UNIVERSITY OF ZAMBIA

SCHOOL OF MEDICINE

DEPARTMENT OF COMMUNITY MEDICINE

Social and Clinical Attributes of Patients who Restart Antiretroviral Therapy at 5 ART Centers in Central and Copperbelt provinces of Zambia

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Master of Public Health-Health Promotion

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DECLARATION

I Chama Mulubwa declare that this dissertation submitted hereby for the Degree of Masters of Public Health (Health Promotion) is my own work and has not been submitted either wholly or in part to for another degree to this or any other University or Institution of higher education.

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DEDICATION

This piece of work is dedicated to my beloved mother Mrs. Christine Bwalya Mulubwaand my beloved young sister Mwansa Bwalya for their relentless love and support. Always remember that “Hard Work” is another name for a miracle.

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CERTIFICATE OF APPROVAL

This Dissertation by Chama Mulubwa is approved in partial fulfilment of the requirements for the award of a Masters of Public Health (MPH) by the University of Zambia.

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ABSTRACT

Background: Treatment outcome of patients on antiretroviral therapy (ART) differ. Some patients default and restart ART. Family Health International (FHI360) in collaboration with Ministry of Health, has been supporting implementation of a program on HIV prevention, care and treatment (ART) services in Zambia and has been collecting routine data on patients who default and restart ART. This study aims to describe and determine the association between the socio-demographic and clinical characteristics of these patients.

Methods: A longitudinal retrospective analysis of data from 535 adult patients restarting ART in 2009 to 2010 and attending ART care services at 5 ART centers in the Copperbelt and Central provinces of Zambia was performed. Patients who were less than 16 years and pregnant women were excluded. To determine the relationship between the socio-demographic characteristic and CD4 cell count over time, quantile regression models were used.

Results: A total of 535 patients adults restarted ART of which 303(56.6%) were female. The proportion of patients that restarted was found to be 21.1%. Most of the patients who restarted ART were above the age of 35 years and had the mean weight of 55.5Kgs. A higher proportion of patients were married (60%, n=321), had attained the highest grade 1-12 (61.1%, n=327) and were either unemployed (35.5% n=190) or self-employed (36.4%, n=195). Female gender had a higher CD4 count by 22 at 6 months and patients in self and formal employment showed an increase in CD4 count. Baseline CD4 count, type of treatment, WHO staging, total duration on treatment, duration lost to follow-up (LTFU) and duration before defaulting were found to be strong predictors of CD4 cell count at 6, 12, 18 and 24 months after restarting ART.

Conclusion: Gender, age of the patient and occupation were the only socio-demographic characteristics predicting CD4 count. The predictors of CD4 count in patients who restart ART are similar to the predictors of CD4 count of patients newly initiated on ART.

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LIST OF ABBREVIATIONS

AIDS – Acquired immune Deficiency Syndrome

ART- Antiretroviral therapy

ARV's- Antiretroviral drugs

DMO- District Medical Officer

HAART- Highly active antiretroviral therapy

HIV- Human Immunodeficiency Virus

LTFU- Loss/ Lost to follow up

MOH- Ministry of Health

PEPFAR-Presidents emergency plan for AIDS Relief

PLHIV- People Living with Human Immunodeficiency Virus

WHO- World Health Organization

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1.0 CHAPTER ONE

1.0 Background

Antiretroviral therapy (ART) has been an essential and vital part of the fight against Human Immunodeficiency Virus (HIV) and Acquired Immunodeficiency Syndrome (AIDS), sustaining human lives for people living with HIV (PLHIV) and preventing HIV/AIDS morbidity and mortality (Piot and Coll Seck, 2001). Standard ART consists of a combination of at least three antiretroviral (ARV) drugs to maximally suppress the HIV virus and stop progression of HIV disease (McGuire et al., 2012).

Early diagnosis and treatment of HIV increases the chance of survival of the patient if the patient is started on ART. As a result, there has been in the last decade, a rapid scale up of ART programs in developing countries largely supported by the World Health Organization and the United States President's Emergency plan for AIDS Relief (Egger et al., 2011, World Health Organisation Report, 2011). While benefits and success of ART scale up has been widely acknowledged, retaining patients in care remain a well-documented challenge globally (Odage et al., 2012) with some people still dropping out of treatment program and risking drug resistance.

In a study done in South Africa, 86% of patients were retained in ART at 6 months, 70% at the end of the 12 months and 60% at 24 months (Fox and Rosen, 2010, Rosen et al., 2007). In another study done in Zambia, 75% of the patients were retained at 12 months and 67% at 24 months (Musheke et al., 2012). Further, a study from Nigeriareported 60% of patients retained in ART care after 2 years of initiation (Odage et al., 2012).

A combination of social, economic and structural factors contribute to retention as well as attrition in ART programs in Sub-Saharan Africa. These factors include direct and indirect costs, poverty, adverse effects of drug, non-disclosure, waiting time, alcohol abuse and use of traditional medicine (Murray et al., 2009). However, the outcomes of patients who re-start ART after defaulting treatment has not received much attention.

Patient retention is a public Health problem because of the risk of HIV related drug resistance and poor patient health outcome (Zulu et al., 2004). There is paucity of published literature on socio-demographic and clinical characteristics of patients who restart ART in Zambia thus creating a knowledge gap. Therefore, there is need to evaluate the socio-demographic and clinical characteristics in patients who default and restart ART.

In Zambia alone, there has been a rapid increase in the number of people living with HIV (PLHIV) on treatment from 30,103 at the end of 2005 to the estimate of 283, 863 at the end of 2007 (Musheke et al., 2012, Central Statistics Office et al., 2009). Despite the provision of free treatment, some PLHIV still drop out of ART care running the risk of developing treatment failure and drug resistance.

There has been a scale up of ART in Zambia since 2004 due to funding from the US President's Emergency plan for AIDS Relief (PEPFAR) and the Global fund to fight AIDS, Tuberculosis and Malaria. The Ministry of Health rolled out free antiretroviral drugs which were accompanied by elimination of user fees for PLHIV with the goal of universal access to HIV care and treatment (Musheke et al., 2012).

This means that all services including drugs and laboratory tests are free of charge (Fox and Rosen, 2010, Rosen et al., 2007). The ART services have also been integrated into health care facilities and offered as one of the primary health care services (Bolton-Moore et al., 2007) were non physician clinicians are used to care for the PLHIV. Despite this roll out of free antiretroviral therapy, patient's retention in care in most Sub Saharan countries (Zambia Included) after 2 years is still less than 70% (Harries et al., 2010, Rosen et al., 2007, Musheke et al., 2012). This means that many patients are likely to be lost to follow-up and retaining them into care is still a challenge for Zambia.

1.1 Problem Statement

Despite integration of ART care in the primary health care services and making them free, only 70% of the Zambian patients are retained into care implying 30% of the patients are either dead, lost to follow-up (LTFU) or transferred (Rosen et al., 2007).Although, ART care centers follow up patients who default and re-start ART and the data from these long term follow up is available, little has been done to describe and document it in Zambia.

Therefore this study sought to describe and document the social and clinical attributes of patients who restarted ART treatment after having stopped treatment at five (5) ART sites in the Copperbelt and Central province of Zambia.

1.2 Study Justification

Programs for HIV prevention and care services need continuous monitoring and evaluation in the various setting they are implemented to determine their performance. In Zambia, ART activities have been carried out for over a decade. However few studies have described the

socio-demographic and clinical characteristics of patients who restart ART after defaulting. The study also aimed to determine how treatment interruption affects the response to ART treatment over time.

The findings from this study will generate knowledge about the attributes of patients who restart ART, which will add to the existing body of knowledge on ART care services. Knowing the patients who restart ART is also important in that it help to stimulate the development or adjustment of HIV/AIDS strategies to specifically include strategies that target patients who purposively default and restart ART.

The results from this study identified areas of ART care services that need improvement and thus positively influencing the planning of ART care related activities. The findings will be useful also to stakeholders especially those in public health in developing strategies that are tailored for patients who default and restart ART so as to reduce drug resistance, which may arise because of treatment interruption.

1.3 Research Question

What are the socio-demographic and clinical attributes of patients who re-start ART?

1.4.0 Study Objectives

1.4.1 General objective

To determine the characteristics and outcomes of people who re-start ART.

1.4.2 Specific Objectives

1. To determine the proportion of clients who restarted ART from January 2009 to December, 2010.
2. To describe the socio-demographic characteristics of patients who restarted ART from January 2009 to December, 2010 (Age, marital status, sex, education and employment status).
3. To describe the clinical characteristics of patients who re-start ART at 6, 12, 18 and 24 months from January 2009 to December, 2010. (Weight, WHO staging, CD4 count, type of treatment and duration of treatment).
4. To determine the association between the social demographic factors and the clinical characteristics of patients who restarted ART from January 2009 to December, 2010.

2.0 CHAPTER TWO

2.0 Literature Review

2.1 Global perspective

Access to antiretroviral therapy (ART) has improved substantially in resource-limited settings in Africa, Asia and South America where 90% of people with HIV/AIDS reside. According to the World Health Organization (WHO), more than four million people with HIV/AIDS in low and middle income countries had initiated treatment by the end of 2008 and about 5.9 million were on ART by the end of 2009 (Musheke et al., 2013). The number of patients both adults and children in need of treatment was reported at 68.4% in 2009 and has increased to 14.8 million by 2012 (World Health Organisation Report, 2012), with only 8 million people on antiretroviral treatment indicating that access to HIV treatment grew by 63% in the last two years.

Globally, antiretroviral therapy has been shown to have saved 14 million life years since 1995 in low-and-middle-income countries(World Health Organisation Report, 2012), including nine million in sub-Saharan Africa resulting in fewer deaths from AIDS-related illnesses has transformed societies: more people regaining their health, are returning to work and taking care of their families. Despite these successes, ensuring that patients remain in care over time remains one of the major challenges globally (Odage et al., 2012) as while as in resource-limited settings.

