FACTORS AFFECTING CD4+T-LYMPHOCYTE COUNT RESPONSE TO HAART IN HIV/AIDS PATIENTS WITHIN 24 MONTHS OF TREATMENT AT CHRESO MINISTRIES ART CENTRES'.

by

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DEDICATIONS

I dedicate this work to my late father Paul Bwalya and my mother Hilda Bwalya for they have made me what I am today.

Also to my wife, Memory Bwalya with deepest love, gratitude and affection for showing understanding even when I arrived home late from school.
I also pay gratitude to my elder brother Andrew Bwalya and, my elder sister Naomi Bwalya for their contribution. They made sure that I had secondary and college education amidst tough economic battles. I would also like to thank uncle Justine Mwenya for his immense efforts he rendered ensuring that I had a stable foundation of Primary Level Education.

DECLARATION

This dissertation is the original work of Marlon Bwalya. It has been prepared in accordance with the guidelines for MPH dissertations of the University of Zambia. It has not been submitted elsewhere for a degree at this or another university.

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This dissertation of Mr. Marlon Bwalya is approved as part of the fulfillment of the requirements of the award of the degree of Master of Public Health by the University of Zambia.

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ABSTRACT

The general objective of this study was to identify factors that affect CD4-TLymphocyte count response in patients commenced on HAART within 24 months of treatment at Chreso Ministries VCT and ART centres. The elements of this study were files of clients of all age groups on HAART above 5 years of age who had at least four consecutive repeat CD4 count rechecks within 24months of treatment with all other necessary information of variables required for this study captured in smartcare at treatment initiation. According to May 2009 statistical report, Chreso Ministries ART centre which happened to be a study site had 7000 HIV positive clients on care and 3900 clients on HAART. This study was a retrospective cohort design and had a sample size of 340 files of clients. The sampling frame generated from the study population was subjected to computerized random selection to come up with the sample size of 340 medical files. The study was purely quantitative and involved reviewing clients' records that have been captured on the smartcare database on clients who have been on HAART for more than 24months. The extracted data was entered in Epidata using Epi Info and was exported to SPSS for analysis. The Chi-Square test at 5% with crosstabulation tables was used to determine associations between the identified variables and CD4-Lymphocyte count response to HAART and the logistic regression analysis was used to predict the probability of CD4 count response to HAART using the variables of this study. The study was completed in 3months following approval from the Ethics Committee of the University of Zambia. The statement of the problem was the observed poor CD4 count response to treatment in most of the clients commenced on HAART. The factors at hand involved the social demographic factors (age, sex, income, alcohol consumption and employment status) ART factors (Adherence and ART regimen) and immunological factor (CD4 count at treatment initiation). In this study it was found that gender, alcohol consumption, nadire and regimen affects CD4 count response to HAART. It was found that men, non alcohol consumers and those that start HAART with baseline CD4 count above 350 cell/µL experienced a good CD4 response to HAART. Additionally, those who commenced treatment on truvada and devoted themselves to 95% adherence also experienced a good CD4 count response to HAART. On the other hand, age, smoking and employment status did not affect CD4 count response to HAART.

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ACRONYMS

1. **HAART**: Highly active antiretroviral therapy.
2. **ART**: Anti retroviral treatment.
3. **CD4**: Cluster of differentiation.
4. **HIV**: Human immunodeficiency virus.
5. **AIDS**: Acquired immunodeficiency syndrome
6. **UN**: United nations
7. **WHO**: World health organisation.
8. **ARV**: Antiretroviral
9. **VCT**: Voluntary testing and counselling.
10. **(NRTI)**: Nucleotide reverse transcriptase inhibitors.
11. **RNA**: Ribonucleic acid
12. **OI's**: Opportunistic infections.
13. **LFT's**: Liver function tests.
14. **STI's**: Sexually transmitted infections.
15. **IDU**: Injection Drug use.
16. **EHR**: Electronic Health Records
17. **IT**: Information Technology.
18. **DEC**: Data entry clerk
19. **SPSS**: Statistical package for social scientists.
20. **HMIS**: Health management information system
21. **PEPFAR**:Presidencies emergency plan for AIDS Relief.

OPERATIONAL DEFINITION OF KEY CONCEPT

1. **CD4 T CELL** : T cell with CD4 receptor that recognizes antigens on the surface of a virus-infected cell and secretes lymphokines that stimulate B cells and killer T cells; helper T cells are infected and killed by the AIDS virus
2. **ADHERENCE:** the extent to which a person's behaviour corresponds with medical advice. The ability to take medication as prescribed
3. **95% ADHERENCE**. Twice a day regimen=2pills per day. If a patient misses 1 pill per week, that is less than 95% adherence. To achieve 96% adherence in a month, a patient should not miss more than 2pills per month
4. **ANTIRETROVIRALS (ARV's):** drugs designed to suppress the progression of HIV/AIDS consisting of double or triple combination.
5. **CLIENT:** a person who uses the ART services
6. **VIRAL LOAD:** level of viruses per 10mL of blood
7. **SOCIAL/DEMOGRAPHIC RELATED VARIABLES:** The list of social/demographic factors in the study includes demographic (age and, sex) as well as social and economic (beer drinking, smoking and socio-economic index of monthly income).
8. **IMMUNOLOGIC RELATED VARIABLES:** factors/variables that are as a result of an individual's state of immunity in relation to there CD4 response to HAART. There is a wide range of immunologic indicators of which mostly used are: total non-paraprotein, immunoglobulin, specific antibody titres, white blood cells and number of CD4 cells. However in ART, CD4 counts and baseline CD4 counts are used to commence and monitor patients' response to HAART respectively.

9. **ART FACTORS:** factors/variables that are mostly drug (ARV's) use related. Examples of these include the type of HAART combination, adherence, and duration of HAART etc.
10. **CD4 COUNT:** is reported as the number of CD4 cells per micro litre.
11. **GOOD CD4 COUNT RESPONSE TO HAART:** gaining 50-100 cells per micro litre per year with successful ART until a threshold is reached.
12. **POOR CD4 COUNT RESPONSE TO HAART:** gaining less than 50-100 cells per micro litre per year with treatment.
13. **CD4 TRENDS ANALYSIS:** studying the general pattern(s) of the client(s) CD4 counts taken over time.
14. **CD4 TRENDS PROGRESS:** an indication of gradual improvement of the client(s) CD4 counts general pattern over time.

CHAPTER 1.

BACKGROUND INFORMATION

1.0 INTRODUCTION

HIV/AIDS (human immunodeficiency virus/acquired immune deficiency syndrome) have posed the world most devastating calamity and threat. According to AVERT. ORG (2009) HIV/AIDS information, more than 25 million people worldwide have died of AIDS since 1981. At the end of 2007, women accounted for 50% of all adults living with HIV worldwide, and for 59% in sub-Saharan Africa. Young people (under 25 years old) accounted for half of all new HIV infections worldwide. An estimated 22 million adults and children were living with HIV in sub-Saharan Africa at the end of 2007. During that year, 22 million adults and children were living with HIV/AIDS and an estimated 1.5 million Africans died from AIDS. The epidemic has left behind some 11.6 million orphaned African children (UNAIDS/WHO 2008). Zambia's problems since the mid 1980's have been similar compounded by this world's most devastating HIV and AIDS epidemics. The statistics alone are shocking. Zambia, in southern Africa, has one of the world's most devastating HIV and AIDS epidemics. More than one in every seven adults in the country is living with HIV (WHO, 2008) and life expectancy at birth has fallen to just 39 years (CIA World Factsbook, 2008). In four decades of independence, Zambia has found peace but not prosperity and today it is one of the poorest and least developed nations on earth.

Zambia's first reported AIDS diagnosis in 1984 was followed by a rapid rise in the proportion of people living with HIV. Although Zambia has received hundreds of millions of dollars for HIV programmes from rich country governments, prevalence rates are not dropping and have remained more or less

stable since the nineties, at as high as 25% in some urban areas (UNAIDS/WHO 2008).

Zambia's prevention of mother-to-child transmission (PMTCT) initiative was launched in 1999, beginning with a three-year pilot programme in Copperbelt Province. In 2004 it had expanded so that 74 health facilities in four provinces offered antiretroviral drugs (primarily nevirapine) to expectant mothers and newborn infants. In 2007 an estimated 47% of pregnant women living with HIV received ARVs for preventing mother-to-child transmission (WHO/UNAIDS/UNICEF, 2008). By 2008 this estimate had increased to 59% (WHO/UNAIDS/UNICEF, 2009). Preventing mother-to-child transmission is a high priority of the United States' PEPFAR initiative. By 2008, 131,900 pregnant women had received ARVs for PMTCT through PEPFAR funding (PEPFAR 2008). State provision of antiretroviral therapy began in Zambia in late 2002, although initially very few people could afford the monthly payments towards the drugs. Provision of free treatment started in June 2004, made possible by an unprecedented amount of funding from the Global Fund (in 2004 it committed $254 million over 5 years), PEPFAR (Zambia is one of the programme's most highly funded focus countries, receiving $149 million in 2006 alone) and other sources. The delivery of the programme relies on the involvement of many NGOs, churches and communities (Stephen, 2008). At the end of 2007, 46% of the 330,000 people in Zambia needing ARV treatment were receiving it, which is above the African average (WHO, 2008).

