AN ASSESSMENT OF THE CHARACTERISTICS OF ADOLESCENTS AT ENROLMENT INTO ANTI-RETROVIRAL THERAPY, AND FACTORS INFLUENCING THEIR RETENTION INTO HIV CARE AND TREATMENT IN ZIMBABWE

RUDO A.P. KUWENGWA
Student Number: 3515795

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University of the Western Cape

Supervisor: Dr. Hanani Tabana

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Adolescents, Adolescent HIV, Anti-retroviral therapy, Characteristics at enrolment, Retention rates, Outcomes, Loss to follow up, Factors influencing retention, Zimbabwe

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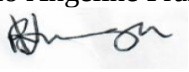
Declaration

I declare that the work presented herein, An assessment of the characteristics of adolescents at enrolment into anti-retroviral therapy, and factors influencing their retention into HIV care and treatment in Zimbabwe, is original and that it has not been submitted for any degree or examination in any other university or institution for the award of a degree or certificate and that all sources of information and data used or quoted have been duly indicated and acknowledged.

Full Name: Rudo Angeline Praise Kuwengwa

Signature: 

Abbreviations

AIDS	Acquired Immune Deficiency Syndrome
ALHIV	Adolescents living with HIV
ART	Antiretroviral Treatment
ARV	Antiretroviral (medicine)
ATP	AIDS and TB Program
BMI	Body Mass Index
CATS	Community Adolescent Treatment Supporter
CD4	Cluster of Differentiation 4
CI	Confidence Interval
DHIS	District Health Information System
ePMS	Electronic Patient Monitoring System
HIV	Human Immunodeficiency Virus
IQR	Interquartile Range
LTFU	Lost-to-Follow-Up
M&E	Monitoring and Evaluation
MICS	Multiple Indicator Cluster Surveys
MoHCC	Ministry of Health and Child Care
MRCZ	Medical Research Council of Zimbabwe
NAC	National AIDS Council
OI	Opportunistic Infection
PLHIV	Persons Living with HIV/AIDS
PMTCT	Prevention of Mother to Child Transmission of HIV
TB	Tuberculosis
UNAIDS	Joint United Nations Program on HIV/AIDS
UNICEF	United Nations Children's Fund
WHO	World Health Organization
VL	Viral Load
ZDHS	Zimbabwe Demographic and Health Survey

Definitions of Key Terms

Adolescents:	The World Health Organization (WHO) defines adolescence as the period in human growth and development that occurs after childhood and before adulthood, from ages 10 to19 years.
Youth:	The WHO defines youth as individuals in the 15 to 24-year-old age group.
Young people:	The WHO defines individuals within the age range 10 – 24 years as young people.
Retention:	refers to patients known to be alive and receiving highly active Anti-Retroviral Therapy (ART) at the end of a follow-up period.
Attrition:	is defined as discontinuation of ART for any reason, including death, loss to follow-up, and stopping ARV medications while remaining in care.
Transfer out:	is Transfer to another ART facility, where reported, is not regarded as attrition—patients who transfer are assumed to be retained.
Loss to follow up:	refers to a scenario where a patient is late by 3 months (90days) or more for a scheduled consultation or medication pickup.
Immunological characteristics	refers to the CD4 cell count for the adolescents.
Clinical characteristics:	refers to the weight, current and emerging opportunistic infections, functional status and WHO clinical stage at baseline.

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Abstract

This study was undertaken within the context of stagnation in the trend of new HIV infections among adolescents globally coupled with increasing mortality within this sub-population as well (UNICEF 2015 report). This trend in no different in Africa and in deed Zimbabwe where low HIV knowledge levels among adolescents, with majority of them demonstrating limitations regarding comprehensive HIV have been observed in key national studies (e.g. Zimstat, 2016). Further, there were concerns regarding disproportionate access to information, services and care among male and female adolescents in the country, with females being worse off and hence more vulnerable to HIV infection as well as the subsequent effects and outcomes even after accessing care and ART. The study problematized adolescents' poor adherence and retention in HIV care and treatment initiatives. Against the backdrop of paucity of nationally-representative adolescent HIV data on retention in care, mortality and attrition rates, as well as factors influencing these observed outcome rates, this was considered as an opportunity to contribute to the knowledge gap. Knowing the factors that influence retention in adolescents is important to devise interventions for improving retention outcomes for this population. The aim of the study is to assess the demographic and clinical characteristics of HIV infected adolescents aged 10 – 19 years who were enrolled onto ART during the period January 2012 – March 2017, to report their retention rates, and explore the possible factors associated with retention outcomes at 3, 6, 12, 24, 36, 48 and 60 months.

Methodology: This study took the form of a retrospective cohort study of adolescents enrolled onto ART between January 2012 and March 2017, then followed up until March 2018 using individual patient medical records within the country-wide encompassing electronic Patient Monitoring System (ePMS). Raw data was then abstracted from the ePMS onto a CSV file, which was exported to STATA v13 and further cleaned for analysis. Of the abstracted 32 208 records of adolescents (10-19years) who had been enrolled onto ART between January 2012 and March 2017, 3 450 records with missing unique identifier, age and sex were excluded from the analysis.

Findings: It was noted among the key highlights from the findings that male adolescents had better retention rates when compared to female adolescents as they had retention consistently higher by 5-8% across the follow up period with the gap widening with time on ART. Both

males and females showed a decline in retention and by 60 months their retention rates were below 50%. Other emerging findings showed that older age (15 – 19 years), pregnancy, referral level facilities and rural located facilities were some of the main *factors associated* with poorer retention rates among adolescents. The study concluded that more work still needs to be done regarding improving adolescent retention in care as prevailing retention rates at the time of the study were still sub-optimal. The study recommends key actions to increase knowledge as well as to develop programmes *meant to* improve adolescent retention rates in HIV treatment and care programmes.

Chapter 1: Introduction

1.1. Background

Since the beginning of the Human Immunodeficiency Virus (HIV) epidemic approximately 76 million people have been infected with HIV and about 35 million people have died due to HIV. By the end of 2016 there were 36.7 million people living with HIV globally with sub Saharan Africa, which is worst affected, by the epidemic accounting for nearly 70% of all people living with HIV worldwide (WHO, 2016; UNAIDS, 2017).

Anti-Retroviral Treatment (ART) has been shown to decrease viral load whilst increasing CD4 T-cell count as well as improving survival for people living with HIV (PLHIV), this evidence led to the scale up of access to ART for people living with HIV being declared a public health emergency by UNAIDS and WHO in 2003. Since that time remarkable progress has been made towards scaling up access ART leading to 19.5 million people receiving ART globally by the end of 2016. These gains in the HIV/AIDS program have seen a global reduction in AIDS related deaths which have decreased by 48%, HIV new infections have also been decreasing but the rate of decline has slowed down over the last couple of years almost becoming static at about 1.8 million in 2016. (UNAIDS, 2016, 2017; WHO, 2016; The Lancet, 2017). There is still however, 19 million people globally who still do not know their HIV status (UNAIDS 2016)

Although there are enormous gains that have been made in the fight against HIV, disparities in these gains still exist among regions and different sub-populations. Women bear a greater burden of the disease when compared to men as women contribute 51 % of all PLHIV. Although more women are infected with HIV, AIDS related deaths were 27% lower among women and girls compared to AIDS related deaths among men and boys (UNAIDS, 2014, 2017). Of the 1.8 million adolescents living with HIV globally less than 1 in 4 adolescents has access to life-saving ART. Eighty-five percent of all adolescents living with HIV are in sub-Saharan Africa. While mortality across all other age groups has been on a down ward trend ever since the roll out of ART, the adolescent population mortality has been increasing with AIDS becoming the leading cause of death in Africa and the second globally among

adolescents (UNICEF, 2015b, 2017, 2018). New HIV infections have also not been decreasing as rapidly in the adolescents as they have in other age groups and uptake of HIV Testing Services (HTS) has been very low amongst adolescents (UNAIDS, 2013; UNICEF, 2013, 2017, 2018).

There are several factors that may contribute to these observed trends of mortality and incidence within the adolescent age group and these include: low basic knowledge on HIV among adolescents, the difficulties that exist in offering the adolescents appropriate HIV testing services to identify them, the difficulties involved in enrolling them into care and high lost to follow up rates(Nglazi *et al.*, 2012; Okoboi *et al.*, 2016). Levels of basic knowledge on HIV among adolescents are very low and in most cases less than 50% of adolescents have any basic information on HIV (Idele *et al.*, 2014). Identifying HIV infected adolescents is very difficult as it has been shown that among adolescents aged 15 – 19 in Eastern and Southern Africa, only 29% and 20% of girls and boys respectively have ever tested for HIV and received their results (UNAIDS, 2013). As testing is the entry point to care and treatment this low coverage of testing means only a few adolescents needing treatment are identified.

In addition to this reduced access to care, it has also been noted that those adolescents currently in care experience challenges with retention and adherence to treatment. Many barriers exist that impact on the identification, linkage to care, retention and viral suppression of HIV infected adolescents most of which are not well understood (Bekker *et al.*, 2015). These factors are further exacerbated by the fact that the adolescent period is a complex developmental period characterized by psychosocial, behavioural, physiological and cognitive changes that impact on the adolescent's perception of their HIV status and their life in general (Nglazi *et al.*, 2012; Sawyer *et al.*, 2012). It is important to understand the epidemiology of HIV among adolescents as disease burden among Adolescents living with HIV (ALHIV) is expected to increase with the projected youth bulge within the population especially in African countries (UNICEF, 2016; United Nations, Department of Economic and Social Affairs, 2017)

1.2. The Zimbabwean Context

Zimbabwe is a country in Sub-Saharan Africa with a population of over 13 million people and is divided into ten provinces. Of these eight are rural and two are metropolitan provinces. Most

of the population is predominantly young with 41% of the population being 15 years and below. Sixty-seven percent of the population resides in rural areas, and the country has high levels of poverty with an estimated 72% of the population surviving below the poverty line (World Bank, 2016). Harare Metropolitan Province is the largest province housing 16% of the country's population and it is also the country's capital city (ZIMSTATS, 2012). Zimbabwe's economic situation has been deteriorating over the years as evidenced by a decelerating GDP over the past few years. Zimbabwe's economy is mainly driven by agriculture and mining. however due to a poor socioeconomic situation, 11.1% of the population is classified as unemployed (Government of Zimbabwe, 2014). Zimbabwe's health system is built on the comprehensive primary health care approach and was one of the best systems in southern Africa before the economic crisis which saw a deterioration in health indicators. The public health system in Zimbabwe is largely decentralized with services being offered at community level by village health workers and at primary, secondary, tertiary and quaternary levels by skilled health professionals (MoHCC, 2012; Zimstat, 2016).

