A review of antiretroviral medicine cost in primary health care clinics in Lesotho

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Abstract

Title: **A review of antiretroviral medicines cost in primary health care clinics in Lesotho**
Key words: antiretroviral therapy, HIV/AIDS, antiretroviral regimens, prophylaxis, cost/prevalence index, *d*-value and cost–effectiveness ratio

HIV/AIDS treatment is costly. Lesotho as a resource-limited country depends mostly on donor funding for HIV/AIDS treatment and care. Knowledge of how much was spent on treatment of HIV/AIDS was lacking. This leads to overstocking of some ART medicines resulting in expiry. Sufficient funds need to be secured for the treatment programme. The main objective of the study is to assess the cost of antiretroviral medication treatments, by specifically assessing the cost of antiretroviral regimens, antiretroviral side effects, and the cost of medicines used for prophylaxis and treatment of opportunistic infections as well as the cost of monitoring laboratory tests and dietary supplements.

The study engaged both public and private ART clinics in the Maseru District in Lesotho. The study population consisted of 1 424 patients and study period was between 12 and 56 months from January 2004 to August 2008. Retrospective observational method was used. The cost for HIV/AIDS treatment comprised the cost of antiretroviral medicines and those used for their side effects, opportunistic infections (OI) prophylaxis and treatment, dietary supplements as well as monitoring laboratory tests. Prescribed daily dose (PDD) was used to calculate the cost of all the medicines used. To determine significant differences in average costs for various regimens *d*- values were used, while a cost/prevalence index was used to determine whether the cost was worth spending on the population or not. Cost-effectiveness ratio was also utilized in order to assess whether the cost born was worth the benefit.

The main findings revealed that regimens 1a (stavudine/lamivudine/nevirapine) and 1c (zidovudine/lamivudine/nevirapine) were the least expensive (cost/prevalence index of 0.6 and 0.7 respectively). Regimens containing efavirenz were found to be more expensive than those containing nevirapine (cost/prevalence index of 1.2 and 1.7 respectively). When using *d*-values, there was a significant difference between the cost of regimens 1a and 1b, 1a and 1d, 1c and 1d and the information could be used for regimen switching decisions. Increase in CD4 cell count was more in stavudine-based regimens than in zidovudine-based regimens, which cost less per treatment. Cost effectiveness ratio was lower in 1a with R9.42/1cell/mm^3 of CD4 cell count increase, and the highest was 1d with R31.77/1cell/mm^3 of CD4 cell count increase.

Therefore it was concluded that stavudine-based regimens are less costly as they have the lowest cost- effectiveness ratio in the Lesotho clinic environment.

Opsomming

Titel: **'n Oorsig van die koste van antiretrovirale medisyne in klinieke vir primêre gesondheidsorg in Lesotho**

Sleutelwoorde: antiretrovirale behandeling, MIV/VIGS, antiretrovirale regimens, profilakse, koste/voorkomsindeks, *d*-waarde en koste-effektiwiteitverhouding

Behandeling van MIV/VIGS is duur. Dit is hoekom die werklike koste van medisyne en meegaande laboratoriumtoetse bepaal moet word om die werklike koste te verkry. So kan genoeg antiretrovirale medisyne vir pasiënte met MIV/VIGS beskikbaar gestel en dit voorkom word dat daardie medisyne verval. Voldoende fondse moet vir behandelingsprogramme gewaarborg word. Die hoof doelstelling van die studie was dan gewees om die koste van antiretrovirale medisyne behandelings te bepaal met spesiale verwysing na assessering van antiretrovirale regimens, koste vir behandeling van newe effekte ervaar, die koste aangewend vir voorkoming en behandeling van opportunistiese infeksies, sowel as koste van laboratorium en dieëtaanvullings.

Die studie het sowel openbare as private klinieke vir antiretrovirale behandeling in die distrik van Maseru in Lesotho betrek. Die studiepopulasie was 1424 en die studieperiode tussen 12 en 56 maande. Die retrospektiewe observasionele metode is gebruik. Die koste vir behandeling van MIV/VIGS behels die koste aan antiretrovirale medisyne en dié vir die behandeling van hulle newe-effekte, medisyne vir die profilakse en behandeling van opportunistiese infeksies, dieetaanvullings en meegaande laboratoriumtoetse. Die voorgeskrewe daaglikse dosis (VDD) is gebruik om die koste van alle gebruikte medisyne te bereken. Om beduidende verskille in die gemiddelde koste van verskillende regimens te bepaal, is d-waardes gebruik, terwyl die koste/voorkomsindeks gebruik is om te bepaal of dit sinvol was om die bedrag op die populasie te spandeer. Die koste-effektiwiteitverhouding is ook gebruik om te bepaal of die voordeel die koste regverdig.

Die belangrikste bevindings was dat regimens 1a (stavudien/lamivudien/nevirapien) en 1c (sidovudien/lamivudien/nevirapien) die goedkoopste was (koste/voorkomsindeks van 0.6 en 0.7 onderskeidelik). Regimens wat efavirens bevat het, was duurder as dié wat nevirapien bevat het (koste/voorkomsindeks van 1.2 en 1.7 onderskeidelik). Volgens *d*-waardes was daar 'n beduidende verskil in die koste van regimens 1a en 1b, 1a en 1d, 1c en 1d en dit is gevind dat die inligting nuttig is om te bepaal na watter regimen oorgeskakel moet word as koste een van die belangrikste redes vir oorskakeling is. In die periode van behandeling is stygings in die CD4-

seltelling meer dikwels in regimens gebaseer op stavudien as dié op sidovudien waargeneem wat goedkoper per behandeling is. Die regimen met die laagste koste-effektiwiteitverhouding was 1a met R9.42/1 sel/mm^3 styging in CD4-seltelling terwyl 1d met R31.77/1 sel/mm^3 styging in CD4-seltelling die hoogste was. Die gevolgtrekking kan dus gemaak word dat stavudiengebaseerde regimens in klinieke in Lesotho goedkoper is omdat hulle die beste koste-effektiwiteitverhouding het.

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TABLE OF CONTENTS

Figures in the study

Tables in the study

Appendices

Abbreviations used in the text

Disease related

ABC:	Abacavir
3TC:	Lamivudine
AIDS:	Acquired immunodeficiency syndrome
ALT:	Alanine aminotransferase
ART:	Antiretroviral therapy
ARV:	Antiretroviral drugs
AZT:	Zidovudine
CD4 cell:	T-lymphocyte bearing CD4 receptor
CMV:	Cytomegalovirus
DDI:	Didanosine
DOTS:	Directly observed treatment short-course
D4T:	Stavudine
EFV:	Efavirenz
FBC:	Full blood counts
FDC:	Fixed dose combinations
FTC:	Emtricitabine
HAART:	Highly active antiretroviral treatment
Hb:	Haemoglobin
HBV:	Hepatitis B virus
HIV:	Human immunodeficiency virus
LPV/r:	Lopinavir/ritonavir
LFT:	Liver function tests
MAC:	Mycobacterium avium complex
MDR TB:	Multi-resistant TB
NNRTI:	Non- Nucleoside Reverse Transcriptase Inhibitor
NRTI:	Nucleoside Reverse Transcriptase Inhibitor
NVP:	Nevirapine
OI:	Opportunistic infections
PCP:	Pneumocystis carinii pneumonia
PI:	Protease inhibitor
RNA:	Ribonucleic acid
SE:	Side effects

STI:	Sexually transmitted infections
TB:	Tuberculosis
TDF:	Tenofovir

Institution Related

ANC:	Anti-natal clinic
BCM:	Baylor College of Medicine
BIPAI:	Baylor International AIDS Initiative
CHAL:	Christian Health Association of Lesotho
HAHPCO:	HIV/AIDS Health Products Coordinating Office
HSA:	Health Service Area
GFATM:	Global Fund for AIDS, Tuberculosis and Malaria
GOL:	Government of Lesotho
LDHS:	Lesotho Demographic Health Survey
LGDP:	Lesotho Gross Domestic Product
LNDC:	Lesotho National Development Corporation
MSF:	Médecins Sans Frontières
MOHSW:	Ministry of Health and Social Welfare
NAC:	National AIDS Commission
NDSO:	National Drugs Service Organization
NGO:	Non-Governmental Organization
OPD:	Out-patient department
OVC:	Orphans and vulnerable children
PLWHA:	People living with HIV/AIDS
PMTCT:	Prevention of mother-to-child transmission
RA:	Research assistant
SSA:	Sub-Saharan Africa
VCT:	Voluntary counseling and testing
USG:	United States Government
UNGASS:	United Nations General Assembly Special Session
UNAIDS:	United Nations Joint Program on HIV/AIDS
WHO:	World Health Organization
ZAR:	South African Rand

Definition of terms

HIV/AIDS patient - a patient who has tested HIV positive and has signs and symptoms of AIDS.

Opportunistic infections – an infection occurring in HIV/AIDS patients only with lowered immune system.

Antiretroviral medicines – antiviral medicines active against HIV.

Antiretroviral regimens - three or more antiretroviral medicines given at the same time to the HIV/AIDS patient.

Antiretroviral side effects – adverse effects emanating from antiretroviral medicines, as reported in the literature which may be long term or short term.

Antiretroviral toxicities- adverse events such as bone marrow suppression, liver toxicities, and renal toxicities caused by antiretroviral medicines. In some cases a medicine may have to be withdrawn and replaced with an alternative medicine.

Monitoring laboratory tests- routine laboratory tests carried out with the purpose of monitoring treatment response in terms of toxicities and success.

ART clinic – clinic where antiretroviral services are provided to the members of the public with HIV/AIDS.

National antiretroviral treatment guidelines – guidelines specifying how to provide treatment and care of the HIV/AIDS patients.

Stavudine-based regimens - regimens that contain three antiretroviral medicines with stavudine as a backbone. The regimen may contain lamivudine with efavirenz or nevirapine.

Zidovudine-based regimens - regimens that contain three antiretroviral medicines with zidovudine as a backbone. The regimen may contain lamivudine with efavirenz or nevirapine.

Dietary supplements - food supplements provided to augment or correct dietary deficiencies that may be caused by lack of food intake, or disease processes.

Synonymous terms in the text

Drugs, medicines and medication

Average and mean

Standard deviation, std dev, and ±

CHAPTER 1

Introduction

Chapter one provides an overview of Lesotho, the health system in Lesotho, supply of antiretroviral drugs, economic matters including employment rates as well as a brief outline of antiretroviral treatment guidelines. The problem statement is defined and general research objective and specific objectives are stated.

1. Background information about Lesotho

A brief background of Lesotho is discussed to give an introduction to the country where the study is carried out.

1.1.1 Geography of Lesotho

Lesotho is a small mountainous kingdom situated in the southern part of Africa and is completely surrounded by the Republic of South Africa. Administratively, it is divided into 10 districts while politically it is divided into 80 constituencies. The ten districts differ in terms of size, topography, climate as well as stage of development. Lesotho has an estimated total area of about 30, 355 square kilometres of which about 10 percent of the land is arable. Lesotho is distinguished by its relatively high altitude terrain. It is divided into two types of residential areas, urban (which refers to towns) and rural (which refers to villages) and further divided into four ecological zones, the lowlands, foothills, mountains and the Senqu river valley (Ministry of Health and Social Welfare , 2007: 9).

1.1.2 Population of Lesotho

Currently, the population of Lesotho is estimated to be 1,880,661 million (Government of Lesotho National Census, 2006). This shows a drop in the Bureau of Statistics population estimates which were 2.2 million in 2003, reflecting an increase from 1.6 million in 1986 to 1.9 million in 1996.

Table 1.1 indicates population distribution by age. It shows that the majority (76 percent) of the country"s population is young with the largest section of the population being between the ages 0 -14 years.

Table1.1 Population distribution by age

Age group (years)	Number of people	Percentage
0-14	900 019	47.9
15-19	277 117	14.7
20-24	249 773	13.3
Above 25	453 752	24.1

Source: Lesotho demographic health survey (LDHS) 2004: 10

According to the Lesotho demographic health survey (LDHS, 2004: 10) the infant mortality rate was 91 deaths per 1,000 while the under-five child mortality rates were 24 and 113 deaths per 1,000 respectively (Ministry of Health and Social Welfare, 2004: 10). Table 1.2 breaks Lesotho population down further according to the ten districts. At that time Maseru had the highest population, followed by Leribe. Qach"s Nek district had the smallest population.

Table 1.2 De jure population distribution by district 2006 census- Lesotho

District	Population	(%) Percentage share of total
Botha Bothe	109,529	5.8
Leribe	298,352	15.9
Berea	256,496	13.6
Maseru	429,823	22.9
Mafeteng	193,682	10.3
Mohale"s Hoek	174,924	9.3
Quthing	120,502	6.4
Qacha"s Nek	71,876	3.8
Mokhotlong	96,340	5.1
Thaba – Tseka	129,137	6.9
Total	1,880,661	100

Source: Government of Lesotho National Census, (2006: 2)

1.1.3 Economy of Lesotho

The currency of Lesotho is Maluti and is equivalent to the South African Rand at 1:1 (International Monetary Fund, 2008: 11). Lesotho is basically a country of subsistence farming where most households grow food for their own consumption. The Gross Domestic Product (GDP) is 8.832 billion Maluti with an annual growth rate of 3.1 percent. The manufacturing

industries are reported to contribute 20.3 percent of the LGDP, while agriculture contributes 17.1 percent (Ministry of Health and Social Welfare, 2004: 1).

1.1.4 Employment rates in Lesotho

The Government of Lesotho employed a population of 46, 921 people, with an increase of 4.1 percent due to increased enrolment of primary school teachers and expansion of the local government structures (Central Bank of Lesotho, 2007: 15). The Lesotho National Development Corporation (LNDC) assisted companies (textile and clothing manufacturers) which employed 48 710 people with an annual increase rate of 10.2 percent of employees. However, some firms closed, resulting in 4.0 percent job losses. Migrant South African mines employment increased by 1.2 percent to 53 467 employees due to favourable performance of gold and platinum. On an annual basis, the increase was higher at 6.5 percent. The annual change was slower than the 7.4 percent in the first quarter (Central Bank of Lesotho, 2007: 16). Table 1.3 reiterated that the numbers of health personnel in Lesotho were lower than in the rest of the African continent, except for laboratory technicians where Lesotho had higher numbers.

Table 1.3 Health workers in Lesotho

Category	Total number	Density per 1000 (Ls)	Density per 1000 (Afr.)
Physicians	89	0.049	0.217
Nurse and midwifes	1123	0.623	1.172
Dentists and technicians	16	0.009	0.035
Pharmacists and techs.	62	0.034	0.063
Laboratory technicians	146	0.081	0.057

Source: WHO 2006 (Ls = Lesotho, Afr. = Africa, Techs- Pharmacy technicians)

1.1.5 Human Immunodeficiency Virus (HIV) / Acquired immuno deficiency syndrome (AIDS) prevalence

Globally, there are an estimated 39.4 million people living with HIV/AIDS. About 95 percent of them live in developing countries of which 70 percent are in Sub-Saharan Africa (SSA) (UNAIDS report, 2004: 54). In 2007, there were 2.7 million new HIV infections and 2 million HIV-related deaths. The annual number of AIDS deaths has decreased due to increased access to treatment in the past ten years. Sub-Saharan Africa remains the region mostly affected by HIV, accounting for 67 percent of all people living with HIV and for 75 percent of AIDS deaths in 2007 (UNAIDS report, 2008: 30).

Lesotho is classified as the country in the world with the third highest HIV/AIDS prevalence of 23.2 percent of adult population between the ages of 15 and 40 (UNAIDS report, 2008: 217). This is the part of the population that is working and providing for their families. There were an estimated 62 new HIV infections and about 50 deaths due to HIV/AIDS each day (UNGASS, 2007: 15). There were further estimated 270,273 people living with HIV in Lesotho at the end 2007. It was estimated that there were 11,801 infected children and 258,472 infected adults. Females were more infected with an estimated 153,581 infected compared to 116,692 males. There has been no significant change in the national adult HIV prevalence since 2005 (UNGASS. 2007: 5). The overall prevalence of HIV among anti-natal clinic (ANC) patients was 25.7 percent while among sexually transmitted infections (STI) patients, prevalence was 56.2 percent. Median HIV prevalence has increased from 22.9 percent to 26.1 percent (Ministry of Health and Social Welfare, 2007: 7).

1.1.6 Health system in Lesotho

The health care delivery is at four levels in Lesotho, namely central level or tertiary level, health service area (HSA) level, health centre level and community level, as stated by the National AIDS strategic plan. The plan further points out that a Health Service Area is a demarcated geographical area (with a hospital as a focus) which supervises several satellite health centres and clinics. Several health centres are located at the hospital periphery (being visited by a medical practitioner at regular intervals) based at the mother hospital of the HSA. At the community level, there are village health workers, traditional healers and faith healers.

According to National AIDS Strategic Plan, there are eighteen HSAs and 160 health centres of which 52 percent are owned by the government of Lesotho (GOL) and 48 percent are managed by the Christian Health Association of Lesotho (CHAL) and other non-governmental organizations (NGO"s). CHAL is a Christian church organization that receives subvention from the government to covering staff salaries and medications, including antiretroviral drugs. There is a signed memorandum of understanding between CHAL and the GOL.

Among the hospitals and clinics, the country has only one tertiary or referral hospital Queen Elizabeth II Hospital which is situated in the Maseru district. It is the only hospital with specialist services and it attends to all complicated cases referred from satellite clinics and the out-patient

department (OPD) of the hospital. Furthermore, Queen Elizabeth II hospital also accepts referrals from all the other nine districts of the country for specialist review and management (Ministry of Health and Social Welfare, 2007: 9).

Public Private Partnership (PPP) is a form of partnership between private practitioners and government of Lesotho to provide antiretroviral drugs. In this way, private service is provided to Basotho patients, partially funded by government. There is a signed memorandum of understanding between the Government of Lesotho and Public Private Partnership. Patients do not pay for antiretroviral drugs and anti-tuberculosis (TB) medicines but pay for consultation and refill fees.

1.2 Maseru district HIV/AIDS and antiretroviral treatment situation

In Lesotho, the total number of patients enrolled at the antiretroviral therapy (ART) clinics is 159 983, according to statistics of July 2007. According to Lesotho demographic health survey (LDHS), for the whole country the total number of HIV/AIDS patients who collected antiretroviral drugs in 2007 was 20, 240 (Ministry of Health and Social Welfare, 2007: 5). The total number of patients enrolled at the ART clinics in the Maseru district is 57 210 which is 36 percent of the population enrolled in the ART clinics. In 2007, the number of patients on antiretroviral treatment in the Maseru district was 6 476 which is about 32 percent of the total population under ART care. Maseru district has about 28 ART clinics. Six of them are managed by CHAL, 13 are under the Ministry of Health and Social Welfare (MOHSW), while nine are run by private practitioners in their medical practices (Ministry of Health and Social Welfare, 2007: 9).

1.2.1 Antiretroviral drugs supply

The supply of antiretroviral drugs is carried out by the National Drug Service Organization (NDSO) which is a trading account for the Ministry of Health and Ministry of Finance. It is responsible for drug procurement, storage and distribution throughout Lesotho. Quantification (which is basically to calculate the quantity of antiretroviral drugs to be given to each clinic) of antiretroviral drugs is done centrally. Reporting of antiretroviral drug usage plays a key role because quantification is based on consumption according to the monthly reports received from the ART clinics. Information is then communicated to NDSO. NDSO supplies various ART clinics, according to their distribution schedule. Highly active antiretroviral therapy (HAART) increases patient survival and reduces mortality and morbidity (Badri *et al.,* 2004: 1159).

Lesotho has to ensure that HIV/AIDS treatment programs are sustainable and have sufficient funds to effectively run such programs (see par. 2.4).

1.2.2 Antiretroviral drugs availability in Lesotho

Because Lesotho is a resource limited country, only the first and second line ART medicines are available for use. First line drugs available are zidovudine 300mg, stavudine 30mg, lamivudine 150mg, nevirapine 200mg, efavirenz 600mg and tenofovir 300mg. Second line drugs available are abacavir 300mg, didanosine 400mg and lopinavir/ritonavir 200mg/50mg (boosted protease inhibitors). HAART prescribing follows the National Antiretroviral Treatment Guideline of 2004 (Ministry of Health and Social Welfare, 2004: 14).

1.2.3 Initiation of antiretroviral treatment

Of the available methods of determining initiation of antiretroviral treatment, two were considered for deciding whether to start antiretroviral therapy or not. These were:

- CD4 cell count of 200 cells/mm^3 or below, or
- World Health Organization clinical staging classification (WHO, 2007: 16)

This allowed initiation of therapy at higher CD4 cell count (Ministry of Health and Social Welfare, 2004: 83)

1.2.4 Highly active antiretroviral therapy (HAART) regimens

HAART is a combination of three ARV"s from two different classes of drugs, as follows:

1.2.4.1 First Line antiretroviral drug regimens

1a – Stavudine/lamivudine/nevirapine

1b - Stavudine/lamivudine/efavirenz

1c – Zidovudine/lamivudine/nevirapine

1d – Zidovudine/lamivudine/efavirenz

1.2.4.2 Second Line antiretroviral drug regimens

1e - Abacavir/didanosine/ lopinavir/ritonavir

1f - Zidovudine/abacavir/ lopinavir/ritonavir

1g - Tenofovir/didanosine/ lopinavir/ritonavir

Any combination of the first line regimen that includes lopinavir/ritonavir

(Ministry of Health and Social Welfare. 2007: 15)

1.2.5 Antiretroviral side effects

All drugs cause side effects. Side effects occurring as a result of antiretroviral drugs may have an impact on patients" adherence to treatment. Their consequent management may improve adherence to medication. Viral suppression depends on good adherence to medicines. This is why it is important to treat side effects of antiretroviral drugs. Consequently, this may impact on the overall cost of medicines used in the treatment of HIV/AIDS (Ministry of Health and Social Welfare, 2007: 27).

1.2.6 Opportunistic infections

For the purpose of this study opportunistic infections are infections that occur in HIV positive patients only. They do not cause disease for people whose immune system is still intact. Some opportunistic infections can be prevented by giving cotrimoxazole to patients whose CD4 cell count is below 200 cells/mm^3 (WHO, 2006: 9). For others, prophylaxis was not found beneficial in the prevention of the opportunistic infection. This is why no prophylaxis was given. Treatment and prophylaxis of opportunistic infections adds cost to treatment of HIV positive patients" overall treatment. However, as patients respond favourably to treatment, there is less need for prophylaxis and treatment mainly because opportunistic infections occur in lower CD4 cell count (WHO, 2006: 9).

1.2.7 National antiretroviral treatment guidelines

National antiretroviral treatment guidelines were first developed in 2004 to guide antiretroviral prescribing as well as laboratory tests for diagnosis and monitoring of HIV/AIDS and response to its treatment. The guidelines came as a pocket reference, covering essential topics in the management of HIV/AIDS including diagnosis, preventive and supportive care, adherence, antiretroviral regimens to be used in Lesotho, side effects and toxicities of HAART, prevention of mother to child transmission and occupational exposure to HIV. The guidelines were revised in 2007, to add management of opportunistic infections and co-infections as well as infection control. In the 2007 national antiretroviral treatment guidelines concerning cotrimoxazole prophylaxis in which groups of patients should start or stop, was specified in detail. Both the 2004 and 2007 antiretroviral treatment guidelines were based on World Health Organization (WHO) antiretroviral guidelines.

1.3 Problem statement

For a long time people were dying of HIV/AIDS-related diseases because they had no access to the relatively high cost HAART. Since HAART was introduced in Lesotho, it continued to play an important role in the management of HIV/AIDS. It is aimed at reducing viral load and increasing CD4 cell count. High CD4 cell count makes patients suffer less from opportunistic infections. It also improves the quality of life of patients (Freedberg *et al.,* 2001: 824). Antiretroviral medicines have side effect like any other medicines, and being a life-time treatment this can cause uncertainty for the patients in need of them. However, according to the study conducted at Scott Hospital, side effects and opportunistic infections commonly occur mostly in the first 6 months of treatment (Cleary *et al*., 2007: 16).

Antiretroviral services are currently free in Lesotho to patients who were seen at Christian Health Association of Lesotho (CHAL) and government clinics, but they were not free from the point of view of the provider. Hence this study assessed the cost of HIV treatment from the perspective of the provider. It is because the provider pays for drug costs, dietary supplements and monitoring laboratory tests. Although at the private clinic patients still pay for consultation and refill fees, (where patients pay for refilling their prescription during drug pick-up), they do not pay for antiretroviral drugs, as the government of Lesotho pays for them. This study also assessed cost changes seen during regimen switching.

The actual cost of medicine treatment for HIV/AIDS comprises of the cost of antiretroviral drugs, their side effects (such as the fact that D4T causes peripheral neuropathy) and the cost of supplements such as multivitamin tablets, prophylaxis of opportunistic infections (such as cotrimoxazole or dapsone given for prophylaxis of *Pneumocystis carinii pneumonia* and toxoplasmosis), the treatment of opportunistic infections occurring and the treatment of tuberculosis (TB). Finally, toxicity monitoring laboratory tests such as the haemoglobin test is carried out on patients who are on zidovudine.

1.3.1 Study objectives

Study objectives include the main objective and specific objectives of both the literature review and the research study**.**

1.3.1.1 Main objective

The main objective of the study was to assess the cost of antiretroviral medication treatments, by specifically assessing the cost of antiretroviral regimens, side effects of antiretroviral drugs, the cost of drugs used for prophylaxis and treatment of opportunistic infections as well as the cost of monitoring laboratory tests and dietary supplements.

1.3.1.2 Specific literature objectives

The literature objectives were as follows:

- To define origin of HIV/AIDS, its diagnosis, and goals of antiretroviral treatment.
- To classify and briefly describe antiretroviral drugs.
- To familiarize the researcher with the local antiretroviral treatment guidelines in order to assess whether antiretroviral prescribing was in accordance with the National Antiretroviral Treatment Guidelines of Lesotho.
- To identify side effects of antiretroviral and their treatment.
- To assess hospitalization of HIV/AIDS patients.
- To define opportunistic infections, their prophylaxis and treatment.
- To determine the reasons for switching antiretroviral drugs in a regimen.
- To evaluate implications of body weight in HIV/AIDS and its role in disease development
- To critically evaluate CD 4 cell count and its role in HIV.
- To evaluate CD4 cell count as an outcome of HIV/AIDS treatment.
- To evaluate body weight as an outcome of HIV/AIDS treatment.
- To evaluate studies that determined the cost of HIV/AIDS treatment in terms of drugs and related monitoring laboratory tests.
- To evaluate studies that assessed cost effectiveness of antiretroviral regimen.

1.3.1.3 Specific research objectives

Specific research objectives of the empirical study were divided into antiretroviral treatment, treatment outcome, treatment cost and economic evaluation

The study had the following objectives concerning the treatment of HIV/AIDS:

- To determine if the antiretroviral prescribing followed National Antiretroviral Treatment Guidelines of Lesotho (2004).
- To assess retention of antiretroviral treatment to first line treatment.

- To assess if switching of antiretroviral therapy from one regimen to another followed recommended policy by the National Antiretroviral Treatment Guidelines of Lesotho (2004).
- To investigate the prescribing patterns of medicines used for the treatment of opportunistic infection and if that was according to National Antiretroviral Treatment Guidelines (2004).
- To determine if side effects of antiretroviral were treated according to National Antiretroviral Treatment Guidelines of Lesotho (2004).

Outcome of antiretroviral treatment

The study had the following objectives concerning the Outcome of antiretroviral treatment:

- To determine CD4 cell count changes brought about by antiretroviral therapy.
- To assess if there was a change in body weight changes before and after antiretroviral treatment.
- To identify incidence of side effects of antiretroviral drugs and how they impacted on overall treatment of HIV/AIDS.

Cost of antiretroviral treatment

The study had the following objectives concerning the cost of antiretroviral treatment:

- To compare the medicine treatment costs of different HAART regimens.
- To assess impact of additional cost imposed by associated monitoring laboratory tests, dietary supplements as well as treatment of side effects at different ART clinics.
- To assess cost implication of antiretroviral regimen switching on overall cost of HIV/AIDS treatment.
- To compare prophylaxis and treatment cost of opportunistic infections in different ART clinics.
- To compare if second line antiretroviral treatment cost implied with first line treatment.
- To assess total cost of HIV/AIDS treatment in private and public clinics.

Economic evaluation of antiretroviral

The study had the following objectives concerning the economic evaluation of antiretroviral treatment:

- To determine cost to effectiveness ratio between two antiretroviral regimens using CD4 cell count as the main measure of outcome.

- To determine cost to effectiveness ratio between two antiretroviral regimens using body weight increase as the subsidiary measure of outcome.
- To calculate the incremental cost effectiveness ratio between the antiretroviral regimens.

1.4 Research methodology

Brief research methodology outline was discussed.

1.4.1 Study design

Observational retrospective study where there was no treatment modification or no direct contact was made with the patients enrolled in the study. Only medical records were used for data collection.

1.4.2 Study sites

Study sites were chosen because of their vicinity. They were all within the radius of 35 km from Roma. The public clinics were Senkatana ART clinic, Bophelong Adult ART clinic, Qoaling ART clinic and Mabote ART clinic. Private clinics included Healthy Life Style and Diabetes clinic®, Medicare Family clinic®, and Khanya Family clinic®. St. Joseph‟s clinic was a Christian Health Association of Lesotho (CHAL) clinic was also included (See appendix C).

1.4.3 Study population

The researcher retrospectively abstracted data from patient files of 1 423 HIV/AIDS patients, who were on antiretroviral treatment for a minimum of one year. All patients who collected their medicines until 31 August, 2008 and who had been on antiretroviral drugs for one year or more were included in the population. Survey forms were used to collect data (see appendix D.1 and D.2) and Excel spread sheet was used to capture the data (see appendix E).

1.4.4 Ethical considerations

Record files for HIV/AIDS patients were used retrospectively. The numbers were used in order to assure patient confidentiality. A confidentiality form was provided and signed by the research assistants and information was kept strictly confidential. Permission to carry out this research was obtained from the Ethics Committee of the Ministry of Health and Social Welfare, and all the ART clinics gave permission. The Ethics Committee of North West University gave permission for the study to be carried out. The number provided is NWU-00101-10-55.

1.4.5 Cost calculations

The following formulae were used to calculate the cost utilized in the public and in private clinics. The cost includes the cost of medicines used for HIV/AIDS and laboratory tests but excludes the cost of hospitalization, surgical consumables, staff remuneration and overheads expenses.