Ultimately, Zambia aspires to provide universal treatment access, so that ARV therapy is equally available to everyone who is clinically eligible. However, some current schemes try to make it easier for particular groups to gain access, including civil servants, teachers, university students and mothers and children (through "PMTCT Plus"). Additionally, some employers run private schemes – particularly the mining companies. In general, accessing treatment is a great deal easier for city-dwellers than for those living in rural areas. The treatment programme's greatest handicap is the inadequacy of the healthcare system, which

suffers from high patient numbers, lack of physical space and infrastructure, and – most critically – too few staff. There is a critical shortage of doctors (in 2006 there were only 646 doctors in a country of almost 12 million people), nurses, lab technicians and other health professionals. Zambia currently has under a third of the doctor-patient ratio recommended by the WHO (The Lancet 2008). The crisis stems from a variety of factors, most notably a large-scale emigration of trained professionals to other countries in Africa and abroad, where salaries and conditions are more favourable. Zambia is now trying to recruit as many health workers as it possibly can, and has implemented a variety of initiatives to retain health staff, expand the workforce, and improve the wellbeing of doctors and nurses. 'Task-shifting' is a strategy that has been introduced to delegate certain health-care duties to lay people or community workers to reduce the workload of doctors and nurses (The Lancet 2008).

There are many ways to help people living with HIV besides treatment. Some organisations run loan schemes that enable groups of HIV-positive people to set up small businesses, so they can provide for themselves and their families. Other projects distribute food or establish cooperative vegetable plots - good nutrition is essential for everyone living with HIV.

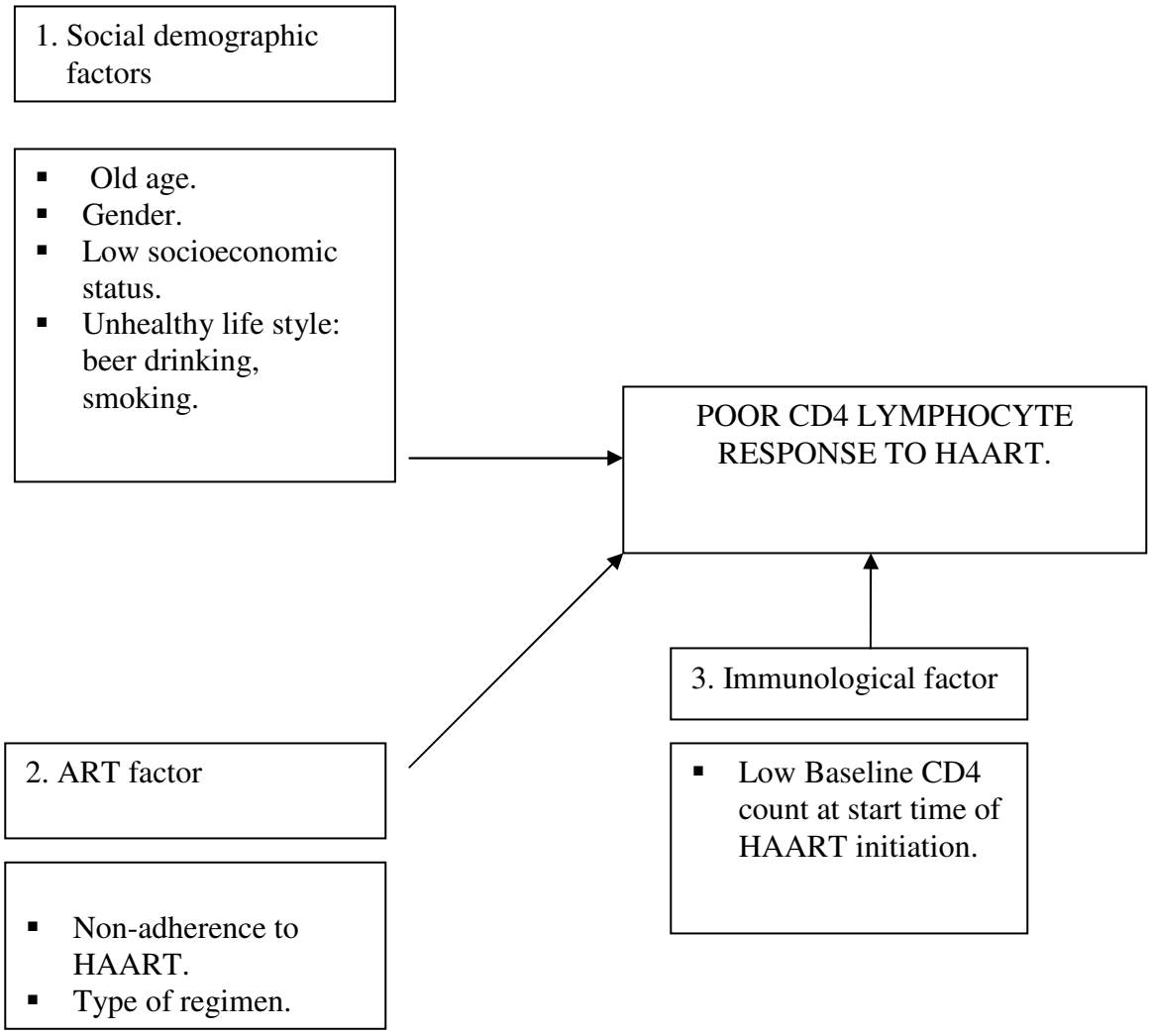
1.2 PROBLEM IDENTIFICATION

Apart from the management of large numbers of HIV/AIDS clients and the costs involved, another challenge exists on the ART programs. This is monitoring the progress of clients/patients immune response to HAART in HIV/AIDS patients'.
Since HIV was first claimed to be the cause of AIDS in 1984, the CD4 count has been widely used to make treatment and diagnostic decisions, but the use of CD4 count has been controversial and recommended actions on how to use them have changed several times over the years (Stohr *et al*. 2007). There are two major arms in the immune system, one which works through antibody produced by B-cells and plasma cells, and the other that works through cells including CD_4+T

Lymphocyte cells. The first is called antibody mediated or humoral immunity and the second is called cell mediated immunity. It is this cell mediated immunity that is profoundly suppressed in people diagnosed with AIDS. The CD4 count still remains the major determinant or measure of the cell mediated immunity. Several patterns of response after initiation of highly active antiretroviral treatment (HAART) have been observed in persons with HIV infection. There are two main approaches regarding when to start antiretroviral treatment. The more aggressive approach recommends starting when the CD4 counts fall below 500, and the second approach is more used in the United States which recommends starting antiretroviral medications immediately in all patients regardless of the patients CD4 counts. Currently, there is not enough evidence showing that all the ART centres in Zambia have implemented research tools to monitor patients' immune (CD4) response to HAART within a specified time frame and identification of factors that might be associated with the poor CD4-Lymphocyte response to HAART. Although Trend analysis studies have been carried out by international research institutions, there has been less focus on the local institutions to carry out and strengthen CD4/viral load trends analysis studies to give a clear indication on the response of HIV/AIDS patients to ART. It should still remain the responsibility of the active ART centres to employ a tool that will constantly monitor the clients' progress in CD4 count since it still remains the major indicator of an individual's immunity. Chreso Ministries that has sprung from Gospel Outreach Church, a faith based organisation whose mission of the statement is to meet the social, psychological, economical, medical/physical and academic needs of people in an effort to achieve sustainable development has a combined unit of VCT and ART that has a total number of 7000 people on HIV care and 3900 people active on ART according to May 2009 statistics (Chreso Ministries Lusaka, May 2009 statistics). The Zambian eligibility criteria is that patients with CD_4-Lymphocytes lower than 350cells/µl, coupled with clinical symptoms, should start ART treatment and their response to treatment should be monitored by checking the response patterns of their CD_4- Lymphocytes levels in the blood (Christopher, 2008). In addition to the above mentioned health centre,

the 21st October 2009 times of Zambia news paper reported that Zambia has about 444 ART centres out of which only 83 are accredited by Medical Council of Zambia. These health centres have relatively high numbers of clients on ART. This calls for serious consideration of managing and monitoring the high number of clients on HAART with well defined strategies to measure their immune response to treatment and identify factors that have the ability to influence their CD4 count recovery.

FIGURE 1: Problem Analysis Diagram showing factors that affect CD4 response to HAART.



The major factors that affect CD4 count response to HAART are best summarised in the diagram above. The diagram illustrates the social demographic, immunological and ART factors likely to cause poor CD4 count response to HAART. These are old age, gender, low social economic status, smoking and

alcohol consumption, non adherence to HAART, type of regimen and low baseline CD4 count.

1.3 Justification of the study

Since 2002 when ART was newly being introduced to Zambia there has been less evidence on the trends analysis studies to determine the effect of treatment on individuals CD4 Lymphocyte counts in the established ART centres to determine drug efficacy and factors that affect the patients' response to treatment. This is mostly because access to free laboratory diagnostic tests was scarce and costly due to shortage of skilled laboratory personnel and the costs involved in procurement of the laboratory equipments and reagents. Therefore in this study, the aim is to identify factors ART health service providers and collaborating members can use to predict who is likely to have their CD4 counts improved and those that are not with regards to HAART. Several factors have been identified to affect the immune response to treatment. However, these findings do not fully convince researchers as being universally applicable. It is for this reason that researchers are encouraged to carry out such studies in other regions and setups to determine if similar findings could be found. There is less evidence showing such a study being carried out in Zambia. This makes it a good reason for such study to be acknowledged especially that most ART centres have been operating for a number of years with a relatively good number of new ART centres mushrooming. In the dynamics of research, this study acts as an aid that helps to emphasize and confirm whether similar findings of identified factors that would influence CD4 counts response to HAART in different regions of the world would be obtained in our local setup (Chreso Ministries ART centre). This would help health service providers to identify those who need more medical attention and treatment strategies during their HAART. Research findings would also help to identify those who are mostly at risk of poor immune response to HAART. It is hoped that this would act as a pioneering piece of study that would help the ministry of health, health related institutions, health practitioners and

academicians to conduct wider research into the dynamics of immunology using CD_4-T Lymphocyte count response to HAART. It is also an attempt to investigate the needs of HIV/AIDS patients and establish the risk factors potentially associated with a low CD4 count response to HAART in our local setting. Research findings would have positive effects/contributions to the rapidly evolving ART guidelines. This would also relay important message to policy makers to integrate and implement CD4 immunological trends analysis tools as a monitoring aid in all ART centres with specified numbers of patients on the programme that have been functional for a recommended time frame. Some of the issues covered in this study might be in-cooperated immediately in the ART guidelines to address urgent issues without necessary with the aid of advanced scientific research. The outcomes of this study may have an important bearing on the survival rates and screening in PMTCT centres for those on ART.