Regional perspective

In Sub-Saharan Africa, records of 2.3 million people were added to treatment programs in the last two years indicating an increase of 59%. South Africa scaled up its treatment services to reach 1.7 million people—an increase of 75% in the last two years. In Zimbabwe, 260 000 additional people accessed HIV treatment, registering a 118% expansion rate. In Kenya, 200 000 people were added—a 59% increase. Upwards of 100 000 people living with HIV were enrolled in HIV treatment in Malawi, Mozambique, Nigeria, Uganda and Zambia each. Five countries in the region have achieved more than 80% coverage of HIV treatment—Botswana, Namibia, Rwanda, Swaziland and Zambia. Outside of sub-Saharan Africa, China has increased the number of people on HIV treatment by nearly 50% in the last year alone.

2.2 ART Care

There has been a number of qualitative research done on factors associated with adherence and patient attrition in both rural and urban settings in Zambia. The most common factors include demographics and physical factors such as insufficient food and side effects, lack of support, fear of stigma/ disclosure and presence of depression and being busy with other activities such as work (Bolton-Moore et al., 2007, Cornell et al., 2010, Sasaki et al., 2012).

Such qualitative studies generate information that can help in formulating effective interventions that are socially accepted. Another study by Musheke (2013) indicated fear of being on the life-long treatment, stigma, fear of straining interpersonal relationships and inadequate/ lack of food and nutritional support as the other factors that contribute to attrition of ART patients from care (Murray et al., 2009, Musheke et al., 2013).

2.3 Loss to follow-up

Loss to follow up has been defined differently by different studies depending on the country and the ART care center. Brinkhof (2009) found that a substantial number 333 (83%) of adults 333 (83%) were LTFU in his study and could not be traced due to incorrect phone numbers and addresses(Brinkhof et al., 2009). Among those who were traced 20% to 60% had died.

Dalal (2008) on the other hand was able to trace most of the patients LTFU in the study; however, 46% of those traced had died meaning 64% were either self-transferred or quit treatment completely (Dalal et al., 2008). Dahab (2008) also reported that 41% had died, 7% had transferred and 52% had voluntarily discontinued treatment or could not be found. Another study done in the Sub-Saharan Africa reported 31% patients defaulting soon after ART initiation had died, 25% had self-transferred themselves and 44% had discontinued treatment voluntarily or could not be traced (Dahab et al., 2008).

Among the reasons for voluntary discontinuation include financial constraints, direct and indirect cost, acceptance of ART and adherence to treatment (Brinkhof et al., 2009). Other causes of LTFU were improvements in the health of the patient, adverse effects, feeling too sick to go to the clinic or being hospitalized, fear of disclosure, social isolation and exposure to discouraging social networks (Brinkhof et al., 2009, Miller et al., 2010).

Studies also found that LTFU included a sizeable group of low–risk patients who self-transferred to another ART center for convenience. Healthier individuals were more mobile

than sicker patients and more likely to leave the catchment area of the ART center in search for work (Brinkhof et al., 2009, Dalal et al., 2008). In addition providing incorrect details may indicate a group of vulnerable patients with little support and low adherence to ART drugs, hence it is more important to pay attention to the patients LTFU and those who re-start treatment.

Mortality was commonly reported to be higher in patients LTFU and mostly from AIDS defining illness differing from patients still in care and ranged from 1.4% to 12.0% at one year while those LTFU mortality ranged from 2.8% to 28.7% at one year (Brinkhof et al., 2009, Egger et al., 2011, Miller et al., 2010) also found that patients who discontinued treatment were at a higher risk of illness and death because of AIDS-relating conditions.

2.3.2 Treatment Interruption

Restarting ART can only occur after there has been treatment interruption and treatment interruption may result in viral rebound, immune decomposition and clinical progression (Kimmel et al., 2012). Potential risks and benefits of interruption vary according to a number of factors, including clinical and immunological status of the patient, the reason for the interruption, the type and duration of interruption and the presence or absence of resistant HIV at the time of interruption (World Health Organisation Report, 2011).

Treatment interruptions planned or otherwise, have been found to increase the risk of opportunistic infection and death with viral load increase and associated CD4 decline most pronounced in the first two months. Interruptions raise similar concerns with respect to drug resistance and increased mortality as sub-optimal adherence (Kranzer et al., 2010).

Temporary treatment interruption to reduce inconvenience, potential long-term toxicity, and/or overall treatment cost was considered as a strategy for patients on ART who had maintained CD4 counts above those currently recommended for initiating therapy (Carlucci et al., 2008, Kimmel et al., 2012). However it was found that treatment interruption even when planned was not safe even though reinitiation was triggered by predetermined CD4 count thresholds (Egger et al., 2002).

El-Sadr (2006) reported that interrupting treatment in patients with CD4 counts >350 cells/mm^3 and reinitiating when <250 cells/mm^3 was associated with an increased risk of disease progression and all-cause mortality compared with the trial arm of continuous ART (El-Sadr et al., 2006).The study alsoshowed that interruption was an inferior strategy such

that interventions in both trials were stopped early because of these findings (El-Sadr et al., 2006).

The same finding were evident in the DART trial which reported a twofold increase in rates of World Health Organization (WHO) Stage 4 events/deaths in the 12-week ART cycling group among African patients achieving a CD4 count >300/mm^3 compared with the continuous ART group (DART Trail team, 2008). These results show that treatment interruption for patients on ART is actually harmful for their health and reduces one's chance of survival (Egger et al., 2011).

Treatment interruption therefore results in viral rebound, acute retroviral syndrome, and increases risk of HIV transmission, decline of CD4 count, HIV disease progression or death, development of minor HIV-associated manifestations such as oral thrush, development of serious non-AIDS complications, development of drugresistance (Kimmel et al., 2012) and the need for chemoprophylaxis against opportunistic infections depending on the CD4 count (Kapata et al., 2012). Treatment interruptions often result in rapid reductions in CD4 counts which are the most likely outcomes in people who are lost to follow-up and the patients who restart ART.

Another study found that when therapy is stopped, there is an immediate increase in viral load (VL) to near the pre-treatment baseline level (Bartllet and Faculty., 2008) and a precipitous decrease in CD4+ cell count that is most marked in the first 2-3 months and followed by a far more gradual decline (Carrieri et al., 2003). They also found treatment interruption to be associated with disease progression.

2.4 Factors associated with Restarting ART

Most studies discussed above reported and defined loss to follow-up as not attending the clinic for more than 3 months and assume that loss to follow-up is a permanent event. Kranzer (2010) on the other hand argued that patients who fulfil the widely used definition LTFU at one point might resume therapy (Kranzer et al., 2010). In this cohort study, the median duration of the probability of ART defaulters to resume therapy within 3 years was 42%. Most ART cohorts report on loss to follow-up defined as not attending the clinic for more than 3 months.

Some of the factors that influence patients to re-start ART include decentralization of services, task shifting to lay care providers, longer drug refill period for stable patients and

provision of transport vouchers for those in need (Brinkhof et al., 2009). Patients who had stopped ART were also reported to re-start by Egger (2011) at the same clinic (Egger et al., 2011). The main reasons for returning to care were mostly structural and social factors relating to transportation and child care and work related responsibilities.

2.4.1 Socio demographic characteristics and re-starting ART

Kranzer (2010) found that restarting ART was also associated with age, gender, and residency, calendar year of defaulting and shorter time since defaulting (Kranzer et al., 2010). The older the patient, the more likely they were to restart treatment and the younger being more at the risk of defaulting.

Geng (2013) reported that women are more likely to default and re-start treatment although defaulter rate and transfer rate are similar for men and women. Defaulter rate was found to be 4% for men and 5% for women while transfer rate is 5% for men and 4% for women (Geng et al., 2013, Miller et al., 2010). Male sex according to Geng (2013) is associated with delay of ART initiation and most likely to be associated with delay in ART re-starting (Geng et al., 2013).

In another study, gender was found to be of influence on the health outcomes and treatment seeking behaviors, Dako-Gyeke (2010) reports more utilization of ART care services by females than in males (Dako-Gyeke et al., 2012). This suggests that gender can affect the health outcomes of people who re-start ART. Further research by Birungi (2010) also show that masculinity attribute to health outcome in that the traditional concepts of masculinity disassociate male identity from disease and portray a picture of an involvement man (Birungi and Mills, 2010), not needing health care. This can be a contributing factor even to the differences in the health of people who re-start ART (Odafe et al., 2012).

According to Kranzer(2010), patients are more likely to restart treatment within the same calendar year of defaulting treatment. As such interventions, for patients LTFU must target patients within their first year of being LTFU (Kranzer et al., 2010). Treatment resumption was more likely in women, patients more than 30 years old and within the first year of stopping therapy.

2.4.2 Clinical characteristics associated with restarting ART

The other risk factors for defaulting ART and factors associated with resuming therapy apart from the socio-demographic include, high baseline CD4 count, WHO staging and recency of ART initiation (Kranzer et al., 2010) and the first 6 months of treatment were associated with a higher risk of defaulting.

The median CD4 count of those resuming therapy was similar to their initial CD4 count prior to restarting treatment, which underscores the potentially negative impact of interruption leading to a reversal in immunological recovery made while on treatment.Industrialized settings suggest that defaulting has detrimental effects on CD4 count, viral load suppression, and clinical progression(Bartllet and Faculty., 2008). Although most programs in developing countries has reported a reduction in CD4 count for patients who restart ART, Kranzer (2010) argued that CD4 count nearest to the time of restarting was not associated with re-starting ART, although up to 14% of patients in care had interrupted treatment at least once (Kranzer et al., 2010).

Odafe (2012) and Yu (2007) also found that baseline characteristics such as CD4 count (<50cells/ul and <250cels/ul respectively) and WHO staging were highly associated with mortality. In this argument, a lower CD4 count and WHO staging of 3 and 4 was related to mortality because of the opportunistic infections that would come in due to the reduce immunity system (Yu et al., 2007). However Reddi (2007) argued that as much as WHO staging was related to mortality, CD4 baseline was not a predictor of mortality but patients with HIV and TB co infections had a high prevalence of dying (Reddi et al., 2007).

Musheke (2013) also found that the people who had stopped treatment were more likely to suffer from opportunistic infections and the common ailments were skin infections, respiratory infection and gastrointestinal tract infections and thus resorted to the use of conventional drugs got over-the-counter (Musheke et al., 2013). This does not only put these patients in the danger of HIV drug resistance but are more likely to develop drug resistance even to other antibiotics that are meant to help them. This also indicates that there is an intermittent decline in the health status and thus the self-care and faith healing strategies might not be as effective as reported.