1.4.5.1 Public clinics

HIV/AIDS treatment cost **Ct = Cta + Ctb + Ctc + Ctd + Cte + Ctf + Ctg**

Where **C-**represents cost in monetary terms; **t**-represents HIV/AIDS treatment; **a-**represents antiretroviral regimen; **b**-represents drugs for prophylaxis of opportunistic infections; **c**-represents drugs used for treatment of opportunistic infections; **d**-represents monitoring laboratory tests; **e**-represents drugs used for treatment of side effects of antiretroviral drugs while **f**-represents supplements; and **g**-represents TB treatment. Financial resources here came from the same source which was government of Lesotho.

1.4.5.2 Private ART clinics

HIV/AIDS treatment cost **Ct = Cta + Ctb + Ctg**

Where **C**-represents the cost in monetary terms, **t**-represents HIV/AIDS treatment, **a**-represents antiretroviral regimen, and **b**-represents drugs for prophylaxis of opportunistic infections and **g**-represents TB treatment.

And

HIV/AIDS treatment cost **Ct = Ctc + Ctd + Cte + Ctf**

Where **C-**represents cost in monetary terms; **t -** represents HIV/AIDS treatment; **c -** represents drugs used for treatment of opportunistic infections, **d -** represents monitoring laboratory tests; **e -** represents drugs used for treatment of side effects of antiretroviral drugs; and **f -** represents supplements. Financial resources came from the patients, paying cash or on a medical aid, and government of Lesotho.

1.5 Chapter summary

Chapter one was divided into an introduction, where Lesotho as a country was introduced, and its location, population and health care system were described in detail. The HIV/AIDS prevalence was also stated as 23.6 percent of the population between the ages of 25-45 years. Antiretroviral drugs available in Lesotho were mentioned and how they are supplied to the facilities was also specified. Antiretroviral treatment guidelines were also introduced.

Statement of the problem was stated as critically assessing the cost of treating patients with HIV/AIDS. Objectives of the study were set out and the main objective being - to assess cost of antiretroviral treatment, by specifically assessing cost of antiretroviral regimens, antiretroviral drug side effects, cost of drugs used for prophylaxis and treatment of opportunistic infections as well as the cost of monitoring laboratory tests and dietary supplements. Specific objectives were also set including those of the literature and research study.

The layout of the rest of the document was introduced as well, including the literature, methods, major results, the conclusion as well as the recommendations. Chapter 2 addresses the literature objectives set for supporting the study and goes on to present reviewed literature.

CHAPTER 2

Literature review

Chapter two presents the search in the literature resources on various topics including the origin of HIV/AIDS, antiretroviral drug classification and when and how to initiate treatment on HIV/AIDS patients using Antiretroviral Treatment Guidelines from Lesotho. World Health Organization (WHO) and South African treatment guidelines were also reviewed. The literature on side effects of antiretroviral and their treatment thereof, opportunistic infections treatment and prophylaxis was searched. The cost of treating HIV/AIDS was assessed from the literature as well.

Specific research objectives of the literature review include the following:

- To define origin of HIV/AIDS, its diagnosis, and goals of treatment.
- To classify and briefly describe antiretroviral drugs.
- To familiarize the researcher with the local antiretroviral treatment guidelines in order to assess whether antiretroviral prescribing was in accordance with the National Antiretroviral Treatment Guidelines of Lesotho.
- To identify side effects of antiretroviral and their treatment.
- To assess hospitalization of HIV/AIDS patients.
- To define opportunistic infections, their prophylaxis and treatment.
- To determine the reasons for switching antiretroviral drugs in a regimen.
- To evaluate implications of body weight in HIV/AIDS and its role in disease development
- To critically evaluate CD4 cell count and its role in HIV.
- To evaluate CD4 cell count as an outcome of HIV/AIDS treatment.
- To evaluate body weight as an outcome of HIV/AIDS treatment.
- To evaluate studies that determined the cost of HIV/AIDS treatment in terms of drugs and related monitoring laboratory tests.

2.1 Origin of HIV and related diagnosis

Origin of HIV and how to diagnose it once it had infected a human being was reviewed.

2.1.1 HIV/AIDS

WHO defines HIV/AIDS in adults as a clinical diagnosis of any stage 4 condition (defined in appendix B) with confirmed HIV infection, and immunological diagnosis in adults with confirmed HIV infection and first-ever documented CD4 count of less than 200 per mm^3 (WHO 2007: 9)

HIV/AIDS is a disease that is caused by HIV-1 or HIV-2. It was suggested that the closest relatives of HIV-1 are simian immunodeficiency viruses (SIVs), infecting wild-living chimpanzees (*Pan troglodytes troglodytes*) and gorillas (*Gorilla gorilla gorilla*) in west central Africa (Sharp & Hahn, 2010: 2487). The likeliest route of chimpanzee-to-human transmission would have been through exposure to infected blood and body fluids during the butchery of bush meat (Hahn *et al*., 2000: 607). HIV-1 subtype A is mainly found in central and Sub-Sahara Africa, including Lesotho (BIPAI, 2007: 16). Among humans, HIV spreads commonly via the sexual fluids during intercourse, intake of blood products and lastly from mother-to-child during pregnancy (Newell *et al*., 1996: 1675), at birth as well as during breastfeeding (Willumsen *et al.,* 2003: 412).

2.1.2 HIV/AIDS prevalence in Lesotho

Lesotho is classified as the country in the world with the third highest HIV/AIDS prevalence of 23.2 percent of the adult population between the ages of 15 and 40 years (UNAIDS report, 2008: 217) (see paragraph 1.1.5).

2.1.3 Diagnosis and monitoring

HIV can be defined by clinical signs and symptoms as well as laboratory tests. The latter include ELISA, Western Blot, Rapid tests and DNA/RNA PCR. Symptoms of early infection of HIV may include lethargy, malaise, sore throat, sweating and fever while the signs and symptoms of late stage HIV are weight loss, diarrhoea, and weakness. Damage to the immune system may be determined by using CD4+ lymphocytes (T-Helper Cell) counts (Daar *et al.*, 2001: 27).

2.2 Treatment of HIV and associated effects

Treatment of HIV starts with goals of HIV treatment, what regimens to give and how to make such decisions.

2.2.1 Treatment of HIV/AIDS with antiretroviral medicines

Matters surrounding decisions to treat HIV/AIDS patients with HAART are critically appraised beginning with the therapeutic goals.

2.2.2 Therapeutic goals of HIV/AIDS treatment

The primary goal of therapeutic interventions is to improve health and prolong survival of an HIV infected patient. This may be achieved by interfering with the viral replication. This results in minimizing damage to the immune system. In turn it makes the patients less susceptible to opportunistic infections, malignancies and other illnesses (Kuritzkes, 2000: 21).

2.2.3 Antiretroviral drug classification

Antiretroviral drug classification is based on the molecular structure according to their mode of action of drugs. They are grouped according to where they inhibit the replication of the human immune-deficient virus.

2.2.3.1 Nucleotide reverse transcriptase inhibitors (NRTI) and nucleoside Inhibitors

Nucleoside and nucleotide reverse transcriptase inhibitors have the same structure as the building blocks of DNA which are the purine nucleoside, adenosine and guanine, the pyrimidine nucleoside, thymidine and cytidine. Their functions are to inhibit DNA synthesis by inhibiting reverse transcriptase, which is the enzyme that copies viral RNA to DNA into the newly infected cell. The reverse transcriptase enzymes incorporate NRTI into the structure of the DNA, consequently blocking all subsequent steps in viral replication. Common examples of NRTI are zidovudine (AZT), stavudine (D4T) lamivudine (3TC), didanosine (ddi), abacavir (ABC) and tenofovir (TDF) is an example of a nucleotide inhibitor (Macchi & Mastino, 2002: 473).

2.2.3.2 Non-nucleoside reverse transcriptase inhibitors (NNRTI)

Non-nucleoside reverse transcriptase inhibitors are non-competitive inhibitors of HIV Reverse Transcriptase. They bind in or close to the hydrophobic pocket near the catalytic site of the HIV Reverse Transcriptase. Examples are nevirapine (NVP) and efavirenz (EFV) (De Clercq, 2004: 44).

2.2.3.3 Protease inhibitors (PI)

An enzyme called protease is necessary for the final stages of viral assembly. Protease is used to make new HIV from the viral materials made in the nucleus. There are the two viral poly-proteins, Gag and the Gag-Pol precursors, which are cleaved by the protease to produce viral proteins such as reverse transcriptase and integrase (Monini *et al.,* 2003: 207). The protease inhibitors prevent the cleavage of the large poly-proteins into structural proteins and viral enzymes. Ritonavir, saquinavir, lopinavir are examples of this group. Commonly used boosted protease inhibitors were a lopinavir/ritonavir (LPV/r) combination called Kaletra® (Zeldin & Petruschke, 2004: 4).

2.2.3.4 Highly active antiretroviral therapy

HAART is a combination of three antiretroviral drugs that are taken once or twice daily (Monini *et al.*, 2003: 207). The common combinations are composed of two NRTI and one NNRTI such as stavudine, lamivudine and nevirapine. If the patient is also on TB treatment containing rifampicin (Ribera *et al.,* 2001: 450), she/he will be given efavirenz instead of nevirapine as rifampicin decreases plasma levels of nevirapine. Another regimen is composed of 2NRTI and a PI and falls under the second line regimens (Monini *et al.,* 2003: 207).

2.2.4 When to initiate antiretroviral treatment and regimen options

Initiation of antiretroviral drugs depends on the antiretroviral treatment guidelines of the specific country, which could either follow WHO or the Centre of Disease Control (CDC) guidelines. Initiation of antiretroviral drugs is based on either CD4 cell count or clinical staging of HIV or both. Clinical staging of HIV/AIDS (see appendix B) guides the decisions to start antiretroviral treatment with or without consideration of CD4 cell count (WHO, 2010: 31).

2.2.5 The role of antiretroviral treatment guidelines

Each country has to develop antiretroviral treatment guidelines in order to form a basis for prescribing and for easy access to the prescribed antiretroviral drugs. WHO plays an important role in the formulation of guidelines for various treatments of various diseases for countries especially developing countries to view and adopt (Gilks *et al.*, 2006: 505). Antiretroviral guidelines were made for first line and second line treatments in order to guide both procurement and prescribing for rational use of antiretroviral drugs (Dybul *et al*., 2002: 381). It was therefore important for Lesotho as a resource limited, and under-developed country to

follow the recommendations of the WHO to develop antiretroviral treatment guidelines. The first antiretroviral treatment guidelines were developed in 2004 when antiretroviral therapy was given to the population for the first time, and later on revised in 2007.

2.2.6 An overview of the antiretroviral guidelines

The guidelines come in the form of a pocket booklet that includes various aspects such as how to test for HIV, patient counseling, when to start HIV treatment, when to monitor treatment outcome, prophylaxis and nutrition so on and so forth (Dybul *et al*., 2002: 382).

The differences between the guidelines are minimal, as the structure does not change. Additional information includes new developments, based on evidence in the treatment of HIV/AIDS, which would normally be a WHO recommendation and that would prompt a review of antiretroviral guidelines in order to include new recommendations. The following guidelines were reviewed to identify their antiretroviral treatment initiation time, especially the CD4 cell count, as an indicator on when to start treatment as well as the regimens to be used for first line and second line treatment.

2.2.6.1 World Health Organization antiretroviral treatment guidelines 2010

WHO has the mandate to guide the treatment of HIV with antiretroviral medicines through antiretroviral treatment guidelines. The guidelines provide information as follows.

2.2.6.1.1 When to initiate antiretroviral treatment using CD4 cell count as a measure:

- CD4 cell count, ≤350cells/mm^3
- Start ART in all pregnant women with HIV and a CD4 count of ≤350 cells/mm^3, irrespective of clinical symptoms.
- Start ART in all HIV/HBV- co-infected individuals who require treatment for their HBV infection (chronic active hepatitis), irrespective of the CD4 cell count or the WHO clinical stage.

WHO antiretroviral treatment guidelines recommend the following for first and second line antiretroviral drug treatment regimen (WHO, 2010: 22):

First line antiretroviral regimens include any combination of three drugs of the following:
AZT or TDF **+** 3TC or FTC **+** EFV or NVP

While second line antiretroviral regimens include any combination of three drugs of the following:

ATV/r or LPV/r **+** AZT or D4T or TDF **+** 3TC or FTC

2.2.6.2 National antiretroviral treatment guidelines of Lesotho 2007

Lesotho adopted the WHO antiretroviral treatment guidelines in order to guide local prescribing of antiretroviral medicines for the treatment of HIV/AIDS

2.2.6.2.1 When to initiate antiretroviral treatment using CD4 cell count as a measure:

All adults and adolescents who are in WHO stage 1 and 2 whose CD4 cell count is ≤350 cells/mm^3 (Ministry of Health and Social Welfare, 2007: 27)

2.2.6.2.2 Antiretroviral regimens in Lesotho

First line treatment consists of any combination of three drugs from the following antiretroviral drugs:
TDF or D4T or AZT **+** 3TC **+** NVP or EFV

Second line treatment consists of any combination of three drugs from the following antiretroviral drugs:
DDI or AZT **+** ABC or 3TC **+** LPV/r

2.2.6.3 South African antiretroviral treatment guidelines (2010)

South Africa as a country has formulated antiretroviral treatment guidelines to guide the prescribing of antiretroviral medicines for the HIV/AIDS population.

2.2.6.3.1 When to initiate antiretroviral treatment using CD4 cell count as a measure:

- CD4 count <200cells/mm^3 irrespective of clinical stage or
- CD4 count <350cells/mm^3 in patients with TB/HIV or pregnant women or
- WHO stage IV irrespective of CD4 count or
- MDR/XDR TB irrespective of CD4

(SA, 2010: 2)

First line antiretroviral drugs regimens include:

- TDF **+** 3TC/FTC **+** EFV/NVP
- Or d4T **+** 3TC **+** EFV/NVP
- Or AZT+ 3TC + EFV/NVP (SA, 2010: 6)

While second line antiretroviral drugs regimens include:

- TDF **+** 3TC/FTC **+** LPV/r and AZT**+**3TC**+** LPV (SA, 2010: 6)

The choice of regimen follows individual patients‟ needs. That is if patients have TB, they are not given nevirapine (Autar *et al.*, 2005: 939). Female of child-bearing age with no reliable contraceptive method are not given efavirenz. Manufacturers do not recommend its use in the first trimester because of its potential teratogenicity (Bussmann *et al.*, 2007: 269). If they have existing renal disease they are not given tenofovir (Karras *et al*., 2003: 1070), and if they have existing anaemia they are not given zidovudine (Ssali *et al.*, 2006: 743). Individual patient factors contribute to the choice of regimen. In choosing second line antiretroviral drugs, prior exposure to the drugs is considered before any choice can be made as no previously used antiretroviral drugs should be re-challenged (WHO, 2010: 31).

2.2.7 Monitoring laboratory tests as specified by the antiretroviral treatment guidelines

According to WHO (2010: 66), monitoring laboratory tests are supposed to be carried out routinely. The purpose of carrying out monitoring laboratory tests is to detect early toxicities, or treatment failure or treatment success that may occur, in order to take prompt decisions should any of the major toxicities occur. The recommended monitoring laboratory tests should be carried out routinely and results be recorded properly in order to use them effectively. Table 2.1 outlines brief toxicities and side effects associated with antiretroviral medicines and as well as high risk situations for early warning and for further treatment steps to be effected.

Table 2.1 Antiretroviral drugs and major toxicities and high risk situations

ARV drug	Major toxicity	High risk situations	Tests required
Stavudine 30mg (D4T)	lipodystrophy	Age >40 years	Lactic acid
	neuropathy	CD4 count of <200 cells/mm^3	
	lactic acidosis	BMI >25 (or body weight >75kg)	
		concomitant use with INH or ddI	
Zidovudine 300mg (AZT)	anaemia	CD4 count of <200 cells/mm3	haemoglobin tests
	neutropaenia	BMI <18.5 (or body weight <50 kg)	
		anaemia at baseline	
Tenofovir 300mg (TDF)	renal dysfunction	underlying renal disease	creatinine clearance tests
		age >40 years	
		BMI <18.5 (or body weight <50 kg)	
		diabetes mellitus	
		hypertension	
		concomitant use of a boosted PI or nephrotoxic drugs	
Efavirenz 600mg (EFV)	teratogenicity	first trimester of pregnancy (do not use EFV)	
	psychiatric illness	depression or psychiatric disease (previous or	
		at baseline)	
Nevirapine 200mg (NVP)	hepatotoxicity	HCV and HBV co-infection	Liver function tests

Source: WHO (2010: 66) HCV (Key: HCV - Hepatitis C Virus, HBV hepatitis B virus)

According to national antiretroviral treatment guidelines of the Lesotho (2004) the following routine laboratory tests are recommended.

Table 2.2 Monitoring laboratory tests

1. Plasma RNA viral load – at the start of therapy, at three months to evaluate initial efficacy, every six months thereafter.
2. CD4 + cell count – every three months
3. Blood chemistry (LFTs, U&E) and haematology (FBC) – at the start of therapy, at 2 weeks to assess toxicity of nevirapine, and every three months thereafter

Source: National Antiretroviral Treatment Guidelines (2004: 28) (key: LTF – liver function tests, U&E – urea and electrolytes FBC – full blood counts)

The National Antiretroviral Treatment Guidelines of the Lesotho (2007) recommends laboratory tests that are more specific for the antiretroviral drugs as viewed in table 2.3 which shows the monitoring laboratory tests for early detection of toxicities for certain antiretroviral medicines in the first line treatment. Monitoring laboratory tests need to be drug specific to avoid unnecessary spending of resources and routine taking of patients‟ samples that do not benefit them.

Table 2.3 Routine laboratory investigations

ARV drug	Recommended laboratory tests
Stavudine 30mg	lactate measurement if symptoms suggest hyperlactatemea
Zidovudine 300mg	haemoglobin at 1 month, 2 months, 3 months and 6 months and every 6 months thereafter
Tenofovir 300mg	serum creatinine, six months after initiation and every six months thereafter
Lopinavir/ritonavir 200mg/50mg	glucose and lipid measurement (additional laboratory test)
Nevirapine 200mg	ALT should be checked at 1 month, 2 months, 6 months and every six months thereafter

Source: Ministry of Health and Social Welfare, (2007: 60) (key: Alt–alanine aminotransferase)

2.2.8 Switching of antiretroviral drugs

Antiretroviral switching could be carried out for various reasons. According to Orrell *et al.,* (2007: 86), the possible reason could be hypersensitivity or lactic acidosis, toxicity, and virologic failure. Other reasons could be pregnancy, as some of the antiretroviral drugs are teratogenic in the first trimester, or drug–drug interactions such as nevirapine and rifampicin (Autar *et al*., 2005: 937). However, Webster *et al.,* (2009: 501) reiterated that the incidence of side effects may be the reason for ARV regimen switching, or single antiretroviral drug switching in the regimen.

2.2.9 Incidence of commonly occurring antiretroviral side effects

Like all other medicines, antiretroviral drugs may show some side effects. These side effects may be classified as short-term and long term. Another classification is minor side effects and adverse drug reactions or toxicities. Short term treatment such as gastrointestinal (GI) upset, require short term treatment. While others are life long or taken as long as the offending drug is provided to the patient such as peripheral neuropathy needs to be treated for prolonged periods of time. The risk of a certain side effect depends on both drug and patient factors (Montessori *et al*., 2004: 229). Forna *et al.,* (2007: 456) showed the frequent incidence of antiretroviral side

effects to occur more in adults than in children. Commonly reported antiretroviral side effects for patients on HAART were found to be anaemia, liver toxicity, skin rash and peripheral neuropathy (Minzi *et al*., 2009: 5).Table 2.4 shows common antiretroviral medicines and possible causes.

Table 2.4 Common antiretroviral side effects and possible causative antiretroviral medicines

Common antiretroviral side effects	**possible causative antiretroviral drug**
Peripheral neuropathy and lipodystrophy	stavudine 30mg
Nausea, headache, rash, anaemia, leukopenia, elevation of liver enzyme levels, elevation of lactic acid level.	zidovudine 300mg
Cough and nasal symptoms and pancreatitis	lamivudine 150mg
Rashes and other skin conditions	nevirapine 200mg
Depression and other central nervous system side effects, rash	efavirenz 600mg
GI upset, low phosphate levels	tenofovir 300mg
Hypersensitivity reaction, which may be characterized by fever, rash, myalgias, arthralgias,and malaise	abacavir 300mg
GI intolerance, pancreatitis, gout, reversible peripheral neuropathy	didanosine 400mg
GI upset, diarrhoea, circumoral paresthesias, elevation of liver enzyme levels, and hypertriglyceridaemia	lopinavir/ritonavir 200mg/50mg

Source: Montessori, (2004: 236)

2.2.10 Treatment of antiretroviral side effects

Treating side effects of the antiretroviral keeps the patient comfortable and consequently increases patient antiretroviral medicines taking behaviour or adherence to medication (Montessori *et al*., 2004: 236). Treatment of side effects of antiretroviral was also specified as a strategy to promote adherence to medication in the 2004 national antiretroviral treatment guidelines. According to Weiser *et al.,* (2003: 281) antiretroviral side effects affected adherence to antiretroviral treatment adversely. Milinkovic *et al.,* (2007: 413) found out that reducing the doses of stavudine from 40mg to 30mg leads to reduced side effects and a recommendation to stop monitoring lactate. This was supported by Ter Hofstede *et al*. (2008: 933) when he suggested that lowering of the doses of stavudine might reduce lypoatropy caused by higher doses of the drug and should consequently improve adherence of the drug. Table 2.5 illustrates

possible treatment of antiretroviral side effects as recommended by antiretroviral treatment guidelines of 2004 and 2007. It shows changes in the suggested treatment of antiretroviral side effects in the 2007 guidelines.

Table 2.5 Possible medicines used in the treatment of antiretroviral side effects

Antiretroviral side effect	2004 National Antiretroviral Treatment Guidelines	2007 National Antiretroviral Treatment Guidelines
Peripheral neuropathy	amitriptyline	pyridoxine 25mg, paracetamol 1g, amitriptyline 25mg
Headache and other pains	paracetamol	paracetamol
Cough and nasal symptoms	cough syrup	
Rashes and other skin conditions	calamine / hydrocortisone	betamethasone chlorpheniramine 4mg
GI effects incl. nausea and vomiting	antacid	metoclopramide 10mg oral rehydration therapy,
Depression and other central nervous system effects	chlordiazepoxide	chlorpromazine
Lypodystrophy	-	-
Anaemia	ferrous salts and folic acid	ferrous salts and folic acid
Pancreatitis	hyosine	

Source: Ministry of Health and Social Welfare (2004: 37), & (2007: 131)

Other recommendations from the 2007 National Antiretroviral Treatment Guidelines were for drug switching within an antiretroviral regimen while no drug treatment was suggested for other side effects besides patient reassurance concerning vivid dreams caused by efavirenz (Ministry of Health and Social Welfare, 2007: 131).

2.2.11 Adherence to antiretroviral drug treatment

The behaviour of the patient towards medicine-taking is crucial for the success of antiretroviral therapy (Amberbir *et al*., 2008: 1). Patient preparation about how to take antiretroviral drugs, their side effects and what to expect from the antiretroviral treatment is necessary. Barriers to

adherence should be addressed at an early stage to avoid non-adherence to antiretroviral therapy (Chestney, 2000: 171).

2.2.11.1 Measurement of adherence

The standard way of measuring adherence in the ART clinics is pill count and determination of how many pills were not taken during the treatment period. Adherence is said to be good when it was 95 percent (Amberbir *et al*., 2008: 3) or greater, and fair when it was 94-85 percent. It was said to be poor below 84 percent. If not more than one tablet was missed in 30 or 28 days adherence is taken to be above 95 percent. When two to four tablets are missed, adherence is between 85-94 percent and if five or more tablets are missed adherence is below 84 percent (Ministry of Health and Social Welfare, 2004: 11).

2.2.11.2 Adherence monitoring

Monitoring of adherence is part of the routine management of patients on antiretroviral therapy. If HIV/AIDS patients fail to adhere to provided antiretroviral regimen the reasons for poor adherence should be known and addressed promptly for continued treatment of HIV/AIDS. If toxicity is the reason for non-adherence, treatment switching is advised and adherence monitoring continued (Roberson *et al.,* 2009: 50). However, Watt *et al.,* (2009: 1793) showed that adherence to medication is good in African population because, among other reasons, HIV/AIDS patients experience immense improvements in their health. This raises their confidence in medicines, as well as the need to meet their family"s responsibilities.

2.2.12 Hospitalization of HIV/AIDS patients

Hospitalization of HIV/AIDS patients is mainly attributed to opportunistic infections (Buchacz *et al*., 2008: 1345) and that is also a major cause of death in HIV/AIDS patients (Garcia-Jardon *et al*., 2010: 81). However, evidence shows that incidence of opportunistic infections or AIDS defining illness (ADI) rates decreases greatly from as high as 27.4 events per 100 PY at HAART initiation (95 percent CI [19.5;38.7]) to linearly by 5 percent per month (95 percent CI = [2;8]) (De Beaudrap *et al.* 2010: 179). According to Buchacz *et al.,* (2008: 1345), the rates of hospitalization for HIV/AIDS opportunistic infections decreased from 7.6 in 1994–1996 to 1.0 in 2003–2005 ($P< 0.0001$). The cause of hospitalisation was not only a result of opportunistic infections but also the side effects as well. Mehta *et al.,* (2008: 396) confirms this by showing

that 6.3 percent of hospitalisation of HIV/AIDS patients was due to adverse drugs reactions that are preventable. Henry (2001: 306) comments that death in the HIV population is reduced by 85 percent after 1 year of treatment and care and treatment of HIV/AIDS patient largely became an outpatient intervention.

2.2.13 Incidence of opportunistic infections in patients with HIV/AIDS

Opportunistic infections are a common occurrence in HIV/AIDS patients with lower CD4 cell counts. They are infections of bacterial, viral or fungal in nature that cause no diseases in HIV negative populations or are rare in occurrence. These infections are major causes of hospitalization and death in HIV/AIDS patients (Garcia-Jardon *et al*., 2010: 81).

2.2.13.1 Treatment of opportunistic infections

Treatment of opportunistic infection is normally short term and requires drugs that are already available in the pharmaceutical market. Early treatment is usually successful. However, there are opportunistic infections that are life-threatening. If prompt treatment is not given death may result. Table 2.6 illustrates commonly occurring opportunistic infections and possible medicines for their treatment.

Table 2.6 Opportunistic infections and possible drug treatment

Opportunistic infection	Symptoms	Medication to use
Oesophageal / oral candidiasis	white plagues in the mouth, difficulty in swallowing	miconazole, fluconazole, ketoconazole, nystatin
Fungal infections	round scaly lesions, hair loss	griseofulvin, ketoconazole, Whitfields®, clotrimazole
Diarrhoea	watery frequent stools	oral rehydration solution, loperamide
Pneumocystis carinii pneumonia	cough, fever, tachypnoea, cyanosis	dapsone, cotrimoxazole
Herpes simplex and zoster	tingling, pain, blisters	acyclovir cream or tablets, gincyclovir
Toxoplasmosis	headache, seizures, focal neurological finding such as facial droop	cotrimoxazole, pyrimethamine

Source: Ministry of Health and Social Welfare, 2007: 132

Table 2.7 provides some information on CD4 cell count where opportunistic infections are most likely to occur in the progression of HIV/AIDS disease**.**

Table 2.7 Type of opportunistic infection and CD4 count at which it occurs

Opportunistic infection	**CD4 count cells/mm^3**
Vaginal candidiasis and herpes zoster	≥400
Tuberculosis and oral candidiasis	≥300
Oesophageal candidiasis, Herpes and *Pneumocystis carinii pneumonia*	≥200
Toxoplasmosis, cytomegalovirus and cryptococcus infections, *Mycobacterium avium complex*	100- 50

Source: Baylor international paediatric AIDS initiative (2007:157)

2.2.13.2 Opportunistic infection prophylaxis

Opportunistic infections may be prevented by giving certain drugs that studies proved to be effective. *Pneumocystis carinii pneumonia* (PCP), now known as *Pneumocystis jirovesi pneumonia,* is an AIDS defining infection that occurs below CD4 count of 200 cells/mm^3 and can be prevented by using a daily dose of cotrimoxazole (a combination of drugs of 800 mg sulfamethoxazole, and 160 mg trimethoprim) (Walker *et al,.* 2010: 2). Patients who develop sensitivity to cotrimoxazole are given a daily dose of dapsone. Prophylaxis of PCP should be discontinued once a patient has had a stabilised CD4 count above 200 cells/mm^3 for a period of 3 months (Egidio *et al.*, 2007: 1711). Cotrimoxazole may also be used for prophylaxis of *toxoplasmosis gondii* (Walker *et al*., 2010: 2). *Mycobacterium avium complex* (MAC) is another common infection for which azithromycin is a recommended drug for prophylaxis (Sendi *et al.*, 1999: 811). It has also been found that improvement in CD4 cell count reduces the incidence of new opportunistic infections as well as a resolution of existing ones (Montessori *et al.*, 2004: 229).

2.2.13.3 Tuberculosis

Tuberculosis (TB) is a disease commonly found in HIV/AIDS patients although it can also affect other people without HIV. It is caused by *Mycobacterium tuberculosis* and mostly affects the lungs. It is referred to as pulmonary TB. Extra pulmonary TB is found mostly in HIV/AIDS patient and affects other parts of the body (besides the lungs). Among patients with TB, HIV/AIDS was found to be encountered in 90 percent of patients, according to the Global Fund factsheet on

Lesotho, there were about 270, 000 people with HIV infection and can be expressed as 14, 356 in every 100, 000 patients with HIV/AIDS, and about 490 in every 100, 000 patients with tuberculosis.This is the fourth highest rate in the world (The Global Fund to Fight AIDS, Tuberculosis and Malaria, 2010).

TB treatment follows TB protocol from WHO guidelines. Directly Observed Treatment Shortcourse (DOTS) is a method used to ensure that all TB patients complete their TB treatment. TB as a public health disease is run by National TB programmes which follows WHO programmes on TB. Pinto (2010: 4) says that even though DOTS is a method used to deliver TB treatment, patients find it unacceptable and intrusive.