CHAPTER 2

LITERETURE RELATED TO THE STUDY

Knowledge and the picture HIV on an individual's immune system is changing rapidly. There is need for close supervision and improve on the existing techniques that would ensure monitoring CD4 trends and variations in trends, in HIV/AIDS patients on HAART (Stohr *et al.,* 2007). A study called Eurosida was conducted using absolute CD4 counts coupled with viral load monitoring. This was a prospective observational study of more than 8500 HIV/AIDS patients who were followed in 63 hospitals of the 20 European countries (Florence *et al*., 2003). The patients for this study were all those who started HAART with moderate immunologic suppression, with base line CD4 count below 350 cells/µl(measured within previous 6months at most). According to Allison (2008), as untreated HIV progresses, CD4 count decreases by about approximately 4% every year. With successful ART the CD4 count might increase by greater than 50 cells per micro litre within weeks after viral suppression. This tends to vary. Additionally, it may increase by 50-100 cells per micro litre per year thereafter, until a threshold is reached (Allison, 2006).

However, it is important to note that in some patients, CD4 count may not increase this quickly or steadily even with durable viral suppression. Association between risk factors potentially associated with a low CD4 count response in the Eurosida study were assessed by using a logic regression model and expressed as odds ratio, with 95% confidence intervals. The risk factors taken into account for low CD4 count response were demographic factors
(age, sex ratio, ethnic origin, HIV transmission group, region), antiretroviral treatment factors(number of nucleotide reverse transcriptase inhibitors(NRTI) use before HAART, start date of HAART, type of HAART, HAART duration), immunological factors(previous episodes of opportunistic infections). Using the SAS statistical software version 6.12, the findings of the study were that although

there is increased CD4 counts in patients commenced on HAART there is a poor immune reconstitution despite a good virological control among patients with a baseline CD4 count of <350 cells/µl. The underlying mechanism leading to this condition seems mainly driven by age and baseline immunological and virological status of patient.

Moore and Keruly (2007) found that patients tends to reach a plateau CD4 increase after four years of HAART with good or highest CD4 peaks among those who started treatment with CD4 counts above 350cell/µL. The study showed that people who commence treatment with CD4 counts much lower than 350cell/µL are less likely to attain Normal CD4-cell counts of ($\geq$750 cells/mm^3). On the other hand, some studies show that good immunological and virological responses to HAART can be achieved regardless of the CD4 count at initiation. For the purpose of this study, it is assumed that the plateau CD4 rise will not be reached within the first two years of HAART (Moore and Keruly, 2007) and that good CD4 response to HAART is a gain of 50-100 cells/µl per year (Allison. 2006).
Stohr *et al* (2007) in their study whose objective was to determine the timing of initiation of antiretroviral therapy(ART) in routine clinical practises, reflected treatment guidelines that evolved toward recommending starting therapy at lower CD4 cell counts. The study analysed the longitudinal data on 10820 patients. The study analysed the effects of non clinical factors such as (age, sex, ethnicity, and exposure category) by logistic regression. Kaplan-meir analysis was used to estimate the proportion of patient who had initiated ART by particular CD4 count among early presenters (initial CD4 count>500cells/µl). The results showed that there was a tendency to initiate ART at lower CD4 counts over the years 1997-2000, especially in the range 200-500cells/µL with little change thereafter. The conclusion of the study was that initiation of ART in the clinics included in this study reflected evolved treatment guidelines. A variety of consensus guidelines have been written and all recommend starting HAART well before the CD4 count fall below 200cells/µL, this being the threshold below which the risk of opportunistic infections(OI's) is reported to increase significantly. The above

studies strongly recommend trends analysis research in HIV patients on ART to determine if there are similar findings in other geographic areas.

A population-based cohort study of unselected adults in Misisi, a shanty compound in Lusaka, was under follow-up since 1999, and CD4 cell counts have been followed in participants since the initial survey (Katubulushi *et al.*, 2009). No antiretroviral drugs were used by any of the participants over the period of the study. Approval was given by the research ethics committees of the University of Zambia and the London School of Hygiene and Tropical Medicine. The initial cohort of 261 adults included 65 HIV-seropositive participants, of whom 12 died, and the researchers were able to obtain repeated measurements (in 1999, 2000, 2001 and 2003) in 24. Among the survivors, the mean age of men (n = 7) was 35 years (SD 7.0) and of women (n = 17) it was 28.6 years (SD 5.7), and the median initial CD4 cell count was 389 cells/µl (interquartile range 255-537). The median initial CD4 cell count was 122 cells/µl among the 12 who died. In the survivors, the mean decline over 4 years was 29 cells/µl per year. The mean percentage decline from baseline was 30%. In six of those who died and who had had at least two measurements separated by at least one year, the mean decline was 15 cells/µl per year. This data indicates that the decline in CD4 cell counts over the period from 1999 to 2003 in adults not treated with highly active antiretroviral therapy was slow, and the estimate of the rate of loss of CD4 cells is in very close agreement with the estimate of 21.5 cells/µl per year from Tanzania. This data support the idea that HIV progression to AIDS and death is slower than at first thought, even in very under-resourced populations living in crowded conditions. The data are unlikely to be skewed by depressed initial CD4 cell counts as a result of intercurrent infection because close analysis of the data depicted reveals only three individuals whose CD4 cell counts rose from an initially depressed level. None of these had any evidence of infection around the date of first sample collection in 1999.

However, the slow rate of progression observed in both of these cohort studies may not fully explain the observed age distribution of HIV infection seen in sub-Saharan Africa. At this rate of decline it would take over 19 years for newly

infected adults in similar populations to progress from a CD4 cell count of 774 cells/µl (the median CD4 cell count in our HIV-seronegative participants) to a count of 200 cells/µl (the level at which AIDS is defined). It is well established that infection occurs in young women at an earlier age than in young men, and AIDS-related deaths start to occur in women in their third decade of life. It could not have taken 19 years for these young women to progress from infection to AIDS if their infections were acquired sexually after puberty, so we must consider alternative explanations. This leads to the understanding that other factors are at play in influencing the rate of decline of the CD4 counts over a period of time. Some studies have demonstrated a number of factors that affect the CD4 count response to HAART such as:

1. Social/demographic factors

Age.

Most doctors confirm that CD4 recovery is slow and less perfect in older people. As in many other diseases, age is an important prognostic factor in HIV infection. Age at seroconversion and age at a given CD4 cell count were shown to be important determinants of progression and survival before the widespread introduction of HAART, starting in 1996 (Sophie *et al*., 2006). Since this date, many studies, including the ART Cohort Collaboration (ART-CC) (Egge., *et al*.,2002) , which includes 13 cohort studies conducted in Europe and North America, had shown that age remains an independent predictor of clinical progression on HAART. The impact of age in the ART-CC study seemed to be less marked than in the pre-HAART era, but a threshold effect was noted at 50 years. Because older patients are usually excluded from clinical trials, controlled data are lacking on this age group. Studies of the response to HAART in elderly patients have mostly involved small populations and relatively short follow-up (Perez and Moore. 2003).

Immunological and clinical responses to first-line HAART according to age at treatment outset in a cohort of 3015 HIV-infected patients, 401 of whom were

over 50 was examined. This analysis, based on the French Hospital Database on HIV (FHDH), showed that patients over 50 had significantly slower CD4 cell reconstitution than younger patients, despite a better virological response. Among patients with baseline HIV RNA levels >5 log copies/mL., The mean CD4 cell increase during the first 6 months of HAART was 42.9 cells/mm^3/month in patients under 50, compared with 36.9 cells/mm^3/month in older subjects. CD4 cell response slowed after 6 months of treatment, counts rising by 17.9 cells/mm^3/month in patients under 50, and by 15.6 cells/mm^3/month in older patients. This impaired immunological response was associated with a more rapid clinical progression in patients over 50. During the first year of HAART, 10.2% of patients over 50 died or had a new AIDS-defining event, compared with 5% of younger patients. After 5 years the respective figures were 21.9% and 12.4%. In contrast, viral suppression, defined by an HIV RNA level <500 copies/mL, was more frequent in patients over 50 than in younger patients [HR (hazard ratio) = 1.23, 95% CI = 1.11–11.38]. In most studies viral suppression was less frequently achieved in younger subjects, a phenomenon usually attributed to poorer adherence to treatment (Grabar. *et al.,* 2004).

Gender

A journal of women's health reported findings that there is no differences in HIV progression and response to HAART attributable to gender among patients accessing the Spanish hospital network. It was a multicenter, hospital-based cohort of HIV-infected patients attending 10 hospitals in Spain from January 1997 to December 2003. Kaplan-Meier and Cox regression were used to assess the effect of sex on time to AIDS, survival from AIDS, onset of a new AIDS event or death, and viral suppression from HAART. The study concluded no differences in HIV progression and response to HAART attributable to gender among patients accessing the Spanish hospital network (Hoyos *et al*., 2007).