The country also has a high burden of HIV with an estimated 1330 000 people living with HIV, including 72,615 adolescents aged 10 -19 years. Zimbabwe has made remarkable progress in scaling up ART access since 2004 when the ART program was launched leading to a decline in AIDS related mortality from 115,117 deaths in 2011 to 31,217 deaths by the end of 2015 (National AIDS Council & MOHCC, 2015). It is estimated that there are 1.3 million people living with HIV in Zimbabwe at an adult HIV prevalence of 13.5% and approximately 74% of HIV infected adults are on ART. ART Services are available in 95% of the health facilities in the country (MOHCC, 2015; AVERT, 2017; United Nations, Department of Economic and Social Affairs, 2017). Adolescent services are offered in the adult ART clinics and adolescents are managed at the clinics as adult clients in 90% of facilities in Zimbabwe (MOHCC, 2015). In some clinics in Zimbabwe peer treatment supporters specifically for adolescents have been trained to assist adolescents on ART with their treatment and also form and convene adolescent support groups, these are known as Community Adolescent Treatment Supporters (CATS) (Pangaea Global, 2015).

Knowledge levels on HIV are still low among adolescents in Zimbabwe with only 46% of female and 47% males having demonstrated comprehensive HIV knowledge in a recent survey(ZimStat, 2016). These low levels of knowledge are worrying as the same survey noted 5% males and 6% females reported having sex before the age of 15 years and 17% young

women 15 – 19years had, had sex with a partner 10 years their senior in the last 12 months. Disparities exist in access to care amongst females and males as 63% of young women had received an HIV test in the past 12 months compared to 39% young men. Young women are also disproportionately affected by HIV as they have a higher prevalence compared to young men (Zimbabwe Ministry of Health and Child Care *et al.*, 2016; Zimstat, 2016).

1.3. Problem statement

Apart from the challenges adolescents face to access services, once identified and enrolled into HIV care and treatment their adherence and retention is also very poor. (Nachega, *et al*, 2009; Bygrave *et al.*, 2012; Mavhu *et al.*, 2013). Data on treatment outcomes of adolescents on ART that include mortality and attrition rates that ultimately impact on retention rates which are nationally representative are not currently available. However, an opportunity exists as there are large amounts of data that are being collected and entered in the electronic Patient Monitoring System (ePMS) which if analysed can give an indication of how well the HIV care and treatment program is doing in the management of adolescents. Identifying the characteristics and factors that are associated with better retention rates assists in planning for improved quality of services among adolescents. The study findings will be useful in informing and guiding programmatic implementation to improve adolescent program performance and ultimately the overall program performance.

1.4. Aim of the Study

The aim of the study is to assess the demographic and clinical characteristics of HIV infected adolescents aged 10 – 19 years who were enrolled onto ART during the period January 2012 – March 2017, to report their retention rates, and explore the possible factors associated with retention outcomes at 3, 6, 12, 24, 36, 48 and 60 months.

1.5. Objectives

1) To determine baseline demographic and clinical characteristics of HIV positive adolescents aged 10 -19 years at enrolment into ART care,
2) To evaluate retention rates and trends of HIV positive adolescents enrolled on ART over time at 3, 6, 12, 24, 36, 48 and 60 months after ART initiation,
3) To identify possible sociodemographic and clinical factors that may be associated with retention among adolescents aged 10 – 19 years

Chapter 2: Literature Review

2.1. Introduction

Due to the observed trends of increased mortality and HIV incidence remaining stable in the adolescent population there is a growing concern to understand the factors behind these trends. Understanding these factors and the outcomes of adolescents in care will help in formulating strategies to reduce the mortality and incidence rates (Dawood, Chb and Sa, 2015). It is estimated that of the 74,000 adolescents living with HIV (ALHIV) in Zimbabwe 32,000 are male and 42,000 are female (UNICEF, 2018). Disaggregated data are not available in the country especially for the age group 10 – 14 years of age (Ministry of Health and Child Care, 2015). Although current data for ART coverage is not readily available it is estimated that ART coverage of children 0 -19 years of age is now around 80% (PEPFAR and Foundation, 2017).

2.2. Characteristics of adolescents enrolled in ART

2.2.1. Socio-demographic characteristics

In terms of the socio-demographic profile, several studies have found that a significant proportion of the adolescents who are enrolled on ART are females, orphaned and do not attend school (A *et al.*, 2007; Ferrand *et al.*, 2007, 2017; Musisi and Kinyanda, 2009). The gender distribution of adolescents on ART shows that there are often more females, and, in most cases, these are pregnant and unemployed (Auld et al., 2014). Emotional and behavioural disorders have also been described in adolescents enrolled for ART. Musisi *et al* (2007) reported that, among 82 Ugandan HIV-infected adolescents, 51% reported psychological distress and 17% attempted suicide. Similarly, in a study in Zambia, about 40% of 127 HIV-infected adolescents reported mental health problems.

2.2.2. Clinical Presentation

Adolescents often present late for care and are consequently enrolled at a more advanced stage of the infection. This is a finding that has been very consistent across most studies carried out to determine the clinical characteristics of adolescences at enrolment (Auld et al., 2014). Studies done in Zimbabwe and Uganda have shown that adolescents often present with a lower CD4 count when compared to either adults and children and in most cases had severe immune-suppression (Bakanda *et al.*, 2011; Shroufi *et al.*, 2013; Nabukeera-Barungi *et al.*, 2015). Although adolescents had a lower median CD4 in Ethiopia when compared to children, adults however had the lowest median CD4 cell count compared to both age groups. In a study done in south Africa there were no significant differences in median CD4 count at baseline (Nglazi *et al.*, 2012; Moshago, Haile and Enkusilasie, 2014).

Ferrand et al (2007) also found out that HIV-infected adolescents who attended HIV treatment clinics in Harare were profoundly immune-suppressed, with characteristics suggesting long-standing HIV infection when they first presented. Recurrent respiratory tract infections, skin complaints, diarrhea, and past tuberculosis are the most common HIV-related complaints with which adolescents present with (Ferrandet al, 2017). Most studies have showed that adolescents present with more advanced clinical disease with a greater proportion presenting with WHO clinical disease stage III and IV.

2.2.3. Retention

It has been noted that there are also challenges with retention in care and adherence for the adolescents with higher rates of loss to follow up noted among this age group. Stigma, discrimination and disclosure problems were noted as some of the major barriers to retention in care and adherence to medication, while peer support, counselling, supportive health care workers, short waiting times and provision of food and transport were notable facilitators (Nabukeera-Barungi *et al.*, 2015). In a study done across 7 countries, it was found that loss to follow up was a major problem among adolescents as evidenced by higher loss to follow up rates among adolescents compared to other age groups. These findings concurred with findings from Ethiopia that saw higher dropout rates of 25.3% among adolescents compared to 17.9% and 20.2% among children and adults respectively (Moshago et al., 2014, Auld et al., 2014) .

Teasdale *et al* (2014), in their cohort study in Kenya also found out that LFT of young people with HIV was high (32.2%) and notably greater among youth compared to young adolescents. They thus concluded that new strategies targeting these populations are urgently needed to improve retention. In Zimbabwe, a study by Matyanga *et al*., from a public-sector clinic in peri-urban Zimbabwe, compared attrition in a non-research cohort between younger (age 10–14 years) and older (age 15–19 years) adolescents and between younger (age 20–29 years) and older (age ≥30 years) adults, over a 2-year period. The rates of retention in care by 24 months were greater than 80% in all age groups except young adults, where 26% were not in care by the end of 24 months (Matyanga *et al.*, 2016).

Mortality is invariably higher among males, patients with low initial CD4 count, those with advanced WHO clinical disease and those with TB coinfection. Retention was not affected by location of service provision whether facility based, or community based as outcomes were comparable at the different service provision locations. However, some community-based service provision models achieved better retention for adolescents when compared to facility-based service provision. Rural location was associated with poor adherence and retention (Bakanda *et al.*, 2011; Massavon *et al.*, 2014; Moshago, Haile and Enkusilasie, 2014; Nabukeera-Barungi *et al.*, 2015).

2.2.4. Viral suppression and immunological response

The effects of poor adherence and retention is lack of immunological response and viral suppression and it has been noted that adolescents have a longer time to viral suppression and are at increased risk to experience a virological rebound. This was a finding in a study done in the United States of America where 48.6% of adolescents experienced a virological rebound during the first 12 months of follow up(Murphy *et al.*, 2005). These findings were similar to a different study carried out in the United States of America as well where viral suppression rates were even lower at 37% and 27% for perinatally infected and behaviorally infected adolescents and young adults respectively (Kahana *et al.*, 2016). In a study done in 7 rural and urban sites in South Africa adolescents and young adults were more likely to have an unsuppressed viral load and were more likely to fail virologically. However, this same study also found that

adolescents and young adults were less likely to fail immunologically and more likely to increase their CD4 count at 6 and 12 months. This finding was also collaborated by the Zimbabwean national HIV outcomes study that was recently concluded. It was also noted that those adolescents with low CD4 count ≥50 cells/mm^3 at baseline were at increased risk of virological failure (Evans et al., 2013; MOHCC, 2016). These findings confirm that indeed adolescents are at increased risk of virological failure and are less likely to achieve viral suppression despite being able to improve their CD4 cell count.

