yes to question 8 or/and 9above, what were the reasons for missing? Put a tick where applicable.

Did not understand instruction ☐ Drugs got finished ☐

Dosage schedule too complex ☐ Forgot ☐

Felt better ☐

Fear of being seen taking drugs ☐

Bad side effects ☐

Other ☐ (Specify)…….

D. Health System Related Factors

1. How would you rate the clinician's behavior (friendly, caring, listening etc.)?

   Excellent = 1 Good = 2 Average = 3 Poor = 4 No response = 5

2. How would you rate the time spent by the clinician in addressing your needs, explaining about your health and your medication, is he/she patient to ensure you leave when totally satisfied?

   Very adequate = 1 Adequate = 2 Inadequate = 3Very inadequate =4 No response = 5

3. How would you rate privacy/confidentiality during examination at this clinic?

   Excellent = 1 Good = 2 Average = 3 Poor = 4 No response = 5

4. How would you rate the information given to you about the drugs you are taking? Excellent = 1 Good = 2 Average = 3 Poor = 4 No response =5

5. How would you 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 No response = 5

6. How would you rate the nursing care in the clinic?

Excellent = 1 Good = 2 Average = 3 Poor = 4 No response = 5

7. How would you rate the provision of health education at this clinic?

Excellent = 1 Good = 2 Average = 3 Poor = 4 No response = 5

8. How would you rate the waiting time during your clinic appointment?

   Adequate =1 long = 2 extremely long = 3 No response = 4

9. Do your appointment dates and time fit with your daily activities?

Yes = 1 sometimes = 2 rarely = 3 No = 4 No response =5

10. How would you rate counseling offered at initiation of therapy?

Excellent = 1 Good = 2 Average = 3 Poor = 4 Don't Know = 5

11. How would you rate the on-going counseling at the clinic?

    Excellent = 1 Good = 2 Average = 3 Poor = 4 No response =5

Appendix 4: Clinical Data Abstraction Tool

1. Date of enrollment in to the Comprehensive care clinic……
2. What was the client's age at enrolment?.....years
3. When was the client initiated on ART? Date……
4. How long has the client been on ART? ……..years
5. What was the WHO disease stage at initiation of therapy (+/- 6months)?

   stage one = 1 stage two = 2 stage three = 3 stage four = 4 Missing= 5
6. What was the CD4+ count at initiation of treatment (or +/- 6 months date of initiation)? .....
7. What was the most recent viral load result done in the last 3 months? .....
8. What is the most recent CD4+ count (must be +/- 6 months of the last VL test)? .....
9. What is the most recent recorded WHO disease stage?(must be +/- 6 months of the last VL test)

   stage one = 1 stage two = 2 stage three = 3 stage four = 4 missing=5
10. What is the current Regimen? 1st line ☐ 2nd line ☐
11. The specific drugs in the regimen……(Drug list, tick as appropriate)