Alcohol consumption

Studies of alcohol use in HIV-1 infected patients have resulted in conflicting and limited information regarding prevalence, as well as impact on HIV replication, disease progression and response to antiretroviral therapy. Alcohol, drug abuse and past medical information, including antiretroviral treatment, were obtained using research questionnaires and medical chart review in 220 HIV-1 infected drug users. A physical examination was conducted and blood was drawn to evaluate immune measures and nutritional status. Heavy alcohol consumption, defined as daily or 3-4 times per/week, was reported in 63% of the cohort. Men (odds ratio (OR) =2.6, 95% CI 1.13-5.99, p =0.013), and participants between 35 and 45 years of age were three times more likely to be heavy alcohol users (p =0.006 and 0.0009, respectively). Low serum albumin levels were more evident in heavy alcohol users than non-drinkers (p =0.003).

Heavy alcohol users receiving antiretroviral therapy were twice as likely to have CD4 counts below 500 than light or non-drinkers (95% CI, 1-5.5, p =0.03), and highly active antiretroviral therapy (HAART)-treated heavy alcohol users were four times less likely to achieve a positive virological response (95% CI, 1.2-17, p =0.04) Maria., *et al* (2002). Alcohol consumption is prevalent in our HIV-1 infected drug user cohort and significantly impacts both immunological and virological response to HAART treatment.

Henrich *et al.,* 2007 examined association of alcohol abuse and injection drug use (IDU) with the immunologic and virological responses to highly active antiretroviral treatment (HAART) in urban community health clinics. The medical records of 293 HIV-infected adult patients who visited either of two urban health clinics in New Haven, Connecticut, from June 2003 to December 2004 were retrospectively reviewed. Changes in mean CD4 lymphocyte counts and undetectable viral loads were compared before and after the initiation of HAART for patients categorized into one of four substance abuse groups: history of neither alcohol abuse nor IDU, alcohol abuse only, IDU only, or both. Unadjusted mean improvements in CD4 count for the four groups were 136, 97, 20, and 27,

respectively. In a linear regression model adjusted for age, gender, and baseline CD4 count, history of IDU only ($p = 0.037$) and a combination of alcohol abuse and IDU ($p = 0.038$) were associated with a lesser increase in CD4 count after HAART compared with those with neither alcohol nor IDU. No significant associations were found between substance abuse history and changes in detectable viral load. Results showed that many patients at urban health clinics have a history of either injection drug use or alcohol abuse, and that injection drug use is negatively associated with the immunologic (CD4) response to HAART in urban HIV-infected individuals. This study highlighted the importance for clinicians of understanding the negative associations of substance abuse with the treatment response of HIV-infected patients at urban health centers (Henrich *et al.,* 2007).

Smoking.

Tobacco smoking is associated with poorer response to antiretroviral therapy and worse disease progression in HIV/AIDS patients especially women, according to a report published in the June 2006 *American Journal of Public Health.* Joseph Feldman, MD, and colleagues analyzed data from 924 participants starting HAART in the Women's Interagency HIV Study; subjects were followed for periods of up to nearly eight years. After controlling for potentially confounding factors such as age, race, illegal drug use, hepatitis C co-infection, and past AIDS diagnosis, the researchers found that women who smoked cigarettes had poorer virological and immunological response to HAART, lower CD4 cell counts, higher HIV viral loads, a 36% greater likelihood of developing AIDS-defining illnesses, and a 53% higher risk of death compared with non-smokers; however, the rate of specifically AIDS-related death was similar. The authors concluded that some of the benefits provided by HAART are not revealed in cigarette smokers, and emphasized the need for smoking cessation efforts targeting HIV positive women (Fieldman *et al*., 2006).

In a study conducted by the University of Miami, the researcher found that HIV positive smokers response to HAART decreased by 40% as measured through drug levels in the body, CD4 counts and viral loads. Another study assessed the association of cigarette smoking with the effectiveness of HAART among low income women in the United States of America. This study showed that apart from poor adherence to treatment, these smokers had poorer viral response, poorer immunologic (CD4 count) response, greater immunologic failure and more frequent immunologic failure.

Social-economic status.

Clinical psychiatry news of September 2003 (Robert, 2003) reported a longitudinal study having study participants highly diverse by ethnicity, gender, and socioeconomic status (ses). The group was 25% white, 43% African American, 28% Hispanic, and 5% other. Males made up 65% of the group. Sixty-two percent of the group earned less than $10,000 annually, 20% earned between $10,000 and $20,000, and the rest earned more than $20,000. Socioeconomic status was defined as a weighted composite of education, income, and job status. This longitudinal study of 186 HIV-positive patients revealed a significant connection between socioeconomic status and disease progression markers, including morbidity, mortality, and CD4 cell count.

2. ART factors

Adherence

HAART adherence predicts treatment response and progression to AIDS and death according to published research from the United States. Although adherence to HAART at a level above 95% has been associated with optimal viral suppression, the impact of different levels of adherence on long-term clinical outcomes has not been determined. Researchers used an objective pharmacy-based measure to examine the association between three levels of adherence to

HAART and disease progression among a population-based cohort of HIV-infected patients attending an urban HIV specialty clinic. Findings were that higher levels of adherence to HAART were significantly associated with longer time to virologic failure ($p<0.001$), greater increase in CD4 cell count ($p=0.04$), and lower risk of progression to clinical AIDS or death ($p<0.007$), Kitahata and coworkers reported. After controlling for other factors, patients with low adherence had over five times the risk of disease progression than patients with moderate adherence ($p=0.007$) or patients with high adherence ($p=0.001$). There was no significant difference in the risk of progression between patients with moderate and high levels of adherence ($p>0.2$). Patients who progressed to AIDS or death had significantly higher viral loads ($p=0.01$) and lower CD4 cell counts ($p=0.03$) than patients who experienced virological failure, but did not progress, the authors concluded (Kitahata *et al.,* 2004).

Similar findings were reported in a study that looked at adherence to antiretroviral therapy and CD4 T-cell count responses among HIV-infected injection drug users (Evan *et al.*, 1996). In this study research findings clearly stated that Overall, the CD4 cell count response rate was slower among injection drug users in Kaplan-Meier analyses (log-rank: $p<0.05$). Injection drug users are poor in adherence to HAART. However, no differences existed when the analyses were restricted to adherent patients (log-rank: $p=0.349$). Similarly, the differences in the time to CD4 cell count response observed in univariate Cox regression analyses for patients with a history of injection drug use [relative hazard: 0.85 (95% CI: 0.75-0.97)] diminished after adjustment for adherence [adjusted relative hazard: 1.02 (95% Cl: 0.89-1.16)]. In Conclusion, these data demonstrate the importance of adherence on CD4 cell count responses and highlight the need for interventions to improve antiretroviral adherence among injection drug user.

3. Immunologic factor

Baseline CD4 count

Patients starting antiretroviral (ARV) therapy gain roughly equal numbers of CD4 cells regardless of their initial count, except for those starting with extremely low or extremely high counts. Patients starting treatment at low counts will probably never reach CD4 counts anywhere near normal. This adds to the weight of evidence that starting treatment earlier, before CD4 cell count fall below 350 cell/μL or so, it is better than waiting until counts have fallen below 200 cells/μL. (Huges *et al.,* 2007).

> The UK CHIC cohort study of over 17,000 UK HIV patients enrolled clients who started ARV therapy between the beginning of 1998 and the end of 2005 and who had maintained undetectable viral loads from six months after the start of treatment to the end of the study. They had to have had at least one pre-treatment CD4 count and another one at least six months after the start of therapy (in practice, the average number of CD4 counts done per patient was 13). They also needed annual viral load measurements to be included. Over 4,100 patients met the testing criteria of which 2,780 (67.6%) maintained undetectable viral loads through to the end of 2005. The study found that the pre-treatment (baseline) CD4 count varied according to the type of patient. For instance, gay men comprised only 38% of those starting with the lowest CD4 counts (below 25 cells/mm^3), but 75% of the 91 patients starting treatment with CD4 counts over 500 cells/mm^3. Conversely, heterosexuals formed 56% of those starting treatment with counts under 25 cells/mm^3 but only 18% of those starting treatment with more than 500 cells/mm^3, according to the Huges *et al* (2007) study. In general, a higher proportion of those starting treatment with CD4 counts below 200 cells/mm^3 were female, African and heterosexual.

The cumulative CD4 increases for each stratum of baseline CD4 count are best summarised in a table below.

FIGURE 2: CUMMULATIVE CD4 INCREASE. (Huges *et al*. 2007)

Baseline CD4 count	Increase over five years
Under 25	389
25-50	322
50-100	309
100-200	285
200-350	289
350-500	281
Over 500	160

It can be seen that those with the very lowest baseline CD4 counts had the highest increase on ARV's, while those with the very highest had the lowest increase. However there was relatively little variation in CD4 increase in those in the middle strata, with patients with 25-50 CD4 cells only gaining 40 more CD4 cells than those starting with 350-500 CD4 cells. The eventual CD4 cell count is therefore much more dependent on the baseline count than on variations in the rate of increase while on treatment, and only those starting treatment with counts above 350 cells/mm^3 achieved CD4 counts nearing normality for people without HIV. The median CD4 count at year five was 169 cells lower in those starting with 25-50 CD4 cells than in those starting with 200-350, and it was 121 higher in those starting treatment with 350-500 cells. The rate of CD4 increase declined every year, and again there was remarkable consistency for all but those starting at the highest or lowest CD4 counts. The average CD4 count gain in the first year, in all baseline groups except those starting with more than 500 cells, was between 172 and 181 cells (those starting with over 500 gained only 98 cells). In the second year the vast majority of patients, namely those starting at counts anywhere between 25 and 350, gained between 52 and 69 cells; in year three between 30 and 43 cells; in year four 19 to 29 cells; in year five 13 to 21 cells.