In all the articles, there was an improvement or increase observed in the CD4 count after treatment initiation. Bolton-Moore (2007) observed the increase of 12.9% to 23.7% at 6 months, 27% at 12 months and 28% at 18 months (Bolton-Moore et al., 2007). Reddi (2007)

also recorded a mean CD4 increase of 10.25% at 6 months and 16.2% at 12 months (Reddi et al., 2007). From this it can be seen that there is an association between initiation on treatment and increase in CD4 count of which the increase can be significant even after 6 months of treatment. However, it is not known if this is the case even in people who have re-started treatment after defaulting.

CD4 was found to be associated to the health related quality of life (HRQL) (Carrieri et al., 2003). According to Cornell (2010), CD4 count was also associated with WHO staging and death. In the same study it was found that those with CD4 count >200cells/ul were more likely to be LTFU than those with CD4 count between 5-199 cells/ul (Cornell et al., 2010). This may mean that as patients attain a self-rated good health, they tend to fall out of treatment because they are asymptomatic and the "self-reported symptoms decreases" (Carrieri et al., 2003).

Weight though it is more used in children than in adults can also be an indicator of the move towards a good patient treatment outcome. In children weight for age is commonly used but is also important in adults. Carrieri (2003) recorded a significant increase in weight after one year in the participants with the standard deviation of 1.29 (Carrieri et al., 2003). Bolton-Moore (2007) also observed an increase in the weight for age among the children who responded well to treatment (Bolton-Moore et al., 2007).

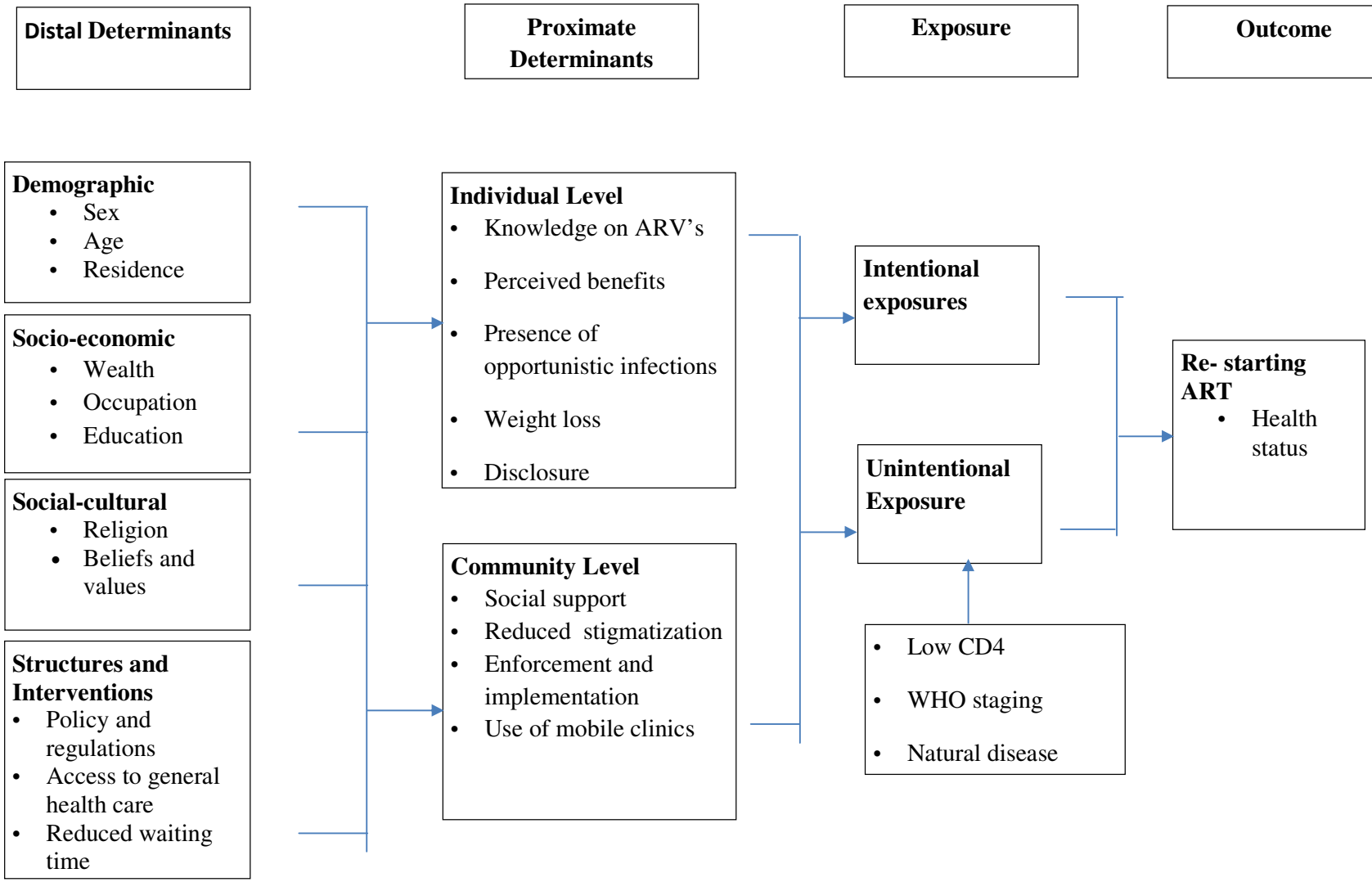
From the literature reviewed, it can be concluded that re-starting ART can be affected by gender, age and social support from both health workers and family members or the community. In addition, restarting ART is also associated with CD4 count, WHO staging and calendar of year of defaulting.

3.0 CHAPTER THREE

3.0 Conceptual Framework

The conceptual framework used in this study was adapted from the works of Boerma and Weir who used it in the study of distribution and determinants of HIV infections in populations (Boerma and Weir, 2005). The proximate determinant model was also used by Bongaarts (1978) and Davis and Blake (1956) in the study on fertility and child survival (Bongaarts, 1978, Davis and Blake, 1956). The proximate determinants model in this study was used to explain the relationships between the distal and the proximate factors associated and affecting the health status of the patients who restart ART. The conceptual framework therefore brings out the details on how various factors interact and affect the health status of the patients who restart ART. This is represented in figure 3.1 below.

Figure 3.1: Conceptual Framework



3.1 Operational definition of concepts

1. Full adherence to ART was defined as when a patient has never missed their drug pharmacy pick up (indirect measure).
2. Restarting ART was defined as patients who were once on ART; they stopped, defaulted or were lost to follow up for more than 90 days and did not have any pharmacy pick-up of antiretroviral drugs during this period, the patients status changed from active to lost. When they came back and were reinitiated on ART, such patients were consideredto have re-started ART.
3. Outcomes in this research were defined as the patient's clinical characteristics on treatment whether poor or better.
4. Patients defaulting treatment was defined as those who had not presented at the pharmacy for ART refills for more than one week after refill date.
5. Treatment interruption was defined as defaulting but patient subsequently resumed treatment
6. Patients lost to follow-up were those who stopped ART for more than 90 days and had not returned to care at the time of reviewing patient records.
7. Adherence to treatment was based on the pharmacy pick-up of the patients. All the patients who picked up ARV's were considered to be on ART.
8. WHO (World health Organization staging) used in this study was based on the staging of the disease as recommended by the World Health organization. In this study T-staging was also considered as WHO staging.

4.0 CHAPTER FOUR

4.0 Study Methodology

4.1 Study design

This study was a Longitudinal study that used a retrospective cohort design to review data of patients who re-started ART from January, 2009 to December 2010 at five different time points namely at time O months (when restarting treatment), 6months, 12months, 18months and 24moths. The study period was selected because it recorded a large number of people restarting ART. This design was selected because the study aimed to describe the characteristics from the same participants in the population at certain points in time as mentioned above and these were treated as independent time points although the data was collected from the same individuals.

The study used secondary data from 5 ART sites that were supported by the Family Health International (FHI360) through the Zambia Prevention, Care and Treatment Partnership (ZPCT II). FHI360 is a USAID funded international organization which works in collaboration with the Ministry of Health (MOH) of Zambia to increase access to and utilization of HIV/AIDS prevention, care and treatment mostly in public health facilities.

Through the ZPCT II program, FHI360 has been working with MOH, and has been enhancing HIV Prevention, Care and Treatment services in Zambia (ZPCT) since 2005 and has been supporting ART centers in Central, Copperbelt, Muchinga, Luapula, Northern and North Western provinces and have been collecting routine data on HIV prevention, care and treatment since then.

Through key service areas of Counselling and Testing, Prevention of Mother to Child Transmission of HIV, Clinical care/ART services and Tuberculosis/HIV services, FHI360 collects program data. These data sets which belong to both MOH and FHI360 were explored in this study.

4.2 Study site

The study was conducted at 5 ART sites which were purposively chosen from two provinces namely Central and Copperbelt Provinces based on the high restarting rates at the ART centers. The ART centers with the highest restarting rates were chosen for this study of which 3 came from Central province and two from Copperbelt Province. These ART centers were chosen because they are situated within the hospital boundaries and are run daily offering

HIV care services to the patients living with HIV/AIDS. Permanent clinical staff employed by the MoH and FHI360 respectively share the responsibility of ensuring that patients receive needed care and support. The sites chosen were Liteta Hospital, Kabwe General Hospital, Mwachisompola Demo Zone (from Central Province) and Kitwe Central Hospital and Chipokota Mayamba clinic (from Copperbelt Province). The chosen study sites gave sufficient numbers required to be collected for the study to be completed within the study period.

4.3 Study Population

Women and men enrolled in the ART care and reported to have defaulted and restarted ART services from January, 2009 to December, 2010 were selected for this study. All the 5 ART centers chosen were high volume centers and serve geographically and socially discrete catchment populations and receive referrals from smaller health centers within their catchment areas. ART health care services are accessible and run throughout the week as part of the primary health services provided by the hospitals. This population was selected because they have access to a comprehensive package of ART care which include counselling, testing and provision of antiretroviral therapy.