2.2.5. Mortality

Global statistics have shown increased mortality among adolescents; however, country level studies have shown a mixed picture with other countries showing increased mortality of adolescents when compared to other age groups where as others have proved there are no significant differences in mortality between the different age groups. In a study at a community based ART clinic in South Africa adolescents had a mortality rate of 1.2 deaths per 100 person years compared to 3.1 in young adults showing that mortality was actually much higher in young adults than in adolescents however these are findings of a single site and might not represent the national picture (Nglazi *et al.*, 2012). In Zimbabwe a study done at one of the central hospitals between 2004 - 2010 also showed that adolescents had a lower mortality when compared to adults and this finding is supported by the recently concluded national HIV outcomes study that showed that mortality was not much different between the different age groups (Shroufi et al., 2013; MOHCC, 2015). In Ethiopia a different picture was observed whereby adolescents had a higher mortality of 2.8 per 1000 person/months compared to 2.5 and 1.9 for children and adults respectively (Moshago, Haile and Enkusilasie, 2014).

2.3. Factors influencing retention of adolescents in HIV care

Various studies have shown that there are differences in retention rates and outcomes across different geographic settings and that factors influencing these outcomes are often similar across countries however some country specific settings may account for the observed differences. (Arrivé *et al.*, 2012) assessed the association of HIV Status Disclosure and Retention in Care among HIV-Infected Adolescents on Antiretroviral in West Africa. They found out that about two-thirds of HIV-infected adolescents on ART were not aware of their

HIV status in these ART clinics in West Africa but disclosed HIV status improved retention in care. They concluded that the disclosure process should be thus systematically encouraged and organized in adolescent populations. In this study, factors that influenced variations in retention included age, CD4 cell count at treatment initiation, WHO clinical stage at treatment initiation as well as parent/caregiver support. Pregnant adolescents have also been reported to have poorer retention than older pregnant women at 50% and 63% respectively at 12 months following diagnosis. (WHO, 2012).

In summary, challenges faced in retaining youth and adolescents in HIV care programs include poor knowledge of ART efficacy and benefits of adherence, inadequate social support, stigma, prolonged waiting times interfering with school / work schedules, costs and a range of social and emotional factors associated with adolescence (Estripeaut *et al.*, 2016; Wadunde *et al.*, 2018). Factors affecting retention can be categorized into site/facility specific factors, community factors, Health system weaknesses, patient/care giver factors and financial barrier. Factors at the facility where the adolescent is receiving care can either promote or impede retention on treatment. Issues that include adolescent services that are not responsive to the needs and preferences of adolescents, long waiting times and inadequate infrastructure among others may present barriers to retention. Health system weaknesses affecting supply chain and logistics, and information systems can lead to trickle down effects on service provision at facility level thus affecting retention on treatment. Financial barriers include out of pocket expenditures to access other supporting services for ART provision such as laboratory and radiologic investigations. Clinical, social and demographic characteristics of adolescents can also affect their retention in care, while community factors that perpetuate stigma and discrimination also affect retention in care (WHO, 2012). Figure 1 shows the interaction of these factors

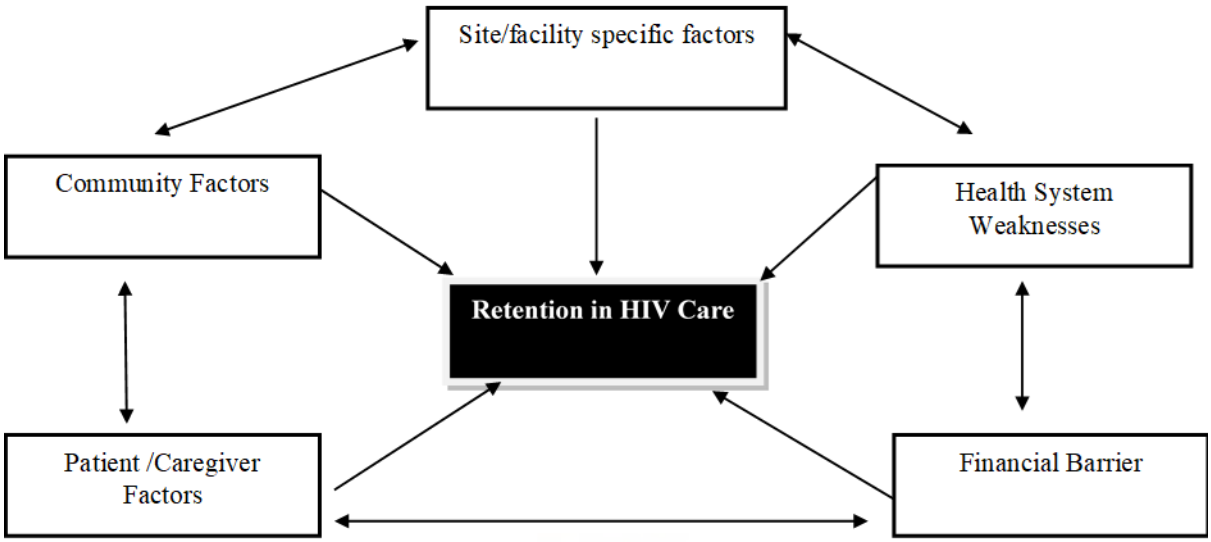

Figure 1: Factors Influencing Adolescent retention on HIV Care. Adapted from WHO, HIV Program 2012

2.4. Conclusion

Various studies have made use of retrospective records review to understand the adolescent HIV treatment outcomes and factors that may influence these outcomes. This is a feasible approach as countries are collecting a lot of valuable data that can assist with defining the factors that influence observed outcomes. Therefore, in the Zimbabwean context where a lot of data has been collected in electronic form it is important to analyze this data to characterize the adolescent clients, their outcomes on ART and the factors influencing these outcomes.

Chapter 3: Methodology

3.1. Study design

A retrospective cohort study of adolescents enrolled onto ART between January 2012 and March 2017, then followed up until March 2018 was carried out using individual patient medical records for all adolescents recorded within the ePMS country-wide. The ePMS has been used in the country since 2012 and contains site level and patient level data. The ePMS is present in 400 high volume sites representing approximately 65% of patients currently in HIV care within Zimbabwe. Using this routinely collected data can give a picture that is nationally representative and can be generalized to most HIV infected adolescents in the country. Data for all the 400 sites was analysed for all adolescents enrolled in care between January 2012 and March 2017 to ensure national coverage. The data in the ePMS covers all the 10 regions of the country (UNDP, 2014).

A retrospective cohort analysis is feasible as Zimbabwe has been implementing the ePMS for patient monitoring since 2012 and as such has a lot of client medical records within an electronic database. The ePMS contains patient level demographic, biological and medical history and it also contains some site level data which are updated at each visit to the clinic, such that it is easy to follow up a client from time of enrolment till to date. A cohort of clients and their baseline characteristics can be obtained and followed up for a period retrospectively as data is available. This a low-cost way to identify outcomes of enrolled clients as it involves analysis of already collected data. It would have been more ideal to do a prospective cohort of adolescents enrolled onto ART; however, this would require more time and resources making it less feasible and expensive to carry out. A cross-sectional study could also be done but would not have been able to show the relationship between baseline characteristics and the specific observed outcomes since exposure and outcomes are measured at the same time (Song and Chung, 2010; Setia, 2016).

3.2. Study population

For the purposes of this study all HIV infected adolescents enrolled into ART during the period January 2012 to March 2017 and followed up until March 2018 were eligible for inclusion in the study. As all client's records for all adolescents seen during this specified period at sites with ePMS were available within the ePMS no sampling was done and all records were analysed. Adolescents enrolled in care during this period were followed up for a period of 60 months up to March 2018 depending on duration on ART. Retention rates at 3, 6 and 12 monthly then at 12 monthly intervals up to 60 months as applies were reported. WHO recommends monitoring number of clients retained on ART at 12 months after ART initiation and 12 monthly thereafter as one of the global indicators for monitoring HIV programs (WHO, 2015). For this study the recommended follow up periods within the WHO Strategic Information guidance for HIV in the health sector were used. Additionally, outcomes at 3 and 6 months were added due to challenges faced in the adolescent age group e.g. self-stigma and disengagement from care due to the need to fit in with other peers leading to poorer outcomes hence the need to pick up outcomes earlier (WHO, 2012).

3.3. Data collection

Raw data, with only the data points required for adolescents aged 10 – 19 years, was exported from the ePMS into a CSV file and cleaning before subsequent analysis was done. Data cleaning involved excluding any clients with missing sex or age as these data elements were necessary for analysis within the study. The data points exported from the ePMS onto the CSV file had several variables, each meant to address the baseline demographic and clinical characteristics as well as the outcomes at 3, 6, 12 and 24 months, up to 60 months as applies.

All ePMS sites submit all their ePMS data back-up monthly in the form of an encrypted USB flash drive which is then stored in a central repository by program staff for all the sites in the country. For the study, back up files for March 2018 were used for analysis and these we received between April and June 2018. De-identified data was then abstracted onto a CSV file and analysed. Considering that the submission of back up files to the AIDS & TB unit is a routine process there was no need to have a separate data abstraction process for purposes of

this study and routinely abstracted data was used in analysis.

3.4. Data Analysis

Data abstracted from the ePMS onto a CSV file was exported to STATA version 13 (STATA Corporation, College Station, TX, USA) for analysis. For baseline characteristics descriptive statistics were done for sociodemographic characteristics and clinical presentation. Age was converted into a categorical variable and categorized into two categories i.e. 10 -14 years and 15 – 19 years, median age at enrolment was also reported with the Inter-quartile range. WHO clinical staging was recategorized into 2 categories i.e. WHO stage I &II and stage III & IV. Functional status was also recategorized as the two categories Work and ambulatory were fused and bed ridden was reported separately. Marital status was also recategorized into two categories i.e. Married and not married with single, widowed and divorced/separated being compressed into the not married category, marital status is only applicable for adolescents aged 16 and above therefore minors who had no marital status were separated and not included under not married. Sex, pregnancy status, education level, health facility level, province and facility geographical distribution were not re-categorized.