    ABC + 3TC + EFV ☐

    AZT + 3TC + EFV ☐

    RAL + 3TC + EFV ☐

    ABC + 3TC + LPV/r ☐

    TDF + 3TC + EFV ☐

    TDF + 3TC + ATV/r ☐

    TDF + 3TC + ATV/r ☐

Other ☐

Specify……

12. Has the client undergone a regimen switch? Yes ☐ No ☐

13. If yes in No.6 above, what was the reason for regimen switch?

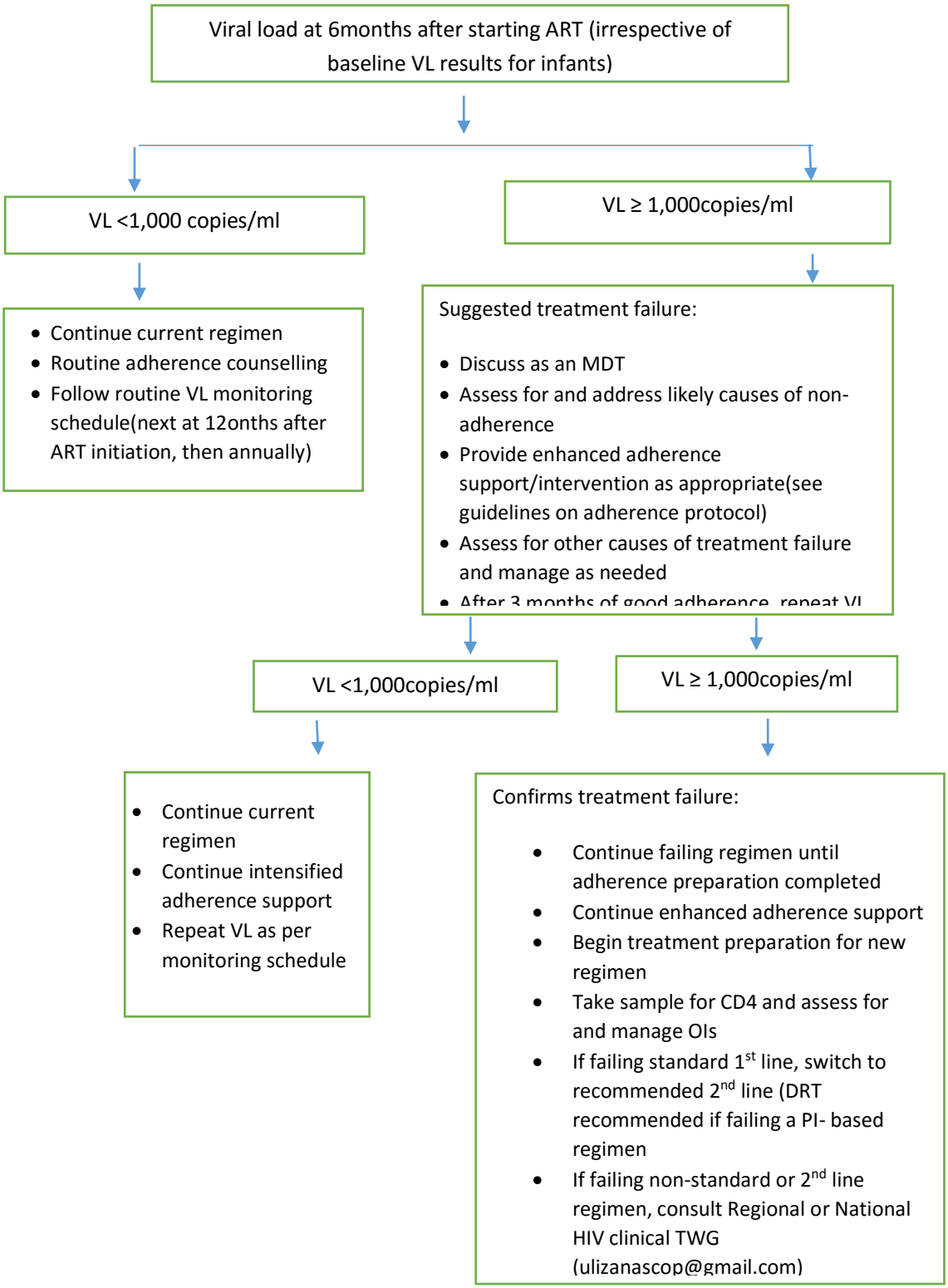
Treatment failure =1

Adverse drug reaction = 2

Drug interaction = 3

Others (specify)…….

Appendix 5: Viral load algorithm



Algorithm for Viral load monitoring of patients on ART (1st or 2nd line)

Appendix 6: Study approval, Institution Review and Ethics Committee, Moi University

MU/MTRH- INSTITUTIONAL RESEARCH AND ETHICS COMMITTEE (IREC)

MOI TEACHING AND REFERRAL HOSPITAL
P.O. BOX 3
ELDORET
Tel: 33471//2/3

MOI UNIVERSITY
COLLEGE OF HEALTH SCIENCES
P.O. BOX 4606
ELDORET

Reference: IREC/2017/185
Approval Number: 0003038

31st May, 2018

Beatrice Muthoni King'ori,
Moi University,
School of Public Health,
P.O. Box 4606-30100,
NAIROBI-KENYA.