2.3 Outcome of HIV/AIDS treatment

This section presents the outcomes of HIV treatment and focuses on CD4 cell count increase and body weight increase

2.3.1 HIV/AIDS and CD4 cell count

CD4 Cell Count measures the number of CD4 cells per cubic milliliter of blood. The CD4 count is used as a measure of the degree of immuno-compromise and stage of HIV disease progression. CD4 cell count is a well accepted laboratory test that is commonly carried out in order to make decisions about initiating ART, or monitoring the recovery of the immune system under the treatment with HAART (Gazzard, 2008: 565). Lower CD4 cell count was associated with incidence of opportunistic infections (Bhat & Saha, 2005: 1645). According to Kimmel *et al.,* (2010: 258), cost-effectiveness of CD4 cell count as a measurement of success of treatment could be used for antiretroviral treatment switching decisions.

2.3.2 HIV/AIDS and body weight

Moyle *et al.,* (2004: 367) defines HIV-associated wasting as 10 percent. Involuntary body weight loss includes a decline in both lean and fat mass. Body weight loss is one of the symptoms of HIV (WHO 2008: 35). The factors that cause malnutrition in HIV/AIDS include infection, which alters the metabolism of energy, carbohydrates, fats, proteins, vitamin and minerals thereby increasing the body"s need for these nutrients. While fever increases caloric needs by 12 percent for each degree centigrade above normal, it may increase protein utilization. Gastrointestinal illnesses such as diarrhoea and mal-absorption can lead to vitamin, mineral,

protein, fat and carbohydrates loss. It has also been found that diarrhoea increases caloric needs by 25 percent. Oral and oesophageal diseases and gastric disease may make eating difficult and painful. Nausea and vomiting may also lead to reduced food intake, leading to decreased nutrients (Baylor International Paediatric AIDS Initiative, 2007: 257). However, Wheeler *et al.,* (1998: 80) associated body weight loss of 5 to 10 percent with the increased risk of opportunistic infections and death among people with HIV. Severe body weight loss leads to the reduced survival period (Wheeler *et al.,* 1998: 80).

Economic and psychosocial issues may include HIV/AIDS patients being too sick to work even if they had a job or too sick to prepare food. They may lose their job because they are too sick to work. This may lead to the loss of income, resulting in lack of money to buy food (Severe *et al*., 2005: 2332). HIV/AIDS is associated with issues such as discrimination and stigma. All these may have an impact on food intake, leading to reduced body weight. On the other hand antiretroviral treatment leads to body weight restoration when the patient can eat well. There is no energy expenditure as a result of reduced opportunistic infections. HIV/AIDS patients may gain body weight because they are employed and can provide nutritious food for themselves (Severe *et al.,* 2005: 2330).

2.3.3 Viral load

Viral load measures the number of virus particles per milliliter of blood by quantifying HIV RNA. The importance of routine measuring of viral load is to determine compliance to medicines, drugs resistance or treatment failure (Gazzard, 2008: 565). With the standard test used in Lesotho, 400 to 750,000 HIV copies per milliliter of blood can be detected.

2.4 Financial resources

Financial resources are important part of HIV/AIDS treatment and without them the treatment would not be possible. That is why it is essential to discuss them in this chapter.

2.4.1 Affordability of antiretroviral therapy services

All ART services are offered at no cost to the HIV/AIDS patient in Lesotho. Antiretroviral drugs are distributed to the ART clinics and are dispensed according to the prescription specified in the National Antiretroviral Treatment Guidelines of Lesotho 2007. Antiretroviral drugs are supplied monthly to HIV/AIDS patients. On the provider side, prices of antiretroviral drugs have

been negotiated and different formulations have been recommended for use by the Clinton foundation for resource-limited countries. Lesotho is among these countries (Médecins Sans Frontières, 2006: 11).

2.4.2 Sustainability of antiretroviral therapy services

Antiretroviral therapy services need robust financing and financial estimates. Accurate financial projections have to be made and money allocations made every year to manage the pandemic. Global spending on HIV/AIDS is presently about 250-300 million U.S. dollars but needs to increase to 8 billion U.S dollars in the next 10 years. It was found that the incremental cost per year of life gained was 240 U.S. dollars in 2002. For prophylaxis with cotrimoxazole alone, it was found that 620 U.S. dollars is needed for antiretroviral therapy and prophylaxis (without CD4 testing), and 1,180 dollars for antiretroviral therapy and prophylaxis with CD4 testing, as each therapy is compared with the next least expensive strategy (Goldie *et al*., 2006: 1441). The Lesotho National HIV/AIDS Strategic Plan for 2006-2011 estimated a total need of 360 million US dollars. Based on the resource needs model, a revised needs estimate was developed by the National AIDS Commission in 2007. It was estimated that a minimum of 547 million US dollars will be required for the period 2006-2011 (National AIDS Commission, 2006: 3).

According to the Lesotho National HIV/AIDS Strategic Plan for 2006-2011 treatment, care and support, was allocated 6.4 million US dollars for 2006/2007 of which 43 percent was spent on antiretroviral drugs, while 33 percent was on nutritional support and 2 percent of the budget was allocated for other drugs used for management of opportunistic infections. The budget would increase to 22.6 million US dollars by 2010/2011 (National AIDS Commission, 2006: 27).

2.4.3 Financing of antiretroviral therapy services

Local and international funds are needed for the successful and sustainable provision of antiretroviral medicines to the HIV/AIDS patients. This is why funds sources were outlined as follows:

2.4.3.1 Domestic funds

The Government of Lesotho has allocated 2 percent of five key ministries budgets. These were Ministry of Health and Social Welfare, Ministry of Finance, Ministry of Education, Ministry of Agriculture, Ministry of Local Government. Approximately 8.4 Million US dollars was spent in

2005/2006 and 8 million US dollars in 2006/2007 fiscal years (FY). The money allocated was supposed to be spent on HIV/AIDS response activities.

2.4.3.2 International fund

There has been a significant increase in the amount of resources pledged and made available for the AIDS response in Lesotho. Following the 9th Donor Round Table Conference on Sustainable Economic Growth and Poverty Reduction, the development partners pledged to support the national AIDS response (UNGASS. 2007: 24). Lesotho has been successful in getting a total of 114,473,978 US dollars from the Global Fund to fight AIDS, TB and Malaria (GFATM). From these 102,922,867 US dollars are for HIV-related programmes. Other significant new grants for Lesotho are from the European Union- (12 million Euros) for orphans and vulnerable children (OVC), USG and Irish AID (UNGASS, 2007: 24).

Funding for HIV treatment is currently available, but the question is its sustainability as allocation of financial resources is largely from external sources. As more people are put on antiretroviral therapy, on one hand more financial resources are spent on antiretroviral medicines. On the other hand, patients on antiretroviral treatment are less sick from opportunistic infections. This results in reduced mortality and morbidity rates. HAART is said to reduce mortality rates by 70 to 80 percent (Palella *et al*., 1998: 857) and morbidity rates of HIV and AIDS by 85 percent (Badri *et al.,* 2004: 1165).

Lesotho as a country officially started providing antiretroviral treatment in 2004 and developed the first National Antiretroviral Treatment Guidelines in the same year. Lesotho has a comprehensive management of HIV with guidelines for treatment of HIV through ART, prophylaxis and treatment of opportunistic infections, monitoring laboratory tests specific to each HAART regimen, as well as treatment of minor and major adverse drug reactions (Ministry of Health and Social Welfare, 2004: 37).

2.5 Evaluation of cost

The cost of treatment of HIV using antiretroviral medicines is evaluated and methods of analysis are briefly discussed.

2.5.1 Direct cost

Direct medical costs are fixed and variable costs that are associated with a medical condition. In the case of this study direct medical costs are the cost of treating HIV/AIDS and these are antiretroviral drugs (Dickson *et al*., 2003: 22)

2.5.2 Indirect cost

Indirect costs are the costs of loss of or reduced productivity, resulting from one"s medical condition or treatment.

2.5.3 Methods of pharmacoeconomic analysis

Methods of economic evaluation are visited in order to give a brief background of how to use them for the understanding of the results**.**

2.5.3.1 Cost minimization analysis (CMA)

Cost minimization analysis is a type of pharmacoeconomic analysis used when two or more products are believed to have the same outcome. The cost of each product is measured and compared to the other. Two products may have the same outcome but differ in acquisition and administration costs.

2.5.3.2 Cost-effectiveness analysis (CEA)

Cost-effectiveness analysis is a method that is used to identify measure and compare the cost and outcomes of two or more alternative interventions. Cost-effectiveness analysis cannot however, be used to compare interventions with different health outcomes. A product or service may be considered cost effective if it is less expensive, but is as effective as the other alternative. It may be more expensive with additional benefit or less expensive and less beneficial when competing with an alternative whose benefit is not worth the extra expense. Table 2.8 shows how to interpret cost-effectiveness results.

Table 2.8 Interpreting cost-effectiveness

Outcome	Cost	
	Higher cost	Lower cost
Higher effectiveness	May be cost-effective	Cost-effective
Lower effectiveness	Not cost-effective	May be cost-effective

Source: Waning & Montagne (2001:151)

2.5.3.3 Cost–benefit analysis (CBA)

Cost–benefit analysis can be used to assess a single programme or to compare multiple programmes. It can compare programmes with dissimilar outcomes. A preferred alternative is the one with lower costs, higher benefits and higher benefit ratio.

2.5.3.4 Cost–utility analysis (CUA)

Cost–utility analysis is a specialised variant of cost effectiveness analysis. Costs are measured in monetary terms while outcomes are measured in preference or utility. CUA considers both the quantity of life which refers to life duration affected by illness or treatment and the quality of life which is the impact that an illness or its treatment has on the well-being of a patient.

2.5.3.5 Cost of illness

Cost of illness is a method used to measure the total of or aspects of a specific disease or illness. An example of HIV/AIDS study which is limited to only the medication cost of treatment of HIV/AIDS patient or it could include all costs direct and indirect for the treatment of an illness.

Table 2.9 Pharmacoeconomic methodologies

methodology	cost measurement	outcome measurement
Costs Minimization	monetary (rand value)	assumed to be equivalent in comparative groups
Cost- Benefit	monetary (rand value)	monetary (rand value)
Cost effectiveness	monetary (rand value)	natural units (life –years gained, mmol/L blood glucose, mm Hg blood pressure, cell/mm^3 CD 4 count)
Cost- utility	monetary (rand value)	quality -adjusted life – year or other utility

Source: (Dickson et al. 2003: 38)

2.6 Cost of treating HIV/AIDS

Cost is the total value of all resources used in order to produce a good or a resource (Dickson *et al*. 2003: 22). In the case of this study cost means the total cost of drugs, laboratory tests and dietary supplements used in the treatment of HIV. Drugs include antiretroviral drugs, drugs used in the treatment of side effects caused by antiretroviral drugs, drugs used for prophylaxis and treatment of opportunistic infections. Laboratory tests include monitoring tests that are required to assess the treatment success and incidence of toxicities and side effects caused by

antiretroviral drugs. Dietary supplements include formulations that are used with the intension to alleviate wasting caused by HIV/AIDS.

2.6.1 Cost of treating HIV/AIDS patients

Rollout of antiretroviral service was carried out in many countries. In order for this to succeed, cost assessment was necessary so as to verify their budgetary allocation (Kumarasamy *et al*. 2007: 509). Cleary *et al.,* (2004: 2) carried out similar assessments in Lesotho and South Africa for the same purpose of rollout of antiretroviral treatment and care for budgetary purposes (Cleary *et al.,* 2006:100, and Cleary *et al.,* 2007: 4). It was reported that cost-effectiveness of antiretroviral treatment compared well with treatment of other chronic illnesses and that antiretroviral therapy was found to be contributing significantly in preventing HIV patient hospital admissions (Gazzard, 2008: 593). Similarly, Badri *et al.*, (2004: 1165) indicated that there was a reduced mortality of patients on HAART, when compared to those who were not on HAART.

On the other hand, Badri *et al.,* (2006: 54) showed that HAART was a cost-effective intervention in South Africa and cost saving when its prices are further reduced. Badri *et al.,* (2006: 52) also showed that use of the HAART could be associated with reduced disease progression, AIDS, and death. Krentz *et al.,* (2006: 463) says that hospital admissions for HIV/AIDS patients after HAART are reduced by 400 percent. This means savings on hospitalization cost for them. Krentz *et al.,* (2004: 93) also found out that initiating ART early has some positive treatment outcome as well as some cost savings as far as hospital admissions are concerned. Median survivorship was also assessed and was estimated to be 8 years with intensive monitoring and first- and second-line antiretroviral drugs (Hogan *et al*., 2007: 1431).

2.6.2 Cost of preventing opportunistic infections

Sendi *et al*., (1999: 811) used cost effective analysis to analyze the cost of azithromycin for preventing opportunistic infections due to *Mycobacterium avium* complex. Outcome measures were expected survival and life years gained. It was concluded that prophylaxis with azithromycin increased life expected survival and reduced health care costs. It was also concluded that it seemed to be more effective if started in patients HIV but without AIDS. Pitter *et al*., (2007: 336) assessed the cost-effectiveness of cotrimoxazole prophylaxis in Uganda among HIV/AIDS patients. The outcome measures were net programme cost and disability adjusted life years gained. It was concluded that giving cotrimoxazole to all HIV infected patients

or to those in WHO stage 2 or more advanced condition was more cost effective than giving it to patients with CD4 count which is less than 500 cells /mm^3 (Pitter *et al*., 2007: 336).

2.7 Chapter summary

Various sources of literature were searched in order to augment this research with the work that has already been carried out on a variety of topics, including the origin of HIV/AIDS, treatment of HIV/AIDS, (which covered antiretroviral treatment guideline and specified which antiretroviral regimens to use, as well as which monitoring laboratory tests to carry out). Antiretroviral regimens, their side effects and opportunistic infections with their treatment and prophylaxis were discussed.

Treatment outcome was found to be CD4 cell count increase and body weight increase. However, viral load was not routinely used as an outcome indicator of antiretroviral treatment. In Lesotho it did not form part of the measurement instruments for the study. Sources of funding and cost assessment methods, as well as cost-effectiveness of HAART were discussed.In Chapter three, the methodology used for this study is addressed. It includes the methods of data collection, measurement instruments and analysis as well as the limitations of the study.

CHAPTER 3

Research Methodology

In Chapter three, the empirical research methodology is presented including the study design, study population and criteria for selection of subjects in the study. Ethical matters are also presented. Data collection tools, analysis and calculations and methods of analysis are also discussed.

3.1 Study objectives

Study objectives are set in order to guide the study process. They are presented as the main objectives and specific objectives of the study.

3.1.1 Main objective

The main objective of the study was to assess the cost of antiretroviral medication treatments. This is achieved by specifically assessing the cost of antiretroviral regimens, antiretroviral drug side effects, the cost of drugs used for prophylaxis and treatment of opportunistic infections as well as the cost of monitoring laboratory tests and dietary supplements.

3.1.2 Specific literature objectives

These objectives were discussed in detail in chapter two of the study. Therefore they would not be discussed in chapter three.

3.1.3 Specific empirical research objectives:

Specific research objectives of the empirical study were divided into antiretroviral treatment, treatment outcome, treatment cost and economic evaluation.

The study had the following objectives concerning the treatment of HIV/AIDS:

- To determine if the antiretroviral prescribing followed National Antiretroviral Treatment Guidelines of Lesotho (2004).
- To assess retention of antiretroviral treatment to first line treatment.
- To assess if switching of antiretroviral therapy from one regimen to another followed recommended policy by the National Antiretroviral Treatment Guidelines of Lesotho (2004).

- To investigate the prescribing patterns of medicines used for the treatment of opportunistic infection and if that was according to National Antiretroviral Treatment Guidelines (2004).
- To determine if side effects of antiretroviral were treated according to National Antiretroviral Treatment Guidelines of Lesotho (2004).

Outcome of antiretroviral treatment

The study had the following objectives concerning the Outcome of antiretroviral treatment:

- To determine CD4 cell count changes brought about by antiretroviral therapy.
- To assess if there was a change in body weight changes before and after antiretroviral treatment.
- To identify incidence of side effects of antiretroviral drugs and how they impacted on overall treatment of HIV/AIDS.

Cost of antiretroviral treatment

The study had the following objectives concerning the cost of antiretroviral treatment:

- To compare the medicine treatment costs of different HAART regimens.
- To assess impact of additional cost imposed by associated monitoring laboratory tests, dietary supplements as well as treatment of side effects at different ART clinics.
- To assess cost implication of antiretroviral regimen switching on overall cost of HIV/AIDS treatment.
- To compare prophylaxis and treatment cost of opportunistic infections in different ART clinics.
- To compare if second line antiretroviral treatment cost implied with first line treatment.
- To assess total cost of HIV/AIDS treatment in private and public clinics.

Economic evaluation of antiretroviral

The study had the following objectives concerning the economic evaluation of antiretroviral treatment:

- To determine cost to effectiveness ratio between two antiretroviral regimens using CD4 cell count as the main measure of outcome.
- To determine cost to effectiveness ratio between two antiretroviral regimens using body weight increase as the subsidiary measure of outcome.
- To calculate the incremental cost effectiveness ratio between the antiretroviral regimens.

3.2.1 Study design

The design of the study was observational retrospective study. Only medical records were examined for collection of the relevant data.

3.2.2 Study sites

Eight Study sites were chosen because of their vicinity. They were all within the radius of 35 km from Roma. The Public clinics were Senkatana ART clinic, Bophelong Adult ART clinic, Qoaling ART clinic, and Mabote ART clinic. Private clinics included Healthy Life Style and Diabetes clinic®, Medicare Family clinic®, and Khanya Family clinic®. St. Joseph clinic, a Christian Health Association of Lesotho (CHAL) clinic was also included (see appendix C).

3.2.3 Study population

The researcher retrospectively abstracted data from patient files of 1 423 HIV/AIDS patients, who were on antiretroviral treatment for a minimum of one year. All patients who collected their medicines until 31 August, 2008 and who had been on antiretroviral drugs for one year or more were included in the population. Survey forms were used to collect data (see appendix D.1 and D.2) and Excel spread sheet was used to capture the data (see appendix E).

3.2.4 Inclusion criteria

The following patients would be included in the study:

- All patients who had been on antiretroviral therapy for at least one year (12 months) and who had come for refills at least 4 times in a year (those who received three months supply of antiretroviral drugs), for a maximum of 12 times a year (those who received monthly antiretroviral drugs supply) were included in the population for the study.
- HIV/AIDS patients who were on both antiretroviral first line and second line drugs were included.
- HIV/AIDS patient who further had TB were included in the study.
- HIV/AIDS patients who transferred into the clinic from another clinic, but who had been on treatment for one year in the clinic were included.

3.2.5 Exclusion criteria

The following patients were not included in the study:

- All HIV/AIDS patients who transferred out of the clinics.
- HIV/AIDS patients who defaulted during the study
- HIV/AIDS patients who died.
- HIV/AIDS paediatric patients (0-14 years)
- Sexually transmitted infections were not considered in the study due to the fact that even though they predispose a patient to HIV/AIDS they had no direct effect on HIV/AIDS treatment and its cost.
- Other medical conditions such as hypertension and its treatment that were not related to HIV/AIDS were not included in the data.

3.2.6 Training of research assistants

Research assistants (who were Pharmacy Honours Programme students of the National University of Lesotho) were trained on how to use research tools and how to extract information from the patient files in the pharmacy or in the records section of the clinics. Some clinics (such as Healthy lifestyle, Bophelong and Senkatana) had a relatively high patient population. Two research assistants were needed for each site. One research assistant was placed in each of the other sites (appendix C).

3.2.7 Monitoring parameters

The following parameters were documented:

- Patient number.
- Gender.
- Age.
- Pre HAART- treatment date.
- Initiation date.
- Treatment regimen.
- CD4+ cell count at initiation and at present for determining immune response.
- Viral load to determine virologic response.
- Full blood counts to assess damage to the blood cells caused by the virus or antiretroviral drug, liver function tests to assess functioning and damage to the liver cells.
- Haemoglobin to determine if zidovudine can be given or not because it causes anaemia.
- Other laboratory tests.
- Opportunistic infections prophylaxis and treatment.

- Side effects of antiretroviral drugs and their treatment.
- Dietary supplements.

3.2.8 Measuring instruments

In this section the variables or instruments that were used to analyse data will be provided

Mean, standard deviation, Median, minimum and maximum

Mean

Mean is a measure of central tendency of the values for the whole group.

Mean can be calculated by adding all the numbers divide by the number in the group

Standard deviation

Standard deviation is a measure of dispersion or variation or how widely the values are spread around the centre. It can be calculated by square adding the value and the mean, adding squared differences and dividing the sum by total number of value minus one, and then find the square root of the result. (Friedman 1994: 19)

Median

Median is the value where up to 50% of recorded values were noted.

Minimum and maximum values

The minimum and maximum numbers recorded in a group or field of related values

Cost-prevalence index = percent cost / percent prevalence

Where the cost-prevalence index would be interpreted as follows:

- If cost-prevalence index < 1 then the drug item utilized is relatively inexpensive.
- If cost-prevalence index = 1 then there is an equilibrium between the cost and prevalence of the drug item.
- If cost-prevalence index > 1 then the drug item utilized is relatively expensive

(Serfontein, 1989: 180)

Effect size or *d*-values

Cohen (1988: 9) stated that the “effect size” is a measurement of the phenomenon in the population.

While Utts & Heckard, (2007: 581) say that "effect size" provides information about how strong a difference effect is in the population relative to another population.

"Effect size" or $d = \frac{\mu_1 - \mu_0}{\sigma}$

where d = effect size, μ_1 is the true population mean and μ_0 is the null value and σ is the largest standard deviation and effect size would be interpreted as follows:

- if *d*- value = 0.2 there is no significant difference between the means
- if *d*-value = 0.5 there is a somewhat significant difference between the means
- if *d*-value ≥ 0.8 there is a practical difference between the means

Cost/patient ratio

Cost/patient ratio = total cost/ total number of patients

Comparison between antiretroviral treatment outcomes

Weighted average CD4 cell count increase /weighted body weight increase ratio

$$= \frac{\sum \text{mean CD4 cell count increase in specific regimens}}{\sum \text{mean body weight increase in specific regimens}}$$

Weighted averages are applied, they were calculated from the mean values recorded and multiplied by the frequency value and added to obtain a weighted average.

Cost–effectiveness analysis expresses an average cost-effectiveness ratio for the alterative treatments being compared**.**

$$\text{Cost-effectiveness ratio} = \frac{\text{average cost of treatment}}{\text{net outcome of treatment (effectiveness)}}$$

(Waning & Montagne, 2001: 151)

Incremental cost-effectiveness ratio measures if the additional cost of a more costly therapy would produce an additional value or benefit, or it assesses added cost per net effectiveness and is calculated using the following formula**:**

$$\text{Incremental cost-effectiveness} = \frac{C_2 - C_1}{E_2 - E_1}$$

Where C_2 and C_1 are the differences in total cost

E_2 and E_1 are the differences in effectiveness

(Waning & Montagne, 2001: 151)

3.3 Ethical considerations

Record files for HIV/AIDS patients were used retrospectively. The numbers were used in order to keep patient confidentiality. Confidentiality forms were provided and signed by the research assistants and information was kept strictly confidential. Permission to carry out this research was obtained from the Ethics Committee of the Ministry of Health and Social Welfare, and all the ART clinics gave permission. The Ethics Committee of North West University gave permission for the study to be carried out with the following number: NWU-00101-10-55.

3.3.1 Pilot study

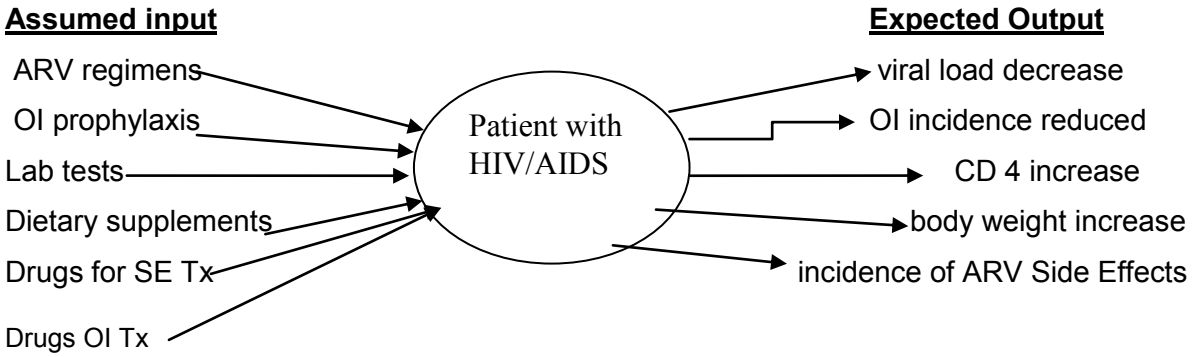
Field testing was done to verify availability of data and presentation of the letter requesting for permission to conduct the study. Five files of patients, who were initiated at Medicare Family Clinic between 1 May and 30 June 2007, were selected for the pilot study. Record of their demographic status, pre-antiretroviral therapy medicines, opportunistic infection treatment, side effects treatment, antiretroviral therapy and laboratory monitoring tests were recorded and the effectiveness of the tool was assessed and reviewed accordingly. A Pilot study was used to further develop the data collection tool. The adherence column as well as weight of the HIV/AIDS patients to record measurement at every visit was included, it was with demographic information in the beginning. Other conditions and prophylaxis columns were also separated and their possible treatment column was drawn. Laboratory tests were recorded at the same time as CD4 cell count. Their column was also drawn.

3.3.2 Representation of input and outputs of HIV/AIDS treatment

The following schematic presentation indicates the variables that were considered in the study. This schematic representation was designed in order to illustrate the inputs and outputs of antiretroviral treatments. The input for standard resources utilisation on patients with HIV/AIDS were antiretroviral medicines, prophylactic medicines and those for treatment of opportunistic

infections, dietary supplements and required laboratory tests. The expected outputs were viral load reduction, incidence of side effects of antiretroviral, reduced opportunistic infections incidence, CD4 cell count increase as well as body weight increase.

Figure 3.1 Schematic representation of input and outputs of HIV/AIDS treatment



(Key: OI – opportunistic infection, lab –laboratory, ARV – antiretroviral drugs, SE- side effects, Tx - treatment)

3.4. Data management

Data was collected using pre-constructed forms and was captured on the excel spread sheet (2007), and calculations of costs were carried out and added to the spread sheet. Finally, data was sent for analysis through SAS version 8.

3.4.1 Data collection instruments

After pilot study, data collection instruments were corrected and finalised. They were printed to collect data from the selected sites (see appendix D.1 and D.2).

3.4.2 Data collection

Data were collected for three months, from September to December 2008, by the research assistants at different study sites and sorted according to sites and antiretroviral regimen.

A calculation instrument was designed (in order to carry out calculations in an easy manner) that consisted of six columns (refer to appendix E). A list of all the drugs used was added on the spread sheet. Their doses were determined and prescribed daily doses (PDD) for a monthly

supply of antiretroviral medicines and medicines for opportunistic infections prophylaxis was calculated. A PDD for medicines used for a short period of time in the treatment of antiretroviral side effects, as well as dietary supplements and treatment for opportunistic infections were also determined. Prices of a monthly supply of medicines, as well as for those medicines that were given for a short time were stipulated from National Drug Service Organization (NDSO) and Tripharm® and put on the spreadsheet.

The total yearly cost of antiretroviral regimens, dietary supplements, and monitoring laboratory tests of each patient were calculated. While for medicines used for opportunistic infection prophylaxis and treatment, medicines used to treat side effects of antiretroviral total costs were then calculated.

For antiretroviral medicines and opportunistic infection prophylaxis, the cost was calculated taking into consideration those patients received monthly supplies. The cost reflected on table 3.2 was for a pack of sixty or thirty tablets depending on the regimen, and, by implication, the number of months of treatment was put on table 3.2 which would automatically calculate the total cost for the months of treatment or prophylaxis.

Laboratory tests were basically CD4 cell count, liver function tests, and blood chemistries, which were carried out once every month. For the treatment duration, they were carried out for a certain number of times. Therefore cost was calculated by putting in the number of laboratory tests done for each test and the total cost was the cost of all laboratory tests done, multiplied by the number of times each test was carried out, and summed together.

For treatment of side effects and opportunistic infections as well as dietary supplement, the actual number of tablets given was put in column 3 of the tool and the answer would automatically be seen in column 5 (see appendix E).

If a patient was given more than one drug, then the total numbers of drugs would be seen in column 6. Once the information was generated, it was transferred to the spread sheet (see appendix E)

3.4.3 Data processing and cleaning

The following list of data was compiled for statistical analysis:

- Demographic information such as age and gender of the patients was compiled, according to the clinics.
- A list of all conditions and possible drugs treatments was compiled. The list of conditions was matched with a list of possible drug treatments using Lesotho National Antiretroviral Treatment Guidelines. Conditions that were neither opportunistic infections nor antiretroviral drug side effects were then excluded, as well as their drug treatments. These were hypertension, long standing diabetes mellitus, sexually transmitted diseases and related information.
- A list of laboratory tests.
- A list of dietary supplements.
- A price list (from 2004 to 2008) of all the drugs, laboratory tests and dietary supplements provided for each patient.

3.4.4 Research instruments used to summarise data

Data instrument (refer to appendix E)

The spread sheet (refer to appendix E) was prepared to summarize the full details of each HIV/AIDS patient. Data were classified according clinic, and who manages it, age, gender and occupation were captured in the spread sheet for individual patient. The following information was also captured:

- Duration of treatment.
- Regimen given.
- Opportunistic infection incidence.
- Opportunistic infection prophylaxis.
- Opportunistic infection treatment and its cost.
- Incidence of antiretroviral side effects.
- Drug treatment of antiretroviral side effects and cost.
- Laboratory tests and their cost.
- Dietary supplements and their cost.
- CD4 cell count before and after treatment.
- Weight before treatment and after the stipulated treatment duration adherence.
- Cost to patient.

- Viral load were included in the spread sheet as well.

3.4.5 Antiretroviral drugs regimens

Antiretroviral regimens were specified by HIV/AIDS directorate of Lesotho and were incorporated into the National Antiretroviral Treatment Guidelines of 2007 (Ministry of Health and Social Welfare, 2007: 50).