CD4 cell gains in patients starting at counts below 25 were consistently higher (in the region of 12 more cells a year than any other group, apart from in the first year), and patients starting over 500 consistently lower. There is of course huge individual variation concealed within these average figures. However the fact that the rate of CD4 increase, in all patients in this large cohort, consistently slowed down from year to year brings with it the sobering conclusion that patients who start therapy with low CD4 counts will never, at least on standard antiretroviral therapy, regain all the immune function that HIV took away (Huges *et al.* 2007).

2.1 Research questions.

This study seeks to answer the following questions:

1. Does HAART have a positive effect on the HIV/AIDS patient's immune system based on an indication of their gained CD4-counts trend analysis within 24 months of treatment at Chreso Ministries ART centre?
2. Are age, gender, social economic class, adherence and baseline CD4 count at treatment initiation important determining factors in HIV/AIDS patients' response to HAART at Chreso Ministries ART centre?

CHAPTER 3

RESEARCH OBJECTIVES AND HYPOTHESIS

3.0 General objective

The study seeks to identify factors that predict CD4-TLyphocyte (immunologic) response in patients commenced on HAART within 24 months of treatment at Chreso Ministries VCT and ART centre.

3.1 Specific objectives:

1. To determine whether there is an association between social demographic factors and improved CD4 Lymphocytes count as a response to HAART
2. To identify association between ART factors (adherence, regimen) and improved CD4T lymphocytes count as a response to HAART.
3. To identify association between the immunological factor of CD4 count above 350 cells/μL at treatment initiation and improved CD4 T Lymphocytes count as a response to HAART.

3.2 Hypothesis:

H_o: Social demographic, immunologic and ART factors cannot be used to predict immune (CD4TLymphocyte) response to HAART.

H_1: Social demographic, immunologic and ART factors can be used to predict immune (CD4TLymphocyte) response to HAART.

CHAPTER 4

RESEARCH METHODOLOGY

4.1 Study variables

FIGURE 3: CONCEPTUAL FRAMEWORK OF VARIABLES THAT INFLUENCE

CD4 COUNT RESPONSE TO HAART

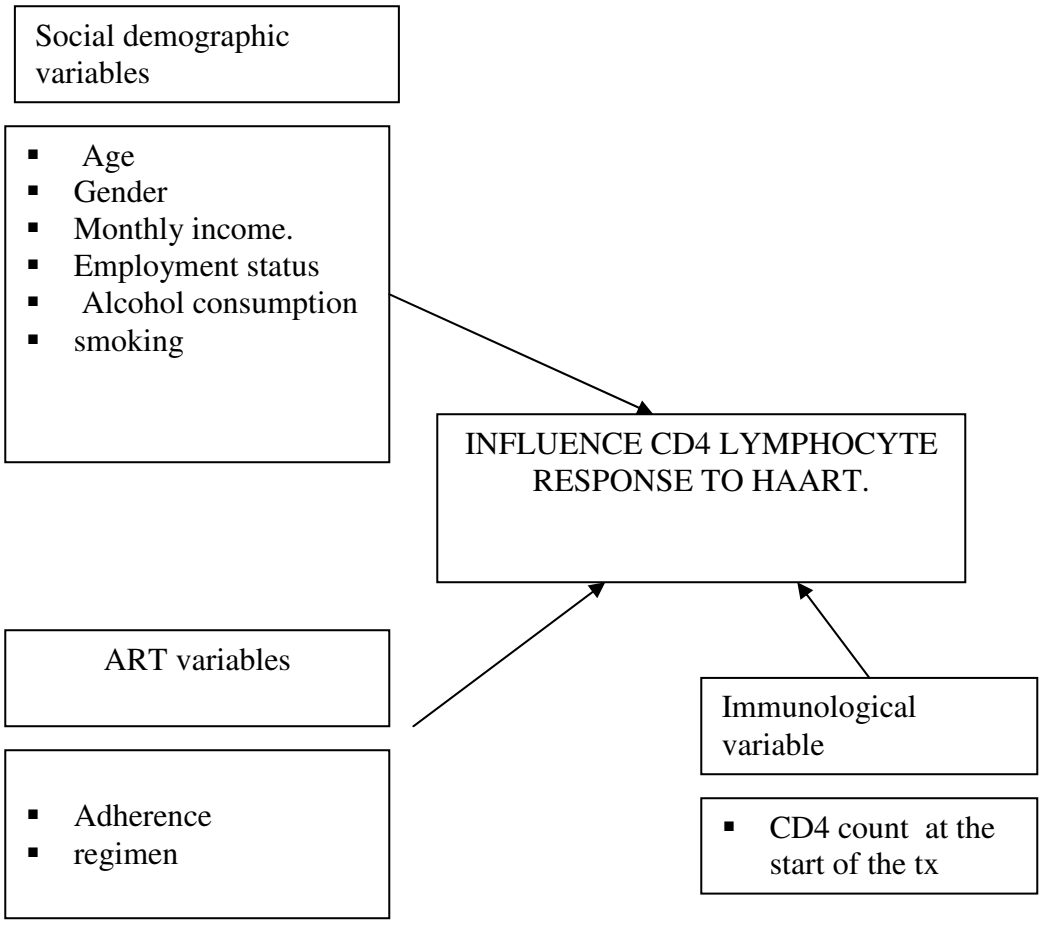


Figure 3 above summarises the variables that affect CD4 response to HAART.

NOTE: Monthly income and employment status are not the best measure of socioeconomical status. For the purpose of this study monthly income and

employment status are used as proxy measures of social economic status due to limited time and resources to complete the study.

4.1.1 Operationalisation of variables

This study was set to examine an association between CD4 response to HAART being dependent variables with Social demographic, immunologic and ART factors being the independent variables.

1. Age was operationalised as a measure according to the following interval scale; 15-20 years, 21-30 years, 31-40 years, 41 years and above.
2. Gender was operationalised as being male or female.
3. Alcohol consumption was operationalised as intake or consuming any locally brewed or commercial alcohol and was categorised into alcohol consumers and non alcohol consumers.
4. Smoking was operationalised and was categorised into smokers and non smokers.
5. Monthly income was operationalised and was measured on nominal scale using the values: High monthly income (>K 500,000) and low income (<500,000).
6. Adherence was operationalised and was measured >95% adherent as adherent and <95% adherence as non adherent.
7. CD4 nadire at treatment initiation was taken as the actual CD4 count recorded when a client commenced HAART.
8. Type of regimen at treatment initiation was operationalised and categorised according to its kind.
9. CD4 response to HAART as a dependant variable was operationalised and categorised as poor CD4 (<50-100cells/μL/year) and good CD4 (≥50-100cells/μL/year) response to treatment.

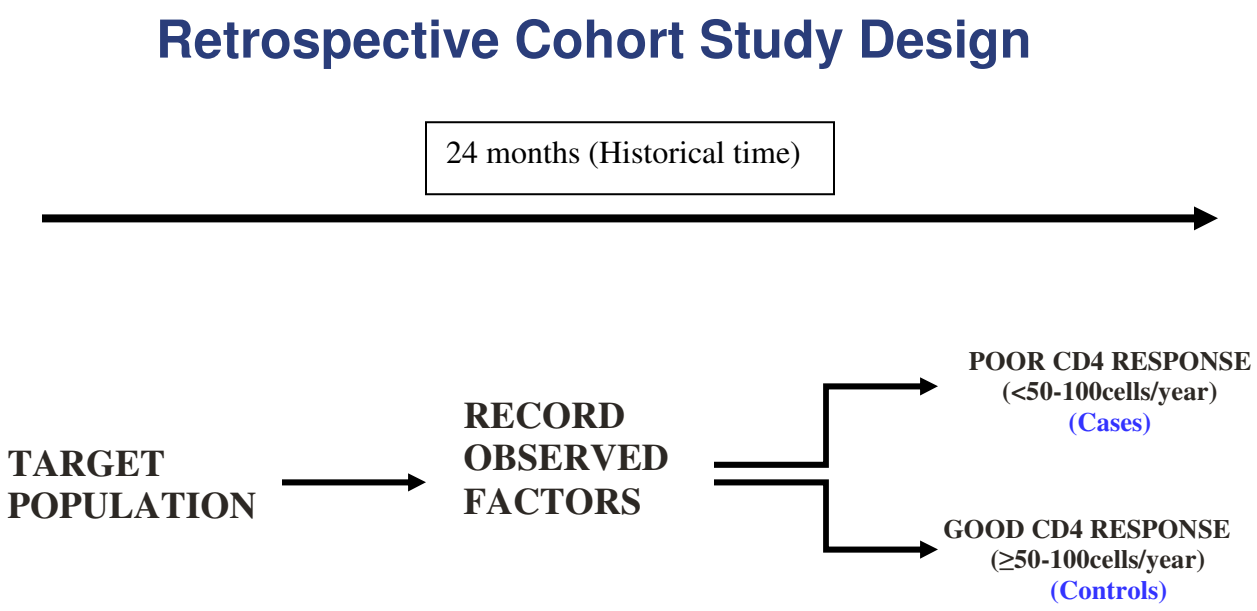
FIGURE 4: TABLE OF VARIABLES

VARIABLES					
#	**INDEPENDENT**	**CLASSICATION**	#	**DEPENDENT**	**CLASSIFICATION**
1	Age at tx initiation	Continuous	1	CD4 response to HAART	Discrete
2	Gender	Discrete			
3	Alcohol consumption	Discrete			
4	Smoking	Discrete			
5	Monthly income	Continuous			
6	Adherence	Discrete			
7	CD4 at tx initiation	Continuous			
8	Type of ART regimen	Discrete			

4.2 Study design and setting

This was a retrospective cohort study that compared factors/variables (age, sex, drinking, smoking, income, adherence, regimen and CD4 count) in immunologicaly poorly responsive (cases) and responsive clients (controls) to HAART, based on their defined CD4 count in response to treatment. The controls were those who have had a significant increase in their CD4count (≥50-100 cells/μL) per year and the cases were those who had their CD4 counts raised by (<50-100 cells/μL) per year in response to 24 months of HAART.