Proportions for all the above-mentioned variables were presented in the descriptive statistics. Longitudinal follow up to report outcomes i.e. currently on ART, lost to follow up, stopped ART, transfer out, defaulted treatment and retained in care, were also done and proportions of clients according to treatment outcome was reported over the specified time frames of 3, 6, 12, 24, 36, 48 and 60 months. For determining factors associated with retention outcomes the reference time point was 12 months after ART initiation this is in accordance with WHO recommendation for mid-term evaluation of outcomes (WHO, 2015). Associations between categorical variables were determined by the chi square test or alternatively Fisher's exact test. Poisson regression with robust error variance was used to calculate crude and adjusted risk ratios (RRs) with 95% confidence interval (CI). Differences at the 5% level ($p<0.05$) were regarded as significant.

3.5. Reliability and Validity of the Study

The reliability of the study is compromised as it relies on routinely collected data which was not originally designed to answer the specific research question being investigated by the study. The fact that the data is being recorded on paper-based records by clinicians and then entered into the electronic system by entry clerks also further compromises the reliability. However, to improve reliability any incomplete records with missing data were excluded from the analysis also data in the ePMS is recorded by nurses and data entry clerks who are well trained in data entry. The software also contains some checks and balances to ensure that errors in data entry are minimized. This will reduce any recording or measurement errors thus increasing reliability. If any errors in recording are available within the database these would affect both the exposed and non-exposed equally and would be independent of the outcome status therefore resulting in non-differential misclassification bringing the association nearer to the null.

The ePMS contains approximately 65% of all clients currently in care in the country and therefore can provide a large proportion of the adolescents in care. Using the ePMS provided a large sample size and this will help improve validity of the study. Because the ePMS is not covering all the ART sites in the country, if adolescents receiving ART at non-ePMS sites are different from those receiving ART at the ePMS sites this would affect validity of the study. However, since the ePMS is available in a third of the sites which are at all levels of care and covering 65% of all clients in care this is not expected to bias the study significantly.

3.6. Study Limitations

The major limitation of this study was incomplete data. Due to the incompleteness of data some very important variables could not be analysed these include CD4 count and Body mass index, which would have added value to the study findings. Longitudinal follow up of these variables and how they changed over time would also have been important in reporting the effect of ART on CD4 count and BMI over time. It is not standard practice to assess and record whether adolescents in care were perinatally or behaviorally infected and this is a weakness as there are known differences between these sub-populations which may influence outcomes. Pregnancy status for females who were pregnant was at point of enrolment and it could not be distinguished whether the females were first diagnosed while pregnant or whether this was

their first pregnancy this too could potentially affect observed outcomes. The data quality for reporting outcomes for those disengaging in ART i.e. Stopped ART and Died was also not complete therefore impacting the study findings negatively since mortality is one of the important outcomes that would have been important to assess. In addition, 11% of records had to be excluded from the analysis due to missing unique identifier, sex and age which were important data elements to enable analysis. These excluded records were random in terms of key characteristics and geographic distribution, and not systematically different from those that were included within the analysis.

3.7. Ethical Considerations

As the study involved an analysis of routinely collected medical records that are part of the national health information system and no actual contact with the clients, there was no direct harm caused to patients. However ethical clearance and approval was sought from University of Western Cape (UWC) and from the Medical research council of Zimbabwe (MRCZ) to conduct this study. The data was abstracted with no personal identification details and serial numbers were used to differentiate the different patients by their unique identifier. Confidentiality for clients was therefore assured as there were no personal identifiers or any link to the actual patients as data was being analysed and reported. The dataset was kept in a password protected laptop in a locked cabinet. Authority was sought from the head of ministry to conduct the study using routinely collected information and permission was granted, see appendices for letters of authority (MRCZ, Ministry of Health).

Chapter 4: Results

4.1. Data cleaning

32 208 records in total for adolescents aged 10 – 19 years who were enrolled onto ART between January 2012 and March 2017 were abstracted from ePMS. 3 450 with missing unique identifier, age and sex were excluded from the analysis (Figure 2).

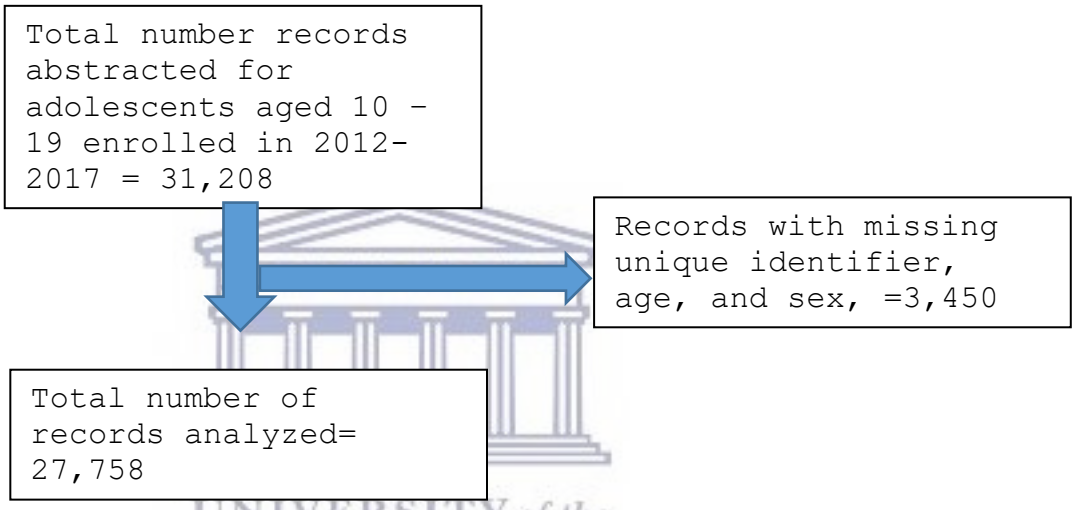

Figure 2: Total Number of Records Analysed After Data Cleaning

4.2. Baseline demographic and clinical characteristics of adolescents 10 – 19 years of age at ART initiation

Table 1: Background characteristics of adolescents initiated on ART during the period January 2012 to March 2018

	Frequency	**Percentage**	**95% CI**
Patients, n (%)			
Sex			
Male, n (%)	7945	28.6	28.1 – 29.2
Female, n (%)	19813	71.4	70.9 – 71.9
Age at enrolment, (Median (Q1-Q3))	16 (13;18)		
10 -14 years	9612	34.6	34.1 – 35.2
15 -19 years	18146	65.4	64.8 – 65.9
Pregnancy status			
Pregnant, n (%)	5685	32.9	32.2 – 33.6
Not pregnant, n (%)	11565	58.6	57.8 – 59.2
Missing	2487	12.6	
WHO Stage			

	Frequency	Percentage	95% CI
Stage 1 and 2, n (%)	18689	67.3	67.2 – 68.3
Stage 3 and 4, n (%)	8890	32.0	31.7 – 32.8
Missing	179	0.7	
Functional status at enrolment			
Work and Ambulatory, n %	27547	99.2	98.8 – 99.6
Bed ridden, n %	78	0.3	0.2 – 0.4
Missing	133	0.5	
Education level			
None	263	0.2	0.16 – 0.20
Primary level	6457	43.7	42.9 – 44.5
Secondary level	7981	54.0	53.2 – 54.8
Tertiary	80	0.5	0.4 – 0.7
Marital status, n (%)			
Married, n (%)	7952	30.7	30.2 – 31.3

Not married, n (%)	10900	42.1	41.5 – 42.7
Minor, n (%)	7039	27.2	26.6 – 27.7
Health facility level			
Quaternary, n (%)	1326	4.8	4.6 – 5.1
Tertiary, n (%)	1038	3.8	3.5 – 4.0
Secondary, n (%)	10197	36.9	36.6 – 37.5
Primary, n (%)	15087	54.6	54.0 – 55.2
Province			
Harare	3,291	11.9	11.5 - 12.3
Manicaland	2,729	9.87	9.5 - 10.2
Mashonaland Central	1,644	5.95	5.7 - 6.2
Mashonaland East	4,167	15.07	14.7 - 15.5
Mashonaland West	3,302	11.94	11.6 - 12.3
Matabeleland North	2,147	7.77	7.5 - 8.1
Matabeleland South	2,392	8.65	8.3 - 9
Midlands	3,468	12.54	12.2 - 12.9

	Frequency	Percentage	95% CI
Masvingo	3,540	12.8	12.4 - 13.2
Bulawayo	968	3.5	3.3 - 3.7
Facility distribution			
Urban, n (%)	8948	32.3	31.8 – 32.9
Peri-urban, n (%)	249	0.9	0.8 – 1.0
Rural, n (%)	18451	66.7	66.2 – 67.3

There were generally more female adolescents compared to males 71.4% (95%CI 70.9 – 71.9) vs 28.6% (95%CI 28.1 – 29.2). Median age at enrolment into ART was 16 years and the interquartile range was 13 - 18 years. Most adolescents enrolled were in late adolescents (15 – 19 years) i.e. 65.4% (95%CI 64.8 – 65.9), while 34.6% (95%CI 34.1 – 35.2) were in early adolescents (10 – 14 years). 32 percent (95% CI 32.2% - 33.6%) of females were pregnant at enrolment, 58.6% (95%CI 57.8 – 59.2) were not pregnant and 12.6% had missing data for pregnancy status.

Most adolescents were initiated ART in WHO stage I and II i.e. 67.3% (95% CI 67.2 – 68.3) and 32% (95% CI 31.7 – 32.8) were in WHO stage III and IV, WHO clinical staging data were missing for 0.7% of adolescents. More than 99% (95% CI 98.8 – 99.6) of adolescents were initiated on ART while still ambulatory and only 0.3% (95% CI 0.2 – 0.4) were bed ridden at initiation. Most of the adolescents had attained secondary school education level i.e. 54.0% (95% CI 53.2% - 54.8%), 43.7% (95% CI 42.9 – 44.5) had attained primary school education while only 0.5% (95% CI 0.4 – 0.7) had tertiary level education. Only 30.7% (95% CI 30.2 – 31.3) were married at the time of ART initiation, 42.1% (95% CI 41.5 – 42.7) were not married and 27.2% (95% CI 26.6 – 27.7) were still minors and therefore not expected to be married according to Zimbabwean law.