4.4 Sampling and Sample size

The study used total sampling in that all the patients who were re-started and on ART from January 2009 to December 2010 and attending ART care services at the 5 ART centers were recruited in the study. This was because there were relatively few people who were restarted on treatment each month. The total number of all the patients restarted during the reviewed period was 535 at all the selected 5 ART centers after the children and pregnant women (fhi360 data) were excluded. To enhance internal validity all the patients who were eligible for the study and met the inclusion criteria were included in the study. The inclusion and exclusion criteria were therefore as follows

Inclusion Criteria

- All adult patients, male and female aged 16 years and above who were re-started on ART from the 5 ART centers with the highest restarting rate (i.e. from January, 2009 to December, 2010).

Exclusion criteria

- All pediatric patients (below 15 years.)
- Pregnant women
- Patients transferred in and out during the study period

4.5 Data collection

Five employees of FHI360 who are stationed at the ART centers were used as research assistants for data collection. These were chosen because they have had previous experience in collecting routine and research data for FHI360 and were well familiar with the patient records and files.

These research assistants were the same people who were responsible for collecting the data from the patient files on a daily basis and recording it in the ART register and entering the data into the Smartcare database. In addition to the previous experience and expertise, the research assistants were also trained on how to use the pre-coded and pre-tested data collection form.

4.5.1 Data collection

The information relating to the research question was collected through the review of Smartcare (electronic database) and Patients files (hard copy). Information for each ART client was sourced using the laboratory form and five smart care forms. The five Smartcare forms used were the Initial history and Patient form, Patient locator, Patient status, Eligibility form and the Clinical follow-up form.

The list of patients that had defaulted and restarted ART was obtained by running a data quality report (DQR) in Smartcare which produced a list of all names and file numbers of the patients. The file numbers were then used to pull the patient files. After pulling both the Smartcare and paper-bases patient file, the information on the data collection form was then filled in.

The data collected on the forms was biological age, weight, duration on ART, education level, marital status, employment status, WHO staging, CD4 count, type of treatment and patient treatment outcome.

This relevant data for each patient was collected at 6 months prospective intervals from the day of restarting up to 24 months. The baseline (0 months) when the patient was restarted

ontreatment; the same information was collected after 6 months, 12 months 18 months and 24 months on treatment. (See appendix III).

To ensure data quality, the principal investigator with the help of the research assistants counter checked whether the data recorded in the Smartcare system patient file was the same as that on the paper-based patients file. The data on the paper based patient files was found to be the same as that which was entered in Smartcare. This data collection was done from December, 2013 to January, 2014.

4.6 Data management and Analysis

At the end of the data collection process, the principal investigator checked the data collected by the research assistants for accuracy, consistency and completeness so as to ensure quality. Most of the data was found to be accurate, consistent and complete. The data was then cleaned and entered into Access database. At the end of data entry, the entered data was again cleaned with the help of the database quality checks and then exported to SPSS version 20.0 for analysis. The data was analyzed as longitudinal data in order to bring out a clear picture of the patients who restart ART at the different time point after restarting (at 0, 6, 12, 18 and 24 months).

Quantile regression was used to determine the association between CD4 count (at 6, 12, 18 and 24 months) as dependent variables and the social demographic characteristics as independent variables (bivariate analysis). Quantile regression was chosen because the outcome variable was typically somewhat skewed. The median rather than the mean was chosen as the base of statistical comparison.

Quantile regression models were used to determine the associations because the normality and the constant variance required by the standard least regression were not satisfied (Tien et al., 2010). Quantile regression models also centers the continuous independent variables at the median when included in the model and reference values for categorical variables. The models used also allowed to control for the baseline confounding variables. Results are presented as proportions, coefficients and 95% Confidence intervals. The *P*-value of less than 0.05 was taken as the level of statistical significance.

4.7 Ethical consideration

The research protocol for this study was reviewed and approved by ERES CONVERGE IRB. Permission to carry out the study was also obtained from FHI360, the Ministry of Health and the District Health Management officer (DHMO) in charge of the study sites.

There was no contact made with the patient because the study used secondary data hence not more than minimum risk was caused. The patient records reviewed were also treated with high confidentiality and continued to be throughout the study period. At data collection, data entry and data analysis all the names of the participants were removed and replaced with identity numbers as such no individual patient data is presented.

There were no direct benefits from the study to participants; however, the findings will indirectly benefit them by suggesting means and ways in which the ART care services and intervention can be improved.

5.0 CHAPTER FIVE

5.0 RESULTS

5.1 Proportion of patients who restart ART

A total number of 2510 patients defaulted ART treatment during the selected period of the study, of which only 535 were reported to have restarted from the same ART centers. Using

the patients that defaulted treatment as a denominator, the proportion of the patients that restarted ART at the same centers was found to be 21.1%

Descriptive characteristics

The socio-demographic and clinical characteristics of the participants are summarized in table 5.1 and table 5.2, respectively. These are presented as follows:

5.2 Socio-demographic characteristics of participants

The socio-demographic features that were evaluated were sex, age, marital status, and occupation and education level of the patients.

Table 5.1: Socio-demographic of patients who restarted ART

Characteristic		Frequency	Percentage (%)
Sex of Participant	Male	232	43.4
	Female	303	56.6
Marital Status	Never Married	77	14.4
	Married	321	60
	Divorced	65	12.1
	Widowed	60	11.2
	Missing	12	2.2
Age Group	15 - 34	148	27.7
	35 - 44	230	43.0
	45+	154	28.8
	Missing	3	0.6
Level of Education	None	103	19.3
	Highest Grade(1-12)	327	61.1
	College/University	88	16.4
	Missing	17	3.2
Occupation	Unemployed	190	35.5
	Self Employed	195	36.4
	Formal Employment	114	21.3
	Other	14	2.6
	Missing	22	4.1

Note: Total sample (N) = 535.

Table 5.1 below show the socio-demographic variables of the patients that were included in this study. Of the 535 patients restarted on ART, 303(56.6%) were female while only 232(43.4%) were male. The age of the participants ranged from 17.2 to 65.5 years with the

majority of the patients [43.0% (n=230)] falling in the age group 35-44 years. In terms of education, 103(19.3%) of the patients had no form of education, 327(61.1%) had attained some form of education (ranging from primary to secondary level of education) while the remaining 88(16.4%) had attained tertiary education (either college or university). Almost equal proportions of the patients were either self-employed [195 (36.4%)] or unemployed [190 (35.5%)] but only 21.3% (n=114) were in formal employment.

5.3Clinical Characteristics of participants

The Clinical characteristics that were assessed in this study were weight, CD4 Count, Type of treatment and WHO staging of the patients at the different stages of ART care from first initiation, restart, 6, 12, 18 and 24 months after restating.

Table 5.2: Clinical characteristics

Variable		**n(%)**				
		0 months	**6 months**	**12months**	**18months**	**24 months**
WHO stage	Stage 1	202(38.0)	264(75.6)	325(89.0)	234(90.3)	279(93.3)
	Stage 2	14(2.7)	63(18.1)	25(6.9)	17(6.6)	13(0.04)

	Stage 3	70(13.2)	15(4.3)	11(3.0)	6(2.3)	4(0.01)
	Stage 4	245(46.1)	7(2.0)	4(1.1)	2(0.8)	3(0.01)
CD4 count	<350cells	438(82.5)	224(52.7)	170(47.6)	109(32.8)	73(24.2)
	>350cells	93(17.5)	201(47.3)	187(52.3)	223(67.2)	229(75.9)
	Median CD4 count	213	323	360	432	476
Type of treatment	1st line	533(99.6)	530(99.1)	523(97.8)	518(96.8)	510(95.3)
	2nd line	2(0.4)	5(0.9)	12(2.4)	17(3.2)	25(4.7)
Weight	Mean weight (Kg)	59.0	60.7	61.4	62.3	63.1

Table 5.2 shows the description of the clinical characteristics of the patients. WHO stage results show thatthe proportion of patients in WHO stage 1 kept increasing as the patients progressed on treatment, from 38% at month 0 (time restarted on ART) to 93.3% by the end of 24 months on treatment. WHO stage 4 on the other hand had the highest number of patients (46.1%) at month 0(ART restart), but as time went by the proportion of patients in WHO stage 4 reduced to as low as 0.01% at 24 months. The proportion of patients in WHO stage 2 and 3 showed similar patterns as that of WHO stage 4 but the drop was less acute.

In terms of CD4 count, table 5.2 shows that 82.5% (n=438) of the patients at ART restart had CD4 count <350 cells and only 17.5% (n=93) had CD4 count >350 cells. This increased to 75.9% at 24 months after restarting ART. The median [Interquartile range (IQR)] CD4 count at ART restart was 213(132-213) and it steadily increases to the median IQR of 476(354-475) at the end of 24 months (see table 5.2).

Out of 535 patients, at least 232(43.6%) had changed treatment regimen by the end of follow-up period. Of which 201(87%) were changed after restarting treatment while 31(13%) were change before LTFU. Of the 535 patients restarted on treatment, 95.3 %(n=510) were still on First line treatment after 24 months while 4.7 %(n=25) were changed to second line treatment (see table 5.2). Those on first line treatment, 42.4% (n=216) were male patients

while 57.6% (n=294) were female patients. Out of the 25 who were changed to second line treatment 64 %(n=16) were male patients while 36 %(n=9) were female.

Table 5.2 also shows that the group mean weight of the patients was at its lowest (59.0Kg) when the patients were restarted on ART (month 0), this increased to 60.7Kg at 6 months, 61.4Kg at 12 months, 62.3Kg at 18 months and finally to 63.1Kg at the end of 24 months on treatment.

Duration on treatment

Patients who restarted ART had experienced 3 main events on ART which are first initiation on treatment, defaulting and Restarting. Duration on treatment was therefore grouped into three categories using the 3 main events mentioned above (see table 5.3).

Table 5.3: Duration on treatment

	Duration in months			
	minimum	**maximum**	**median**	**SD**
Total duration	31	119	59	17.4
Duration before defaulting	2	80	20	15.5
Duration LTFU	4	61	11	8.9

Table 5.3 shows that total duration on treatment ranged from the minimum of 31 months (2.57 years) to the maximum of 119 months (9.92 years) with the median months being 59 (SD =17.5). The second one was duration on treatment before defaulting and it ranged from the minimum of 2 months (1.18 years) to the maximum of 80 months (6.6 years, median months = 2.0, SD=1.5.5). The third category was duration of defaulting or duration LTFU which ranged from 4months (5.1years) with the median being of 11 months and SD of 8.9.