First Line antiretroviral drugs combinations were as follows:

1a –Stavudine 30mg /lamivudine150mg/ nevirapine 200mg
1b – Stavudine30mg / lamivudine150mg / efavirenz 600mg
1c - Zidovudine 300mg/ lamivudine150mg/ nevirapine 200mg
1d - Zidovudine 300mg / lamivudine150mg / efavirenz 600mg

Second line antiretroviral drugs combinations were as follows:

1e – Stavudine 30/ lamivudine 150mg / lopinavir/ritonavir 200/50mg
1f - Zidovudine 300mg/ lamivudine 150mg/ lopinavir/ritonavir 200/50mg
1g – Didanosine 400mg/ abacavir 300mg / lopinavir/ritonavir 200/50mg
1h-Tenofovir 300mg/ lamivudine 150mg / lopinavir/ritonavir 200/50mg
1i –Tenofovir 300mg/ lamivudine 300mg/ efavirenz 600mg

Antiretroviral regimen switches from first line to other first line drugs or first line to second line antiretroviral medicines, was denoted as 1s.

3.5 Cost calculations for HIV/AIDS treatment

The costs included and not included in the calculations are spelt out below.

Costs of medicines and monitoring laboratory tests included for the study duration (Jan 2004-August 2008) were:

- The yearly cost of antiretroviral medicines
- The cost of opportunistic infection prophylaxis and treatment
- The cost of antiretroviral side effects treatment
- The yearly cost of dietary supplements

- The yearly cost of laboratory tests that is CD4 cell count, liver function tests, and blood chemistries

NB: Prices were obtained from invoices issued to Ministry of Health and Social Welfare by the supplier, and each respective year prices were used to calculate yearly costs for ARV"s, when a patient was not given a certain regimen for a year, monthly costs were calculated and added to the yearly costs. This applied for laboratory tests and supplement as well as opportunistic infections prophylaxis if it was given for a period longer than a year. However, treatment of opportunistic infection and side effects was short in duration and the cost calculations followed the duration of treatment not necessarily the yearly costs and also the number of episode that were treated was considered. Prices used were according to the year stated in the invoices which were from 2004 to 2008.

Costs <u>not</u> included in the study were:

- The cost of HIV/AIDS counseling and testing
- The cost of prevention of mother to child transmission (PMTCT)
- The cost staff remuneration
- The cost of hospitalization
- The cost of overheads

3.5.1 Cost calculations in the public ART clinics

The following formulae were used to calculate costs incurred in the public clinics and in private clinics, including the cost of medicines used for HIV/AIDS and laboratory tests but excluding cost of hospitalization, staff emoluments and overheads.

HIV/AIDS treatment cost **Ct = Cta + Ctb + Ctc + Ctd + Cte + Ctf + Ctg**

Where **C** represents cost in monetary terms; **t** -represents HIV/AIDS treatment; **a-** represents antiretroviral regimen; **b** - represents medicines for prophylaxis of opportunistic infections; **c -** represents medicines used for treatment of opportunistic infections; **d -** represents monitoring laboratory tests; **e -** represents medicines used for treatment of side effects of antiretroviral while **f -** represents supplements; and **g -** represents TB treatment. Financial resources here came from the same source which was the government of Lesotho.

3.5.2 The cost calculations in private ART clinics

- HIV/AIDS treatment cost **Ct = Cta + Ctb + Ctg**

Where **C-** represents cost in monetary terms, **t** - represents HIV/AIDS treatment, **a -** represents antiretroviral regimen, and **b -** represents drugs for prophylaxis of opportunistic infections and **g -** represents TB treatment.

And

- HIV/AIDS treatment cost **Ct = Ctc + Ctd + Cte + Ctf**

Where **C -** represents cost in monetary terms; **t -** represents HIV/AIDS treatment; **c** represents drugs used for treatment of opportunistic infections; **d** - represents monitoring laboratory tests; **e** - represents drugs used for treatment of side effects of antiretroviral; and **f** - represents supplements. Financial resources came from the patients, through cash or medical aid, and the government of Lesotho.

Table 3.1 represents antiretroviral regimens and their packaging, according to their daily doses. Antiretroviral drugs were commonly available in individual unit packs as seen on table 3.1. Most adult HIV/AIDS were given sealed unit packs monthly, based on the daily doses that they were given as a regimen. A unit pack was divided by the unit pack size to obtain the daily dose for 30 days. If the daily dose consisted of 2 tablets, then the patient would be given 60 tablets monthly in a sealed unit pack. If 1 tablet was a daily dose, 30 tablets were given for the month. A monthly supply (30 or 60 tablets) of each antiretroviral drug was multiplied by number months of treatment. This was done for all the three antiretroviral drugs and their monthly costs were added together to provide the total cost.

Table 3.1 Packaging of antiretroviral regimens

Antiretroviral regimen	Daily dose (number of tablets/drugs in an regimen)	Unit pack
1a (Stavudine30mg/lamivudine150mg/nevirapine 200mg) fixed dose combination	2	60
1a (Stavudine30mg/lamivudine150mg/nevirapine200mg) single tablets of each	2 + 2 +2	60 + 60 +60
1b (Stavudine30mg/lamivudine 150mg/efavirenz600mg) fixed dose combination of stavudine/lamivudine	2 + 1	60 + 30
1b (Stavudine30mg/lamivudine150mg/efavirenz 600mg) single tablets of each	2 + 2 +1	60 + 60 + 30
1c(Zidovudine300mg/lamivudine150mg/nevirapine200mg) fixed dose combination	2	60
1c(Zidovudine300mg/lamivudine150mg/nevirapine200mg) single tablets of each	2 + 2 + 2	60 + 60 +60
1d (Zidovudine300mg/lamivudine150mg/efavirenz600mg)	2 + 1	60 + 30
1d (Zidovudine 300mg/lamivudine 150mg/efavirenz 600mg) single tablets of each	2 + 2 +1	60 + 60 +30

The prices of antiretroviral drugs were obtained from the NDSO from the invoices that were sent to the Ministry of Health and Social Welfare for payment of ARVs in 2004, 2005, 2006, 2007 and 2008. Table 3.2 showed that how the cost calculations for antiretroviral medicines were carried out using prices from different years of acquisition. These were the prices of antiretroviral regimen used to calculate the total amount of money spent on each patient for the period of time that they had been on antiretroviral drugs.

The combination tablets consisted of the following drugs:
Triomune (stavudine/lamivudine/nevirapine), Combivir (zidovudine/lamivudine), Zidolum N (zidovudine/lamivudine/nevirapine), Lamivir (stavudine/lamivudine), LPV/r (lopinavir/ritonavir)

Table 3.2 Calculation of antiretroviral regimen cost according acquisition year.

Antiretroviral regimen and the year in which it was bought	Number of months	Unit price	Total
1a			
Triomune® 30/200/150 2008		52.08	
Triomune® 30/200/150 2007		52.84	
Triomune® 30/200/150 2006		106.78	
Triomune® 30/200/150 2005		175.89	
Triomune® 30/200/150 2004		106.98	
tenofovir/3TC 300/300MG 2007/8		132.60	
efavirenz 600mg 2008		99.19	
1b			
Lamivir® 30/150 2008		31.29	
efavirenz 600mg 2008		99.19	
Lamivir® 30/150 2007		36.5	
efavirenz 600mg 2007		93.29	
Lamivir®30/150 2006		46.93	
efavirenz 600mg 2006		213.94	
Lamivir® 30/150 2005		60.63	
efavirenz 600mg 2005		213.94	
Lamivir® 30/150 2004		60.63	
efavirenz 600mg 2004		240.35	
1c			
Zidolum N®150/300/200 2008		111.16	
Zidolum N®150/300/200 2007		104.24	
zidovudine 300mg 2006		85.02	
nevirapine 200mg 2006		42.46	
lamivudine 150mg 2006		37.51	
zidovudine 300mg 2005		97.76	
nevirapine 200mg 2005		57.18	
lamivudine 150mg 2005		42.18	
zidovudine 300mg 2004		97.76	
nevirapine 200mg 2004		43.13	
lamivudine 150mg 2004		89.88	
1d			
Combivir® 300/150 2008		67.93	
efavirenz 600mg 2008		93.29	
Combivir® 300/150 2007		70.2	
efavirenz 600mg 2007		99.19	
Combivir® 300/150 2006		138.99	
efavirenz 600mg 2006		213.94	
Combivir® 300/150 2005		171.64	
efavirenz 600mg 2005		213.94	
Combivir® 300/150 2004		131.06	
efavirenz 600mg 2004		240.35	
Second line drugs			
Abacavir		533.2	
LPV/r 2006		293.18	
LPV/r 2007		308.42	
Lamivir® 30/150 2006		46.93	
LPV/r 2008		329.83	

3.5.3 Regimen switching

For antiretroviral drugs regimen switches, monthly costs of each regimen was calculated and multiplied by the number of months that the antiretroviral regimen was given. When the patient switched to another regimen for some reason, the cost of the new antiretroviral regimen was still multiplied by the number of months that it was given. The total was computed by summing all the costs of all antiretroviral regimens given to that patient. Below is the example of one patient who had been on antiretroviral drugs since 2005. Regimens were frequently changed and the cost of all regimens that the patient was put on was calculated for all the years.

Table 3.3 Calculation of the cost of switched regimens

Name of regimen and year it was given	No. of months	Unit cost ZAR	Total
Lamivir® 30/150 2005		60.63	
efavirenz 600mg 2005		213.94	
Lamivir® 30/150 2006		46.93	
efavirenz 600mg 2006		213.94	
zidovudine 300mg 2006		85.02	
nevirapine 200mg 2006		42.46	
lamivudine 150mg 2006		37.51	
Zidolum N®150/300/200 2007		104.24	
Zidolum N®150/300/200 2008		111.16	

3.5.4 Opportunistic infection prophylaxis

Commonly known opportunistic infections were identified, based on the literature (WHO, 2006: 7). WHO states that prevention of *Pneumocystis carinii pneumonia* and toxoplasmosis by giving cotrimoxazole is part of the important care of HIV/AIDS patients. When a patient developed sensitivity to cotrimoxazole, dapsone is used (Ministry of Health and Social Welfare, 2007: 119-124).

Cotrimoxazole

A course of 30 tablets of cotrimoxazole double strength is given monthly as prophylaxis that costs (2007) R2.76 for 30 tablets. Therefore the cost of 30 tablets (monthly treatment) was multiply by the number of months of treatment to obtain total cost of prophylaxis for the patient.

Total cost (2007) of cotrimoxazole prophylaxis = price of 30 tablets x duration of treatment
= R2.76 x 4 month
= R11.04

Dapsone

A course of 30 tablets of dapsone is given monthly. The amount multiplied by the number of months of prophylaxis of opportunistic infections gives the total cost of prophylactic treatment. The price of 30 tablets is R8.70 (2007) and this is multiplied by the number of months that the patient is on prophylaxis. For example

Total cost (2007) of dapsone prophylaxis = price of 30 tablets x duration of treatment
= R8.70 x 4 month
= R34.80

3.5.5 Opportunistic infections and treatment

Commonly known opportunistic infections are identified, using the literature (Ministry of Health and Social Welfare, 2007: 119-124). Some of the opportunistic infections such as diarrhoea can also be side effects of antiretroviral drugs, if it is bothersome to the patient before initiation of ART, then it is taken as opportunistic infections. However, if it never occurred before but is seen as a new problem a month after therapy it is taken as a side effect of the new antiretroviral drug. In the spread sheet the number of opportunistic infections is specified as well as the number of drugs for treating opportunistic infections. Table 3.4 portrays commonly opportunistic infection, their presenting signs and symptoms and possible available medicines for treatment of each infection.

Table 3.4 Opportunistic infections and possible drug treatment.

Opportunistic infection	Symptoms	Alternative treatment
Oesophageal / oral candidiasis	white plaques in the mouth, difficulty in swallowing	miconazole, fluconazole, ketoconazole, nystatin
Fungal infections	round scaly legions, hair loss	griseofulvin, ketoconazole, Whitfields®, clotrimazole
Diarrhoea	watery frequent stools	oral rehydration solution, loperamide
Pneumocystis carinii pneumonia	cough, fever, tachypnoea, cyanosis	dapsone, cotrimoxazole
Herpes simplex and zoster	tingling, pain, blisters	acyclovir cream or tablets, gincyclovir
Toxoplasmosis	headache, seizures, focal neurological finding such as facial droop	cotrimoxazole, pyrimethamine

3.5.6 Calculations of opportunistic infections treatment cost.

The number of opportunistic infections that occur during the number of months of ART from the patient"s file, the number of drugs used for treatment, and the cost per tablet is determined. The quantity of each drug is calculated and multiplied by the cost of each tablet. If more than one kind of drug is used, the cost of all drugs used is calculated and added together to give the overall cost of opportunistic infection treatment for the respective patient.

Cost (2007) of acyclovir cream and acyclovir tablets for treatment of Herpes Zoster

Total cost of opp. infection treatment = cost of 30g acyclovir cream + cost of 35 acyclovir tablets

= R11.00 + R37.1

= R48.10

3.5.7 Tuberculosis

Tuberculosis occurs commonly in people with HIV but is not a disease for HIV infected people only. Therefore it is not included among opportunistic infections but separated as a disease commonly seen in HIV patients. TB is treated using standard treatment guidelines and followed DOTS method (Ministry of Health and Social Welfare, 2004: 21). Treatment usually consists of four, namely ethambutol, isoniazid, pyrazinamide and rifampicin in the first two months of treatment, followed by four months of two drugs, namely isoniazid and rifampicin. PDD of TB

medicines is usually 4 tablets of the fixed dose combination. Pyridoxine is always supplemented, as long as the patient is given isoniazid. Total duration of standard pulmonary TB treatment is six months, and it is longer for extra pulmonary TB which is exclusive for patients with HIV (Ministry of Health and Social Welfare, 2007: 75).

The cost (2007) of TB drug regimen

Total cost of TB drug regimen = Total cost of fixed dose kit (Stop TB®) that lasts for 6 months

= R 155.48

3.5.8 Antiretroviral drug side effects

Ill-effects appearing after treatment is initiated that persisted as long as the associated drug was given to the patient a month or a few months later. It should not have been a common complaint that a patient had before initiation of ART. The side effects should disappear on withdrawal of a causative drug. On the spread sheet the number of side effects occurs in the specified duration as well as the number of drugs for treating them is recorded (Ministry of Health and Social Welfare, 2007: 131-134). Table 3.5 illustrates common antiretroviral medicine side effects and the possible treatment, according to antiretroviral treatment guidelines as well as practice.

Table 3.5 Common treatable antiretroviral side effects with possible treatments

Side effect	Commonly Associated antiretroviral drug	Antiretroviral Treatment Guidelines	Alternative treatment
Peripheral neuropathy	stavudine	amitriptyline	carbamazepine, Neurobion®, pyridoxine, phenytoin, pyroxicam, Sundilac®,
Headache and other pains	zidovudine	paracetamol	ibuprofen, diclofenac, Panacod®, tramadol, Adcodol®, Codorol®,
Cough and nasal symptoms	lamivudine	cough syrup	Drixine®, Benylin®, Alcophylline®
Rashes and other skin conditions	nevirapine	calamine / hydrocortisone	betamethasone, prednisone
GI effects incl. nausea and vomiting	zidovudine	antacid	omeprazole, cimetidine, ranitidine, Buscopan ®, Maxolon®, Fybogel®, Medigel®, Gaviscon®, Stemetil®
Depression and other central nervous system effects	efavirenz	chlordiazepoxide	fluoxetine, Zopex®
Lypodystrophy	stavudine	-	-
Anaemia	zidovudine	ferrous salts and folic acid	
Pancreatitis	lamivudine	hyosine	

3.5.9 Calculations for drugs used to treat antiretroviral drug side effects

A number of side effects is specified, using the list of known antiretroviral drug side effects after verifying the possibility of the condition being an antiretroviral drug side effects. The number of drugs used to treat the side effects is also specified and from the data appendix F, the quantity of each drug is multiplied by the cost of a single tablet. Finally, the total cost of different drugs is computed.

The cost (2007) of treating painful feet

Total cost of ARV drug side effects treat. = cost 21 amitriptyline tablets + cost of 21diclofenac tablets

= R1.47 + R1.85

= R3.32

3.5.10 Dietary supplements

The following dietary supplements were given at different facilities - Ensure®, ferrous sulphate, Prenatal®, multivitamins, Centrum®, folic acid, calcium gluconate, ascorbic acid, vitamin B co, Instameal®, VMA®, Suthalandria®, thiamine and pyridoxine.

Dietary supplements are calculated by the units given and multiplied by the cost of each. If more that one dietary supplement is given then the two are added together to give the total amount spent on the patient.

Cost (2007) of dietary supplements

Total cost of dietary suppl. = cost of 5 cans of Ensure® + 280 tablets of multivitamin

= R200.95 + R5.60

= R206.55

3.5.11 Monitoring laboratory tests

The following monitoring laboratory tests were carried out for different regimens at different clinics CD 4 count, full blood count (FBC), liver function tests (LFT), X-rays, viral load, electrolytes and urea, creatinine, haemoglobin (Hb), alanine aminotransferase (alt)/ Aspartate aminotrasferase (ast) (Ministry of Health and Social Welfare, 2004: 28).

The cost is calculated by counting the number of laboratory tests done throughout the study period. The number of times each test is carried out is multiplied by its cost. If more than one test is carried out, the total cost of the tests is added together to calculate the final cost.

The cost (2007) of monitoring laboratory tests

Total cost of Laboratory tests = cost of 5 CD4 cell count tests + 4 LFT tests

= R700.00 + R160

= R860.00

3.6 Adherence classification

The standard way of measuring adherence in the ART clinics is pill count. However, the determination of how many pills is not taken during the treatment period. If one tablet is missed in 30 or 28 days, adherence is taken to be above 95 percent. When 2 to 4 tablets are missed, adherence is between 85-94 percent and if 5 or more tablets are missed adherence is below 84 percent (Ministry of Health and Social Welfare, 2004: 11).

3.7 Treatment outcome

Treatment outcome of HIV/AIDS could be quality of life, increased body weight, reduced incidence of opportunistic infections and increase CD4 cell count, reduced viral load. For the purpose of this study CD4 cell count and body weight increase would be considered.

3.7.1 CD4 cell count

CD4 Cell Count measures the number of CD4 T helper cells per cubic milliliter of blood and is a measure of the degree of immuno-compromise and stage of HIV/AIDS disease progression. The CD4 count is an important test for deciding whether ARV therapy is required and for monitoring the recovery of the immune system under treatment.

3.7.2 Body weight

Why is the body weight a problem for HIV/AIDS patients? There are various reasons why people may have a body weight problem in HIV/AIDS. These are

- High energy output because of the HIV infection and opportunistic infections.
- Incidence of opportunistic infection that may affect food intake such as oesophageal or oral candidiasis.
- The HIV/AIDS patient is too sick to work even if they had a job.
- The HIV/AIDS patient is too sick to prepare food.

- The HIV/AIDS patient is unemployed. Therefore, there is no money to buy food (WHO 2008: 35).

3.7.3 Incidence of opportunistic infections as an outcome of antiretroviral treatment

Effects of opportunistic infections on patients with reduced immunity could result in the patient‟s frequent visits to the clinic. Patients might miss work days or other important life activities because they become sick with opportunistic infections (Casale, 2006: 7). Some opportunistic infections may cause a lot of pain such herpes zoster, while others cause the patient to cough, or have unpleasant lesions on their body. Incidence of opportunistic infections may result in death of the patient. Therefore prevention or reduction in the incidences of opportunistic infections by increasing the body‟s defense through antiretroviral therapy becomes an important outcome of antiretroviral treatment as they reduce mortality and morbidity in the HIV/AIDS patient (WHO, 2006: 8).

3.7.4 Methods of cost analysis

Methods of cost analysis are evaluated in order to choose a suitable method that may be used to analyze the cost of HIV/AIDS treatment.

3.7.5 Cost of treating HIV/AIDS patients

The cost is the total value of all resources used in order to produce a good or a resource. In the case of this study cost would mean the total cost of drugs, lab tests and dietary supplements used in the treatment of HIV/AIDS. Medicines include antiretroviral drugs as well as drugs used in the treatment of side effects of antiretroviral drugs and drugs used for prophylaxis and treatment of opportunistic infections. Laboratory tests include monitoring tests that are required to assess the treatment success or failure, incidence of toxicities and side effects caused by antiretroviral drugs. Dietary supplements include formulations that are used with the intension to alleviate wasting caused by HIV/AIDS.

Cost-minimization method is used in this study because the outcomes of HIV/AIDS treatment with antiretroviral drugs are the same. They are the CD4 count measurement, weight measurement and incidence of opportunistic infections. However, Dickson indicates that effectiveness and toxicities of the proposed drug should be no worse than the other. This is why the antiretroviral regimens triple nature makes the analysis somewhat difficult. Different

individual antiretroviral drugs in a combination cause different unwanted effects and their toxicities may be measured differently. Therefore it is not a suitable method of analysis (Dickson *et al*., 2003: 22).

Cost-benefit analysis method poses a challenge of costing weight and CD4 cell count measurements which is not practical**. Cost –utility** analysis is difficult to measure as it included measurement of the quality of life (Dickson *et al*., 2003: 22).

The preferred method of analysis is the **Cost- effectiveness** analysis for the following reasons:

Cost is measured as direct medical costs, including the cost of antiretroviral drugs, laboratory tests and opportunistic infections treatment cost as well as prophylaxis, and dietary supplements. Indirect medical costs refer to treatment of side effects caused by the use of antiretroviral drugs. Outcome means average CD4 cell count (cells/mm^3) increase and the average weight (kg) increase.

The following outcomes were also considered:

Incidence of opportunistic infections avoided at CD4 cell count above 200cells/mm^3 that are intermediate measurements for treatment success. CD4 cell count is indirectly influenced by antiretroviral treatment, and measures the recovery of the immune system. Higher CD4 cell count results in lowered incidence of opportunistic infections because they commonly occur in lower CD4 cell counts. For example, *Pneumocystis carinii pneumonia* (PCP) occurs below CD4 cell count of 200cell/mm^3 (WHO, 2006: 9). Body weight increase is a direct measure of increased food intake because patients have no difficulty in swallowing and the food eaten can be absorbed easily. Lowered incidence of opportunistic infections requires high energy expenditure as well as lowered viral load that is directly affected by antiretroviral drugs. Lower incidence of or no opportunistic infections result in patients living **sickness-free days for prolonged periods.** For example no PCP incidence leads to no coughing, no pain, no off-sick days, no chest x-rays, no prophylaxis as well as no drug treatment. **Viral load reduction** is not used as an outcome because it is not routinely tested in Lesotho. However only mean CD4 cell increase and mean weight increase are used. In the subsequent research sick free days and reduced incidence of opportunistic infections may be used as an outcome of antiretroviral treatment.

3.8 Statistical analysis

Excel spreadsheet (2007) is used to compile data and it was sent to North West University where SAS version 8 is used for data analysis.

3.9 Limitations of the study

The following limitations were observed during the study:

- Laboratory tests were not recorded properly in the paper based medical record and that led to insufficient information about which laboratory tests were carried out routinely according to the antiretroviral guidelines.
- Hospitalization of the patients was not included in the study. This information could have been useful in order to determine which patients were hospitalized because of opportunistic infections and those who were hospitalized as a result of antiretroviral toxicities. The information could have an impact on the cost of treating the HIV/AIDS patients.
- Paper based medical records with missing data.
- Variable sample size at different clinics.
- Retrospective study shows what has happened to the HIV/AIDS patients from the diagnosis to the point of data collection. No follow up or any interview of the patients themselves was done.
- Adherence was recorded by the pharmacy staff and not the data collectors. The latter did not have any contact with the HIV/AIDS patients themselves, therefore information could be somehow misleading.
- Assumption was made when deciding whether the drug was used for treatment of side effects or opportunistic infection or even an unrelated condition that the HIV/AIDS patient presented with.
- Indirect costs such as transport and missed days at work were not considered

3.10 Chapter summary

In this methodology chapter, various topics were dealt with. This is an observation retrospective study with a sample size of 1 424 HIV/AIDS patients carried out in eight ART clinics in the Maseru district, of which three were private clinics and five were public clinics. Sample selection with exclusion and inclusion was decided on (3.2.4 and 3.2.5). Monitoring and measuring parameters were also decided on (3.2.7 and 3.2.8). Ethical permission was received from the

Ethical committee of the Ministry of Health and Social Welfare and North West University. Confidentiality forms were signed by data abstractors who were also trained. A Pilot study was carried out for one month in one of the ART clinics, and data collection tool was designed corrected and finalised.

Data collection was carried out in all eight ART sites for three months. Daily and monthly amounts of medicines given were calculated and costs were calculated and assigned to each medicine and total costs per patient were also calculated according to the disease being treated or prevented, or supplemented. Monitoring laboratory tests were also identified and cost assigned per patient. Data was cleaned and was put on Excel spread sheet (2007) and sent to North West University for analysis using SAS version 8. Methods of analysis were decided upon and cost/prevalence index, *d*-values as well as mean and standard deviation were used. An appropriate pharmacoeconomic method was decided upon to calculate the cost-effectiveness analysis. Chapter 4 discusses the major findings of the study.

CHAPTER 4

Findings of the study

In Chapter 4 results are displayed in tables, graphs and figures, and in each stage discussion is made on key findings from those tables, graphs and figures. The chapter is divided into several sections: patient demographics, drug treatment, monitoring laboratory tests, treatment outcomes and costs analysis. A comparison is made between different ART clinics on the subtopics.

4.1 Study population demographics

Demographic information of the study population would be described to form a basis for the discussion of the population under the study.

4.1.1 Study population in different clinics in Maseru

From Table 4.1.1 it is observed that Senkatana (334, 23.47 percent), Healthy Life Style (296, 20.80 percent) and Bophelong Adult (237, 16.65 percent) clinics had the highest number of patients on antiretroviral drugs included in the study population. The sample size of some clinics was smaller due to the fact that most patients did not meet the criterion which was for patients to be on antiretroviral drugs for at least 12 months. Most patients were on antiretroviral treatment for less than 12 months, because some ART clinics were first opened in mid 2005 or mid 2006.

Table 4.1.1 described the study population in the clinics over the duration of the study, those who met the selection criteria and those who did not. The percentage of patients in each ART clinic was calculated from the total number of patient in the specific clinic for both clinic population and study population using total number of patients in all the clinics.

Table 4.1.1 HIV/AIDS patients' population distribution from 2004 to August 31, 2008.

Name of clinic	Total no. of patients on antiretroviral drugs (n=7 286)	Percent (%)	Study population (n=1 424)	Percent (%)
Bophelong Adult	1839	25.24	238	16.65
Healthy Life style	904	12.41	296	20.80
Khanya	500	6.86	146	10.26
Mabote	168	2.3	89	6.25
Medicare	220	3.02	134	9.42
Qoaling	289	3.97	92	6.47
Senkatana	2816	38.65	334	23.47
St. Joseph"s	550	7.55	95	6.68
Total	7 286	100.00	1 424	100.00

4.1.2 HIV/AIDS patients' population distribution by ART clinic type

From figure 4.1.1 it is deduced that there were more HIV/AIDS patients from public clinics (752, 53 percent) than from private clinics (576, 40 percent). CHAL had (95, 7 percent) in the study population.

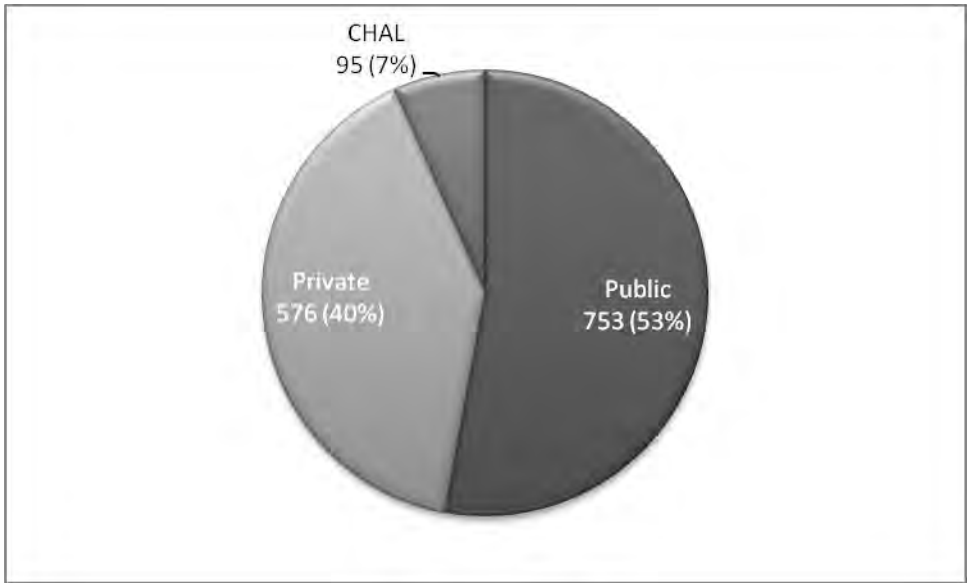


Figure 4.1.1 Study population according to the type of clinic. (n=1424)

4.1.3 Age distribution of the study

From figure 4.1.2 it is noted that the study population being treated for HIV /AIDS concentrated the age group beween 26 years to 45 years of age (75.11 percent). This was also observed in the national statistics of Lesotho where HIV prevalence is 40 percent around this age group (25-49 years) (UNGASS, 2007: 15).

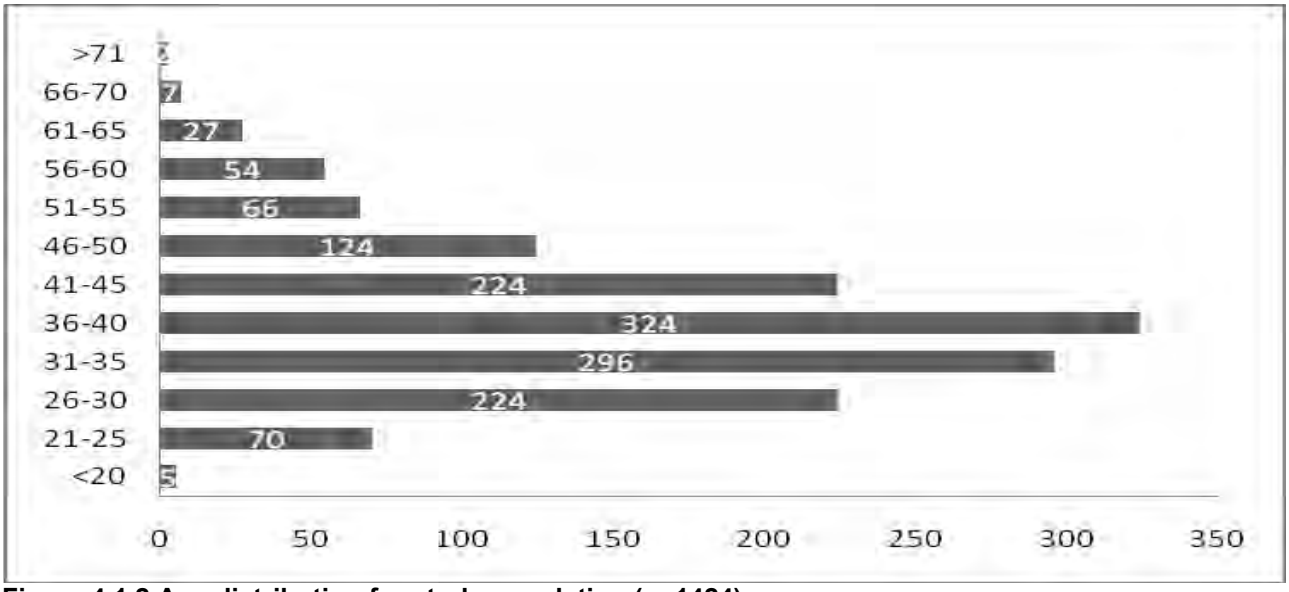


Figure 4.1.2 Age distribution for study population (n=1424)

4.1.4 Gender distribution of patients in all the clinics in Maseru

Figure 4.1.3 indicates that there are more females (890, 63 percent) than males (534, 37 percent). This is commensurate with HIV/AIDS statistics of Lesotho as there are more females (56 percent) than males (44 percent) infected with HIV. Therefore, the figures in the study show similar trend and may be accepted as a true picture of HIV/AIDS seen in Lesotho (UNGASS, 2007: 15).