The majority [54.6% (95% CI 54.0 – 55.2)] of the adolescents were initiated ART at the primary level health care facilities, followed by secondary level facilities [36.9% (95% CI 36.6 – 37.5)] with tertiary and quaternary level facilities contributing 4.8% and 3.8% respectively. Mashonaland East Province contributed the largest number of adolescents with 15% (95% CI 14.7 -15.5) of adolescents being initiated in Mashonaland East and Bulawayo metropolitan province had the least contribution of only 3.5% (95% CI 3.3 – 3.7). 66.7% (95% CI 66.2 – 67.3) of adolescents were initiated in rural facilities, 32.3% (95% CI 31.8 – 32.9) were at urban facilities while only 0.9% (95% CI 0.8 – 1.0) were at peri-urban facilities. Table 4.1 summarizes the baseline demographic and Clinical characteristics.

4.3. Adolescent on ART outcomes at 3, 6, 12, 24, 36, 48 Up to 60 months

Figure 3 shows outcomes of adolescents on ART over time up to 60 months post initiation,

retention in care was 90.7%, 87%, 82.7%, 76.2%, 69.7%, 63.1% and 53.8% respectively at 3, 6, 12, 24, 36, 48- and 60-months post ART initiation. The balance of non-retained clients is reported as lost to follow up with mortality, stopped ART and transfer out being almost zero across the follow up periods. The actual figures are shown in table 2 after the graph below.

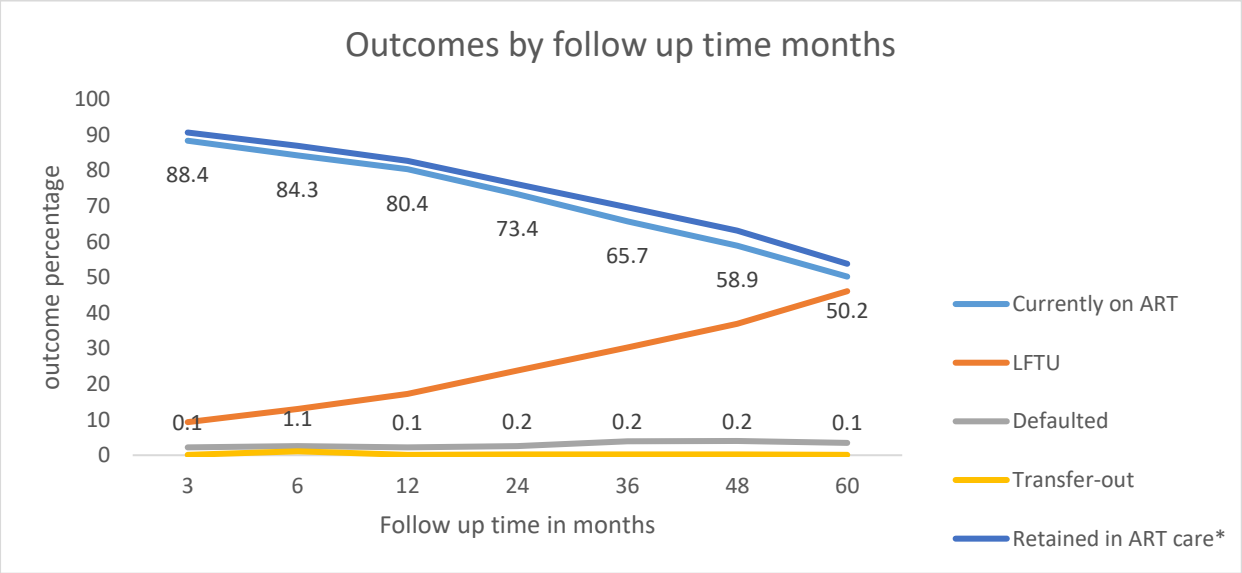

Figure 3: Outcomes of Adolescents Initiated onto ART between January 2012 and March 2017 depicted by follow up months

Table 2: Overall Retention Frequencies by time of follow up

Outcome	Follow-up time (in months)													
	3 months		6 months		12 months		24 months		36 months		48 months		60 months	
	Frequency	Total	Frequency	Total	Frequency	Total	Frequency	Total	Frequency	Total	Frequency	Total	Frequency	Total
Currently on ART	23,818	26,946	21,496	25,489	18,338	22,819	13,561	18,473	9,228	14,055	5,762	9,779	3,637	7,242
Died	0	26,946	0	25,489	0	22,819	0	18,473	0	14,055	0	9,779	0	7,242
LFTU	2,510	26,946	3,312	25,489	3,936	22,819	4,390	18,473	4,256	14,055	3,606	9,779	3,341	7,242
Defaulted	597	26,946	651	25,489	510	22,819	0	18,473	543	14,055	395	9,779	254	7,242
Stopped ART	-	26,946	1	25,489	1	22,819		18,473		14,055		9,779		7,242
Transfer-out	21	26,946	29	25,489	34	22,819	34	18,473	33	14,055	16	9,779	10	7,242
Retained in ART care*	24,415	26,925	22,147	25,460	18,848	22,785	14,049	18,439	9,771	14,022	6,157	9,763	3,891	7,232

**Retained in ART care consists of those who were alive on ART or defaulted ART at the respective follow-up time points and also excludes transfers-out from the denominator and the numerator due to uncertainty of these patients being alive and on ART at health facilities they transferred into.*

Male adolescents had better retention rates when compared to female adolescents as they had retention consistently higher by 5-8% across the follow up period with the gap widening with time on ART. Both males and females showed a decline in retention and 60 months their retention rates were below 50%. This is summarized in Figure 3.

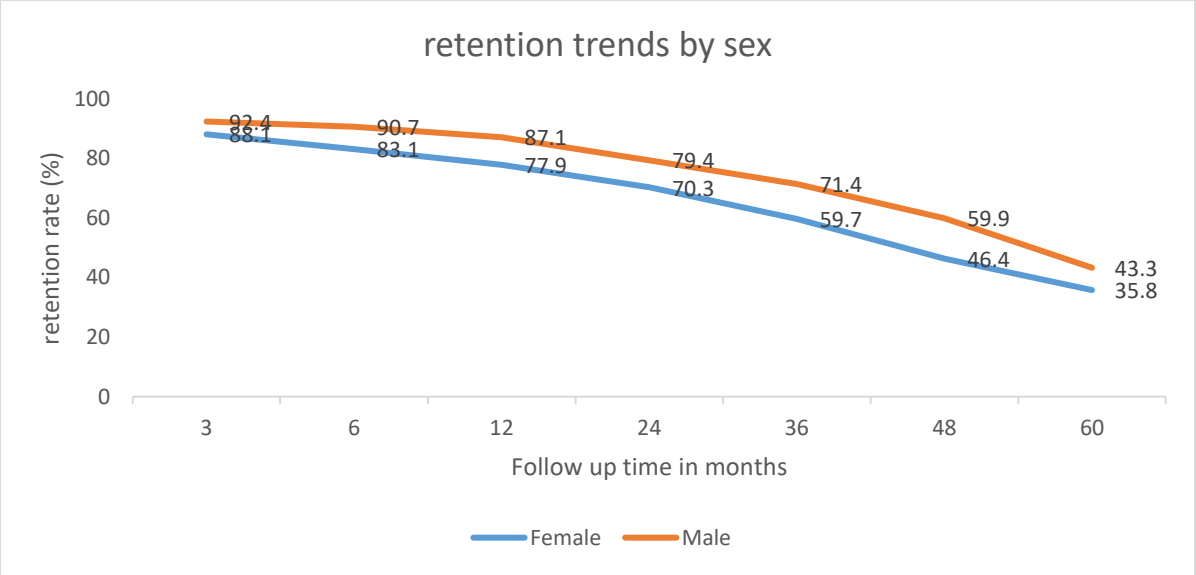

Figure 4: A comparison of retention rates over time between female and male adolescents up to 60 months post ART initiation

Figure 5 below shows that younger adolescents (10 -14 years) had better retention rates when compared to older adolescents (15 – 19 years) across the follow up time frame. The differences in retention were by 3 – 10% with the biggest difference being at 48 months after ART initiation. However, for both age groups there is a worrying steep decline in retention with retention rates below 50% for both age groups by 60 months.

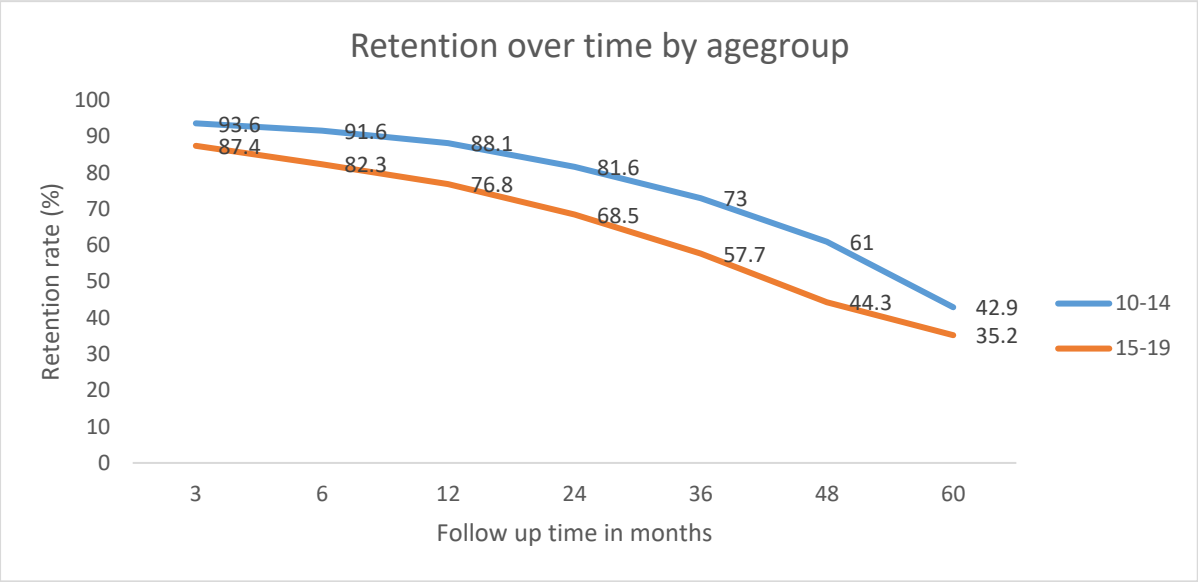

Figure 5 : A comparison of retention rates over time between adolescents aged 10 -14 years and those aged 15 – 19 years up to 60 months post ART initiation

Female adolescents who were not pregnant at ART initiation had better retention rates over time when compared to those who were pregnant at initiation. The differences between these two groups widens with increasing time with the most marked difference being seen at 48 months where there was a difference of over 20% between these 2 groups. By 60 months after initiation only 30% of adolescent girls who were initiated during pregnancy and 42% of those who were not pregnant at initiation were still on treatment as summarized in Figure 6 below.