5.4Quantile regression

Quantile regression was performed to assess the ability of the socio-demographics (sex, age group, education level, marital status, occupation) to predict levels of CD4 count (median CD4 count) of the patients after controlling for type of treatment, duration on treatment and WHO staging. The socio-demographics were entered at step 1, explaining 8% of the variance

in median CD4 count. After entry of type of treatment, duration on treatment and WHO staging at step 2, the variance explained by the model was at 18.9%, $P<0.001$. In step 3, CD4 count at different stages on ART was controlled for and the total variance explained by the model as a whole was 59%, $p<0.001$. The results from the quantile regression model are presented below.

Table 5.4: Quantile logistic regression model on CD4 count of the patients at 6, 12, 18 and 24 months

Independent variable		Median CD4 count							
		At 6 months		At 12 months		At 18 months		At 24 months	
		UC‡ (95% C.I)	AC* (95% C.I)	UC‡ (95% C.I)	AC* (95% C.I)	UC‡ (95% C.I)	AC* (95% C.I)	UC‡ (95% C.I)	AC* (95% C.I)
Sex	Male	1	1	1	1	1	1	1	1
	Female	54.3 (-1 4, 62.3)	22.4* (4.5, 39.7)	30.1 (-1.5, 61.5)	-2.9 (-29.9, 24.1)	38.3 (-25.0, 101.0)	-28.6 (-62.2, 5.4)	35.8 (-24.9, 94.9)	14.3 (-13.9, 42.0)
Age Group	15-29	1	1	1	1	1	1	1	1
	30-34	24.5 (-9.7, 117.7)	-18.1 (-49.5, 13.4)	34.3 (-24.9, 92.9)	-4.5 (-51.5, 42.5)	-5.1 (-108.8, 98.8)	-22.9 (-78.8, 34.4)	38.7 (-58.9, 136.9)	-38.9 (-86.9, 9.3)
	45+	13.4 (-53.4, 103.4)	-26.8 (-62.2, 7.4)	17.1 (-46.0, 80.0)	-15.4 (-67.3, 36.8)	-42.2 (-153.8, 69.8)	-40.6 (-103.6, 24.4)	-9.3 (-116.0, 98.0)	-62.4* (-166.5, -7.8)
Occupation	Unemployed	1	1	1	1	1	1	1	1
	Self-employment	29,9 (-19.9; 79.9)	37.4* (16.3; 58.5)	45.2* (10.7, 79.3)	12.8 (-17.5; 44.1)	18.9 (-45.6; 83.6)	-1.1 (-39.1; 36.9)	17.6 (-47.6; 83.6)	-14.5 (-45.9; 15.5)
	Formal employment	-37.1 (-67.8, 47.8)	50.3* (21.3, 79.8)	24.8 (-14.7, 64.9)	31.7 (-10.3, 73.5)	-22.9 (-95.5, 49.9)	-13.4 (-65.9, 39.6)	22.6 (-54.2, 100.2)	12.1 (-28.5, 52.1)
Education	None	1	1	1	1	1	1	1	1
	Highest grade (1-12)	-48.7 (-121.6, 23.6)	-4.9 (-29.0, 18.9)	-45.1* (-75.8, -14.2)	-14.4 (-50.1, 21.9)	-21.4 (-92.8, 50.8)	11.9 (-32.3, 56.9)	-4.3 (-76.2, 68.2)	-15.2 (-50.4, 21.2)

	College/ University	-46.1 (-135.1, 43.1)	-21.5 (-56.6, 12.6)	25.3 (-15.6, 61.6)	-30.1 (-80.1, 20.8)	-34.7 (-120.4, 52.5)	20.2 (-42.3, 82.9)	36.9 (-55.9, 127.9)	-22.6 (-72.9, 28.7)
Marital status	Unmarried	1	1	1	1	1	1	1	1
	Married	14.8 (-50.1, 80.2)	-18.2 (-44.5, 8.2)	33.1 (-31.7, 97.7)	-13.8 (-56.4, 27.8)	-36.6 (-122.1, 48.1)	-18.5 (-70.2, 32.9)	26.3 (-69.4, 121.4)	53.4* (11.8, 94.9)
	Divorced	32.6 (-54.4, 120.4)	-12.4 (-46.1, 21.7)	73.1 (-6.9, 152.9)	14.8 (-37.5, 67.7)	45.4 (-61.1, 151.0)	39.7 (-24.2, 103.5)	59.9 (-57.8, 177.9)	48.4 (-4.3, 99.3)
	Widowed	-1.1 (-90.3, 88.3)	-24.4 (-60.7, 11.8)	-1.3 (-87.1, 85.1)	-16.5 (-71.6, 0.5)	-42.4 (-151.1, 67.1)	-2.3 (-69.8, 65.2)	-10.1 (-132.1, 112.1)	49.6 (-3.2, 103.3)
Type of treatment	1st line	1	1	1	1	1	1	1	1
	2nd line	-137.2* (-206.7, - 67.3)	-66.4* (-102.0, -29.2)	-167.1* (-261.7, -72.3)	23.8* (-75.9, 0.1)	-200.3 (-276.2,123.8)	-24.7 (-86.8, 37.5)	-66.3 (-319.2, -58.8)	-23.1 (-75.5, 29.4)
WHO staging	Stage 1	1	1	1	1	1	1	1	1
	Stage 2	-112.4* (-157.8, -66.2)	-50.6* (-71.9, -27.3)	-181.2* (-252.8, -109)	-59.4* (-109.7, -7.9)	-210.2* (-306, -113.5)	-98.0* (-160.3, -35.5)	-282.8* (-422, -143.9)	5.4 (-23.0, 32.3)
	Stage 3	-152.2* (-240, -66.2)	-61.4* (-102, -19.9)	-189.7* (-298, -86.7)	-49.8 (-117, 18.4)	-415.3* (-570, -259.2)	-169.1* (-285.5,-52.4)	-382.4* (-604, -159.4)	-5.6 (-47.9, 36.6)
	Stage 4	-271.3* (-389, -152.7)	-175.1* (-234.0, -116.3)	-133.9* (-260.3, -7.7)	-150.7* (-256.2, -46.1)	-389.2* (-414, -363.2)	-103.1* (-183, -23.9)	-312.5* (-555, -71.1)	-98.8* (-177.5, -20.1)
CD4 count	ART restart	0.8* (0.7, 0.9)	0.8* (0.7, 0.84)	0.7* (0.6, 0.8)	-0.01* (-0.1, 0.1)	0.5* (0.4, 0.7)	-0.005 (-0.1, 0.1)	0.6* (0.4, 0.7)	-0.2* (-0.3, -0.1)
	6 months			0.8* (0.8, 0.9)	0.8* (0.7, 0.9)	0.8* (0.7, 0.9)	0.1 (-0.1, 0.3)	0.6* (0.5, 0.8)	-0.1* (-0.2, 0.5)

12 months					0.8* (0.7, 0.9)	0.7* (0.6, 0.9)	0.9* (0.8, 0.9)	0.2* (0.1, 0.4)
18 months							1 (0.9, 1.1)	0.9 (0.8, 1.0)
Total Duration	1.4* (0.03, 2.7)	27.1* (16.7, 37.1)	16.4* (5.9, 25.1)	-6.3 (-23.0. 10.5)	15.8* (1.6, 29.9)	6.3 (0.4, 15.9)	18.4* (1.6, 34.1)	17.9 (0.1, 36.6)
Duration LTFU	2.1 (-0.4, 4.7)	-26.0* (-36.5, -15.6)	16.1* (2.0, 30.6)	-0.3 (-2.2, 1.6)	6.6* (3.0, 10.3)	2.8 (0.3, 5.3)	6.7* (2.2, 11.3)	-10.4 (-29.8, 9.4)
Duration on treatment before LTFU	1.3 (-0.1, 2.7)	27.1* (6.7, 36.2)	5.2* (1.3, 9.5)	6.0 (-12.5, 23.9)	13.8 (-3.7, 30.8)	12,6 (-11.0, 36.3)	7.9 (-13.9, 30.7)	2.4 (-0.2, 3.9)

‡Unadjusted coefficient (UC); *Adjusted coefficient (AC), adjusted for sex, age group, occupation, education level, marital status, occupation, type of treatment, duration and CD4 count

Quantile regression at 6 months

As shown in table 5.4 under 6 months, eight variables (sex, occupation, type of treatment, WHO staging, CD4 at restart, total duration and duration LTFU) were significantly associated to CD4 count at 6 months at multivariate analysis. In the bivariate analysis, patients on 2nd line treatment compared to those on 1st line had a decrease in CD4 count by 137.2 (95% CI, -206.7 to -67.3). This result remained significant after adjusting for all the variables in the model(AC,-66.4;95% CI, -102.0 to -29.2).

WHO was significantly associated with CD4 count at 6 months both at bivariate and multivariate analysis.At bivariate analysis, patients in WHO stage 4 compared to those in WHO stage 1 had a decrease in CD4 count by 271.3 (95% CI, -389 to -152.7) and these results were significant at bivariate analysis and after adjusting for the variables in the model (AC, -175.1 (95% CI,-234.0 to -116.3). The patients in WHO stage 3 as compared to those in WHO stage 1 also showed (see table 5.4) a decrease in CD4 at 6months by -152.2(95% CI,-240 to -66.2). This result was also significant after adjusting for all the variables in the model (AC, -61.4; 95% CI, -102 to -19.9). WHO stage 2 patients as compared to those in WHO stage 1 (table 5.4) had a decrease of CD4 count at 6 months by 112.4 (95% CI, -157.8 to -66.2) which remained significant after adjusting for all the variables in the model (AC, -50.6; 95% CI, -71.9 to -27.3).

According to table 5.4, CD4 count at restart was significantly associated to CD4 count at 6 months. One unit increase in CD4 count at restart increases the CD4 at 6 months by 0.8 (95% CI, 0.7 to 0.9). This increase can be as low as 0.7 to as high as 0.9. Total duration on treatment was significantly associated with CD4 count at 6 months. One month increase in total duration on treatment increases the CD4 count at 6 months by 1.4 (95% CI, 0.03 to 2.7). This result also remained significant after adjusting for all the variables in the model (AC, 27.1; 95% CI, 16.7 to 37.1).