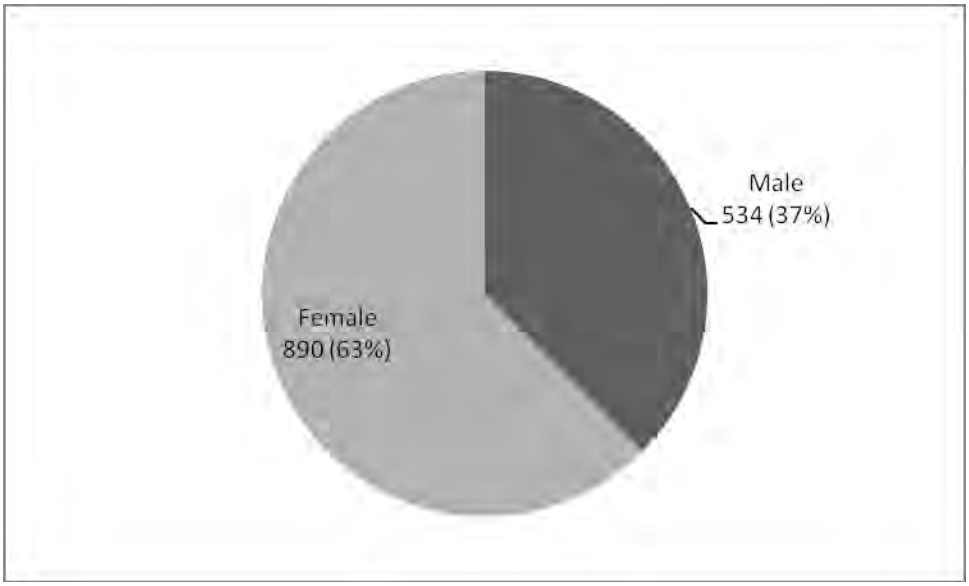


Figure 4.1.3 Gender distribution among the study population (n=1424)

4.1.5 Employment status of the HIV/AIDS patients in all the ART clinics in Maseru

Figure 4.1.4 shows that among this population, there are as many patients working (49 percent) as those that are not working (50 percent) and this is comparable to the employment rate of Lesotho which was 45 percent in 2002 (Central Intelligence Agency (CIA) Fact Sheet, 2009).

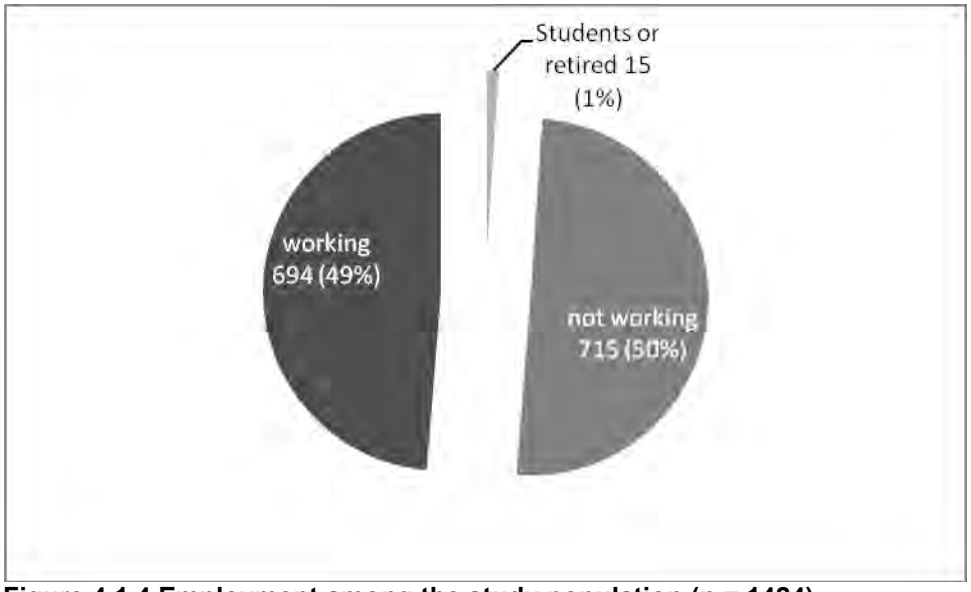


Figure 4.1.4 Employment among the study population (n = 1424)

4.1.6 Employment status of male and female HIV/AIDS patients

From the figure 4.1.5 it is perceived that there are more females who are employed and who are unemployed than males.

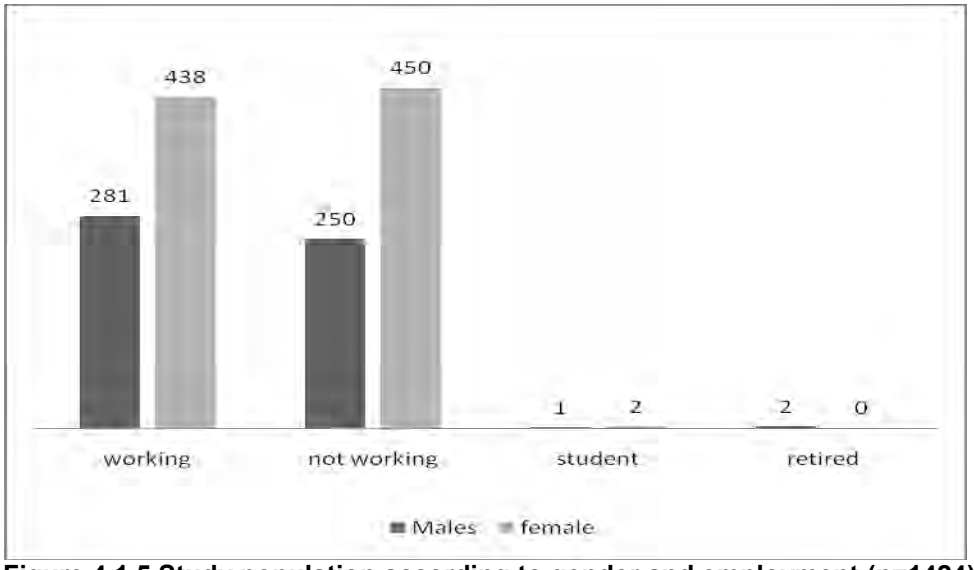


Figure 4.1.5 Study population according to gender and employment (n=1424)

It is observed that most of the patients in the study are around the age group of 26-45 years, the HIV/AIDS statistics of Lesotho that showes HIV prevalence to be 40 percent among the age range or 25-49 years while the national prevalence was 23.6 percent (UNGASS, 2007: 15). This is further comparable to South African HIV/AIDS prevalence which is 18 percent around the same age group while the national prevalence was 11 percent (Dorrington *et al.* 2004:14).

There are more females (62 percent) than males (38 percent) on antiretroviral treatment which also is consistent with the Lesotho statistics that shows the percentage of females to be 56 percent, and male to be 44 percent (UNGASS, 2007: 15). According to Dorington (2004: 15) HIV/AIDS prevalence was highest amongst females between the age of 25-29 years which was 28.1 percent in South Africa. The unemployment rates of the study population are relatively similar to the national unemployment rates (2002) which are 50 percent and 45 percent respectively (CIA Fact Sheet, 2009). This is comensurate with the efforts of keeping people living with HIV/AIDS employed mainly by Apparel Lesotho Alliance to Fight AIDS (ALAFA) which employs about 45,000 factory workers. This indicates poverty reduction alleviation strategies carried out by different government bodies for people living with HIV/AIDS (see Lesotho under documents). It is determined that there are more than 80 percent of the study population that can be employed as they are within the economically viable group. Lesotho still needs to employ more people, especially HIV positive patients.

4.2 Disease incidence and drug treatment

In this section antiretroviral treatment is discussed as an input as well as treatment and prophylaxis of opportunistic infection, and antiretroviral side effects according to figure 3.1**.**

4.2.1 Year in which antiretroviral treatment was started

From figure 4.2.1 it is noted that most patients are initiated antiretroviral therapy in 2006 with 547 patients and followed by 2007 with 442 patients.

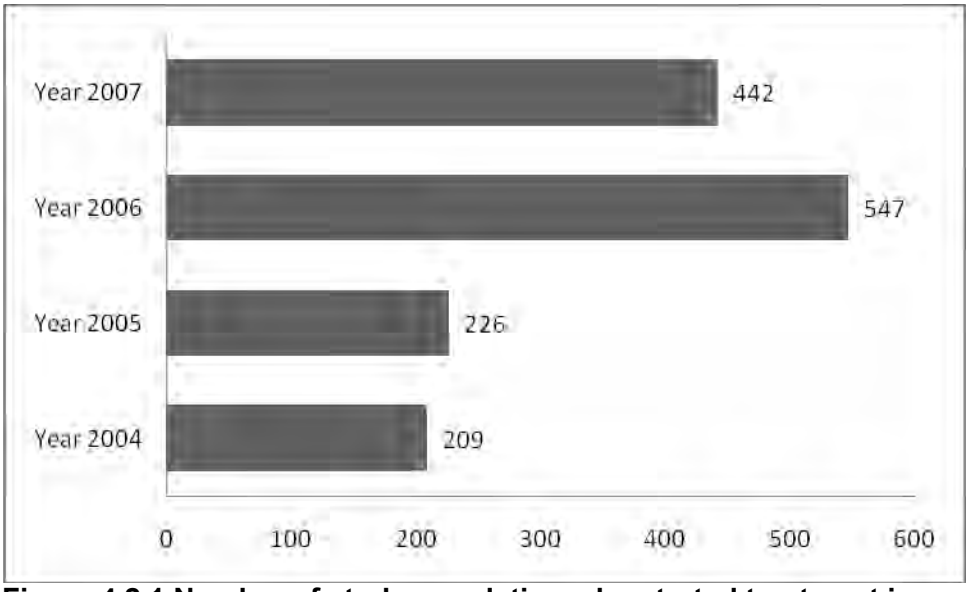


Figure 4.2.1 Number of study population who started treatment in a specified year. (n=1424)

4.2.2 Antiretroviral treatment duration

The majority of the study population are on antiretroviral treatment for 12 to 24 months, while fewer patients are on treatment between 49 to 60 months.

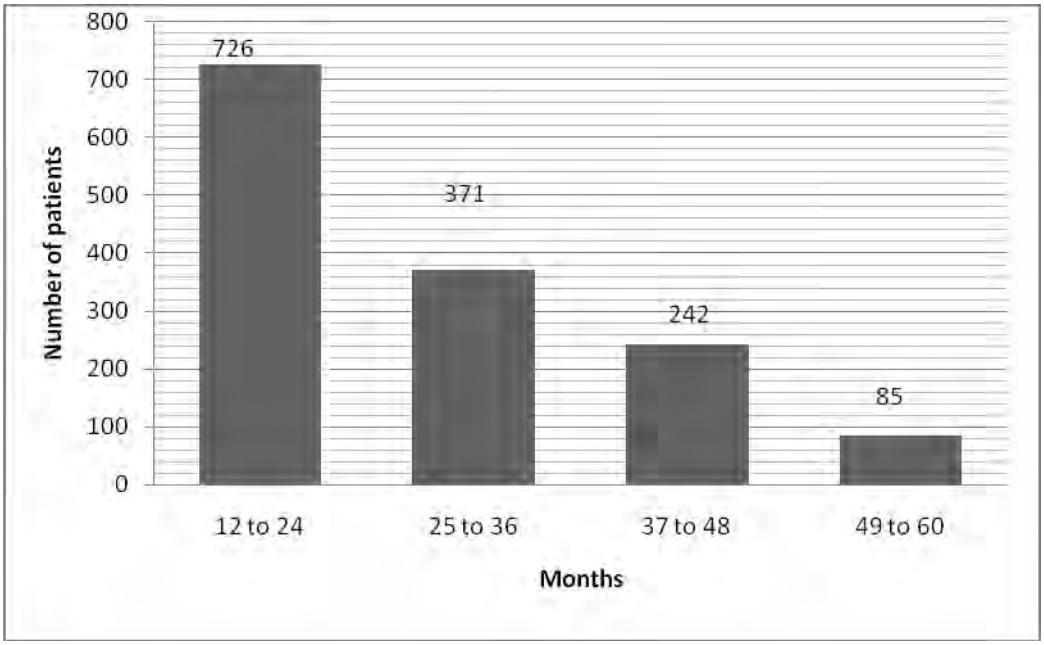


Figure 4.2.2 Antiretroviral treatment duration in months. (n=1424)

More patients (1097) were on antiretroviral treatment between 12-36 months, mainly because more ART clinics were opened to enable easy access to treatment.

4.2.3 Antiretroviral treatment regimen

From Table 4.2.1 it is observed that most patients are on regimen 1a (37.03 percent) and 1b (30.71 percent). Switching of regimens (1s) (18.14 percent) from one to the other is also relatively less common.

Table 4.1.2 Types of antiretroviral regimens used in treatments (n=1424)

Antiretroviral regimen	freguency	percentage
1a (Stavudine/lamivudine/nevirapine)	527	37.03
1b (Stavudine/lamivudine/efavirenz)	437	30.71
1c (Zidovudine/lamivudine/nevirapine)	109	7.66
1d (Zidovudine/lamivudine/efavirenz)	89	6.25
1s (Switched regimens)	262	18.14

Antiretroviral treatment was started in 2004 as the initiative of the Ministry of Health and Social Welfare at the same time National Antiretroviral Treatment Guidelines of 2004 were developed and published in order to guide prescribing of antiretroviral drugs in all the clinics that were intended to provide HIV care and treatment in the clinics prescribing of antiretroviral regimens followed the Ministry of Health and Social Welfare (2004: 16). Fifteen percent of the study population started antiretroviral treatment in 2004 and some patients remained in their original therapy since then. Retension of original therapy is preserved mostly among the in patient who are on regimen 1a, 1b, 1c and 1d. They are on only one kind of regimen.This is the case with 81.61 percent of the study population from Maseru ART clinics. Rational prescribing and retention of patients on first line regimen for one year are considered to be the early warning of indicators used by WHO in order to determine emergence of resistance to antiretroviral drugs (Hedt et *al.*, 2008: 72).

4.2.4 Switching from one antiretroviral drug to the other

The percentage of patients who switch therapy is 18.14 percent. This is a relatively low number compared to those who remained on the same therapy (81.86 percent) throughout the period from 2004 to 2008. The reasons for changing regimen varied from serious drug toxicities such as Stevens John Syndrome which warranted an immediate switch of nevirapine to a boosted protease inhibitor. This was done according to National Antiretroviral Treatment Guidelines (Ministry of Health and Social Welfare, 2004: 85). Another reason is the lack of response to treatment where CD4 cell count remains low, and the viral load remains at detectable levels. In

this case a sensitivity test is done and therapy changed, after ensuring that the problem is not adherence to therapy. Switching of therapy is done with antiretroviral drugs that are within the first line or second line drugs.

The common switching is within the first line antiretroviral drugs (250 patients out of 258). Therefore it may be concluded that the clinics reserved second line antiretroviral drugs by all means. In Lesotho only first and second line antiretroviral drugs are currently available from the national antiretroviral services. If a patient has a virus that develops resistance to those drugs, there will be no third line drugs available. That is why it is important for the ART clinics to make sure that they exhuast all the options in the first line before moving on to the second line.

4.2.5 Prophylaxis, incidence and treatment of opportunistic infections

This section deals with opportunistic infections that are observed, and it includes prevention, incidence, and treatment of opportunistic infections.

4.2.5.1 Prophylaxis of opportunistic infections

From figure 4.2.3 it is noted that most patients (n=882) are on opportunistic infection prophylaxis for 1 to 20 months. There is also a relative large number of patients (n=484) who do not receive prophylactic drugs for opportunistic infection.

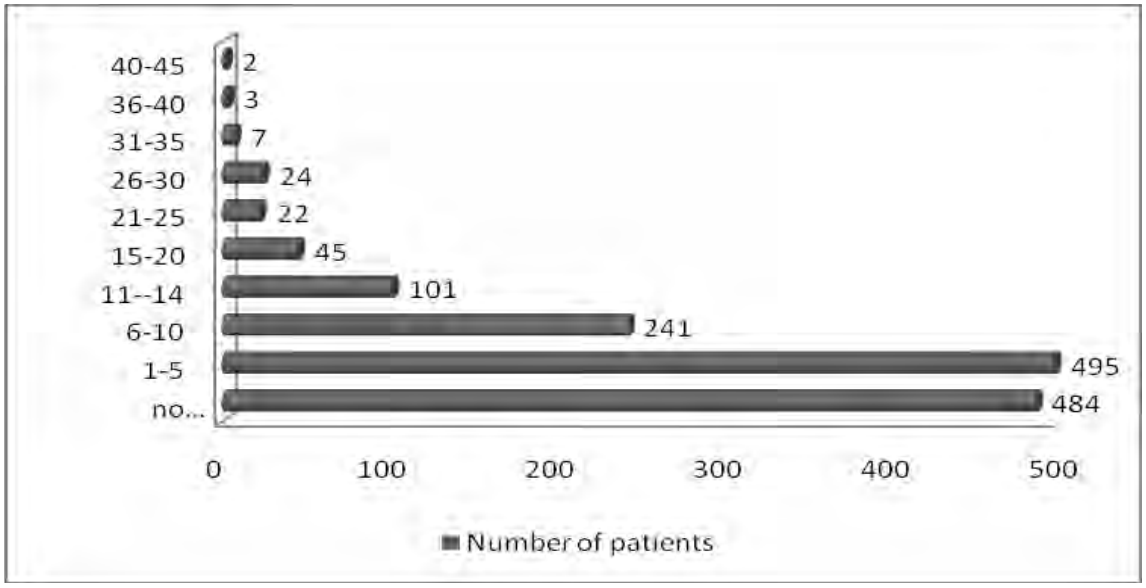


Figure 4.2.3 Duration of opportunistic infections in months (n=1424)

4.2.5.2 Incidence of opportunistic infections among the study population

The majority(n= 1052, 73.98 percent) of the HIV/AIDS patients do not experience any incidence of opportuinistic infections. About (n= 294, 20.68 percent) patients have one type of opportunistic infection while (n=67, 4.71 percent) have two opportunistic infections.

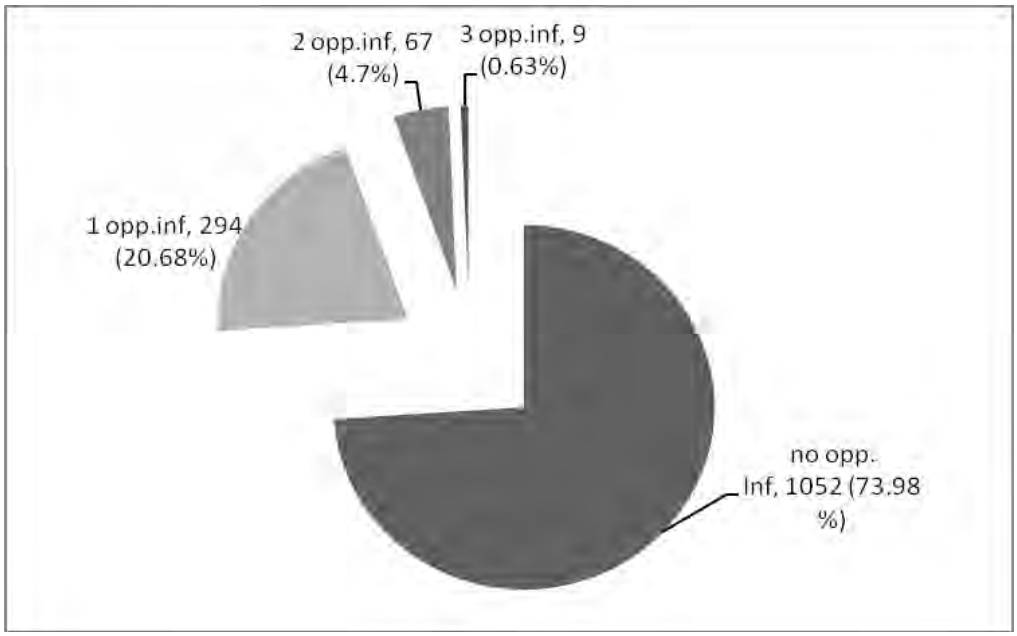


Figure 4.2.4 Percentage of patients who experienced opportunistic infections (n=1424) (Key – opp.inf. is opportunistic infections)

4.2.5.3 Opportunistic infections treatment

Due to the low incidence of opportunistic infections, the majority of patients do not receive treatment of opportunistic infections. Patients who have opportunistic infections are treated accordingly. Overall, drug treatment of opportunistic infection is presented in figure 4.2.5 where some HIV/AIDS patients seem to have received a certain number of drugs to treat different kinds of opportunistic infections over a period of time.

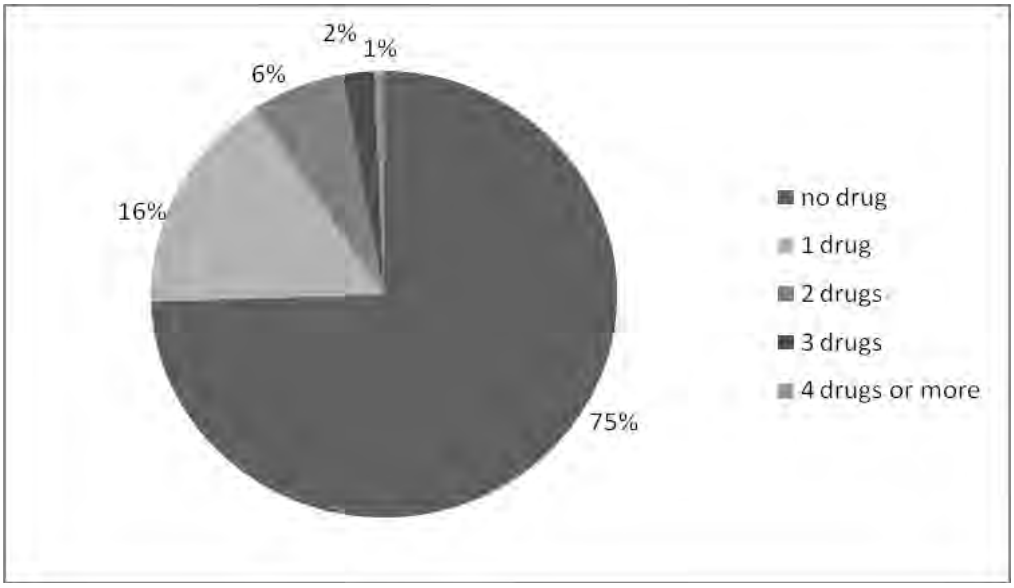


Figure 4.2.5 Percentage of patients who received medication or not for treating opportunistic infections according to the number of medicines (n=1424)

Opportunistic infections occur commonly in patients with HIV/AIDS due to lowered immune responses. However, the study finds that 20.68 percent of the HIV/AIDS patients have one type of opportunistic infection while 4.7 percent experience two types, it is observed that the majority of the HIV/AIDS patients do not experience any opportunistic infections (73.98 percent). The first possible reason may be the fact that HIV/AIDS patients begin ART treatment that leads to CD4 cell count increasing hence immune response against the infecting organism. The second reason is that HIV/AIDS patients are given cotrimoxazole or dapsone prophylaxis which prevents *pneumocystis cariini pneumonia*, and *toxoplasmosis gondii.* These are preventable common opportunistic infections (Ministry of Health and Social Welfare, 2007: 119). The third reason may be attributed to the efforts carried out by the government of Lesotho, especially the "know your status" (KYS) campaign which was launched in 2004 and carried on up to the end of 2007, during the campaign people were encouraged to test for HIV and go for appropriate referral for services when needed. These steps lead to more people going to the ART clinics early and getting treatment before the occurrence of major opportunistic infections. The fourth possible reason was the opening of more ART clinics, thus increasing access to treatment with the result of a lower incidence of opportunistic infections.

Cotrimoxazole prophylaxis was provided for more than 60 percent of the HIV/AIDS patients even though duration of prophylaxis varied from one month to 45 months in some clinics. However, the majority of the patients were given cotrimoxazole prophylaxis between one and 15

months. The National Antiretroviral Treatment Guidelines 2004 did not specify for how long the patients should be kept on opportunistic infections for prophylaxis of cotrimoxazole or at what level of CD4 cell count they should stop. In the 2007 guidelines prophylaxis information against various opportunistic infections was laid out although it did not specify when to start or to stop. (Ministry of Health and Social Welfare, 2007: 113) However, WHO specified when to start cotrimoxazole prophylaxis for opportunistic infections and when to end. According to WHO guidelines, P*neumocystis carinii pneumonia* prophylaxis should be discontinued once a patient has had a stabilised CD4 cell count above 200 cells/mm^3 for a period of 3 months (WHO, 2007: 9).

According to the Ministry of Health and Social Welfare (2004: 12), cotrimoxazole is given as a pre-treatment drug to assist in observing patients‟ habits to adhering to medicines. Pill count is done accordingly and if the patient is adhered to cotrimoxazole, that determined the drug taking behavoiur of the patient, according to antiretroviral treatment initiated in the form of regimen. Guidelines specify however, that this was not supposed to be used to exclude patients from being initiated on ART, but to show which patients needed more help on drug taking behaviour. The most commonly occurring opportunistic infections were oral and oesophageal candidiasis, herpes zoster, and to a lesser extend topical fungal infections (Amirali *et al.,* 2004: 228). The drug treatment given to the HIV/AIDS patients who presented with opportunistic infection was appropriate, even though it was not specified in the 2004 National Antiretrtoviral Treatment Guidelines. The ART clinics still managed opportunistic infections rationally. However treatment was specified later when review was made in 2007 (See Chapter 3 table 3.2).

4.2.6 Tuberculosis (TB) incidence among the study population

Patients who were on HAART as well as received treatment for TB infection constituted (n=144, 10.12 percent). The national incidence of TB infection among patients with HIV was 40 percent in 2004 when HAART was not as commonly used as it later was in 2007. However, this was not included in the Sentinel Survey of 2007.

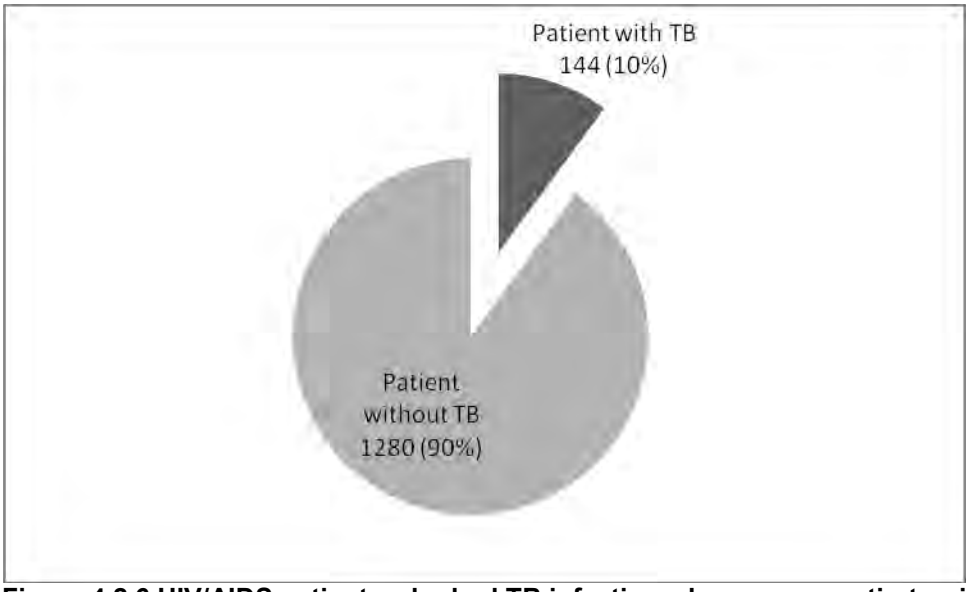


Figure 4.2.6 HIV/AIDS patients who had TB infection who were on antiretroviral drugs. (n=1424)

The statistics taken appears much higher than the actual cases of HIV patients with TB as recorded in recent literature from Lesotho. Among the patients with TB, HIV is found to be very common for up to 90 percent of the patients. According to the Global fund factsheet there are about 270, 000 people with HIV infection, which translates to 14 357 in every 100 000 patients with HIV and about 490 in every 100 000 patients with tuberculosis, which is the highest in the world (Global Fund Fact Sheet, 2010)

TB treatment was provided according to TB protocol, following WHO guidelines. DOTS is followed to ensure that all TB patients complete the treatment for TB. This was shown to reduce inicdence and mortality of TB (Salomon *et al.,* 2006: 1307). Management of TB and HIV/AIDS is not done through similar programmes. It is run differently. While TB is run by TB programme and HIV/AIDS is run by the HIV/AIDS directorate. This somehow affects both the drug managemnt of HIV/AIDS and of TB. Patients received both treatments in one ART clinic. However, the patient has to go to the clinic everday for DOTS, while they take their antiretroviral drugs at home in the morning and in the evening. This may have been intergrated to ease the life of the patient with HIV.

4.2.7 Dietary supplements

Although most patients receive dietary supplements some patients do not receive. Some of them receive one item while others receive more items.