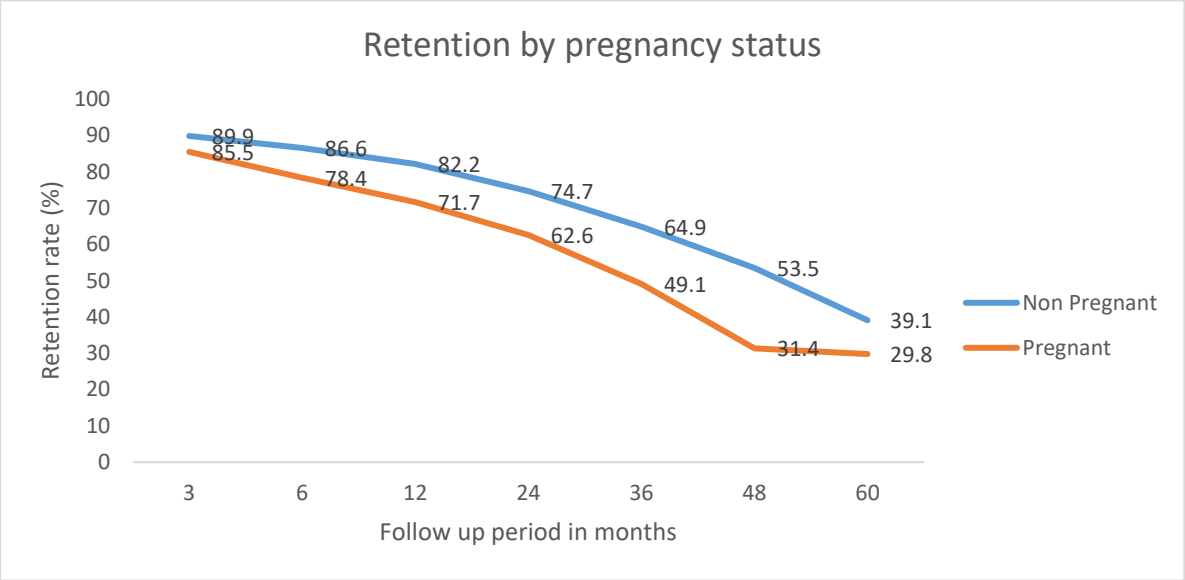

***Figure 6**: A comparison of retention rates for pregnant females and non-pregnant females over the follow up period of 60 months post ART initiation*

4.3. Factors associated with retention in care

Table 4 below summarizes the factors that were associated with retention in care at 12 months after ART initiation.

Having secondary school education at enrolment into ART was the only factor associated with increased retention, while older age at enrolment, pregnancy at enrolment for female adolescents, enrolment at a secondary level facility and enrolment at a facility located in the rural area were associated with a lesser probability to be retained in care at 12 months after ART initiation. Adolescents with secondary school education had a risk ratio of 1.14 (CI 1.02 – 1.28; P- 0.017) in comparison with those with no education at enrolment thus those with secondary school education were 1.14 times more likely to be retained in care compared to those with no education at enrolment. No statistical differences were noted for those with primary or tertiary education.

Older adolescents aged 15 – 19 years at initiation had a risk ratio of 0.89 (CI 0.85 – 0.92; P < 0.001) compared to younger adolescents aged 10 – 14 years at time of enrolment onto ART thus they were less likely to be retained in care at 12 months after initiation in comparison to the younger adolescents. The risk ratio for female adolescents who were initiated on ART while pregnant was 0.91 (C1 0.88 – 0.95; P < 0.001) compared to non-pregnant adolescent girls at enrolment 12 months after ART initiation. Adolescents enrolled at the secondary level facilities had a reduced likelihood to be retained on ART when compared to those initiated at the primary level facilities (risk ratio = 0.90; CI 0.88 – 0.93; p < 0.001), those initiated at tertiary level facilities also had a reduced probability to be retained on ART at 12 months when compared to those initiating at primary level facilities (risk ratio = 0.90; CI 0.83 - 0.97; P – 0.007). Differences with those initiating ART at quaternary level were not statistically significant. Adolescents who were initiated at a facility located in the rural areas were 0.96 (CI 0.94 – 0.99; P – 0.02) times less likely to be retained in care compared to those initiating at urban facilities. No significant differences were noted for those initiating at a peri-urban facility.

Table 3: Predictors of ART Outcome at 12 Months after ART Initiation

Characteristic	Number on ART	Number (%) Retained	Unadjusted RR (95% CI)	P value	Adjusted RR (95% CI)	P value
Age, n						
10 – 14 years	9426	7072 (75)	Ref		ref	
15 – 19 years	17499	11492(65.7)	0.87 (0.86 – 0.88)	0.000	**0.89 (0.85 – 0.92)**	**0.000**
Gender, n						
Female	19179	12896 (67.2)	ref		ref	
Male	7746	5668 (73.7)	1.08 (1.07 – 1.10)	0.000	1.07 (0.86 – 1.33)	0.541
Marital status, n						
Not married	13593	9228 (67.9)	ref		ref	
Married	7693	5063 (65.8)	0.94 (0.92 – 0.95)	0.000	1.01 (0.98 – 1.04)	0.642
Pregnancy status (females), n						
Not Pregnant	11257	7667 (68.1)	ref		ref	
Pregnant	3485	5523 (78.0)	0.90 (.088 – 0.92)	0.000	**0.91 (0.88 – 0.94)**	**0.000**
Facility level, n						
Primary level	14639	10085 (68.9)	ref		ref	
Secondary level	9957	6769 (68.0)	0.93 (0.92 – 0.95)	0.000	**0.90 (0.88 – 0.93)**	**0.000**

Characteristic	Number on ART	Number (%) Retained	Unadjusted RR (95% CI)	P value	Adjusted RR (95% CI)	P value
Tertiary level	1015	708 (69.8)	0.94 (0.91 – 0.96)	0.000	**0.90 (0.83 - 0.97)**	**0.007**
Quaternary level	1314	1002 (80.9)	0.99 (0.98 – 1.02)	0.856	1.03 (0.97 – 1.09)	0.294
Facility distribution, n						
Urban	8698	6020 (69.2)	ref		ref	
Peri-urban	237	197 (83.1)	1.11 (1.05 – 1.16)	0.000	1.13 (1.02 – 1.24)	**0.011**
Rural	17990	12347 (68.6)	1.0 (0.99 – 1.02)	0.597	**0.96 (0.94 – 0.99)**	**0.020**
WHO clinical stage, n						
Stage 1 & 2	17989	12293 (68.3)	ref		ref	
Stage 3 & 4	8760	6155 (70.3)	1.03 (1.02 – 1.04)	0.000	0.99 (0.97 – 1.02)	0.490
Functional status at enrolment						
Work and Ambulatory, n %	26716	18438 (69.0)	ref		ref	
Bed ridden, n %	77	44 (57.1)	0.81 (0.70 – 0.93)	0.004	0.83 (0.61 – 1.14)	0.272
Education level						
None	262	171 (65.3)	ref		ref	

Characteristic	Number on ART	Number (%) Retained	Unadjusted RR (95% CI)	P value	Adjusted RR (95% CI)	P value
Primary level	6414	4647 (72.5)	1.09 (1.01 – 1.16)	0.013	1.1 (0.99 – 1.23)	0.082
Secondary level	7917	5338 (67.4)	1.06 (0.99 – 1.14)	0.090	**1.14 (1.02 – 1.28)**	**0.017**
Tertiary	80	47 (58.8)	1.12 (1.01 – 1.24)	0.024	1.16 (0.98 – 1.37)	0.079

NB. what is in bold is statistically significant

Chapter 5: Discussion

5.1. Sociodemographic characteristics of adolescents enrolling onto ART

There are more female adolescents than males enrolled onto ART due to differences in prevalence in the 15 – 19-year age group causing the overall HIV prevalence for adolescents to be disproportionately higher for girls compared to boys and in general girls' access services more frequently than boys (WHO, 2019). Findings of the Zimbabwe Demographic and health Survey (ZDHS) and the Zimbabwe Population based HIV Impact Assessment (ZIMPHIA) collaborate these findings although differences noted within the ZDHS were not as marked as those seen in the All -in assessment and the ZIMPHIA (Ministry of Health and Child Care, 2015; Zimbabwe National Statistics Agency, 2015; Zimbabwe Ministry of Health and Child Care *et al.*, 2016). This pattern of distribution between girls and boys in HIV care was also found in other studies in sub-Saharan Africa including studies done in Uganda, South Africa and another specific one in Zimbabwe (Nglazi *et al.*, 2012; Shroufi *et al.*, 2013; Okoboi *et al.*, 2016).