FIGURE 5: DIAGRAMATIC REPRESENTATION OF RETROSPECTIVE COHORT STUDY



The study began immediately after approval and clearance form the ethics committee of the University of Zambia. The study was done at Chreso ministries ART centre. Chreso Ministries is a privately own faith based organisation in Lusaka funded through president bush's PEPFAR initiative. A pre-test of the study was done at circle of hope ART centre another beneficiary of PEPFAR based in Makeni, Lusaka. All the above mentioned ART centres provide free VCT, ARV's and the necessary clinical support and treatment to clients. All the centres were equipped with laboratories equipped to run tests such as: CD4's,

LFT's, HIV including other STI's and routing tests necessary to commence and monitor patients on HAART. Chreso Ministry had 7000 patients on care and 3900 patients on ART with the survival rate of 91% (Chreso Ministries Lusaka, May 2009 statistics Report).

4.3 Data collection tools

The study was purely quantitative. The quantitative method used was retrospective review of electronic patients' medical records to extract the baseline data from the smartcare and or careware database. Since 2006, Chreso Ministries used a Computer software's known as smartcare which is electronic health record (EHR) system that has been developed in the nation of Zambia for Zambians by Zambians and their international partners. It also contained the 2004 electronic health records that were imported from careware software. Smartcare was used to retrieve and review the patients' medical records. The findings were confirmed using the patients' medical files or charts from the filing cabinet. Therefore electronic health record system and medical files or charts were used in identification and categorising of study subjects. It was ensured that security processes were in place in a fully secured storage and work environment prior to receiving or transfer of data, and that all these processes could be demonstrated upon request. No persons other than the persons approved in written protocol were allowed to see the data before the final analysis was done as a measure of securing access and use of data.

4.4 Sample Size.

Factors that would influence the patients CD4 count rate of response to HAART were determined and assuming they would improve CD4 response to treatment from 90%-95% and the power of study of 50%, one tailed taste at a significant level of 5%. The required sample size was calculated from the following:

$$n = \frac{(P1Q1 + P2Q2)}{(P1 - P2)^2} * f(\alpha,\beta)$$

Where;

- (P1) Expected proportion in the control group
- (P2) Expected proportion in the intervention group
- (α) Significance level
- (1-β) Power of the study

$$n = \frac{(90x10 + 95x5)}{(90 - 95)^2} \text{ x } 2.71$$

$$n = \frac{(900 + 475)}{25} \text{ x } 2.71$$

n = 149.05 = 150

Considering an average response rate of 90%, the required number in each group came to

$$n = \frac{149.05}{0.9} = 170$$ files of clients in each group giving a total of 340

4.5 Sampling.

Chreso Ministries ART centre was selected because it is geographically located at the heart of Lusaka and had relatively high number of patients on ART that would give a representative sample size. The centre was equipped with computerised patients' records coupled with the smartcare computer software that makes clients' data retrieval and analysis easier and faster. The researcher used computerised random sampling in selection of study subjects because the sampling frame was computerised patients records thus being quick, effective and more representative. Furthermore, the researcher with the help of the IT specialist cleaned the patients' medical records from smartcare by removing the records of children of the age of 5 years and below including clients who had less than four CD4 rechecks within 24months of HAART to come up with a study population. The study population was then exposed to computer randomisation to generate the required sample size. In this type of sampling, each sample element in the population had an equal chance of being selected. From the population the researcher determined an ideal sample at 0.95 confidence interval. Data Entry Clerks and Information Technology Specialist from the department of HMIS were used as research assistants to identify patients who had at least four CD4 counts recheck within 24 months of HAART.

4.5.1 Enrolment procedure

The **inclusion criterion** was that respondents had to be:

- All age groups above 5years who have had at least four consecutive repeat CD4 count checks within 24months of HAART.

- Recruited on ART and their names and ID appeared in the computerised files.

- With medical records having all the necessary information (variables) required for this study captured at treatment initiation.

The **exclusion criteria** was that respondents:

- Were not to be of any age groups less than 5years of age.

- Were not to have their names and ID missing in the electronic health record (EHR) SMARTCARE.

- Were not to lack any of the necessary information (variables) required for this study captured at treatment initiation.

- Were not to be on HAART for less than 24 months.

NOTE: Children under five were excluded from the enrolment procedure because WHO recommends use of CD4% under this age group due to their significant variations in absolute CD4 counts.

4.5.2 Target Population

The target population comprised files of HIV positive clients who have been accessing HAART services from Chreso Ministries ART centre in Lusaka for a period of 24months.

4.6 Testing of Data Collection Tool/pre-test

Data collection tools were pre-tested as a pilot study from Circle of Hope on files of 40 clients. This ART centre was conveniently sampled because it has similar strategies and formats of patients' management to Chreso Ministries. Therefore,

having considered the short time frame in which the study had to be undertaken, it was found convenient to pick Circle of Hope for pilot study. The pilot test was done two weeks before the commencement of the actual study. The objectives of the pilot study were:

1. To determine the potential of the data collection tools to yield reliable results
2. To determine the length of time it would take to locate and analyse data from the randomly selected patients' records.
3. To identify the expected challenges during the study
4. To estimate the required materials/resources

4.7 Study Sites

The study was undertaken from Lusaka at Chreso Ministries ART centre.

4.8 Data Entry and Analysis

The obtained data was entered in Epi Info and exported to SPSS were analysis was done. The Chi-Square test was used to determine associations between the identified factors and CD4 count response to HAART using the crosstabulation tables. The cut-off point for statistical significance was set at 5%. The logistic regression model was used to determine the probability of predicting the improved CD4 Lymphocyte count using the factor mentioned in the null hypothesis.

4.9 Ethical Considerations.

Clearance was sought from the Research Ethnics Committee of the University of Zambia and the Directorate of Graduate studies before undertaking the study. Since this study involved retrieval and analysis of clients' confidential files, it was

paramount to obtain permission to undertake this study from the hospital board and the designated research and ethics committees. No consent was obtained from the owners of the selected files since there was no direct contact or interaction with these clients. Approval from the Research Ethics Committee and Directorate of Graduate studies was used as a waiver to undertake this study at Chreso Ministries ART centre. Clients' data was abstracted from smartcare system and was confirmed using clients charts in cases where irregularities were noted. During the course of the study, there was no identified harm likely to occur to the owners of selected medical files

CHAPTER 5

PRESENTATION OF DATA AND ANALYSIS

5.0 Introduction

Following retrospective review of medical records, 340 files of clients who were registered for ART at Chreso Ministries were selected for analysis. 170 files of clients whose CD4 count increased by ≥50-100 /year within 24 months of treatment were selected as controls. On the other hand, 170 files of clients whose CD4 count had not increased by ≥50-100/year were selected as cases. 34.7% of those selected were above 40 years of age and 65.3% were below the age of 39. Out of 340 clients files selected, (52.9%) were males and 160 (47.1%) were females. 68.2% of the clients files reviewed 95% adherence to ART, 14.1% were smokers and 24.1% were alcohol consumers. The frequency data captured from the smartcare is best summarised in Table 1.

Table 1: Frequency data of social demographic, immune and ART variables

VARIABLE	FREQUENCY	VALID PERCENTAGE
Social demographic variables		
AGE		
15-20 years	16	4.7
21-30 years	76	22.4
31-40 years	148	43.5
41 and above	100	29.4
SEX		
Male	180	52.9
Female	160	47.1
SMOKING		
Smoker	48	14.1
Non Smoker	292	85.9

ALCOHOL		
Drink alcohol	82	24.1
Do not drink alcohol	258	75.9
INCOME		
>K 5OO,OOO per Month	186	54.7
<K 500,000 per Month	154	45.3
EMPLOYMENT		
Formaly employed	196	57.6
Not formaly employed	144	42.4
ART Variables		
REGIMEN		
Combivir	174	51.2
Truvada	166	48.8
ADHERENCE		
Adherent (95% Adherence)	232	68.2
Not Adherent (<95% Adherence)	108	31.8
Immune variable		
CD4 NADIRE		
Baseline CD4 > 350 cells	220	64.7
Baseline CD4 <350 cells	120	35.3

5.1 Social demographic factors and CD4 count response to HAART.

In order to determine association between social demographic factors and CD4 response to HAART, 6 variables were identified; age, sex, smoking, alcohol consumption, income and employment status.

Table 2: Association between age and CD4 response to HAART

	CD4		Total
	Increased CD4 by ≥50-100 cells/year	Increased CD4 by < 50-100 cells/year	

AGE	15-20 years	7(43.8%)	9(56.3%)	16(100%)
	21-30 years	36(47.4%)	40(52.6%)	76(100%)
	31-40 years	74(50%)	74(50%)	148(100%)
	41 and above	53(53%)	47(47%)	100(29.4%)
Total		170(50%)	170(50%)	340(100%)

The observed differences in CD4 response to HAART in 24 months according to age in Table 1 could have been due to chance (Chi-Square=1.30; p=0.255).

Table 3: Association between Gender and CD4 count response to HAART

		CD4		Total
		Increased CD4 by ≥50-100/year	Increased CD4 by < 50-100/year	
Gender	Male	72(40%)	108(60%)	180(100%)
	Female	98(61.3%)	62(38.8%)	160(100%)
Total		170(50%)	170(50%)	340(100%)

The observed proportions of CD4 response to HAART according to gender in table 2 was highly statistically significant (Chi-Square=15.30; p<0.001).