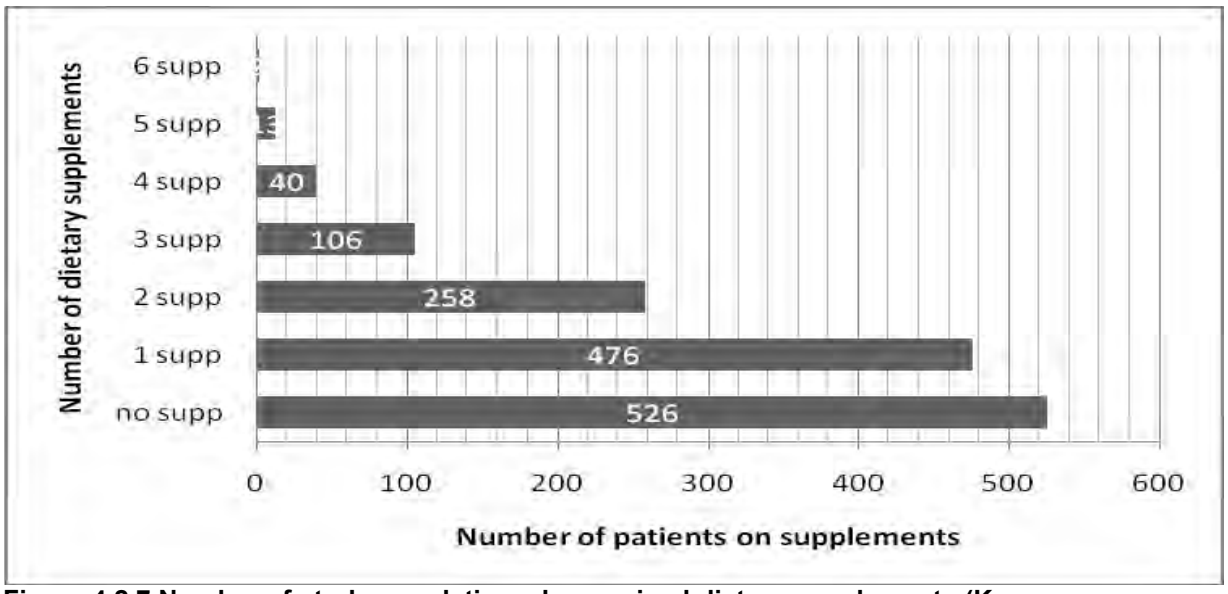


Figure 4.2.7 Number of study population who received dietary supplements (Key – supp: represents dietary supplement) (n = 1424)

Patients with HIV/AIDS suffer from nutritional deficiencies due to the high energy output caused by the HIV infection, other opportunistic infections as well as resticted food intake (Tang et al., 2002: 233). Therefore the majority of HIV/AIDS patients with lower body weights are given dietary supplements in order to augment dietary deficiencies that may not be found from the normal food intake.

4.2.8 Incidence of antiretroviral side effects in patients on treatment

The number of patients who did not show any side effects to antiretroviral treatment was (n=387, 25.23 percent) while a significant percentage of patients (n=1037, 72.94 percent) suffered from one to five side effects that may have been caused by different antiretroviral drugs. The side effects that were recorded were similar to the ones stipulated in the National Antiretroviral Treatment Guidelines 2007 (Ministry of Health and Social Welfare, 2007: 134)

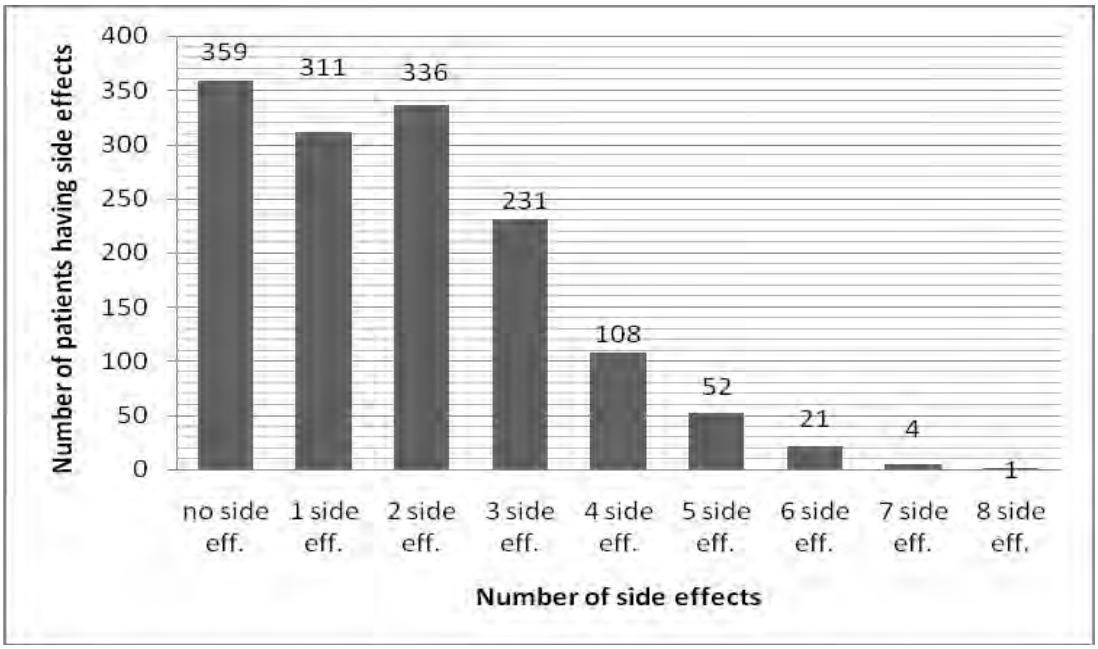


Figure 4.2.8 Incidence of side effect caused by HAART (Key: side eff. - represents side effects) (n=1424)

4.2.9 Number drugs used to treat antiretroviral side effects.

It is observed that (n=387) patients were not treated for side effects. The rest of the patients were treated with a certain number of drugs, with the majority being treated with one to five drugs.

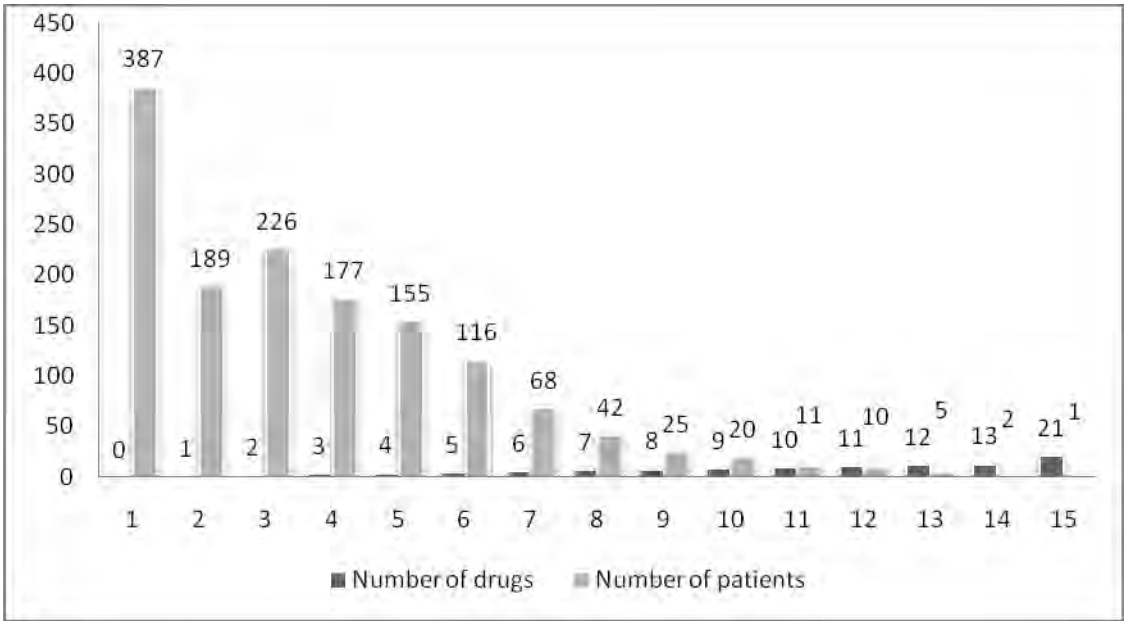


Figure 4.2.9 Number of medicines provide for the treatment of antiretroviral side effects

The side effects caused by individual antiretroviral drugs were a common occurrence in patients who were on HAART (Montessori *et al.,* 2004: 229). Some side effects were transient and lasted for a short time while others were prolonged. This means that as long as the patient is on the drugs the side effect persist. Upon the removal of the offending drug, the side effect disappear (Montessori *et al.,* 2004: 230). Treatment of side effects depends on the ART clinic. The type of drugs used in government clinics were the generic while branded drugs were used more by private clinics. This may affect the cost of drugs that the patients receive. The number of drugs seen on Table 4.2.9 represents the number of drugs that are used to treat different side effects of the antiretroviral treatment over a period of time not imply that one patient is treated for one type of side effects with 21 drugs. Commonly occurring antiretroviral side effects dependent on the antiretroviral regimen that the patient received and decisions to treat side effects depended on the severity of the side effect, as well as whether it was life-limiting or not.

4.3 Monitoring laboratory tests

Certain laboratory tests have been specified to be carried out at certain times because they could detect any toxicities caused by the antiretrovrial drugs or be able to monitor the disease progression or treatment success.

4.3.1 Number of monitoring laboratory tests carried out on the study population

Only one monitoring laboratory test was carried out on (n=696, 48.91 percent) patients. This was for the CD4 cell count. More than one monitoring laboratory tests were carried out for other patients.

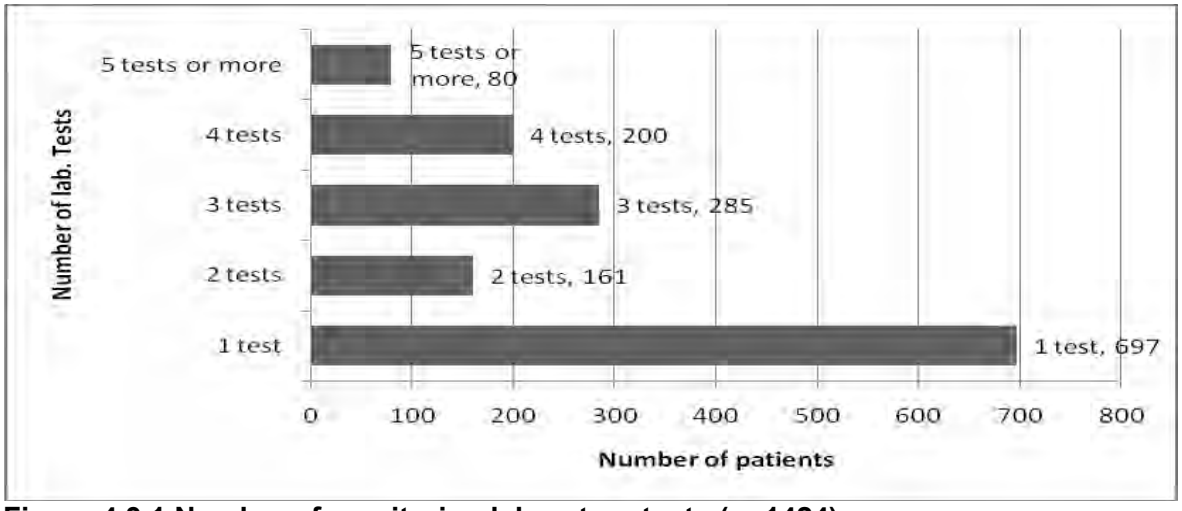


Figure 4.3.1 Number of monitoring laboratory tests (n=1424)

It is noted that in most of the patients only one laboratory test is carried out. This is the CD4 count. Other laboratory tests, such as the liver function tests, urea and electorlytes, as well as full blood count were not carried out routinely. According to the Ministry of Health and Social Welfare (2007: 60), CD4 cell count, liver function tests, and the full blood counts are mandantory in order to determine disease progression, treatment success, or toxicities. Therefore, one monitoring laboratory test is not enough. There is a recommended schedule for monitoring laboratory tests (see Chapter 2, table 2.3)

There may be reasons why laboratory tests appear not to have been carried out. They may have been done but record was not properly kept in the patients‟ medical records, since the study was retrospective any information that was missing from the files was taken as not done. Medical records were mainly paper-based, as a result some of the information may have been missed. The medical record files are used each time the patient visits the clinic. In ART clinics, routine blood draws are a normal practice. They are offered for free and patients continue to go for consultation or to collect medicines. There is no reason why laboratory tests are not carried out. Therefore, the low number of laboratory tests is attributed to a poor recording system.

4.3.2 Viral load tests

The viral load tests was carried out only for 67 patients in the study population.

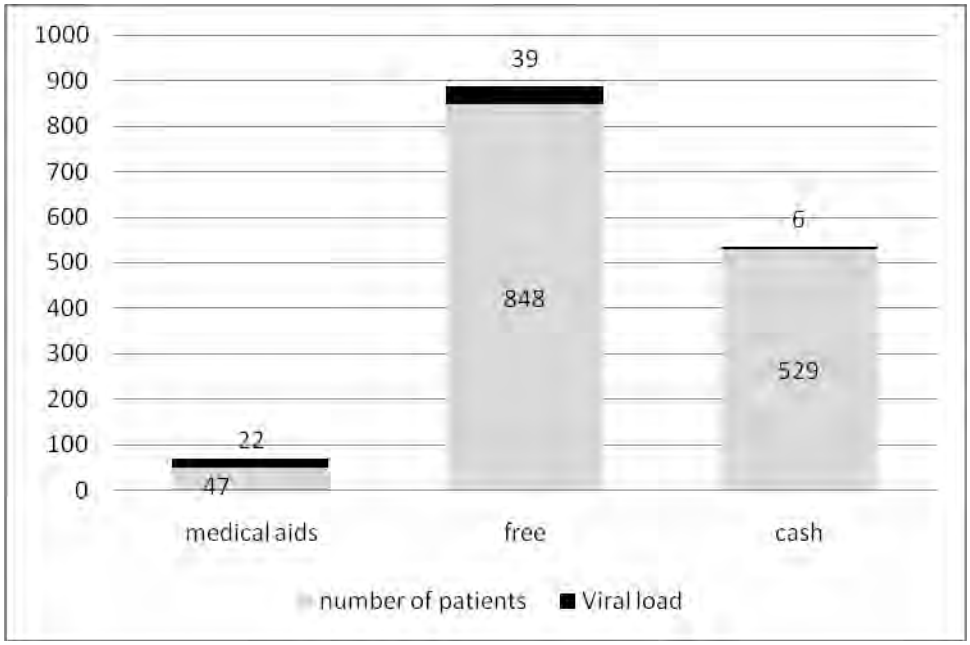


Figure 4.3.2 Viral load carried out on study population with respect to method of payment (n =1424)

Viral load tests are not routinely done in Lesotho because of their relative high cost and because they have to be done outside Lesotho. It is also observed that the tests carried out mainly for patients who are on a medical aid (22 out of 47 patients) in private clinics. In public clinics viral load tests are carried out in patients who show poor response to antiretroviral therapy in order to determine treatment failure. Once treatment failure is acertained treatment switch is carried out.

4.4 Outcome of HIV/AIDS treatment

The outcomes of HIV/AIDS treatment discussed in this section are the CD4 cell count and body weight increase. (refer to chapter 3, figure 3.1 resource input assumed and outcome expected)

4.4.1 CD4 cell count

It is observed from figure 4.4.1 that the majority of patients (n=1 024) started antiretroviral therapy at a CD4 cell count of between zero and 199 cell/mm^3. After treatment, more patients had a higer CD4 cell count (n=1277) and more detected at the CD4 cell count above 500 cells/mm^3.

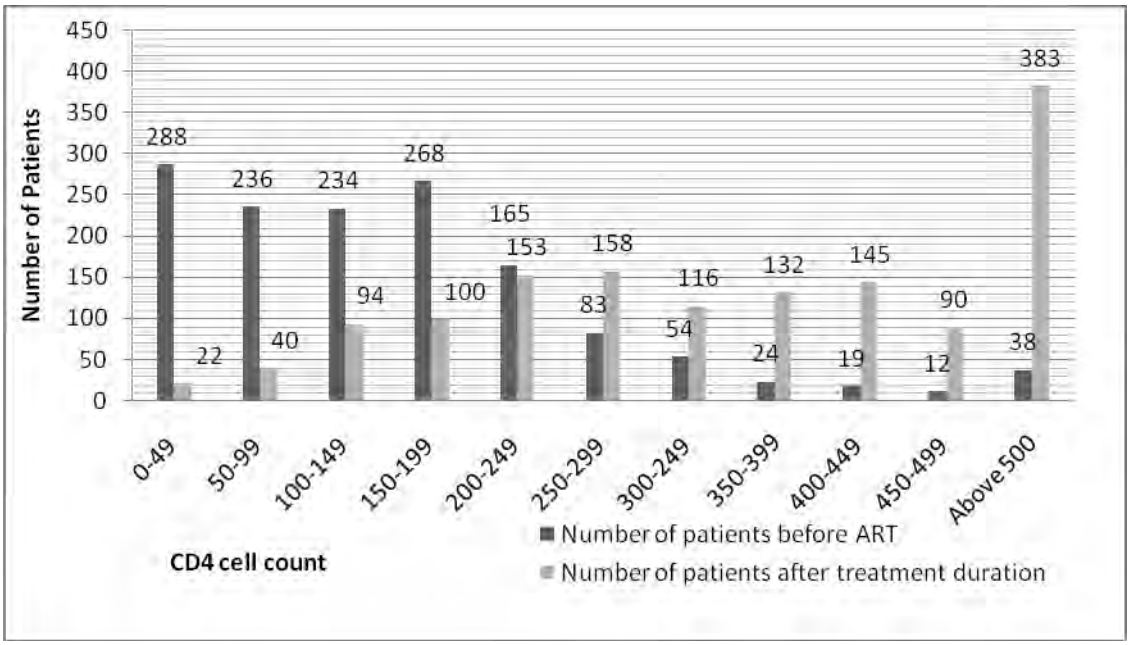


Figure 4.4.1 CD4 cell count at the start of antiretroviral therapy

The viral load which is a direct measure of antiretroviral treatment outcome but the usage as an outcome measurement had limited value due to the fact that it was carried out on a small number of patients who can pay for it in private ART clinics, and in one public ART clinic. Even

though the Ministry of Health and Social Welfare, (2004: 28) specify that the viral load is a routine test to be done at the start of therapy and every 3 months thereafter, it is not part of the routine tests that are carried out in many ART clinics in Maseru. The outcome of HIV/AIDS treatment was measured using CD4 cell count increase, and body weight increase.

One important outcome of HIV/AIDS treatment is found to be CD4 cell count increase. Even though it is an indirect outcome, for the purpose of the study it is taken as a direct and useful measure as it is a measurement of the degree of immuno-compromise, stage of HIV/AIDS disease progression and for monitoring the recovery of the immune system under treatment. If CD4 cell count increases, the effects of immune system recovery are observed. Patients become less sick hence contribute more towards their own well-being (De Beaudrap *et al*. 2009: 2). CD4 cell count is also utilized to determine the need to switch regimens (Kimmel *et al*, 2010: 268). While Diabaté & Alary, (2009: 640) notes the CD4 cell count increase of 50cells/mm^3 after six months of initial treatment.

It seems that there is a strong relationship between CD4 cell count and incidence of opportunistic infections. CD4 cell count increase means that there is a remarkable decrease in incidences of opportunistic infection which is common in HIV/AIDS patients with lower CD4 cell counts. Incidence of opportunistic infection is relatively low for patients on antiretoviral treament, the patients with no incidence of opportunisitc infections comprised 73.98 percent, while the remaining suffered from 1 to 3 types of opportunistic infections.

CD4 cell count increase is a success measure for HIV/AIDS treatment as it protects against opportunistic infections and malignancies (Wolbers *et al*., 2007: 889).This was because if patients do not have incidences of opportunistic infection, they lead a healthier life. They can work, look after their families and socialise without a problem. With any of the opportunistic infection such as oral or oesophageal candiasis, they experience reduced appetite and difficulty in swallowing and hence would have reduced food intake leading to loss of weight. If a patient suffers from *Peumocystis cariini pneumonia*, he/she is sick and miss his/her job. Increased CD4 cell count is attributed to the absence of opportunistic infection and prophylactic treatment is given at lower CD4 cell count (Phair *et al*., 1990: 164). Prevalent opportunistic infections are those that have no prophylactic treatment recommended such as herpes, diarrhoea, oral and oesophageal candidiasis, as well as fungal infections.

4.4.2 Body weight

From figure 4.4.2 the study finds that the majority of paptients have body weight around 40 to 79 kg, with less people below 40kg and above 80 kg. After HAART, the body weight of patients increases between 40 and 80 kg.

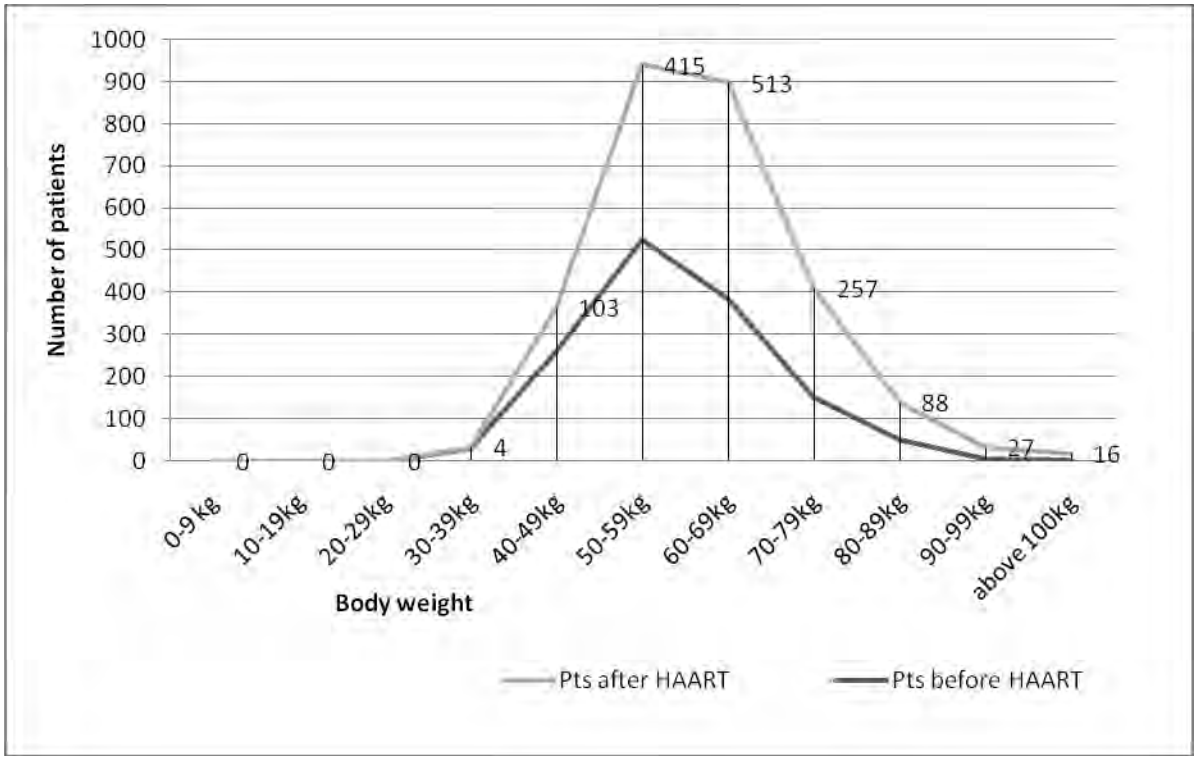


Figure 4.4.2 Body weight before and after antiretroviral treatment (n=1424)

4.4.3 Body weight increase for patients on dietary supplements

Body weight increase was observed when patients were not given any supplements and also when they were provided with supplements. HIV/AIDS patients were given dietary supplement in all ART clinics. However, some clinics issued more than one supplement while others did not provide supplements to most of the patients.

The Ministry of Health and Social Welfare, (2004: 64) recommended the use of dietary supplements such as multivitamin. In addition they recommend well cooked balanced meals. However, the clinics give dietary supplements such as suthalandria to most patients which is not recommended in the guidelines. The guidelines do not prohibit patients from using dietary supplements if it is the preference of the patient to use them. It is a common practice to give a number of dietary suppements, especially in private practice where patients receive most of the

other supplements. Multivitamin are mostly given in public clinics. Dietary supplements are provided to increase body weight as most adult patients go to the ART clinics late, with unacceptably low body weights (31-49 kg).

Body weight gain is attributed to dietary supplements and to the absence of opportunistic infections, particularly oral and oesophageal candidiasis which makes food intake difficult. When patients do not have such a condition they eat easily and do not suffer from severe body weight loss. Opportunistic infection leads to energy expenditure and a patient may end up with reduced body weight. The absence of opportunistic infection contributes to patient body weight gain in the treatment of HIV/AIDS. Therefore, indirectly increased CD4 cell count results in the absence of opportunistic infection and leads to body weight gain.

The study finds that some patients are able to regain ideal body weights and may even be described as being obese. Some research subjects weighed more than 100 kg, with the highest body weight being 123 kg (see figure 4.4.2). The implication of obesity is the development of life style diseases such as diabetes and hypertension. However, there are also those patients who remain with lower body weights even with increased CD4 cell count, no opportunistic infection, good food intake, dietary supplementation. Their low body weight is not related to HIV/AIDS. but They probably have high metabolism rates. However, these disease aspects are not investigated as they are outside the scope of the study.

4.5 HIV/AIDS patients' adherence to antiretroviral treatment

The majority of patients adhere to treatment. The study finds that 92 percent of patients achieving over 95 percent of adherence rate.

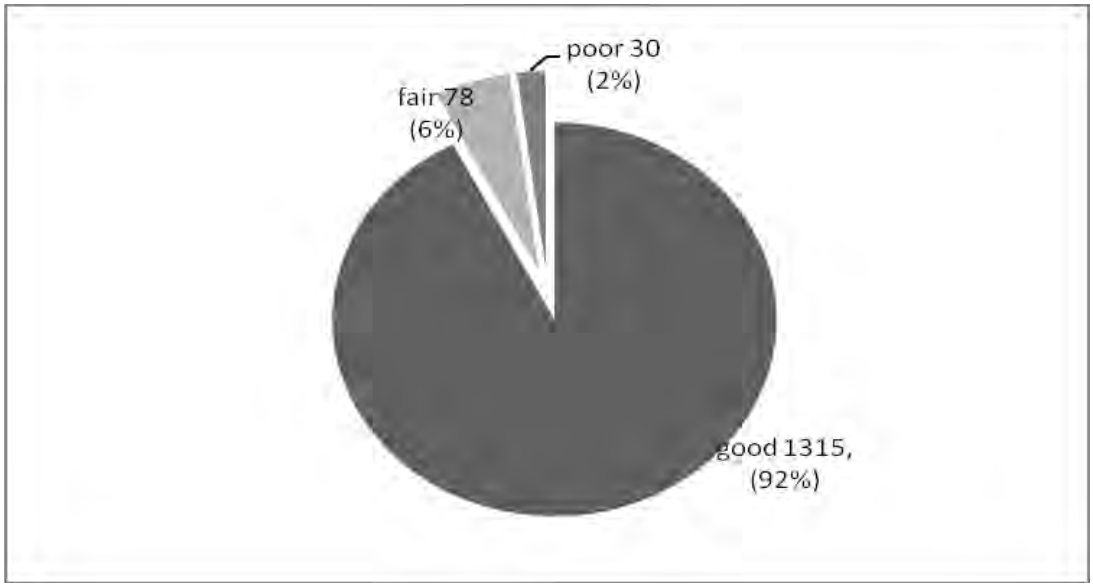


Figure 4.5.1 Patients' adherence to antiretroviral treatment. (n=1424)

Adherence of patients to antiretroviral therapy is mostly above 95 percent. This rate was achieved by 92 percent of the study population. Only 2 percent of the study population had poor adherence (below 84 percent). According to the Ministry of Health and Social Welfare, (2004: 12) good adherence is when the patient has missed not more than one table in 30 days which is more than 95 percent, and fair adherence is when more than three tablets are missed (94 -85 percent). Poor adherence is when more than three tablets are missed in a month (below 84 percent). This was also observed in the study carried in Côte d'Ivoire where adherence used was 95 percent (Diabaté & Alary, 2009: 640). In other countries, 90 percent is accepted as good adherence.

4.6. The cost of treating HIV/AIDS in ART clinics

The cost of treating HIV/AIDS patients in the study is assessed.

4.6.1 Theoretically expected cost of regimens for one year of treatment in 2008.

Figure 4.6.1 depicts the cost of different antiretroviral regimens available in Lesotho. It is observed that the cost of second line regimen (1g) has the highest cost and that the efavirenz containing regimens (1b, 1d, and 1f) appear to be more expensive than their nevirapine based regimens (1a, 1c and 1e). Wolf, et al (2007: 8) expresses the need to lower second line antiretroviral cost.