Duration on treatment before being LTFU and duration LTFU were not statistically significant at bivariate analysis (see table 5.4) but became significant after adjusting for all the variables in the model. One month increase in duration LTFU decreases the CD4 count at 6 months by 26.0 (95% CI, -36.5 to -15.6)while duration before LTFU increased the CD4 count at 6 months by 27.1 (95% CI, 6.7 to 36.2).

As shown on table 5.4 (under 6 months), all the socio-demographic characteristics were not statistically significant at bivariate analysis. However, sex and occupation were significant after adjusting for all the variables. Females compared to males had an increase in CD4 count at 6 months of 22.4 (95% CI, 4.5 to 39.7). Patients in formal employment as compared to patients unemployed had an increase in CD4 count at 6 months by 50.3 (95% CI, 21.3 to 79.8) while patients in self-employment showed an increase in CD4 count by 37.4 (95% CI, 16.3; 58.5).

Quantile regression at 12 months

Running the same model at 12 months with CD4 count at 12 months at the dependent variable, only two variables (WHO stage and CD4 count at 6 months) made a significant contribution to the model. The results are shown in table 5.4 above.

Table 5.4 shows that both CD4 count at 6 months and CD4 count at restart were significantly associated with CD4 count at 12 months. At multivariate analysis, one unit increase in CD4 count at 6 months increases the CD4 count at 12 months by 0.8 (95% CI, 0.7 to 0.9). This result was also statistically significant at bivariate analysis (UC, 0.8; 95% CI, 0.7 to 0.9). At bivariate analysis, one unit increase in CD4 count at restart, increases the CD4 count at 12 months by 0.7 (95% CI, 0.6 to 0.8) but this result was not significant after adjusting for all the variables in the model.

According to table 5.4, WHO stage 4 and 2 were significantly associated with CD4 count at 12 months.At multivariate analysis, the patients in WHO stage 4 as compared to those in stage 1 had a decrease in CD4 at 12 months by 150.7 (95% CI, -256.2 to 46.1). This result was alsosignificant at bivariate analysis(UC, 133.9 (95% CI, -260.3 to -7.7)and after adjusting for all the variables in the model. The patients in WHO stage 2 as compared to those in stage 1 had a decreases in CD4 count at 12 months (UC, 181.2; 95% CI, -252.8 to -109) at bivariate analysis. This was significant even after adjusting for all the variables in the model (AC, 59.4; 95% CI, -109.7 to -7.9). WHO stage 3 results at 12 months did not contribute significantly to the model but were statistically significant at bivariate analysis (UC, -189.7; 95% CI, -298 to -86.7).

At 12 months total duration on treatment (UC, 16.4; 95% CI, 5.9 to 25.1), duration before LTFU (UC, 16.1; 95% CI, 2.0 to 30.6) and duration on treatment before LTFU (UC, 5.2; 95% CI, 1.3 to 9.5) were only significant at bivariate analysis but made no significant

contribution to the model (see table 5.4). Similarly, type of treatment was only significant at bivariate analysis. Patients on 2nd line treatment regime as compared to those on 1st line treatment regime had a decrease in CD4 count at 12 months by 167.1 (95% CI, -261.7 to -72.3) but this result made no significant contribution to the model.

Among the socio-demographic characteristics, occupation was significantly associated with CD4 count at 12 months at bivariate analysis.Patients in self-employment as compared to those unemployed had an increase in CD4 count at 12 months by 45.2 (95% CI, 10.7 to 79.30) but this result was not significant after adjusting for all the variables in the model. On the other hand, those who had attained the highest grade 1-12 as compared with patients with no education had a decreases in CD4 count at 12 months by 45 (95% CI, -75.8 to -14.2).. This result equally made no significant contribution to the model after adjusting for all the variables.

Quantile regression at 18 months

At 18 months, only 3 variables (WHO staging, CD4 count and total duration on treatment) made a statistically significant contribution to the model. The results of the model with CD4 count at 18 months as a dependent variable are presented in table 5.4.

As shown in table 5.4, CD4 count at 12 months was significantly associated with CD4 count at 18 months at both bivariate and multivariate analysis. CD4 count at 6 months and at restart were only significant at bivariate analysis but ceased to be significant upon adjusting for all the variables in the model. At bivariate analysis, one unit increase in CD4 count at 12 months increases the CD4 count at 18 months by 0.8 (95% 0.7 to 0.9). This result was significant after adjusting for all the variables in the model (AC, 0.7; 95% CI, 0.6 to 0.9). One unit increases in CD4 count at 6 months increases the CD4 count at 18 months by 0.8 (95% CI, 0.7 to 0.9) while one unit increase CD4 count at restart increases the CD4 count at 18 months by 0.5(95% CI, 0.4 to 0.7). These were only significant at bivariate analysis.

Table 5.4 also shows that total duration on treatment was significantly associated with CD4 at 18 months.One year increase in total duration on treatment at bivariate analysis, increases the CD4 count at 18 months by 15.8 (95% CI, 1.6, 29.9), this increase can be as low as 1.6 to as high as 29.9. The result was significant even after adjusting for all the variables in the model (AC, 6.3; 95% CI, 0.4 to 15.9). At 18 months, duration LTFU was only significant at bivariate analysis (UC, 6.6; 95% CI, 3.0 to 10.3) but was not significant after adjusting for all the variables in the model.

All the stages of WHO contributed significantly to the model. Patients in WHO stage 4 as compared to those in WHO stage 1 had a decrease in CD4 count at 18 months by -389.2 (95% CI, -414.5 to -363.2) at bivariate analysis. This result remained significant after adjusting for all the variables in the model (AC, -103.1; 95% CI, -183.6 to -23.9). At bivariate analysis, those in WHO stage 3 as compared to WHO stage 1 had a decrease in CD4 count at 18 months by 415.3 (95% CI, -570 to -259.2). Those in Stage 2 had a decrease of 210.2 (95% CI, -306 to -113.5). The results remained significant after adjusting for all the variables in the model (WHO Stage 3 AC, -169.1; 95% CI, -285 to -52.4 and stage 2 AC, -98.0; 95% CI, -160.3 to -35.5).

At 18 months all the socio-demographic characteristics were not statistically significant at bivariate analysis and they made no significant contribution to the model.

Quantile regression at 24 months

Using the same model at 24 months with CD4 count at 24 months as a dependent variable, five (5) variables (total duration on treatment, CD4 count at 12 and 18 months, WHO staging, marital status and age group) contributed significantly to the model.

Table 5.4 shows that CD4 count at 12 and 18 months were significantlyassociated with CD4 count at 24 months both at bivariate and multivariate analysis. At bivariate analysis, one unit increase in CD4 count at 18 months increases CD4 count at 24 months by 1.0 (95% CI, 0.9 to 1.1) while one unit increase in CD4 count at 12 months increase CD4 count at 24 months by 0.9 (95% CI, 0.8 to 0.9). These results remainedsignificant after adjusting for all the variables in the model (CD4 at 12 months AC, 0.2; 95% CI, 0.1 to 0.4 and CD4 at 18 months AC, 0.9; 95% CI, 0.8 to 1.0).CD4 count at restart and at 6 months were only significantly associated to CD4 count at 24 months at bivariate analysis. CD4 count at restart and at 6 months respectively increases CD4 count at 24 months by 0.6 (CD4 at restart AC, 0.6; 95% CI, 0.4 to 0.7 and CD4 count at 6 months AC, 0.6 95% CI, 0.5 to 0.8).

In terms of duration on treatment, total duration was significantly associated to CD4 count both at bivariate and multivariate analysis. One (1) year increase in total duration on treatment at bivariate analysisincreases the CD4 count at 24 months by 18.4 (95% CI, 1.6 to 34.1). This result (see table 5.4) remainedsignificant after adjusting for all the variables in the model (AC, 17.9; 95% CI, 0.1, 36.6). Duration LTFU was only significant at bivariate analysis (UC, 6.7; 95% CI, 2.2 to 11.3) but made no significant contribution to the model.

All WHO stages were significantly associated to CD4 count at 24 months at bivariate analysis but only WHO stage 4 remained significant after adjusting for all the variables in the model. WHO stage 4 patients (table 5.4) as compared to those in WHO stage 1 had a decrease in CD4 count at 24 months by 313.5 (95% CI, -555 to -71.1) and the results remained significant after adjusting for all the variables (AC, -98.8; 95% CI, -177.5 to -20.1). WHO stage 3 and stage 2 were only significant at bivariate analysis (stage 3 UC, -382.4; 95% CI, -604 to -159.4and stage 2 UC, -282.8; 95% CI, -422 to -143.9)

Table 5.4 also show that among the socio-demographic characteristics, only marital status and age group were significantly associated with CD4 count at 24 months at multivariate analysis.Patients who are married as compared to those who have never married had an increase in CD4 count at 24 months by 53.4 (95% CI, 11.8 to 94.9). The age group of patients who were 45+ (and above) as compared to the age group 15-29 years showed a decrease in CD4 count at 24 months by 62.4 (95% CI, -166.5 to -7.8). Both of the socio-demographic characteristics were not significant at bivariate analysis.

6.0 CHAPTER SIX

6.0 DISCUSSION

The findings in this studyrevealed that out of the patients who were declared LTFU, only 21.1% restarted ART. The majority of the patients who restarted ART were Female and that most of them were married with the least being widowed. Most of the patients did attain some form of education with the highest level of education being grade 1 to 12. An equal proportion of the patients were either unemployed or self-employed with the minority being in the formal employment sector.

Among the factors found to be independently associated to CD4 count at 6 months was sex, occupation, type of treatment regime, WHO staging of the patients, CD4 count at restarting ART and duration on treatment. Level of education, type of treatment, WHO staging, CD4 count (at ART restart and 6 months), and duration on treatment were the independent factors associated with CD4 count at 12 months. Furthermore, type of treatment, WHO staging, CD4 count and duration were also found to be independently associated with CD4 count at 18 months after treatment resumption.