Table 4: Association between smoking and CD4 count response to HAART

		CD4		Total
		Increased CD4 by ≥50-100/year	Increased CD4 by<50-100/year	
SMOKING	Smoker	24.0(50%)	24.0(50%)	48.0(100%)
	Non Smoker	146.0(50%)	146.0(50%)	292.0(100%)
Total		170.0(50%)	170.0(50%)	340.0(100%)

The table shows that we had equal number of people from the category of those that used to smoke and had increased CD4 by ≥50-100cells/µL/year in 24 months of HAART (50.0%) compared to the category of those that did not smoke and had increased CD4 by ≥50-100cells/µL/year in 24 months of HAART (50.0%), the observation could have been due to chance as this was not statistically significant (Chi-Square=0.00; p=1.000).

Table 5: Association between alcohol and CD4 count response to HAART

		CD4		Total
		Increased CD4 by ≥50-100/year	Increased CD4 by <50-100/year	
ALCOHOL	Drink alcohol	26(31.7%)	56(68.3%)	82(100%)
	Do not drink alcohol	144(55.8%)	114(44.2%)	258(100%)
Total		170(50%)	170(50%)	340(100%)

The observed association between alcohol use and CD4 count response to HAART was highly statistically significant (Chi-Square=14.46; p<0.001). Those who drink alcohol (31.7%) were less likely to have increased CD4 by ≥50-100cells/µL/year in 24 months of HAART compared to 55.8% of those who do not drink alcohol.

Table 6: Association between income and CD4 count response to HAART

		CD4		Total
		Increased CD4 by ≥50-100 cells/year	Increased CD4 by <50- 100 cell/year	
INCOME	>K 500,000 per Month	82(44.1%)	104(55.9%)	186(100%)
	<K 500,000 per Month	88(57.1%)	66(42.9%)	154(100%)
Total		170(50%)	170(50%)	340(100%)

Association between income and CD4 response to HAART was statistically significant (Chi-Square=5.75; p=0.017). Among proportion of clients who earned more than K500,000, 44.1% had increased CD4 by ≥50-100cells/μL/year in 24 months of HAART, compared to 57.1% in clients who earned less than K500,000

Table 7: Association between employment status and CD4 count response to HAART

		CD4		Total
		Increased CD4 by ≥50-100 cells/year	Increased CD4 by <50-100 cells/year	
EMPLOYMENT	Formally employed	96(49%)	100(51%)	196(100%)
	Not formally employed	74(51.4%)	70(48.6%)	144(100%)
Total		170(50%)	170(50%)	340(100%)

The association between employment status and CD4 response to HAART was not statistically significant (Chi-Square=0.19; p=0.661).

5.2 ART factors and CD4 count response to HAART

In order to determine association between ART factors and CD4 count response to HAART, 2 variables were identified; regimen and adherence.

Table 8: Association between regimen and CD4 count response to HAART

		CD4		Total
		Increased CD4 by ≥50-100/year	Increased CD4 by <50-100/year	
REGIMEN	Combivir	74(42.4%)	100(57.5%)	174(100%)
	Truvada	96(57.8%)	70(52.2%)	166(100%)
Total		170(50%)	170(50%)	340(100%)

The association between the two types of regimen and CD4 count response to HAART status was statistically significant (Chi-Square=7.96; p=0.005).

Table 9: Association between adherence and CD4 count response to HAART

		CD4		Total
		Increased CD4 by ≥50-100 cell/year	Increased CD4 by <50-100cell/syear	
ADHERENCE	Adherent (95% Adherence)	148(63.8%)	84(36.2%)	232(100%)
	Not Adherent (<95% Adherence)	22(20.4%)	86(79.6%)	108(100%)
Total		170(50%)	170(50%)	340(100%)

Table 9 shows association between adherence and increased CD4 count by ≥50-100/year in 24 months of HAART. Clients who adhered to treatment were likely to have an increased CD4 response to HAART (Chi-Square=55.581; p<0.001).

5.3 Immune factors and CD4 count response to HAART

CD4 nadire was the only identified immune factor captured at treatment initiation from the smartcare database. It was also of interest to determine if there is an association between the captured CD4 count at treatment initiation and CD4 response to HAART within 24 months.

Table 10: Association between CD4 nadire and CD4 count response to HAART

		CD4		Total
		Increased CD4 by ≥50-100 cells/year	Increased CD4 by <50- 100cells/year	
NADIRE	Baseline CD4 above 350 cells	128(58.2%)	92(41.8%)	220(100%)
	Baseline CD4 below 350	42(35%)	78(65%)	120(100%)
Total		170(50%)	170(50%)	340(100%)

A test of significance (Chi-Square=16.69; $p<0.001$) indicates that the observed proportion of clients with baseline CD4 count above 350 cells/µL at treatment initiation among those that had increased CD4 count (58.2%), was statistically different from proportion of clients who did not have increased CD4 count (41.8%) as shown in table 9. This shows that there was an association between baseline CD4 and CD4 count response to HAART.

5.4 Electronic Record Reviews to Determine the Probability of Predicting CD4 Response to HAART.

Table 11: Probability of predicting CD4 response to HAART using logistic regression model

NUMBER	VARIABLE	PROBABILITY VALUE	p VALUE
1	Age	0.529	0.255
2	Gender	0.606	< 0.001
3	Adherence	0.688	< 0.001
4	Smoking	0.500	1.000
5	Alcohol	0.588	<0.001
6	Income	0.565	0.170
7	Employment	0.512	0.661
8	Regimen	0.576	0.005
9	CD4 nadire	0.606	<0.001

The probabilities of predicting CD4 count response to HAART for age, sex, adherence, smoking, alcohol consumption, income, employment status, ART regimen, CD4 nadire were between 0.500 and 0.606 with adherence having the highest probability of 0.688.

CHAPTER 6

DISCUSION OF RESULTS

6.0 Introduction

In this study, associations between social demographic variables (Age, sex, income, employment status, smoking and consuming alcohol), ART factors (Adherence and ART regimen) and immune factor(CD4 nadire) on one hand and CD4 count response to HAART on another were examined. Also in this study, we tried to determine the probability of predicting CD4 response to HAART using the above mentioned variables captured at commencement of treatment. It would be important to note that adherence was not captured at enrolment or treatment initiation but during follow up visits reflected in smartcare database.

6.1 Limitations of the study

The following were the limitations of the study;

1. Definitions of adherence: Defining adherence was a problem. Because there was no universally accepted definition of adherence, we found it very difficult to define the adherent and the non adherent. It is possible that some of the files of clients we classified as non adherent could as well have been wrongly classified.
2. Limited number of variables captured during patient enrolment: In order to determine probabilities of predicting CD4 response to HAART, we needed to identify some variables that were found in the records of the respondents, captured during commencement of ARV therapy. The problem was that variables considered for this study was not recorded in all the files of clients on HAART and this limited us to determine

probabilities of predicting only by using income, employment status, age, sex, smoking, alcohol consumption, adherence, regimen and CD4 nadire.

3. Limited number of variables to measure social economic status. Only income and employment status were used as proxy measures of social economic status.
4. Sample size: The sample size was too small. A bigger sample size is recommended with a power of study of at least 80%.
5. This study relies so much on the details provided by the clients at enrolment on ART program. The study is likely to be affected in cases were clients give wrong details.

6.2 Discussion on associations between social demographic variables and CD4 count response to HAART.

Age, sex, smoking, alcohol consumption, income and employment status were the identified social demographic variables in this study.

6.2.1 Age and CD4 count response to HAART

In this study no association was found between age at treatment initiation and CD4 response to HAART. This is in line with the findings of the other study (Grabar *et al.* 2004) which reported that age was not an independent predictor of CD4 response to HAART unless at a threshold age of 50 years. Clients over the age of 50 years were less likely to have their CD4 increased during HAART. However, in our study no analysis could be made directly on clients over the age 50 years because of limited number of clients above this age in the smartcare data base.

6.2.2. Gender and CD4 count response to HAART

In this study there was an association between Gender and CD4 response to HAART. 42.4% of clients who had their CD4 count increased by ≥50-100cells/year in 24 months of treatment were male and 57.6% were female. This was contrary to the study by Hoyos *et al* (2007) which reported no difference in HIV progression and response to HAART attributed to gender. This could be explained by the fact that most males who access treatment at Chreso Ministries come in there late stages (WHO stage 3&4) of HIV due to stigma. This makes it very difficult for males who seek treatment late to have good immunological response to HAART at Chreso Ministries ART centre. Additionally, this study captured more males (52.9%) compared to females (47.1%) different from the general trend observed in other studies because it has been successful in the male involvement campaign programs.

6.2.3. Smoking and CD count response to HAART

In this study, no association was found between cigarette smoking and CD4 count response to HAART. This was different from the findings of other studies that reported poor immunological and virological response to HAART among smokers especially in women (Fieldman *et al*. 2006). This could be due to the fact that the 24 months used in this study compared to the 8 years used in Fieldman *et al* (2006) study, was not enough to reveal the effects of smoking on CD4 count response to HAART. The effect of smoking on the immune system is very slow and also depends on the quantity of cigarettes consumed in a given period of time. In this study, cigarette smoking quantification into heavy smokers and moderate smokers could not be done because the numbers of cigarettes smoked by clients were not captured in smartcare database. Therefore, it is recommended that more time and indicators were needed in this study to appreciate the effect of smoking on CD4 count response to HAART.

6.2.4 Consuming alcohol and CD4 count response to HAART

A study by Maria *et al* (2002) indicates that heavy alcohol users receiving antiretroviral therapy were twice as likely to have CD4 counts below 500 as light or non-drinkers, and highly active antiretroviral therapy (HAART)-treated heavy alcohol users were four times less likely to achieve a positive immunologic and virological response. Similarly, this study showed an association between alcohol consumption and CD4 count response to HAART within 24 months. There was 55.8% non alcohol consumers who had increased CD4 count compared to the 31.7% alcohol consumers. These findings agree with the findings of other studies on alcohol and CD4 count response to HAART, though alcohol users were not further categorised into heavy and light alcohol users.