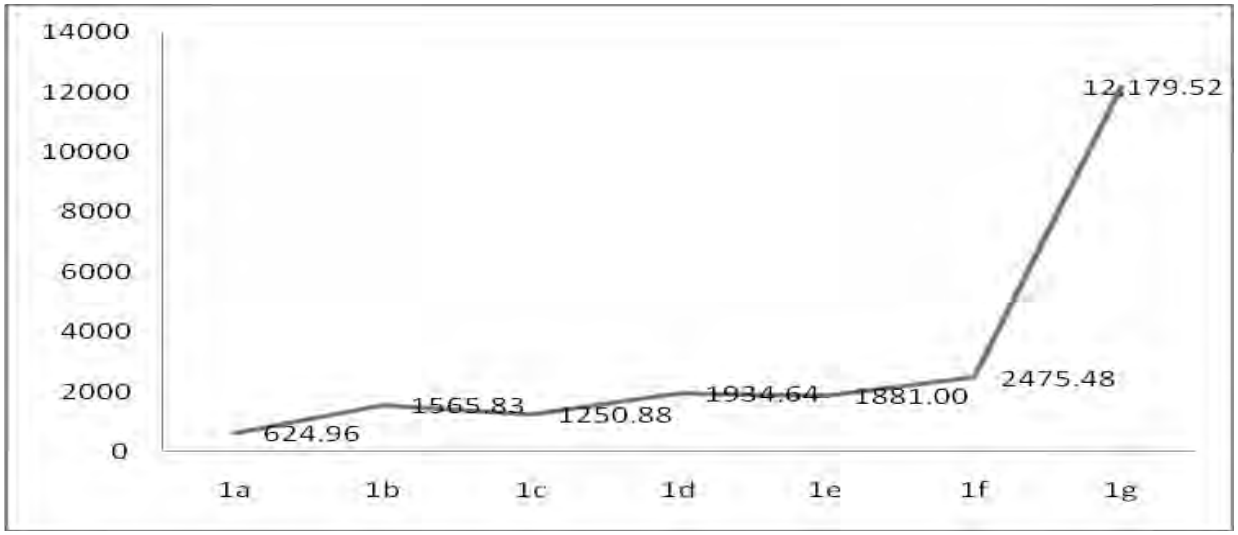


Figure 4.6.1 Illustration of theoretical expected cost of antiretroviral regimens in ZAR for 2008

(1a-stavudine/lamivudine/nevirapine, 1b-Stavudine/lamivudine/efavirenz, 1c–zidovudine/lamivudine/nevirapine,1d-zidovudine/lamivudine/efavirenz, 1e-tenofovir/lamivudine/nevirapine, 1f-tenofovir/lamivudine/efavirenz, 1g-abacavir/didanosine/lopinavir/ritonavir.)

4.6.2 Actual cost of treating HIV/AIDS in the ART clinics over the duration of treatment (from 2004 January to 2008 August).

The cost of treatment of HIV/AIDS patients comprised of cost of ARVs, dietary supplements, TB, opportunistic infection treatment as well as prophylaxis, antiretroviral side effects and laboratory tests as appeared in table 4.1.4. The major spending was on antiretroviral medicines, followed by laboratory tests. Other costs were minor compared to the cost of antiretroviral medicines.

Table 4.1.4 Total cost of treatment of HIV/AIDS in ART clinics in Maseru

Variable	Number of patients in the clinic	Mean and Std dev. cost (ZAR)	Minimum cost in (ZAR)	Maximum cost (ZAR)	Median cost (ZAR)	Total cost in (ZAR)
Cost of ARV side effects	1037	40.7±59.1	0.1	579.6	16.4	42,207.59
Cost of OI treatment	360	3.6±2.4	1.0	9.0	3.0	1,295.00
Cost of TB treatment	134	160.3±29.2	155.5	362.8	155.5	29,482.92
Cost of dietary supp	896	31.7±70.1	2.0	678.6	3.0	28,354.19
Cost of ARVs	1424	3809.4±3066.6	629.5	30686.88	2991.86	5,424,673.63
Cost of laboratory tests	1424	717.2±482.4	8.4	4292.00	560	1,021,220.7
cost of OI prophylaxis	939	20.04±19.52	0.87	121.40	13.80	18,818.94
Total						**R 6,566 052.97**

OI - opportunistic infections, ARV - antiretroviral drugs, TB - tuberculosis

4.6.2.1 The cost of treating HIV/AIDS patient

Figure 4.6.2 shows the cost of treating HIV/AIDS patients in the ART clinics throughout the duration of treatment. The results reveal that the cost of antiretoviral medicines contributes 83 percent of the total cost of treating HIV/AIDS. The cost of laboratory tests contribute 15 percent while other drugs contribute 2 percent of the total cost.

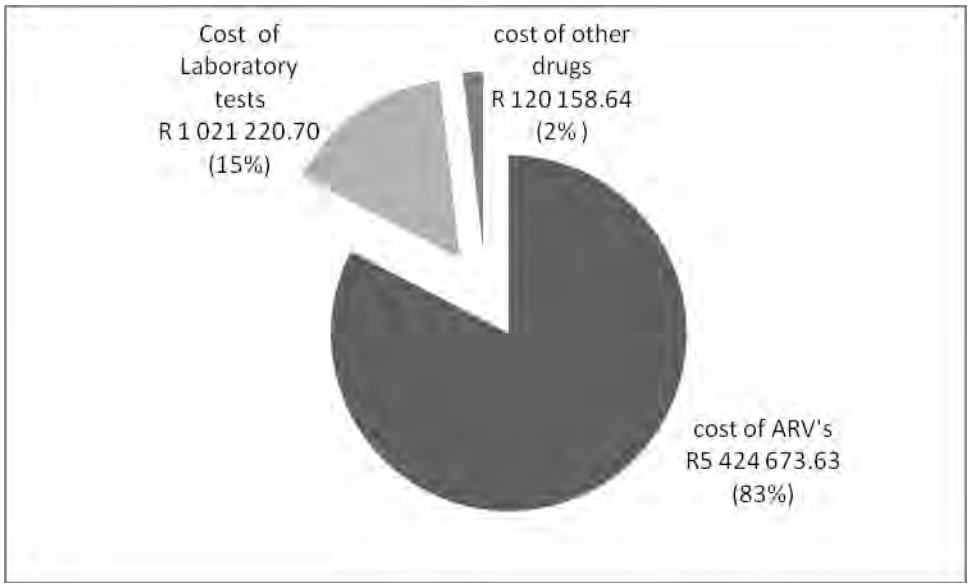


Figure 4.6.2 Illustration of the cost of other drugs and laboratory tests for all the clinics throughout the duration of treatment

Table 4.1.5 shows average cost of ARVs in all the clinics for all regimens including paitents who swtiched regimens. The cost-prevalence index is also calculated.

Table 4.1.5 Cost contribution of ARVs, for all ART clinics throughout the duration of treatment in South African Rands (ZAR)

ARV regimens	Number of patients per regimen	Mean and Std dev cost	Minimum cost	Maximum cost	Median cost	Total cost	Cost/ prevalence index
1a	527	2253.8±1622.1	629.5	6530.64	1426.52	1,187,770.25	0.6
1b	437	4621.1±2663.7	1561.62	11263.16	3774.5	2,019,410.58	1.2
1c	109	2509.9±1148.2	1403.56	7734.68	2070.52	273,574.46	0.7
1d	89	6315.5±3611.0	1995.84	16841.36	5286.97	562,064.93	1.7
1s	262	5274.3±4261.5	850.84	30686.38	4304.67	1,381,853.41	1.4
Total cost of antiretroviral drugs						**5,424,673.63**	

The cost/prevalence index included in table 4.1.5 reveals that regimens 1a and 1c are relatively inexpensive while regimen 1b and 1d are relatively expensive. 1s indicates a code for all switched regimens, including switching to second line regimens.

Table 4.1.6 Comparison of the effect size or *d*-value of cost of antiretroviral drug regimens

Regimen	**1a**	**1b**	**1c**	**1d**	**1s**
1a		**0.89**	0.16	**1.12**	0.71
1b	**0.89**		0.79	0.47	0.15
1c	0.16	0.79		**1.05**	0.65
1d	**1.12**	0.47	**1.05**		0.24
1s	0.71	0.15	0.65	0.24	

There are practical difference significances between the cost of regimen 1b and 1a, 1d and 1c, 1d and 1a as their *d*-value is above 0.8. There are also nearly practical differences in regimens 1c and 1b and 1s and 1a. There is no practical significant difference between the cost of other regimens.

The reason of switching of regimens depends on other factors such as toxicity of the regimen and resistance developed by the virus to the specific drug. If the cost is the main reason for switching, the switching of antiretroviral drugs may be made between the regimen with no significant difference between the costs. However, this difference must be known to the personnel incharge of budgets and procurement who stock enough medicines in order to avoid stockout and expiry of overstocked medicines. The prescriber makes informed decisions about

the cost of regimens while prescribing and switching HIV/AIDS patients‟ regimens, if this information is made available to them.

Table 4.1.7 Cost of ARV side effects per regimen in (ZAR)

Regimen	Number of patients in the clinic	Mean and std. dev cost	No. of patients	Minimum cost	Maximum cost	Median cost	Total cost	Cost/prevalence index
1a	527	33.27±53.05	360	0.14	420	13.31	11,977.49	0.82
1b	437	40.22±56.05	323	0.1	579.6	20.03	12,990.73	1.02
1c	89	38.56±66.06	65	0.6	424.24	4.62	2,506.6	0.95
1d	62	52.18±86.3	62	0.14	369	11.7	32,87.35	1.28
1s	262	50.64±61.11	226	0.21	476	23.31	114,45.42	1.24

The study finds that cost of treatment of side effects caused by antiretroviral of regimens 1b, 1d and 1e is slightly more expensive in comparison to 1a and 1c. However, the decision to treat antiretroviral drugs side effects is important to the management of HIV/AIDS as it improves the medicine taking behaviour of the patient.

Table 4.1.8 Effect size (*d*-value) between the cost of treating antiretroviral side effects in specific antiretroviral regimens

Regimen	**1a**	**1b**	**1c**	**1d**	**1s**
1a		0.12	0.08	0.12	0.28
1b	0.12		0.02	0.14	0.17
1c	0.08	0.02		0.16	0.18
1d	0.12	0.14	0.16		0.02
1s	0.28	0.17	0.18	0.02	

The cost of medicines used for treating antiretroviral side effects for specific regimens is found to have no significant difference. Therefore, the decision to switch from one regimen to the other is not based on the cost of medicines used to treat antiretroviral side effects. It is based on other reasons which may be more serious, life threatning toxicities that are usually not treated but warrant a switch of regimen, or certain drugs in the regimen. This piece of information may be useful when a new ART clinic is opened and with an inexperienced HIV/AIDS prescribers in private clinics. Another reason may be some of the side effects such as lipoatrophy are not routinely treated and their cost is not included.

4.7 A comparison of different ART clinics providing HAART.

This section compares prescribing practices of individual clinics, in terms of cost and outcome of antiretroviral treatment regimens.

4.7.1 Patients demographics

Patients" demographics of different ART clinics are discussed.

4.7.2 Number of patients on all available regimens in the clinics (n=1424)

Table 4.1.9 shows that the distribution of patients who are on all regimens among the clinics. There are more people at Senkatana clinic (n=334). Mabote clinic (n=89) has the lowest number of patients.

Table 4.1.9 Number of patients according to clinics.

ART Clinic	Number of patients	Percentage (%)
Bophelong	238	16.65
Healthy Lifestyle	296	20.8
Khanya	146	10.26
Mabote	89	6.25
Medicare	134	9.42
Qoaling	92	6.47
Senkatana	334	23.47
St. Joseph	95	6.68
Total	**1424**	**100**

4.7.3 The employment status of patients in the ART clinics

Most patients are employed in Healthy Lifestyle and Khanya ART clinics, while most patients are not employed in public clinics except for Qoaling clinic where most patients are employed.

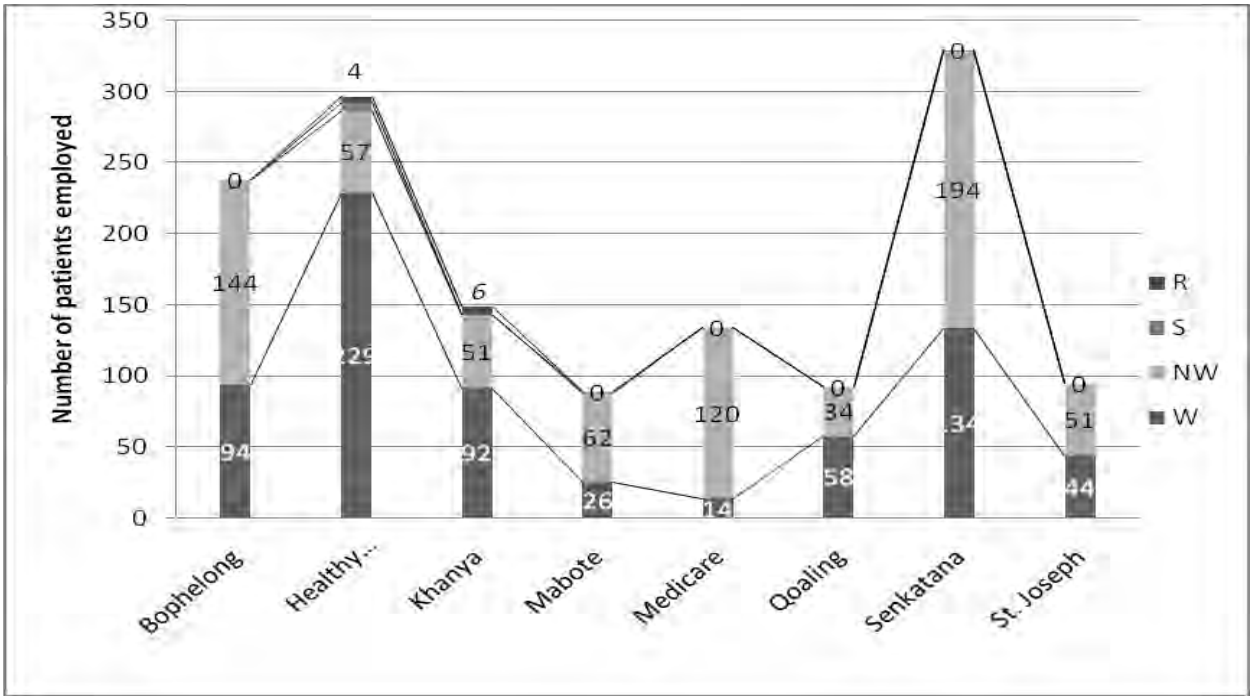


Figure 4.7.1 HIV/AIDS patients according to employment status and ART clinics (Key: Healthy - Healthy Life Style, NW – not working, W – working, S –student, R- retired))

4.7.4 Outcome of antiretroviral treatment

Outcomes of antiretroviral treatment to be discussed are CD 4 count and body weight increase

4.7.4.1 CD4 count increase

Table 4.2.1 compares the CD4 cell count increase of patients who were on regimen 1a, 1b, 1c and 1d in all eight ART clinics in Maseru. The average CD4 cell count increase is above 100 cell/mm^3 in all the clinics, with the highest CD4 cell count increase noted at Senkatana clinic for patients on regimen 1a which is 456 cells/mm^3.When these results are compared with another study Mocroft *et al*., (2006: 1141) compares drug nucleoside backbones, there was a poorer CD4 cell count increase for zidovudine/lamivudine and for those on tenofovir when compared to lamivudine/stavudine.

Table 4.2.1 CD cell count average increase (in cell/mm^3) for four different regimens according to ART clinics

	Antiretroviral regimen given in the clinics and average CD4 cell increase							
	1a		1b		1c		1d	
ART Clinic	n	Mean and std. dev.	n	Mean and std. dev	n	Mean and std. dev	n	Mean and std. dev
Bophelong	70	193.2±160.8	65	229.9±170.4	43	163.0 ±140.1	15	153.6 ±132.0
Healthy Lifestyle	79	162.7±184.5	102	174.7±166.4	29	212.2 ±238.3	18	226.9 ±223.9
Khanya	17	219.0±145.4	93	188.4±123.2	7	237.0 ±74.4	13	289.1 ±137.8
Mabote	57	139.3±134.4	9	152.2±185.5	8	124.4 ± 225.7	0	No patients
Medicare	73	156.1±180.6	42	223.0±225.0	4	335.0 ±246.1	2	157.0 ±87.7
Qoaling	71	142.4 ±119.4	6	202.5 ±91.9	6	187.3 ±197.5	1	267.0
Senkatana	130	456.4±294.1	97	343.3 ±208.2	2	429.5 ±590.4	15	200.6 ±202.0
St. Joseph's	30	237.7±188.1	23	144.3±120.8	10	180.1 ±172.4	25	144.3 ±138.2

n denotes the number of patients on certain antiretoviral regimen in a particular clinic.

CD4 cell count increase is found to be an important marker of treatment success. When its increase results in lowering of incidence of opportunistic infections and without which a patient has a better health outcome (Mezzaroma, *et al.,* 1999: 1187). It is noted that patients at the Senkatana clinic had a better outcome as an average CD4 cell count increase was more than 200 cells/mm^3 in all those patients who did not switch regimens. Similarly in this ART clinic patients had a better treatment outcome with mean CD4 cell count of 456.4 ± 294.1cells/mm^3 from regimen 1a, the least costly regimen. All the patient have their CD4 cell count increased on average by a minimum of 100 cells/mm^3.

4.7.4.2 Significance of CD4 count increase

Table 4.2.2 shows effect sizes and shows that there is practical difference the average CD4 cell count increases in regimen 1a between all the eight clinics when using the highest average CD4 cell count as that of Senkatana.

Table 4.2.2 CD4 cell count in cells/mm^3 increase significance using *d*-values

	Antiretroviral regimens			
ART clinic	**1a**	**1b**	**1c**	**1d**
Bophelong	**0.9**	0.5	0.4	0.6
Healthy Lifestyle	**1.0**	**0.8**	0.4	0.3
Khanya	**0.8**	0.7	0.3	-
Mabote	**1.1**	**0.9**	0.	No patients
Medicare	**1.0**	0.5	0.2	0.6
Qoaling	**1.1**	0.6	0.4	0.1
Senkatana	-	-	-	0.4
St. Joseph's	0.7	1.0	0.4	0.7

4.7.4.3 Body weight increase

The results in table 4.2.3 reveal that body weigth increase with regimen 1a, 1b, 1c and 1d in the eight ART clinics in Maseru. The highest average body weight increase is with 13.3±12.8 kg with regimen 1c in St Joseph"s clinic.

Table 4.2.3 Mean body weight (kg) increase in the clinics for individuals regimens

	Means body weight (kg) in antiretroviral regimen provided in the clinics							
	1a		**1b**		**1c**		**1d**	
ART Clinic	n	Mean and std dev.	n	Mean and std dev	n	Mean and std dev	n	Mean and std dev
Bophelong	70	4.8 ±7.1	65	6.6±7.1	43	0.6±8.1	15	4.5±7.3
Healthy Lifestyle	79	5.7 ±8.6	102	6.9±6.3	29	5.7±5.5	18	7.7±6.8
Khanya	17	4.7 ±5.1	93	4.5±6.0	7	0.3±5.8	13	6.9±9.2
Mabote	57	4.5 ±6.5	9	6.2±6.6	8	3.3±4.4	0	No patients
Medicare	73	4.4 ±7.9	42	6.6±7.9	4	2.8±3.2	2	1.0±2.8
Qoaling	71	6.9 ±6.7	6	12.0±8.7	6	2.0±13.2	1	9.0
Senkatana	130	7.0 ±9.3	97	6.1±7.6	2	2.0±7.1	15	5.4±8.5
St. Joseph's	30	7.1 ±8.6	23	6.3±5.6	10	13.3±12.8	25	3.4±6.9

Body weight increase for patients on HIV/AIDS treatment may be a result of a number of factors such as dietary supplementation, improved food intake, wellness of the patient as a result of freedom from other infections and presence of nutritious food in the home. However, obesity is observed in some patients and that can cause other medical problems associated with obesity.

Table 4.2.4 shows the practical significant differences in body weight increase between various clinics.

Table 4.2.4 Practical significant increase in body weight

	Antiretroviral regimens *and d-* values			
ART clinic	**1a**	**1b**	**1c**	**1d**
Bophelong	0.3	0.6	0.5	0.6
Healthy Lifestyle	0.2	0.6	0.5	0.2
Khanya	0.3	**0.9**	0.7	0.2
Mabote	0.3	0.7	0.6	No patients
Medicare	0.3	0.6	0.5	**1.1**
Qoaling	0.02	0	0.1	0
Senkatana	0.01	0.7	0.6	0.4
St. Joseph's	0.3	0.7	0.6	0.8

There is no practical significant difference in body weight increase resulting from the use of the regimen at the clinics except for regimen 1b provided by Khanya clinic and 1d provided by Medicare clinic.

4.7.5 Cost of antiretroviral treatment in different ART clinics

Cost of antiretroviral treatment was compared between the clinics

4.7.5.1 Cost of antiretroviral drugs

Table 4.2.5 shows the average cost of antiretroviral regimens at different ART clinics. Cost/prevalence index is calculated to show how each ART clinics spent resources.

Table 4.2.5 Aspects of the average cost of antiretroviral drugs in eight ART clinics (ZAR)

ART clinic	No. patients in the clinic	Mean and std. dev. cost	Minimum cost	Maximum cost	Median cost	Total cost	cost / prevalence index
Bophelong	238	2852.8±1939.7	629.5	9142.73	2210.57	678,958.96	0.73
Healthy Lifestyle	296	2928.7±2238.1	629.5	18120.48	2247.2	866,879.90	0.76
Khanya	146	4393.4±3405.2	893.72	30686.38	4052.31	641,438.36	1.0
Mabote	89	1362.8±882.3	629.5	7089.38	999.4	121,249.55	0.35
Medicare	134	3699.8±3743.1	682.36	29053.64	3021.99	495,776.36	1.0
Qoaling	92	1340.0±572.4	682.36	3522.82	1212.96	123,278.90	0.35
Senkatana	334	6358.6±3058.6	735.2	14984.31	5353.86	2,1237,57.67	1.67
St. Joseph"s	95	3929.8±2282.8	682.36	9299.8	3252.76	373,333.93	1.03

By observation of the total cost highlights that most financial resources are used by the Senkatana clinic. It is the clinic with the largest patient population and has the highest number of patients on treatment since 2004. The length of treatment and prevalence contribute to the highest cost **(R 2,123,757.67)**. However, the use of certain regimens more than others also resulted in higher costs that were not proportional with patient populations. This conclusion is based on assessment of the cost/prevalence index. It is observed that some ART clinics (Bophelong, Healthy Lifestyle, Mabote and Qoaling) choose inexpensive regimens for the majority of patients. Others probably have more patients on relatively expensive regimens (Senkatana and St. Joseph‟s). However Medicare and Khanya clinics have a balanced relationship between expenditure on ARV regimen between the cost and prevalence. Table 4.2.6 shows the *d*-values between the average costs of antiretroviral regimens when various ART clinics are compared.

Table 4.2.6 Practical significant (*d*-values) of regimen costs between the clinics

ART clinic	Bophelong	Healthy Lifestyle	Khanya	Mabote	Medicare	Qoaling	Senkatana	St. Joseph
Bophelong		0.03	0.46	**0.77**	0.23	**0.78**	**1.15**	0.47
Healthy Lifestyle	0.03		0.43	0.7	0.21	0.71	**1.12**	0.44
Khanya	0.46	0.43		**089**	0.18	**0.9**	0.58	0.14
Mabote	**0.77**	0.7	**0.89**		0.62	0.03	**1.63**	**1.12**
Medicare	0.23	0.21	0.18	0.62		0.63	0.71	0.06
Qoaling	**0.78**	0.71	**0.9**	0.03	0.63		**1.64**	**1.13**
Senkatana	**1.15**	**1.12**	0.58	**1.63**	0.71	**1.64**		**0.79**
St. Joseph's	0.47	0.44	0.14	**1.12**	0.06	**1.13**	**0.79**	

There are some observed practical significant differences in cost of treating HIV/AIDS patient with antiretroviral regimens among ART clinics. The differences may be due to the fact that some clinics have been running for longer periods, while others have had shorter running period. Another difference may be attributed to the type of regimen that patients are treated with. For example if more patients are treated with a more costly regimen for a longer period, that would show an increase in the cost of treatment regimens in the clinic.

4.7.6 Dietary supplementation and CD4 cell count increase

It is observed that CD4 cell count increase does not depend on dietary supplementation. There is a higher CD4 cell count increase for patients who do not receive any dietary supplements than for those who receive 6 dietary supplements.

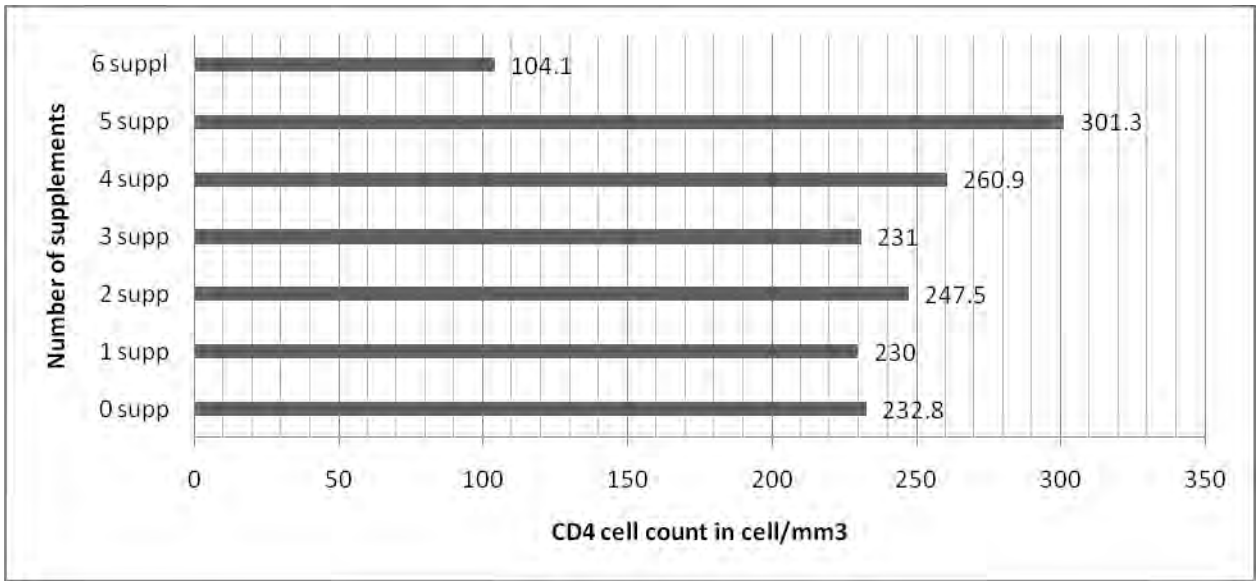


Figure 4.7.2 CD4 cell count increase according to the number of dietary supplements. (key – supp stands for dietary supplements) (n=1424)

Dietary supplements are commonly given to patients who are on HAART. Their body weight increase is mostly observed when patients are given supplements. Therefore, probably body weight gain for these patients is a result of all the factors put together. However, the result does not show any relationship between the number of dietary supplements and CD4 cell count increase.

4.7.6.1 Cost of dietary supplements in the eight ART clinics for the duration of the study

Dietary supplement are given to HIV/AIDS patients in the ART clinics and their cost is calculated and analysed. Similarly cost-prevalence ratio was calculated for each clinic.

Table 4.2.7 Aspects of cost of dietary supplements in the ART clinics (ZAR)

ART clinic	Number of patients in the clinic	Mean and Std. dev cost	Number of patients given supplements	Minimum cost	Maximum cost	Median cost	Total cost	Cost-prevalence index
Bophelong	238	2.5 ±5.8	47	0.28	40.99	1.5	117.63	0.002
Healthy Lifestyle	296	76.2 ±102.2	264	0.56	678.6	44.4	20124.89	2.4
Khanya	146	64.1 ±64.1	70	0.4	258.8	49.5	4488.89	2.02
Mabote	89	2.8 ±1.4	76	1	6	2.4	213.4	0.1
Medicare	134	53.6 ±91.2	39	2	434.4	2.4	2089.42	1.7
Qoaling	92	4.1 ±2.2	84	1.2	10.2	4.8	344.6	0.1
Senkatana	334	1.8 ±2.3	221	0.3	31.2	1.2	407.08	0.06
St. Joseph‟s	95	6.0 ±2.5	95	1.2	12.6	5.2	569	0.02

By using a cost/pravalence index, it is observed that dietary supplements are relatively expensive in private clinics (2.4, 2.02 and 1.7), compared to the public clinics which are all below cost-prevalence index of 1. This is in line with the type of supplements used in the private clinics and those used in public clinics. When average cost is used (76.2 ± 102.2, 64.1 ± 64.13 and 53.6 ± 91.2) of dietary supplements are mostly used in private clinics with higher costs. This is due to the fact that patients who are attending private clinics are mostly employed therefore they can afford more costly dietary supplement except for Medicare clinic, where most patients are not working. Patients in public clinics receive basic free dietary supplements. Probably acquisition costs between private and public differ as public clinics buy from NDSO which is able to negotiate costs from bulk sales, and private clinics buy from private company in smaller quanties.

Table 4.2.8 Analysis of dietary supplements costs in the ART clinics using *d*- values

ART clinic	Bophelong	Healthy Lifestyle	Khanya	Mabote	Medicare	Qoaling	Senkatana	St. Joseph
Bophelong		0.46	0.61	**0.92**	0.6	**0.78**	0.62	0.67
Healthy Lifestyle	0.46		0.37	0.39	0.11	0.27	0.14	0.17
Khanya	0.61	0.37		0.41	0.014	0.19	0.02	0.06
Mabote	**0.92**	0.39	0.41		0.35	0.16	0.27	0.25
Medicare	0.6	0.11	0.014	0.35		0.19	0.03	0.07
Qoaling	**0.78**	0.27	0.19	0.16	0.19		0.14	0.11
Senkatana	0.62	0.14	0.02	0.27	0.03	0.14		0.04
St. Joseph's	0.67	0.17	0.06	0.25	0.07	0.11	0.04	

A comparison of the *d* - values of cost used for dieteray supplements in all the ART clinics in the study shows that there is no practical significant cost difference of dietary supplements in both private and public ART clinics. With the exception of comparisons between Bophelong with Mabote and also Bophelong with Qoaling clinics.

4.7.7 Incidence of side effects, opportunistic infections and TB

It is observed that incidence of TB was relatively low as well as opportunistic infection, while incidence of antiretroviral side effects is relatively high. Due to the tripple nature of antiretroviral treatment, patients may have suffered side effects from one medicine or two or even all three medicines bringing the rates to more than 100%, indicating that each patient has more than one side effect related to antiretroviral medicines

Table 4.2.9 Incidence of side effects, opportunistic infections and TB (n =1424)

ART Clinic	Number of patients	Side effects incidence	Opportunistic infection incidence	TB incidence
Bophelong	238	252 (106%)	25(11%)	11(5%)
Healthy Lifestyle	296	782(264%)	170(57%)	39(13%)
Khanya	146	40(27%)	36(25%)	6(4%)
Mabote	89	84(94%)	33(37%)	0
Medicare	134	252(188%)	81(60%)	26(19%)
Qoaling	92	82(89%)	43(47%)	27(29%)
Senkatana	334	993(297%)	49(15%)	24(7%)
St. Joseph's	95	45(47%)	18(19%)	8(8%)
Total	**1424**	**2530(178%)**	**455(32%)**	**141(10%)**

Incidence of antiretroviral side effects seem to be more because one patient has more than one side effect. Infact there is a ratio of 1.78 side effects per patient. Antiretroviral side effects are classified as adverse outcome of antiretroviral treatment, however patients may not necessarily be affected by side effects because if benefit outweigh risks, the drug treatment may be issued and where risks outweighed benefit the drug may be switched to another one that the patient can tolerate better.