INSTITUTIONAL RESEARCH & ETHICS COMMITTEE
31 MAY 2018
APPROVED
P. O. Box 4606 - 30100 ELDORET

Dear Ms. Muthoni,

RE: FORMAL APPROVAL

The MU/MTRH- Institutional Research and Ethics Committee has reviewed your research proposal titled: -

"Factors Associated with HIV Viral Non-Suppression among Adolescents on Anti-Retroviral Therapy, Chulaimbo County Hospital, Kisumu County, Kenya".

Your proposal has been granted a Formal Approval Number: ***FAN: IREC 3038*** on 31st May, 2018. You are therefore permitted to begin your investigations.

Note that this approval is for 1 year; hence will expire on 30th May, 2019. If it is necessary to continue with this research beyond the expiry date, a request for continuation should be made in writing to IREC Secretariat two months prior to the expiry date. You will be required to submit progress report(s) on application for continuation, at the end of the study and any other times as may be recommended by the Committee.

Furthermore, you must notify the Committee of any proposal change (s) or amendment (s), serious or unexpected outcomes related to the conduct of the study, or study termination for any reason. You will also be required to seek further clearance from any other regulatory body/authority that may be appropriate and applicable to the conduct of this study.

Sincerely,

DR. S. NYABERA
DEPUTY-CHAIRMAN
INSTITUTIONAL RESEARCH AND ETHICS COMMITTEE

cc CEO - MTRH Dean - SOP Dean - SOM
Principal - CHS Dean - SON Dean - SOD

Appendix 7: Permission to conduct Research by AMPATH

Academic Model Providing Access To Healthcare
Telephone: 254 53 2033471/2P.O. BOX 4606, ELDORET Fax: 254 53 2060727

RESEARCH

Ref: RES/STUD/2/2018 June 18, 2018

Beatrice Muthoni Kingo'ri
Moi University
School of Public Health
P.O Box 4606-30100
Eldoret

Dear Ms. Muthoni,

RE: PERMISSION TO CONDUCT RESEARCH AT AMPATH

This is to inform you that your study *"**Factors Associated with HIV Viral Non-Suppression among Adolescents on Anti-Retroviral Therapy, in Chulaimbo County Hospital, Kisumu County, Kenya**" has* been reviewed by the AMPATH Research Program Office. Permission is therefore granted to begin collecting your data at AMPATH Chulaimbo Clinic.

Please note that your research activities should not in any way interfere with the care of patients. This approval does not support access to AMRS data at AMPATH.

You are required to submit a final report of your findings to the AMPATH Research Program Office.

Should you wish to publish your research findings, permission has to be sort from AMPATH Publications Committee. Please contact the AMPATH Research Office research.manager@iukenya.org in case of any enquiry regarding this matter.

Thank you,

Appendix 8: Permission to conduct study by Kisumu County Health Department

Beatrice King'ori
School of Public Health
Moi University, Eldoret

25.06.2018

Approved

TO
THE DIRECTOR OF HEALTH SERVICES
KISUMU COUNTY HEALTH DEPARTMENT
P.O. Box 2738-40100
KISUMU

REF: PERMISSION TO CONDUCT STUDY AT CHULAIMBO COUNTY HOSPITAL

I am a postgraduate student at the Moi University undertaking MSc.in Applied Epidemiology. I have planned to conduct a study at Chulaimbo hospital for my thesis, on **"Factors associated with viral non-suppression among adolescents on ART at Chulaimbo County Hospital".** The study protocol has been reviewed by Moi University/MTRH Institutional Research and Ethics Committee (IREC) and approved. I have also sought permission from AMPATH as you will find in the documents attached to this application. I kindly request your office to allow me collect the relevant data. Your support will be highly appreciated.

Thanks in advance.

Yours faithfully,

Beatrice King'ori