At 24 months after restarting ART, age group and marital status were two of the socio-demographic factors that were independently associated with the levels of CD4 count in addition to type of treatment regime, CD4 count, WHO staging and duration on treatment.

It is not surprising that the females restarting ART outnumbered the males because this has been the pattern in the health seeking behavior where HIV/AIDS epidemic is concerned. In most African countries, male sex has been associated with delay of ART initiation and most likely ART restarting (Geng et al., 2013). Woman have been generally reported to utilize ART care services more than men and hence more likely to restart ART treatment than males (Dako-Gyeke et al., 2012).

The differences in the health seeking behavior between men and women could have contributed to the fact that women showed a much higher increase in CD4 count 6 months after restarting ART than the men. Review of national AIDS/STI data in in Ghana found that the health seeking behavior influenced the health outcome of the patient suffering from AIDS/STI (Dako-Gyeke et al., 2012).

6.1 Socio-demographic characteristics

Findings from the socio-demographic also revealed that most of the patients who restarted ART were above the age of 35. Although these findings are consistent with the study which was done in adults in South Africa which stated that resumption of treatment is more likely in patients more than 30 years old than those who are younger (Kranzer et al., 2010). There is a variation in age as patients older than 30 were more likely to resume treatment unlike in the current study where the patients aged 35 and above were more likely to restart.

In this study, Patients in formal and self-employment as compared to patients unemployed had an increase in CD4 count at 6 and 12 months. Most studies have suggested that the income status of an individual and family dynamics influence the health outcome of the patients ART. Patients with less income were reported to have the likelihood of experiencing 10 times more negative life events than patients with high income (Tesfaye and Bune, 2014, Wouters et al., 2014).

On the other hand, those who had attained the highest grade 1-12 as compared with patients with no education had a decrease in CD4 count at 12 months. This result though significant is not logical as the definition of highest grade 1-12 on the Smartcare forms was too broad. Although an option to specify the exact grade has been provided, this option has been less utilized and the information is not collected both at ART initiation and when the patient is restarted on treatment.

Other socio-demographic characteristics associated with CD4 count are marital status and age group. Patients who are married as compared to those who have never married had an increase in CD4 count at 24 months by 53.4. Further, the age group of patients who were 45 and more as compared to the age group 15-29 years showed a decrease in CD4 count at 24 months by 62. This is contrary to the study in which individuals who are 50 years and more showed better CD4 recovery over time (O'connor et al., 2014).

6.2 Duration on treatment

The patients restarting ART in this study experienced 3 main events namely 1st initiation on ART, defaulting and restarting ART. Using these events duration on treatment was categorized into 3, the first one was total duration on treatment which ranged from the minimum of 31 months to the maximum of 119 months with the median months being 59. The second one was duration on treatment before defaulting and it ranged from the minimum of 2 months to the maximum of 80 months median months equal to 2.0. The third category

was duration of defaulting or duration LTFU which ranged from 4months with the median being of 11 months. All the 3 categories of duration were significantly associated with CD4 count.

In this study, one unit increase in total duration and duration on treatment before LTFU were positively associated with CD4 count while a unit increase in duration of the patient LTFU showed a negative relationship with CD4 count. The median time taken by the patients to resume treatment (11 months) also shows that most of the patients restarted treatment within the same year. These results are similar to the finding that most patients are likely to restart treatment within the same calendar year of defaulting (Kranzer et al., 2010). It is therefore important for ART interventions to target patients LTFU within the first year of defaulting.

6.3 CD4 count and other Clinical Characteristics

The mean weight of the patients who restarted ART was observed to be very low (55.5Kg) the first time they were initiated on treatment. This increased to the mean weight of 65.5Kg at the time they were recorded as defaulted treatment. At the time of restarting ART the mean weight had dropped to 59Kg but was seen to gradually increase as the patient continued on treatment. After 24 months on treatment, the mean weight had increased by about 5Kgs. The increase in weight when patients restart ART is consistent with the results from the French cohort study which recorded an increase in weight of the patients after a year of highly active ART (Carrieri et al., 2003). Further it is argued that although weight is more useful in children than adults, it can be a good indicator towards good patient health outcome (Bolton-Moore et al., 2007, Carrieri et al., 2003).

Most of the patients who restarted treatment were still on first line treatment regime and more than 80% were at least changed to a different ARV combination. However, reviewing the patient treatment regime at 24 months showed that only 5% of the patients were changed to second line treatment while 95% were still on 1st line.

Throughout the study period, the results show that patients on 2nd line treatment regime had a decrease in CD4 count as compared to those on 1st line treatment regime even after continuing on treatment for the same period of time. Further research is needed to establish and ascertain whether this association between treatment regime and CD4 count in patients who restart ART is not due to chance.

The findings reviewed that, most of the patients restarted on ART were in WHO stage 4 but as they continued on treatment more and more patients moved to stage 1. As a result, over 90% of the patients were in WHO stage 1 by the end of 24 months. Patients who were in WHO stage 2, 3 and 4 as compared to those in WHO stage 1 consistently showed a decrease in CD4 count. This was expected in the present study and was consistent with other studies that have shown that even though there are improvements observed in CD4 count and WHO staging of the patient (Bolton-Moore et al., 2007, Reddi et al., 2007), treatment interruption in patients whether planned or not is not safe (El-Sadr et al., 2006).

These studies found that interruption of treatment is actually harmful to the patients' health as it reduces one's chance of survival. Treatment interruption is also associated with increased risk of disease progression and death (DART Trial team, 2008, Egger et al., 2011). This could explain why the majority of the patients restarting ART were in WHO stage 4.

The increment in the number of patients in WHO stage 1 is a sign that patients restarting treatment can still respond well to treatment after restarting ART as suggested by the study which was done in rural Zambia and in settings with inadequate HIV treatment availability (Carlucci et al., 2008, Kimmel et al., 2012). On the contrary, the current study also shows that the CD4 count of the patients in WHO stage 2, 3 and 4 were inferior to those in WHO stage 1. Two studies, one done in South Africa and the other in Zambia reported similar findings, in both studies WHO stage 3 and 4 were found to be highly associated with mortality because of the opportunistic infections due to the reduced immune system (Yu et al., 2007, Reddi et al., 2007).

Median CD4 count was observed to be lowest at first ART initiation and much higher at restart. After restart there was a steady increase of the median CD4 up to the end of 24 months. The median CD4 count indicates that the CD4 count of the patients who restart treatment recover after reinstitution of treatment. This was similar to the findings reported by Richard (2008) where the CD4 count of the patients improved after reinstitution on treatment. Monforte (2005) also reported patients with lower CD4 count being more likely to restart treatment and those with higher CD4 count more likely to interrupt treatment (Mocroft, 2001). This might be the reason why most of the patients who restarted ART in the current study had CD4 count below 350 cells at ART restart.

CD4 count in this study was associated with sex, age group, occupation, type of treatment, WHO staging, baseline CD4 when restarting ART and duration of treatment. These

significant associations were observed as early as 6 months after restarting ART and seemed to be confounding.

6.4 Limitations of the study

This study used secondary data hence during data collection some information in patient files were missing this affected the sample size. The fact that the data was reviewed at 6 months intervals made that sample size to differ as patients are allowed to send someone to collect the ARV's on their behalf. Adherence to treatment was therefore based on the records from the pharmacy pick-up of the medication. The study was conducted at only 5 ART centers in the Copperbelt and central provinces of Zambia which were purposively sampled. Therefore, the findings in this study can only be generalized to similar settings but can be difficulty to generalize to the rest of Zambia.

7.0 CHAPTER SEVEN

7.0 CONCLUSION AND RECOMMENDATIONS

The proportion of patients who restarted ART was 21.2% indicating that only 1 in 5 patients who default ART restart. The socio-demographic characteristics show that patients that restart are more likely to be female, aged 35 years and above, married, and must have gone to either primary or secondary level of education. There was a linear relationship of patients responding better in terms of mean weight, median CD4 count and WHO staging.

Type of treatment regime, WHO staging , duration on treatment and baseline CD4 count were strong predictors of having an increased CD4 count at 6, 12, 18 and 24 months. Duration LTFU was a main predictor of having a reduced CD4 count at all the stages on ART. These predictors of CD4 count in patients who restart ART are similar to the predictor of CD4 count in patients initiated on ART for the first time. Sex and occupation were also strong predictors of CD4 count at 6 months after treatment resumption. At 12 months, level of education was also independently associated with CD4 count. Contrariwise, there was no association between the socio-demographic characteristics and CD4 count of the patients at 18 and 24 months after restarting ART.

All these findings gained insight on the patients that default and restart ART, however more studies need to be done to validate these findings and better understand this at risk population. The ministry of health together with its partners who are involved in improving ART care services should put more effort in encouraging the patients who default ART and are LTFU. Further, ART care services must focus on the patients who are more vulnerable to defaulting and these are the male sex, those below the age of 30 and have no form of education.