Median age at enrolment was 16 years of age this was higher than the median age previously found by Shroufi et al. in another study done to compare treatment outcomes of HIV infected adolescents with those of adults at a Zimbabwean central hospital in 2010 which was 13.3 years. This difference may be due to the location of the central hospital in the capital city an urban area where access to health services and health related information is better therefore leading to earlier enrolment into care unlike the analyzed dataset which includes rural based facilities with reduced access leading to late enrolment in care. A Kenyan study found a mean age of 16.8 in a study comparing survival on ART for children, adolescents and adults (Moshago, Haile and Enkusilasie, 2014). The distribution between early adolescents (10 – 14 years) compared to late adolescents (15 – 19 years) was as expected as data within the country showed that prevalence of HIV in late adolescents is higher than in early adolescents (Zimbabwe Ministry of Health and Child Care *et al.*, 2016). Most of the adolescents were in secondary school education level followed by primary school education level, with very few being at tertiary level. This distribution is expected as the age of entry into secondary school in Zimbabwe is 13 years of age, statistics however show that though attendance at primary level is quite high at 93.3% it drops drastically to 47.7% at secondary school level (ZIMSTAT,

2014). In this study 54% of adolescents enrolled were at secondary school level, this is an encouraging finding as studies have shown keeping children in school especially girls has a protective effect towards HIV acquisition(Stoner *et al.*, 2017; Marie *et al.*, 2018) .

The number of female adolescents who were pregnant at enrolment was quite high with 32% of females being pregnant at enrolment. This is however in keeping with recent statistics that show that the adolescent birth rate in Zimbabwe is 120/1000 and has been on the increase and births by age of 18 were sitting at 22.4% for the general population (ZIMSTAT, 2014). The percentage is higher for adolescents enrolling in ART than what is in the general population as this population also includes adolescents who are sexually active and have acquired HIV infection and are more likely to be sexually active compared to the general adolescent. This is in keeping with the proportion of adolescents that were married at initiation which was around 30% of adolescents above 16 years of age the 2015 Multiple indicator survey reported that 24.5% of young women aged 15 -19 years were in a union compared to 1% for males, additionally 5% of women 15 – 24 years that were in union had married before the age of 15 years (ZIMSTAT, 2014). These statistics show an alarming high number of early marriages and teenage pregnancies which have been shown to contribute to the increased acquisition of HIV among adolescent girls and young women in Zimbabwe contributing to the high HIV prevalence among girls (PEPFAR and CDC, 2014).

5.2. Clinical Characteristics

Approximately a third of the clients enrolled were WHO clinical stage I and II this was similar to findings of the Kenyan and Ugandan studies however in a number of studies adolescents were typically enrolled onto ART late in stage III and IV (Massavon *et al.*, 2014; Moshago, Haile and Enkusilasie, 2014; Koech *et al.*, 2016). This finding also differed with the study done at a Zimbabwe central hospital in 2010 where almost 80% of enrolled clients were in stage III and IV, this difference may be attributed to the fact that our study involved 400 hundred facilities at different levels of the health system where as the other study was done at a central hospital which is a referral institution and most patients initiated at a referral hospital would be complicated and presenting with advanced disease (Shroufi *et al.*, 2013). Most of the

adolescents were ambulatory and able to work at enrolment and this was similar to the study done in Ethiopia where the majority of adolescents were either ambulatory or able to work at initiation (Moshago, Haile and Enkusilasie, 2014). The data for CD4 cell count, weight and height on initiation was largely incomplete and the numbers were too small to analyze, this points to an issue with data quality as CD4 count investigation and anthropometric measurements were not being updated at enrolment despite physical examination being done at every visit and evidence from program reports showing CD4 coverage to be high especially prior to 2017 when CD4 count was used as an eligibility criteria for ART initiation (World Health Organization, 2011; MOHCC, 2014).

5.3. Level of care and geographic location of facility

The HIV program in Zimbabwe is largely decentralized and this is evident in the findings as 54% of clients were initiated at primary level facilities, this proportion however is a bit lower than expected as quite a considerable number of adolescents were initiated at secondary level pointing towards lack of confidence among health care workers in the management of adolescents infected with HIV (Ministry of Health and Child Care, 2015; MOHCC, 2015; UNICEF, 2015a). Most of the facilities are located in the rural areas and accounted for 67% of adolescent ART initiation, findings are in keeping with the general population distribution in the country which shows that 67% of all people living in Zimbabwe are located in rural areas (Zimstat, 2012). The distribution of adolescents across the provinces was somewhat similar to previous findings with Midlands, Masvingo and Harare being found to have been contributing a large number of adolescents both in the All-in assessment and the finding of our study. However, Mashonaland East and Mashonaland West which contributed high proportions of adolescents within our study were not collaborated in the All-in assessment, this may point to the distribution of the ePMS sites being more in these provinces compared to other provinces(Ministry of Health and Child Care, 2015). Bulawayo contributed the least to adolescents initiated on ART and this finding was similar to what was found in the ART outcomes assessment (Ministry of Health and Child Care (MOHCC) and National AIDS Council (NAC), 2016).

5.4. Adolescent outcomes on ART

ART outcomes for adolescents have generally been shown to be poor however studies in Zimbabwe have shown retention rates for adolescents were comparable to adults. Our study did not compare outcomes across different age groups however retention rates at 3, 6, 12 and 24 months for adolescents were more or less similar to what has been found in other studies in Zimbabwe including the ART outcomes assessment (Shroufi *et al.*, 2013; UNAIDS, 2013; Ministry of Health and Child Care (MOHCC) and National AIDS Council (NAC), 2016). Most of the adolescents that were not in care however were mostly reported as lost to follow up (LTFU) with other outcomes such as death and stopped ART having negligible figures. This finding shows that the outcome of patients not continuing in care is largely unknow as most of them are just recorded as lost to follow up. This points to gaps in data and information systems especially for patients disengaging in care as the outcome events happen away from facilities i.e. death and stopping treatment and as such are difficult to report at a largely health facility dependent information reporting system. This also points to challenges in client tracking systems which was found to be a factor contributing to attrition even prior to ART initiation in another assessment (World Health Organization, 2011; Bergmann, Heather, Heather Pitorak, 2013). Although graph 4.2 seems to show that males had better retention than females after multivariate analysis there were no statistically significant differences between males and females. Other studies have also not picked up any significant differences on retention among males and females (Matyanga *et al.*, 2016).

5.5. Factors associated with retention in care

Older adolescents were less likely to be retained in care when compared to younger adolescents, these findings concur with several other studies done in Uganda, Kenya and South Africa (Koech *et al.*, 2016; Maskew *et al.*, 2016; Okoboi *et al.*, 2016). In a different setting in the USA younger adolescents were the ones less likely to adhere to treatment compared to older adolescents (Murphy *et al.*, 2005). The increased risk of loss to follow up for older adolescents is however supported by changes in brain structure and cognitive development in older adolescents which is responsible for increased risk taking and rebellion (Sawyer *et al.*, 2012).

This age group being the transition age to adulthood as the legal age of majority in Zimbabwe is 18 years and age of sexual consent is 16 years is associated with increased mobility due to transition out of school towards a search for livelihoods and better life opportunities (Bygrave *et al.*, 2012; Sawyer *et al.*, 2012; Zimbabwe, 2013). This mobility may cause the adolescents to leave their area of usual residence without notifying the health staff to obtain an official transfer while others may transfer to another facility silently and others may completely stop treatment. Younger adolescents maybe more likely to be retained as they may still be in the care of their caregivers and rely on the caregiver for clinic visits therefore are more likely to be retained if they have a supportive caregiver(Mavhu *et al.*, 2013; Nabukeera-Barungi *et al.*, 2015). Treatment fatigue with age for those who start ART early may contribute to the observed poorer retention among older adolescents as studies have shown that adolescents are likely to develop treatment fatigue due to long term treatment

Those who had secondary school education were more likely to be retained this finding was similar to what was found in the ART outcomes assessment where secondary and tertiary education were associated with 2 times likelihood of being retained in care (Ministry of Health and Child Care (MOHCC) and National AIDS Council (NAC), 2016). This may suggest that a higher education level brings increased understanding of the benefits of ART leading to better retention. This is supported by Sawyer et al who suggest that access to education may enhance decision making capabilities among adolescents (Sawyer *et al.*, 2012).

Pregnancy was shown to be associated with poorer retention in care among adolescents although data from the ART outcomes assessment shows poorer retention among pregnant woman there is no accessible data on retention of pregnant adolescents in Zimbabwe. It can however be extrapolated that they would have poorer retention being adolescent and pregnant, a study in Zimbabwe showed that pregnant adolescents were unlikely to know their HIV status at ANC booking and lower PMTCT service uptake compared to adults though findings were not statistically significant. These findings were also reported for other sub-Saharan countries and summarized in a commentary by Callahan et al. (Ministry of Health and Child Care (MOHCC) and National AIDS Council (NAC), 2016; Callahan *et al.*, 2017; Musarandega *et al.*, 2017). Pregnant adolescents are identified as an important sub-population among adolescents that may require even more tailored interventions to improve not only their

outcomes but also the outcomes of their infants.

Initiating ART at secondary and tertiary level facilities was associated with poorer retention, similarly Apollo et al also found that initiating ART in a referral site was associated with increased attrition. This finding was also the same as in the ART outcomes assessment (Mutasa-Apollo *et al.*, 2014; Ministry of Health and Child Care (MOHCC) and National AIDS Council (NAC), 2016). This may be due to patients initiating at a referral facility being more likely to be complicated with advanced disease and advanced disease has been shown to be associated with increased attrition in other studies (Mutasa-Apollo *et al.*, 2014; Koech *et al.*, 2016). Long travel distances may also attribute to this observed finding as patients initiating in the referral site may have been referred from another facility such that the referral hospital will not be as geographically proximal to their area of residence. Long distances have been documented as a barrier to ART retention along with long waiting times at facilities which may be the case at referral facilities (World Health Organization, 2011; Maskew *et al.*, 2016).

Adolescents in rural areas had a reduced likelihood of being retained in care however another study in Zimbabwe found that clients registered at urban sites were marginally at increased risk of attrition (Mutasa-Apollo *et al.*, 2014). A study in South Africa which was not specifically targeted at adolescents also showed that outcomes in rural facilities were comparable to urban based facilities as no significant difference in outcomes were noted (Omole and Semenya, 2016). A study in Zambia comparing treatment outcomes of paediatric patients on ART in rural facilities with those in urban facilities showed that lost to follow up increased in rural areas over time contributing to lower retention rates although overall care for pediatrics improved in rural facilities (Sutcliffe *et al.*, 2010). Poorer retention in rural areas may be associated with accessibility of health facilities as transportation networks are not as developed in rural areas compared to urban areas.