6.2.5 Income and CD4 count response to HAART

Our study reviewed an association between income and CD4 response to HAART. Among proportion of clients who earned more than K500, 000 per month, 57.1% had increased CD4 by ≥50-100cells/µL/year in 24 months of HAART, compared to 44.1% in clients who earned less than K500, 000 per month. Clients who earned more than K 500,000 per month were more likely to have an increased CD4 count response to HAART. Though this study agrees with other studies that have been done on socioeconomic status (Robert, 2003), it is not ideal to make full comparison to such studies based on income alone. The K 500,000 income per month that was used as a cutoff point of the low and high income earners is subject to be criticised because of Zambia's current poor economic state. Additionally, the geographic location of Chreso Ministries ART centre being surrounded by shanty compounds entails that most clients who access treatment at Chreso Ministries are of low socioeconomic status. Socioeconomic status in other studies was well defined as a weighted composite of education, income, job status and amount of assets. It is for this reason that income cannot be used as an independent measure of socioeconomic status. It is recommended to carry out such a study in remote setups were most peoples

incomes fall far much below K 500,000 per month and determine whether similar findings would be obtained.

6.2.6 Employment status and CD4 count response to HAART

In this study, there was no association between employment status and CD4 response to HAART. This does not agree with Robert (2003) study on socioeconomic status. The definite reason for the difference in findings is that employment status on its own is not the best measure of socioeconomic status.

6.3 Discussion on association between ART factor and CD4 count response to HAART

ART regimen and adherence were the only two variables identified as ART factors captured in smartcare database.

6.3.1 ART regimen and CD4 count response to HAART.

This study revealed that there was an association between the type of ART regimen clients begin treatment with and CD4 count response to HAART. Out of the two regimen types used as first line choice in Zambia (Combivir & Truvada), clients who started treatment with truvada were more likely to have an improved CD4 count response to HAART by ≥50-100 cell/μL/year. This agrees with the study conducted by Ronald (2007) whose findings were that clients on truvada were more likely to achieve a good immunological and virological response to HAART. According to Ronald (2007), it is not recommended that Truvada be used as a component of a triple nucleoside regimen. Truvada should not be coadministered with Atripla, Emtriva, Viread or lamivudine-containing products, including Combivir (lamivudine/zidovudine), Epivir® or Epivir-HBV® (lamivudine), Epzicom (abacavir sulfate/lamivudine) or Trizivir (abacavir

sulfate/lamivudine/zidovudine). In treatment-experienced patients, the use of Truvada should be guided by laboratory testing and treatment history.

6.3.2 Adherence and CD4 count response to HAART

Findings in this study were that there was an association between adherence and CD4 count response to HAART. Kitahata and coworkers reported optimal viral suppression and good immunological response being associated with 95% adherence. Therefore, our study tally with the findings of Kintahata and cowokers study including other studies that state that adherence is a strong indicator of CD4 count response to HAART. It is recommended that other studies to determine the effects of different levels of adherence on CD4 count response to HAART should be conducted.

6.4 Discussion on association between immune factor and CD4 count response to HAART.

In our study, CD4 nadire was the only immune factor captured in smartcare database at treatment initiation.

6.4.1 CD4 nadire and CD4 count response to HAART

This study showed that there was an association between baseline CD4 count at treatment initiation and the way ones CD4 count responds to ART. In our study it was noted that clients who commence treatment with CD4 counts less than 350 cells/µL were less likely to have an improved CD4 count response to HAART compared to clients who begin treatment with CD4 counts above 350 cells/µL.
This agrees with the findings from other studies (Huges *et al.* 2007) which indicate that clients who start treatment with low CD4 counts, especially lower than 200 cells/µL, are less likely to have a good CD4 count response HAART.

6.5 Discussion on probabilities of predicting CD4 count response to HAART

The probability of predicting CD4 count response to HAART using adherence was 0.688. This means that health care providers would be certain that 68.8% of clients who commit themselves to 95% adherence will have a good CD4 count response to HAART. Using alcohol consumption at treatment initiation would give a probability of predicting CD4 count response to HAART of 0.588. Gender and CD4 nadire would give 0.606, while ART regimen would give a probability of predicting CD4 count response to HAART of 0.576. On the other hand, age, smoking, income and employment status cannot be used to predict CD4 count response to HAART as shown by their probability significance values.

CHAPTER 7

CONCLUSION

7.1 Critics of methods used

Most of the information captured in smartcare is based on the information provided by the client at enrolment into care and treatment. Therefore the study is likely to be affected in cases where the client does not provide the real information. Additionally, 50% power of study used in sample size determination could not have been good enough. It could have been ideal to use a power of 80% and above. It was also difficult to analyse some variables such as age, drinking and smoking due to the way these variables appear in smartcare database. Smartcare has no provision of categorising smoking and drinking into heavy smokers, moderate smokers and light smokers or into heavy alcohol consumers, moderate alcohol consumers and light alcohol consumers and very few clients above the age of 50 exist in the database.

7.2 Major findings

In this study gender, alcohol consumption, income, ART regimen and baseline CD4 at treatment initiation affects CD4 count response to HAART. It was found that men, non alcohol consumers and those that start HAART with baseline CD4 count above 350 cell/μL experienced an increased CD4 response to HAART. Additionally, those who commenced treatment on truvada and devoted themselves to 95% adherence also experienced a good CD4 count response to HAART. On the other hand, age, smoking and employment status did not affect CD4 count response to HAART. From the variables captured on enrolment(age, gender, smoking, alcohol consumption, income, employment status, regimen and CD4 nadire), only alcohol use, ART regimen and CD4 nadire could be used to

predict CD4 count response to HAART. Additionally, clients who commit themselves to 95% adherence during their HAART are more likely to have increased CD4 count response to HAART by > 100 cells/μL/year. HAART has a positive effect on clients CD4 count response. However factors such as low levels of adherence, low socioeconomic status, heavy alcohol consumption and seeking treatment when CD4 count falls far much below 350 cells/μL has been shown to negatively affect CD4 count response to HAART.

Even with the above findings, there is still much work to be done on factors affecting clients' response to HAART. The progressive change in guidelines shows that HIV/AIDS is still in its learning phase. It is hereby suggested that further studies are needed in this area.

CHAPTER 8

RECOMMENDATIONS

- Despite the fact that no association was found between clients age at treatment initiation and CD4 count response to HAART, there is need to pay particular attention to clients who present themselves for treatment in their late age, especially those above 50 years of age.
- With the observed association between consuming alcohol and CD4 count response to HAART, it is necessary to involve a component of educating clients on the effects of alcohol use during periodic counselling.
- In this study, there was an association between clients' income and clients CD4 count response to HAART. It would be vital to go an extra mile in helping clients that come from impoverished households. Such help would involve nutritional counselling and giving food supplements where possible. Nutritional counselling would involve advising clients the type of foods they would derive the highest nutritional benefits.
- Though there was no association between employment status and clients CD4 count response to treatment, it is important to pay close attention to the unemployed since they lack a consistently stable income. The unemployed who are identified to earn low income should be given special attention such as occasional home visits and home based care.
- There was an association between ART regimen (truvada and combivir) and CD4 count response to HAART. This tallied with Ronald (2007) comparative study of truvada and combivir. Therefore, it would be logical for clinicians to prioritise combivir at treatment initiation in ideal situations.
- Our study showed an association between adherence and CD4 count response to HAART. Therefore adherence counselling is needed to all HIV clients at treatment preparation and during clients follow up visits.

- There was an association between baseline CD4 count at treatment initiation and clients CD4 count response to treatment. It was found that clients who begin treatment with CD4 counts below 350 cells/µL, were less likely to have a good immunological response to HAART. It is for this reason that clinicians should not delay commencing ART until the CD4 count falls far much below 350 cells/µL.

CHAPTER 9

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CHAPTER 10

APPENDICES

APPENDIX 1: BUDGET

An estimated budget of all the requirements for the study.

FIGURE 6: BUDGET BREAKDOWN

NUMB	BUDGET ITEM	UNIT COST	MULTIPLYING FACTOR	TOTAL COST
1	DEC ALLOWANCES @ CHRESO	ZK 50,000	25 PERSON WORKING DAYS	ZK1,200,000
2	TRAVELING EXPENCES			ZK3,800,000
3	STATIONERY	ZK 400,000	2 STUDY SITES	ZK 800,000
4	PHARMST. ALLOWANCES @ CHRESO	ZK 50,000	4 PERSON WORKING DAYS	ZK 200,000
5	LAB ALLOWANCES @ CHRESO	ZK 50,000	4 PERSON WORKING DAYS	ZK 200,000
	GRAND TOTAL			**ZK 6,200,000=00**

APPENDIX 2: WORK PLAN

Summary of the work plan for the study.

FIGURE 7: DIAGRAMATIC REPRESENTATION OF WORK

NO	TASK TO BE PERFORMED	PERSON RESPONSIBLE	MONTH(2009/2010)					
			NOV	DEC	DEC	DEC	JAN	JAN
1	FINALISING RESEARCH PROPOSAL	RESERCHER						
2	APROVAL BY ETHICS COMMITEE	PERSON INCHARGE						
3	PILOT TESTING	RESEARCHER						
4	DATA COLLECTION AT CHRESO	DATA ENTRY CLARKS						
5	DATA ANALYSIS	RESEARCHER						
6	STUDY COMPLETION AND PRESENTATION	RESEACHER						