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Appendix I: Data Collection Form

Social and clinical attributes of patients who restart antiretroviral therapy at 5ART Centers in the Central and Copperbelt provinces of Zambia

Name of data collector

Code

Date form filled in

Date: D D M M Y Y Y Y

Section A: General Information

			Source of information (See Smart care forms)
1	Sex	1 ☐ Male 2 ☐ Female	Initial History and patient or patient locator
2	Date of birth	☐☐ / ☐☐ / ☐☐☐☐ (D D / M M / Y E A R)	Initial History and patient or patient locator
3	Health Centre	Province 1 ☐ Copperbelt 2 ☐ Central Province	Standard
		District 1 ☐ Kitwe ART Centre 1 ☐ Chipokota Mayamba	Standard

		2		Ndola	2	Kabwe General
		3		Chibombo	3	Kitwe General
		4		Kabwe	4	Liteta
					5	Mwachisompola
4	Marital status	1		Never married		Patient locator
		2		Married		
		3		Divorced		
		4		Widowed		
5	Highest	1		None		Patient locator
	Education Level	2		Highest Grade (1-12) ……..		
	at time of starting ART	3		College/university		
		4		Other (specify)……		
6	Patient Occupation	1		Unemployed		Patient locator
		2		Self-employed (specify)		
		3		Formal employment		
		4		Other (Specify) ……		

7			
a	Height (meters)	……..	Initial History and patient
b	Baseline weight when		Eligibility form
	Initiated on ART	…….	
c	Weight at time		Clinical Follow up
	declared lost	…….	
d	Baseline Weight when		Patient Status/clinical
	Restarted on ART	….. …….	Follow up
8a	Date of Baseline	D D M M Y Y Y Y	Eligibility form
	Initiation on ART		
8b	Date declared Lost	D D M M Y Y Y Y	Patient status
9	Date Restarted on ART	D D M M Y Y Y Y	Patient status/clinical
			Follow up

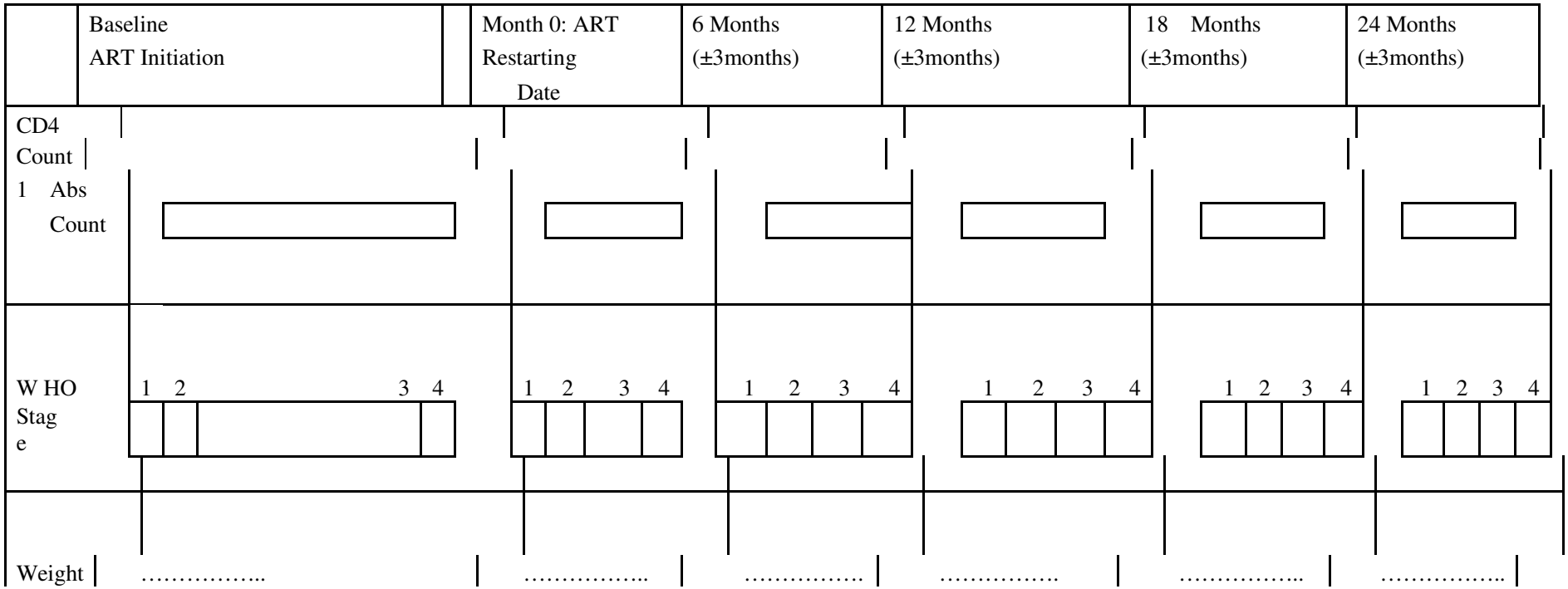
Section B: Type of Treatment

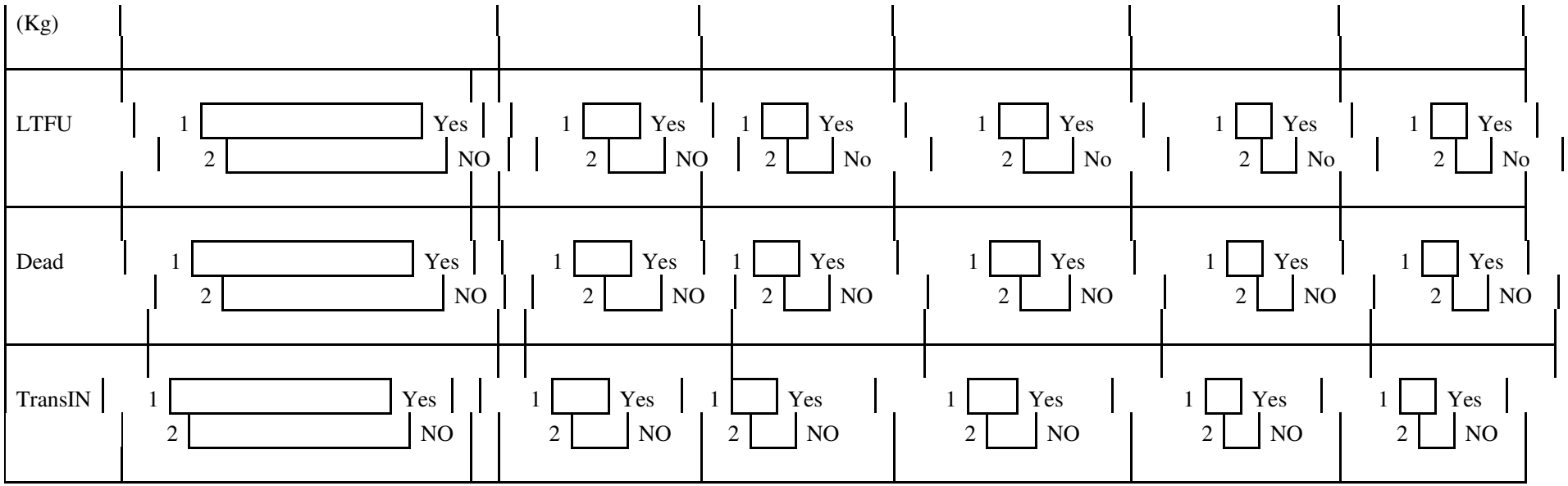
11	Current ARV (Specify	(e.g AZT/3TC/NVP/EFV)
	Combination)	
		…….…….…….……..
12		
a	Has the patient ever	1 ☐ Yes
	been changed on ARV	2 ☐ NO (If No go to section c)
	Combination?	
	If yes specify Previous	(e.g. AZT/3TC/NVP/EFV)
	ARV combination	…….…….…….……..
b	Switch made after	1 ☐ Yes
	Restarting ART	2 ☐ NO
c	Date Switched	☐☐ ☐☐ ☐☐☐☐
		D D M M Y Y Y Y

Section C: Six Monthly CD4 Count, Weight and WHO Staging after restarting ART

See the following forms

1. Eligibility or lab form for Baseline CD4 count at ART initiation
2. Initial History and physical examination form for WHO stage at baseline ART initiation
3. For the rest of the information see the clinical follow up form or lab form

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Appendix II: FHI Approval letter

fhi360

Date: 17th September, 2013

Dear Sir/Madam:

Subject: Letter of Introduction: MPH Student – Chama Mulubwa

This letter serves to introduce the subject **Chama Mulubwa**, who is a University of Zambia Master of Public Health student. She is doing an internship with FHI360 through the ZPCT II project for 10 months. This arrangement is formalized through an MOU signed between FHI360 and UNZA School of Medicine.

As part of the development of her academic process, FHI360 will support the subject logistically and otherwise to work on her MPH Dissertation. This also involves working with strategic information unit to access data in supported health facilities. All the standard ethical and academic approvals will be followed to the letter.

This is one sure way of analyzing available data and adding to the body of knowledge on AR".

Thanking you in advance.

Michael Welsh, Ph.D.
FHI360 Zambia Country Director,
ZPCT II Chief of Party.

FHI - ZAMBIA Plot 3055, Nasser road P.O. Box 320303, Woodlands, Lusaka Telephone: (260-211) 360100 - 60 Facsimile: (260-211) 297328URL: http://www.fhi360.org

Appendix III: Ministry of Health Approval letter

REPUBLIC OF ZAMBIA
MINISTRY OF HEALTH
KITWECENTRALHOSPITAL

Telefax : 260 – 2 – 2226

Kuomboka Drive
P O Box 20969
Kitwe
Zambia

Telefax: 224365/228604
EM-kchmb@zamtel.zm

All Correspondence to Be Addressed to the Senior Medical Superintendent

Our Ref: MH/KCH/
Your Re:

4th October, 2013

Mr. Chama Mulubwa
University of Zambia
School of Medicine
LUSAKA

Dear Sir,

RE: APPLICATION TO CONDUCT A RESEARCH - YOURSELF

We refer to your letter dated 13th September, 2013 in which you applied to undertake a Research on "Social and Clinical attributes of Patients who restart Antiretroviral Therapy".

We are pleased to inform you that authority has been granted for you to do your Research at our hospital at ART Clinic.

Please report to the Head of Department with the letter.

We wish you all the best in your Research.

Yours faithfully,
KITWE CENTRAL HOSPITAL

Nsakasha

Memory Nsakasha (Ms)
Ag/Senior Human Resource Management Officer
FOR/SENIOR MEDICAL SUPERINTENDENT

REPUBLIC OF ZAMBIA
MINISTRY OF HEALTH
KABWE GENERAL HOSPITAL

All correspondence to be addressed to the Executive Director and not to individuals

Our Ref:

Your Ref:

P.O. Box 80917
KABWE
Tel: 260-5-222301-6
TelFax:260-5-223049
Cell No. 0972-757283
Email: kabwegeneral@gmail.com

11th October 2013

The University of Zambia
School of Medicine
Department of Public Health
LUSAKA

Dear Sir,

RE: REQUEST FOR PERMISSION FOR MASTERS STUDENT – CHAMA MULUBWA

Refer to the above.

We hereby grant you permission to conduct the Research for academic purposes only. You are expected to adhere to the standards with regards patient's right to confidentiality and privacy.

All the best.

Yours faithfully,

Dr. G. Chipulu
MEDICAL SUPERITENDENT

REPUBLIC OF ZAMBIA
MINISTRY OF HEALTH
KITWECENTRALHOSPITAL

Telefax : 260 – 2 – 2226

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