6.0. Conclusion and Recommendations

6.1 Conclusion

This study focused on a population that is becoming increasingly important for control of the HIV epidemic. The availability of program data that is nationally representative presents an opportunity to measure progress and identify gaps for informing programmatic improvements. This study has added to the body of nationally available evidence and shows that there is still more work to be done with improving adolescent retention in care as it is still sub-optimal. Secondary school education level was associated with an increased chance to be retained in care. Older age (15 – 19 years), pregnancy, referral level facilities and rural located facilities were associated with poorer retention rates among adolescents, reasons for poorer retention associated with these variables need to be further investigated to come up with interventions targeted at improving retention for the subpopulations with these characteristics. Even the variables associated with better retention also need to be further investigated and used as a basis for interventions towards improving retention.

6.2. Recommendations

6.2.1. Improving data quality

Most reports have pointed out the need for good information systems to track patient outcomes over time, suggestions have been made to make use of electronic systems although these need to be implemented together with systems to ensure data quality and completeness (World Health Organization, 2011; Bergmann, Heather, Heather Pitorak, 2013). Pertaining to adolescent data most countries do not have disaggregated adolescent data for program decision making and these disaggregation are important as the study findings show disparities in gender and age (Idele *et al.*, 2014; Ministry of Health and Child Care, 2015; UNICEF, 2015a). As such the ePMS system has to be improved to reduce incomplete data entry installation of checks and balances that flag a reminder on crucial data elements that need to be entered at each visit and

at determined intervals should be installed. An analysis of why some data fields are not being updated while others are being updated may need to be carried out at selected sites and remedial actions taken to close the gap exactly where it is happening in the chain from the clinical consultation to the time data is entered in the system. Supervision of the process from consultation to data entry on a regular basis and checking of data for completion should be instituted by the nurse in charge of the ART clinic.

6.2.2. Improving outcomes

The first thing which will be crucial is to improve reporting of outcomes, the AIDS and TB unit developed a defaulter tracing tool that stipulates a client is followed up through telephone or the use of community health workers once they have missed a single appointment this system enables patients to be brought back before they have fully disengaged from care. This follow up procedure if fully implemented will enable the reporting of adolescents that self-transfer. It will also assist with processing transfers for those adolescents who are moving as they transition out of school to seek employment and other opportunities; this system will also enable the reporting of adolescents that may have demised if implemented well. The proper outcomes of followed up clients would then need to be updated in the ePMS. Although the SOP and tools for the defaulter tracing are available, they are not being fully implemented at all sites. As a recommendation going forwards the defaulter tracing needs to be rolled out to all sites with district and provincial managers monitoring its implementation on a regular basis. Use of technologies such as SMS reminders have also been shown to improve retention and should be considered especially for adolescents.

6.2.3. Facilitators and barriers of retention

Tailored adolescent responsive services have been shown to improve retention in adolescents on ART (Ruria *et al.*, 2017). There is need to come up with differentiated approaches targeting older adolescents, pregnant adolescents, adolescents with advanced disease seen at referral facilities and those in rural areas. The adolescents need to be consulted on what ideal tailored service delivery looks like to them and tailored service delivery models can be designed for

specific sub-populations of adolescents and the general adolescents. Involvement of adolescents in decision making for their care has been suggested as a good practice (UNICEF, 2015a). Community based support for the adolescents as well as the care giver has also been shown to improve outcomes by reducing social isolation and stigma, and imparting coping mechanisms (Laughlin, Wyatt and Ware, 2012; Ferrand *et al.*, 2017; PEPFAR and Foundation, 2017). Zimbabwe has been implementing a community-based peer led support by adolescents and within DREAMS districts this is coupled with care giver support, scale up of these interventions to all sites should be prioritized to improve treatment outcomes of adolescents on ART.

Keeping children in school has been shown to be associated with better outcomes, empowering adolescents with education is important in improving treatment outcomes for adolescents. This requires a multi-sectoral approach with other ministries and departments to ensure adolescents stay in school and attain higher levels of education. This is something that cannot be achieved overnight however advocacy towards this vision should start with creating a multi-sectoral forum where the various ministries and departments sit together to discuss such issues. The provinces with better outcomes should document the best practices that have contributed to better outcomes for sharing with other provinces this creates a platform for learning from each other and exchange of ideas.

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Appendix 1: MRCZ Approval;

Telephone: 791792/791193
Telefax: (263) - 4 - 790715
E-mail: mrcz@mrcz.org.zw
Website: http://www.mrcz.org.zw

Medical Research Council of Zimbabwe
Josiah Tongogara / Mazoe Street
P. O. Box CY 573
Causeway
Harare

APPROVAL LETTER

REF: MRCZ/B/1304 **14 June, 2017**

Dr.A.P.Rudo Kuwengwa
University of Western Cape
Private Bag X 17
Bellville 7535
South Africa

RE: An Assessment of the Characteristics of Adolescents at Enrolment into Anti-retroviral Therapy, and Factors Influencing their Retention Rates in Zimbabwe

Thank you for the above titled proposal that you submitted to the Medical Research Council of Zimbabwe (MRCZ) for review. Please be advised that the Medical Research Council of Zimbabwe has **reviewed** and **approved** your application to conduct the above titled study. This is based on the following documents that were submitted to the MRCZ for review:

a) Study proposal
b) Data extraction tools

APPROVAL NUMBER : MRCZ/B/1304
This number should be used on all correspondence, consent forms and documents as appropriate.

- **APPROVAL DATE : 04 June, 2017**
- **TYPE OF MEETING : Expedited**
- **EXPIRATION DATE : 03 June, 2018**
  After this date, this project may only continue upon renewal. For purposes of renewal, a progress report on a standard form obtainable from the MRCZ Offices should be submitted one month before the expiration date for continuing review.
- **SERIOUS ADVERSE EVENT REPORTING**: All serious problems having to do with subject safety must be reported to the Institutional Ethical Review Committee (IERC) as well as the MRCZ within 3 working days using standard forms obtainable from the MRCZ Offices.
- **MODIFICATIONS**: Prior MRCZ and IERC approval using standard forms obtainable from the MRCZ Offices is required before implementing any changes in the Protocol (including changes in the consent documents).
- **TERMINATION OF STUDY**: On termination of a study, a report has to be submitted to the MRCZ using standard forms obtainable from the MRCZ Offices.
- **QUESTIONS**: Please contact the MRCZ on Telephone No. (04) 791792, 791193 or by e-mail on mrcz@mrcz.org.zw.

Other

- Please be reminded to send in copies of your research results for our records as well as for Health Research Database.
- You're also encouraged to submit electronic copies of your publications in peer-reviewed journals that may emanate from this study.

Yours Faithfully

.....

MRCZ SECRETARIAT
FOR CHAIRPERSON
MEDICAL RESEARCH COUNCIL OF ZIMBABWE

MEDICAL RESEARCH COUNCIL OF ZIMBABWE
2017 -06- 14
APPROVED
P.O. BOX CY 573 CAUSEWAY, HARARE

PROMOTING THE ETHICAL CONDUCT OF HEALTH RESEARCH

Appendix 2: MoHCC Mini Thesis Research Study Approval

Telephone 730011

Telegraphic Address
"MEDICUS", Harare
Fax: 729154/793634 (702293 FHP)
Telex: MEDICUS 22211ZW

ZIMBABWE

Reference:
MINISTRY OF HEALTH
AND CHILD CARE
P.O. Box CY1122
Causeway
Zimbabwe

12 April 2017

To: The Director AIDS and TB Programmes

Dear Dr Owen Mugurungi

RE: APPROVAL TO CARRY OUT SECONDARY DATA ANALYSIS ON THE ELECTRONIC PATIENT MONITORING SYSTEM (EPMS) TO ASSESS THE CHARACTERISTICS OF ADOLESCENTS AT ENROLMENT INTO ANTI-RETROVIRAL THERAPY AND THE FACTORS INFLUENCING THEIR RETENTION FOR DR R KUWENGWA

This letter serves to confirm approval for Dr R Kuwengwa to carry out a secondary data analysis on the electronic Patient Monitoring System as a requirement to fulfilling her Masters Degree studies

This approval is done with the expectation that findings from this study will be shared with the Ministry of Health and Child Care, AIDS and TB programmes.

Thank you for your support

SECRETARY FOR HEALTH & C/C
(PRINCIPAL DIRECTOR
PREVENTIVE SERVICES)
19 APR 2017
P.O. BOX CY 1122, CAUSEWAY
ZIMBABWE

Regards

Brigadier General (Dr) G. Gwinji
SECRETARY FOR HEALTH AND CHILD CARE

Appendix 3: UWC Ethics approval letter

UNIVERSITY of the WESTERN CAPE

OFFICE OF THE DIRECTOR: RESEARCH
RESEARCH AND INNOVATION DIVISION

Private Bag X17, Bellville 7535
South Africa
T: +27 21 959 2988/2948
F: +27 21 959 3170
E: research-ethics@uwc.ac.za
www.uwc.ac.za

19 January 2017

Ms R Kuwenga
School of Public Health
Faculty of Community and Health Sciences

Ethics Reference Number: BM/17/1/32

Project Title: An assessment of the characteristics of adolescents in enrolment into anti-retroviral therapy, and factors influencing their retention rates in Zimbabwe.

Approval Period: 15 December 2016 – 15 December 2017

I hereby certify that the Biomedical Science Research Ethics Committee of the University of the Western Cape approved the scientific methodology and ethics of the above mentioned research project.

Any amendments, extension or other modifications to the protocol must be submitted to the Ethics Committee for approval. Please remember to submit a progress report in good time for annual renewal.

The Committee must be informed of any serious adverse event and/or termination of the study.

Ms Patricia Josias
Research Ethics Committee Officer
University of the Western Cape

PROVISIONAL REC NUMBER -130416-050

FROM HOPE TO ACTION THROUGH KNOWLEDGE.