Incidence of opportunistic infections seem to be relatively higher for patients who are treated in the private clinics. This may result from the fact that the patients receive less prophylaxis to prevent the incidence. Patients who are treated at public clinics suffer from opportunistic infections less frequent. They receive opportunistic infections prophylaxis. TB incidence is generally low. While opportunistic infections and TB incidence are positive outcome of treatment. Low incidences are positive indication of treatment success, and a better quality of life for the patient. As the quantity of life increases for the patient, the quality improves. There is less disease incidence, fewer sick off days. When not treated side effects bring back the symptom incidence. However, if they are treated, the life of the patient improves. In practice, the imbalances lead to patients being more sick in private clinics, than in public clinics.

4.7.7.1 Cost of drugs used for treating antiretroviral side effects at various ART clinics

The highest average cost (R87.3 ± 66.7) for drugs is used for treating antiretroviral side effects at Medicare clinic. The least average cost (R9.2 ± 10.6) is observed in the figures from the Qoaling clinic.

Table 4.3.1 Aspects Cost of treating antiretroviral side effects at the clinics in (ZAR)

ART clinic	Number of patients	Mean and std. dev cost	Number of patients with SE	Minimum cost	Maxi Mum cost	Median cost	Total cost	Cost/prevalence index
Bophelong	238	12.1 ±53.9	143	0.1	579.6	4	1,729.99	0.3
Healthy Lifestyle	296	67.6±70.3	275	0.3	424.24	50.5	18,594.14	1.7
Khanya	146	22.1±22.5	88	1.56	94.1	12.62	1,947.46	0.5
Mabote	89	21.3±71.8	46	1	476	6.1	978.84	0.5
Medicare	134	87.3±66.7	94	7.1	321.23	65.1	8,209.78	2.1
Qoaling	92	9.2±10.6	51	1	64.87	6.21	468.2	0.2
Senkatana	334	31.5±34.3	312	0.14	198.62	19.61	9,828.92	0.8
St. Joseph"s	95	16.1±69.2	28	1	369	2.63	450.26	0.4

SE- side effects

When the cost-prevalence index is used, it becomes clear that Medicare and Healthy Lifestyle clinics treat antiretroviral side effects in a relatively expensive manner. In other clinics the cost is contained below the cost-prevalence index of 1, implying that less expensive medicines are utilised. The reason for this is that here the patients are treated for antiretroviral side effects with branded medicines, as opposed to generic medicines that are used in the public clinics. This can be verified with the list of medicines used in the appendix. (see appendix F) Table 4.3.2 shows the practical significant differences in the average cost of treatment of antiretroviral side effects between the clinics using *d*- values

Table 4.3.2 Differences between the average cost per antiretroviral side effects medicines using according to the clinics using *d* –value

ART clinic	**Bophelong**	**Healthy Lifestyle**	**Khanya**	**Mabote**	**Medicare**	**Qoaling**	**Senkatana**	**St. Joseph**
Bophelong		0.46	0.61	**0.92**	0.6	**0.78**	0.62	0.67
Healthy Lifestyle	0.46		0.37	0.39	0.11	0.27	0.14	0.17
Khanya	0.61	0.37		0.41	0.014	0.19	0.02	0.06
Mabote	**0.92**	0.39	0.41		0.35	0.16	0.27	0.25
Medicare	0.6	0.11	0.014	0.35		0.19	0.03	0.07
Qoaling	**0.78**	0.27	0.19	0.16	0.19		0.14	0.11
Senkatana	0.62	0.14	0.02	0.27	0.03	0.14		0.04
St. Joseph's	0.67	0.17	0.06	0.25	0.07	0.11	0.04	

When *d*-values are used, it is observed that there are practical significant differences in the cost of treating antiretroviral side effects between Mabote and Bophelong clinincs and Qoaling and Bophelong clinics. The practice for treatment of antiretroviral side effects is not the same in

public and private clinics. Antiretroviral side effects occurr in both, but they are mostly observed in public clinics because there are more patients receiving services from public clinics, however it is observed that more financial resources were spent on treatment of antiretroviral side effects. For incidences of opportunistic infection (see Table 4.2.9).

4.7.7.2 Cost of treating opportunistic infections

The average cost of treating opportunistic infections in the ART clinics was assessed and cost–prevalence index is utilized to determine how expensive the cost of treating opportunistic infection is in different clinics. Table 4.3.3 illustrates how opportunistic infections are treated in the clinics.

Table 4.3.3 Aspects of cost of treating opportunistic infection in the ART clinics in (ZAR) (n= 1424)

ART clinic	Number of patients in the clinic	Mean and std. dev cost	Number of patients with OI	Minimum cost	Maximum cost	Median cost	Total cost	Cost/prevalence index
Bophelong	238	5±2.5	21	1	8	5	105	1.5
Healthy Lifestyle	296	3.8±2.7	127	1	9	3	481	1.1
Khanya	146	3.5±1.8	30	1	7	3	101	1.0
Mabote	89	2.7±1.4	26	1	6	3	71	0.8
Medicare	134	3.5±2.21	58	1	9	3	203	1.0
Qoaling	92	3.1±2.1	38	1	8	2	117	0.9
Senkatana	334	3.4±2.6	42	1	9	2.5	144	1.0
St. Joseph"s	95	3.3±2.4	18	1	8	3	60	0.9

OI –opportunistic infections

Assessing cost-prevalence index in most clinics the average cost of treating opportunistic infections is relatively inexpensive.

Results in table 4.3.4 indicates the calculation of *d*- values in order to assess if there are any practical significant differences between the average costs of treating opportunistic infections in all the ART clinics in the study.

Table 4.3.4 Effect size [or *d*- value] of the cost of treating opportunistic infections in the ART clinics

ART clinic	Bophelong	Healthy Lifestyle	Khanya	Mabote	Medicare	Qoaling	Senkatana	St. Joseph
Bophelong		0.46	0.61	**0.92**	0.6	**0.78**	0.62	0.67
Healthy Lifestyle	0.46		0.37	0.39	0.11	0.27	0.14	0.17
Khanya	0.61	0.37		0.41	0.014	0.19	0.02	0.06
Mabote	**0.92**	0.39	0.41		0.35	0.16	0.27	0.25
Medicare	0.6	0.11	0.014	0.35		0.19	0.03	0.07
Qoaling	**0.78**	0.27	0.19	0.16	0.19		0.14	0.11
Senkatana	0.62	0.14	0.02	0.27	0.03	0.14		0.04
St. Joseph's	0.67	0.17	0.06	0.25	0.07	0.11	0.04	

Table 4.3.4 shows that from the *d*- values, it is observed and deduced that there is no difference in average cost in the ART clinics as far as treatment of opportunistic infection is concerned. However, there is a practical significant difference in the average cost of treating opportunistic infections between Mabote and Bophelong clinicsas well as Qoaling and Bophelong clinics. Apart from those differences, the average cost of treating opportunistic infections is the same.

When considering private clinics alone there is no practical significant differences in average cost in the treatment of opportunistic infections beween the private clinics. When comparing average cost differences between public and private clinics there are also no practical significant differences. Therefore it is concluded that there is mainly no differences in cost and also practice of treating opportunistic infection prevalent in HIV/AIDS patient in the ART clinics in Maseru.This information may be used to analyse usage and cost patterns and also for annual budgetary purposes, to avoid overstocking and expiry of opportunistic infections medications.

4.7.7.3 Cost of preventing opportunistic infections

Cotrimoxazole is used commonly to prevent opportunistic infections mainly *Pneumocystis carinii pneumonia*, and to a lesser extend dapsone is used for mainly patient who developed sensitivity to cotrimoxazole. Table 4.3.5 shows the cost of preventing opportunistic infections in the clinics as well as cost-prevalence index.

Table 4.3.5 Aspects of cost of preventing opportunistic infections (ZAR) (n=1424)

ART clinic	Number of patients in the clinic	Mean and std dev. cost	Number of patients given prophylaxis	Minimum cost	Maximum cost	Total cost	Cost/ prevalence index
Bophelong	238	19.49±16.27	232	1.74	99.36	4,521.344	1.0
Healthy Lifestyle	296	14.79±7.44	225	1.72	33.12	3,328.502	0.7
Khanya	146	3.24±0.30	80	2.76	19.32	259.47	0.2
Mabote	89	11.46±5.10	86	2.76	24.84	985.24	0.6
Medicare	134	16.09±19.86	33	0.87	88.32	530.83	0.8
Qoaling	**92**	**37.24±10.47**	**91**	**2.76**	**57.96**	**3,389.20**	**1.9**
Senkatana	334	5.83±5.61	97	2.58	27.6	565.83	0.3
St. Joseph's	**95**	**55.14±34.54**	**95**	**28.0**	**121.40**	**5,238.52**	**2.8**

It is observed out that more resources are spent on prophylaxis of opportunistic infection in public clinics than in private clinics. The cost spent on prophylaxis is not in line with the number of patients being treated at the clinics, because clinics with less patient numbers spent more financial resources For example. St. Joseph"s and Qoaling clinics show cost-prevalence index of 2.8 and 1.9 respectively. Fewer resources are used at both Senkatana and Khanya clinics. The length of prophylaxis at St. Joseph"s and Qoaling clinics are the reasons for the increase in the average cost of prophylaxis, since they do not use different drugs or different branded drugs. WHO antiretroviral treatment guidelines are not followed to stop giving prophylaxis when the patient reaches CD4 cell count 200 cell/mm^3 (WHO, 2006: 21). Table 4.3.6 shows the differences of average cost of preventing opportunistic infections in the different clinics providing HAART.

Table 4.3.6 Effect size or *d*- values for preventing opportunistic infections

ART clinic	Bophelong	Healthy Lifestyle	Khanya	Mabote	Medicare	Qoaling	Senkatana	St. Joseph's
Bophelong		0.29	**1.07**	0.5	0.16	**1.07**	**0.83**	**1.03**
Healthy Lifestyle	0.29		**2.14**	0.45	0.07	**2.14**	**1.2**	**1.16**
Khanya	**1.0**	**2.14**			0.65	**3.25**	**3.0**	**1.50**
Mabote	0.5	0.45	**2.46**		0.23	**2.46**	**1.0**	**1.26**
Medicare	0.16	0.07	**1.07**			**1.07**	0.52	**1.13**
Qoaling	**1.07**	**2.14**	**3.25**	**2.46**	1.07		**3.0**	0.52
Senkatana	**0.83**	**1.2**	**3.0**	**1.0**	0.52	**3.0**		**1.42**
St. Joseph's	**1.03**	**1.16**	**1.50**	**1.26**	1.13	0.52	**1.42**	

There is a practical significant difference in the average cost of opportunistic infection prevention in clinics where *d* value is greater than 0.8, as observed mostly between St Joseph's and the ART clinics except the Qoaling clinic. The Qoaling clinic has the highest average cost of opportunistic infection prophylaxis. The difference is observed with Khanya clinic whose average cost is the lowest for preventing opportunistic infections. This translates to some ART clinics spending a lot of resources on prophylaxis of opportunistic infections while others spend fewer resources.

In practice terms, some ART clinics prevent opportunistic infections more, while others prevent them less. This means that without prevention some patients suffer from opportunistic infections that require treatment. Treatment of opportunistic infection may be short in duration. However, the opportunistic infections may result in hospitalization of the patient, and increase the cost tremendously. As Freedberg, *et al*., (2001: 830) says CD4 cell count is the predictor of opportunistic infections and mortality, prophylaxis of opportunistic infections has to be guided by CD4 cell count of the patient. If the patient is not hospitalized, the cost spent on him/her may appear smaller. In practice terms, one should not be denied prevention while his/her CD4 cell count is lower than 200cell/mm^3. It is not good practice to wait until a patient gets sick while prevention could have been given.

4.7.7.4 Aspects of cost of drugs used for the treatment of tuberculosis

Generally, TB treatment is found to be the same at all the clinics except for one clinic that treated patients for more than 6 months. The average cost of treatment for that appears to be higher than it is for other clinics.

Table 4.3.7 Aspects of average cost of drug treatment for TB in ZAR

ART clinic	Number of patients in the clinic	Mean	Number of patients	Minimum	Maximum	Median	Total cost
Bophelong	238	155.48	11	155.48	155.48	155.48	1710.28
Healthy Lifestyle	296	155.48	39	155.48	155.48	155.48	6063.72
Khanya	146	155.48	4	155.48	155.48	155.48	621.92
Mabote	89	-	-	-	-	-	-
Medicare	134	155.48	26	155.48	155.48	155.48	4042.48
Qoaling	92	180.43±63.28	26	155.48	362.79	155.48	4691.08
Senkatana	334	155.48	21	155.48	155.48	155.48	3265.08
St. Joseph"s	95	155.48	7	155.48	155.48	155.48	1088.36

Treatment of TB in Lesotho follows the recommended treatment guidelines and number of patients who have TB are treated in the same way for six months. However, for those who suffered from extra–pulmonary TB continue treatment for nine months and 14 months. There is no difference in the treatment cost of patients. Data collected from Mabote clinic do not include any TB patients.

4.8 Cost of antiretroviral treatment in public and private ART clinics

The total cost of treating HIV/AIDS is carried out for the purpose of having an idea of how much it costs to treat one patient in a month.

4.8.1 Calculating the cost of antiretroviral treatment in public ART clinics

Public ART clinics included in the study are Bophelong, Mabote, Qoaling, Senkatana and St. Joseph"s. They are financed by the government of Lesotho. The formula that the study uses to calculate the total cost of treating HIV/AIDS in these public clinics is

HIV/AIDS treatment cost **Ct = Cta + Ctb + Ctc + Ctd + Cte + Ctf + Ctg**

Financing and services provided at CHAL clinics is the same as that provided in government clinics, this is why the government and CHAL clinics are grouped together.

HIV/AIDS treatment cost **Ct = Cta + Ctb + Ctc + Ctd + Cte + Ctf + Ctg**

Where **C -** represents cost in monetary terms, **t** - represents HIV/AIDS treatment, **a -** represents antiretroviral regimen, **b -** represents drugs for prophylaxis of opportunistic infections, **c -**

represents drugs used for treatment of opportunistic infections, **d** - represents monitoring laboratory tests, **e** - represents drugs used for treatment of side effects of antiretroviral drugs. Financial resources here came from the same source which was the government of Lesotho

Table 4.3.8 Aspects of cost of HIV/AIDS and related treatment in public ART clinics in (ZAR) (n = 848)

ART clinic	Number of patients	Cost of ARV (Cta)	Cost of OI prophylaxis (Ctb)	Cost of OI treatment (Ctc)	Cost of laboratory tests(Ctd)	Cost of ARV side effects (Cte)	(Ctf) Cost of dietary supp.	Cost of TB Treatment (Ctg)
Mabote	89	121 249.6	985.24	71	49 425	798.84	213.4	0
Qoaling	92	123 278.9	3389.20	117	47 075	468.20	344.6	4691.08
Senkatana	334	212 3758	565.83	144	388 559	9828.92	407.08	3265.08
St. Joseph‟s	95	37 3333.9	5238.52	60	61 915	450.26	569	1088.36
Bophelong	238	678 959	4521.34	105	171 489.5	1729.66	117.63	1710.28
Sum	**848**	**3 420 579**	**14 700.13**	**497**	**718 463.5**	**13 275.88**	**1651.71**	**10 754.8**

HIV/AIDS treatment cost **Ct =Cta + Ctb + Ctc + Ctd + Cte + Ctf + Ctg**

=R3 420 579 + R14 700.130 + R497 + R718 463.5 + R13 275.88 + R1 651.71 + R10 754.8

= R 4, 179, 922.00

This is the amount of the money that the government of Lesotho pays for antiretroviral treatment including relevant laboratory tests of these patients in the public clinics.

Cost /patient ratio of treating one patient in the public clinic

$$\frac{\text{R 4, 179,922.00}}{848} = \textbf{R4929.15} \text{ per patient in a public ART clinic}$$

4.8.2 Calculating the cost of antiretroviral treatment private ART clinics

Private ART clinics are Healthy Lifestyle, Khanya and Medicare. The calculation of cost in the private sector is divided into two parts, what the government of Lesotho contributes, and what the provider pays. This is because the cost of running the clinic is partially provided by the government of Lesotho. The government basically contributes antiretroviral drugs, TB drugs and cotrimoxazole while the patient pays for other drugs and laboratory tests.

The cost born by the government of Lesotho was calculated as follows:

HIV/AIDS treatment cost **Ct = Cta + Ctb + Ctg**

Where **C-** represents cost in monetary terms, **t** - represents HIV/AIDS treatment, **a** - represents antiretroviral drugs, **b -** represents drugs for prophylaxis and **g** - represents TB treatment.

And

HIV/AIDS treatment cost **Ct = Ctc + Ctd + Cte + Ctf**

Where **C -** represents cost in monetary terms, **t** - represents HIV/AIDS treatment, **a** - represents antiretroviral regimen, **b** - represents drugs for prophylaxis of opportunistic infections, **c -** represents drugs used for treatment of opportunistic infections, **d** - represents monitoring laboratory tests, **e** - represents drugs used for treatment of side effects of antiretroviral drugs, **f** -represents supplements. Financial resources came from the patients, paying cash or on medical aid, and government of Lesotho.

In Table 4.3.9 total cost of HIV/AIDS treatment in private clinics was calculated most of the cost came from antiretroviral medicines followed by laboratory tests.

Table 4.3.9 Aspects of cost of HIV/AIDS treatment in Private ART clinics (n= 576)

Private ART clinic	**n**	**Cost of ARV (Cta)** (ZAR)	**Cost of OI prophylaxis (Ctb)**(ZAR)	**Cost of OI treatment (Ctc)** (ZAR)	**Cost of lab tests (Ctd)** (ZAR)	**Cost of ARV side effects (Cte)** (ZAR)	**Cost of TB Tx (Ctg)** (ZAR)	**Cost of dietary supp (Ctf)** (ZAR)
Medicare	134	495776.4	530.83	203	92839.2	8209.78	4042.48	2089.42
Healthy Lifestyle	296	866879.9	3328.50	481	143138	18594.14	6063.72	20124.89
Khanya	146	641438.4	259.47	104	66780	1947.46	621.92	4488.89
Total cost	**576**	**2004095**	**4118.80**	**788**	**302757.2**	**28751.38**	**10728.12**	**26703.2**

HIV/AIDS treatment cost **Ct = Cta + Ctb + Ctg**

= 2,004,095.00 + 4,118.80 + 10,728.12

= R 2, 008,224.5

The cost to patient ratio of treating one patient was

$$= \frac{\text{R 2, 008224.5}}{576} = \text{R 3,486.5}$$

This is the contribution of the government of Lesotho in monetary terms to the private clinics in the treatment of HIV. The contribution of the ART clinic in the treatment of patients with HIV was

HIV/AIDS treatment cost **Ct = Ctc + Ctd + Cte + Ctf**

= R788 + R302 757.2 + R28 751.38 + R26 703.2

= **R 360,703.25**

Cost to patient ratio for one patient was = $\frac{\text{R 360,703.25}}{576}$ = **R626.22**

The amount of money spent by the private clinic for one patient ratio for HIV treatment R 626.22, with the contribution of R3 486.5 per patient provided by the government of Lesotho. This analysis of the cost of HIV treatment excludes treatment of other diseases Table 4.3.10 shows spending of resources for different types of medicines and laboratory tests.

Table 4.3.10 Compares both public and private spending on HIV/AIDS treatment in ZAR

Type of cost	**Public clinic cost per patient ratio n=848**	**Private clinic cost per patient ratio n=576**
Cost of ARVs	4033.70	3479.31
Cost of OI prophylaxis	17.33	7.16
Cost of OI treatment	0.59	1.37
Cost lab tests	847.00	71.50
Side effects	15.66	49.91
Cost of TB	12.68	18.62
Cost of supplements	1.95	46.35
Total	**4928.91**	**3674.22**

The actual spending of resources between public and private clinics is somewhat unbalanced. For antiretroviral side effects treatment, the cost in private clinics is three times more than the cost utilized in public clinics and the possible reason is the use of generic medicines in the public clinics that leads to lower spending of money. Cost of treatment of opportunistic infection is also higher for the same reason that more of not using generic medicines in the private clinics. Prophylaxis of opportunistic infections is carried out mostly in public clinics than in private clinics. Antiretroviral medicines cost is higher in public than private and the reason may be the choice of regimens, this means that regimens containing expensive medicines are used more frequently in public clinics than in private clinics. High proportion of money is used in public clinics for laboratory tests than in private clinics, which means that fewer laboratory tests are carried out in private clinics. These are monitoring tests that show when the patient is

responding well to treatment and also reveal incidence of serious toxicity to the antiretroviral medicines. The carrying out of fewer tests is not good practice in the private clinics. Dietary supplement are costing more in private clinics because more expensive dietary supplements are used.

4.9 Relationship between outcomes of antiretroviral treatment.

Possible relationship between weighted average CD4 cell count increase and body weight increase amongst the regimens provided by the clinics as demonstrated in table 4.4.1. Information used on this table comes from table 4.5.2 and table 4.6.1

Table 4.4.1 Comparison of weighted CD4 cell increase and weighted body weight increase in the clinics

Treatment outcome	1a	1b	1c	1d
Weighted CD4 cell count increase	239.2±138.1	226.4±184.2	192.1±194.6	198.8±169.8
Weighted body weight increase	5.78± 8.04	6.17±6.90	2.53.±8.88	5.31±7.53
Weighted CD4 cell increase to cause 1 kg of body weight increase	**41.4**	**36.7**	**75.9**	**37.4**

The result in table 4.4.1 shows that regimen 1c has the highest CD4 cell count weighted average increase needed for body weight to increase by 1 kg, that means that the highest CD4 cell count weighted average increase to body weight increase by 1kg ratio, followed by regimen 1a. These are the regimens that contained nevirapine, and those with efavirenz (1b and 1d) have lower CD4 cell count weighted average increase to body weight increase ratio.

The importance of this information is related to wasting that is common in HIV/AIDS patients and is found to be an independent predictor for mortality (Tang, 2002: 230). It is important to observe the relationship between CD4 cell count increase and body weight in order to know which regimen may be selected for patients who present with severe wasting at the start of antiretroviral treatment and hence the decision to provide regimen that shows the lowest weighted CD4 cell count increase to raise body weight by 1kg.

4.10 Cost-effectiveness analysis for the antiretroviral treatment of HIV/AIDS

Cost-effectiveness of the regimen is assessed by using the average cost of regimen and its outcome which is average CD4 cell count increase and average body weight increase. Table

4.5.1 shows the average cost of regimens with zidovudine is higher than those with stavudine and also average cost of efavirenz-based regimens is higher than those with nevirapine.

Table 4.5.1 Determination of cost of different antiretroviral regimens in (ZAR)

Antiretroviral regimens	Number of patients per regimen	Mean and Std dev. cost	Minimum cost	Maximum cost	Median cost	Total cost
1a	527	2253.8±1622.1	629.5	6530.64	1426.52	1,187,770.25
1b	437	4621.1±2663.7	1561.62	11263.16	3774.5	2,019,410.58
1c	109	2509.9±1148.2	1403.56	7734.68	2070.52	273,574.46
1d	89	6315.5±3611.0	1995.84	16841.36	5286.97	562,064.93
1s	262	5274.3±4261.5	850.84	30686.38	4304.67	1,381,853.41

4.10.1 The average CD4 cell count as treatment outcome measurement

The average CD4 cell count is taken as an outcome of HIV/AIDS treatment and it is observed that stavudine-based regimens have higher average CD4 cell count increase while zidovudine-based regimens have lower average CD4 cell count increase. In comparison with Wolbers *et al.,* (2010: 889) where he finds out those stavudine-based regimens produces higher CD4 cell count increase than tenofovir-based regimens. Table 4.4.3 shows CD4 cell count increase as an outcome measure of antiretroviral treatment.

Table 4.5.2 The CD4 cell count in cell/mm^3 as an antiretroviral treatment outcome

Antiretroviral regimens	**Number of patients on regimen**	**CD4 cell count increase**			
		Mean and standard deviation	**Number of patients with CD4 increase**	**Maximum**	**Median**
1a	527	239.2 ±238.1	526	1641.0	177.5
1b	437	226.4±184.2	435	1179.0	191.5
1c	109	192.1±194.6	109	847.0	184
1d	89	198.8±169.8	88	675.0	181.5
1s	262	275.0±239.2	259	1106.0	231.0

4.10.2 Cost-effectiveness analysis

The calculations for cost-effectiveness ration is carried out in table 4.5.3, incremental cost-effectiveness is also calculated. Cost-effectiveness ratio for regimen 1a is found to be lower than that of regimen 1b.

Table 4.5.3 Determination of cost-effectiveness ratios between regimen 1a and 1b using average CD4 cell count as an outcome measurement

Regimen	Mean cost	Outcome – mean CD4 increase cell/mm3	Cost-effectiveness ratio
1a	R 2253.8	239.2	R 2253.8/ 239.2= **R9.42 /1cell per mm^3**
1b	R 4621.1	226.4	R 4621.1/ 226.4= **R20.41 /1cell per mm^3**
Incremental cost-effectiveness ratio = R 4621.1– R 2253.8= R2367.30 = **R184.96/1cell per mm^3** 226.4-239.2 (-)12.8			

Interpretation
For regimen 1a to increase CD4 cell count by 1 cell/mm^3, R9.42 is spent, while for regimen 1b to increase CD4 cell count by 1 cell mm^3, a total amount of R20.41 is spent.

Incremental cost-effectiveness is R184.96 meaning that to get additional CD4 cell increase of 1cell/mm^3, this is the amount of money that is supposed to be spent this would enable the patient to receive additional benefit of 1 cell/mm^3. In table 4.4.4 similar calculation are carried out for regimens 1a and 1c, still with cost-effectiveness ratio of 1a being the lowest.

Table 4.5.4 Determination of cost-effectiveness ratios between regimen 1a and 1c using average CD4 cell count as an outcome measurement

Regimen	Mean cost	Outcome – mean CD4 increase cell/mm3	Cost-effectiveness ratio
1a	R 2253.8	239.2	R 2253.80/ 239.2= **R9.42 /1cell per mm^3**
1c	R 2509.9	192.1	R 2509.90/ 192.1= **R13.07 /1cell per mm^3**
Incremental cost-effectiveness ratio = R 2509.90 – R 2253.80= R256.10 = R**4.26/1cell per mm^3** 192.1- 239.2 (-)60.16			

Interpretation
For regimen 1a to increase CD4 cell count by 1 cell/mm^3, **R9.42** is spent, while for regimen 1c to increase CD4 cell count by 1 cell mm^3, **R13.07** is spent. Incremental cost-effectiveness is **R4.26** this means that to get additional benefit of CD4 cell increase of 1cell/mm^3, the amount of R4.26 is supposed to be spent.

Results in table 4.4.5 also show similar calculations between regimens 1b and 1d, with the former showing lower cost-effectiveness ratio.

Table 4.5.5 Determination of cost-effectiveness ratios between regimen 1b and 1d using average CD4 cell count as an outcome measurement

Regimen	Mean cost	Outcome – mean CD4 increase cell/mm3	Cost-effectiveness ratio
1b	R 4621.1	226.4	R 4621.1/ 226.4= **R20.41 /1cell per mm^3**
1d	R 6315.5	198.8	R 6315.50/ 198.8= **R31.77 /1cell per mm^3**
Incremental cost-effectiveness ratio = R 6315.50- 4621.1 / 198.8 – 226.4 = R1694.40 / (-)27.6 = R**61.39/1cell per mm^3**			

Interpretation

For regimen 1b to increase CD4 cell count by 1 cell/mm^3, R20.41 is spent, while for regimen 1d to increase CD4 cell count by 1 cell mm^3, R31.77 is spent. Incremental cost-effectiveness is R61.39. The interpretation of this situation is that to get additional benefit of CD4 cell increase of 1cell/mm^3, Lesotho is expected to spend R61.39.

Results in table 4.5.6 also show similar calculations between regimens 1c and 1d, with the former showing lower cost-effectiveness ratio.

Table 4.5.6 Determination of cost-effectiveness ratios between regimen 1c and 1d using average CD4 cell count as an outcome measurement

Regimen	Mean cost	Outcome – mean CD4 increase cell/mm3	Cost-effectiveness ratio
1c	R 2509.9	192.1	R 2509.90/ 192.1= **R13.07 /1cell per mm^3**
1d	R 6315.5	198.8	R 6315.50/ 198.8= **R31.77 /1cell per mm^3**
Incremental cost-effectiveness ratio = R 6315.50 - R 2509.90 / 198.8 – 192.1 = R 3805.6 / 6.7 = R**568.00/1cell per mm^3**			

Interpretation

In order for regimen 1c to increase CD4 cell count by 1 cell/mm^3, Lesotho spends R13.07, while for regimen 1d to increase CD4 cell count by 1 cell mm^3, R31.77 is spent. Incremental cost-effectiveness is R 568.00. Therefore, to get additional CD4 cell increase of 1cell/mm^3, Lesotho is supposed to spend this amount.

Results in table 4.5.7 show both cost-effectiveness ratio and incremental cost-effectiveness ration between regimens 1a and 1d, with the former showing lower cost-effectiveness ratio.

Table 4.5.7 Determination of cost-effectiveness ratios between regimen 1a and 1d using average CD4 cell count as an outcome measurement

Regimen	Mean cost	Outcome – mean CD4 increase cell/mm3	Cost-effectiveness ratio
1a	R 2253.8	239.2	R 2253.80/ 239.2= **R9.42 /1cell per mm^3**
1d	R 6315.5	198.8	R 6315.50/ 198.8= **R31.77 /1cell per mm^3**
Incremental cost - effectiveness ratio = R 6315.50– R2253.80= R 4061.70 = **R 92.10/1cell per mm^3** 236.2 – 192.1 44.1			

Interpretation

For regimen 1a to increase CD4 cell count by 1 cell/mm^3, R9.42 is spent, while the amount to be spent for regimen 1d to increase CD4 cell count by 1 cell mm^3, R31.77. Incremental cost-effectiveness was R 92.10. This figure shows that to get additional CD4 cell increase of 1cell/mm^3, would be R92.10.

Summary determination of cost-effectiveness ratios

The results show that cost-effectiveness ratio is high for regimen 1d and low for regimen 1a. The regimens containing efavirenz (1b and 1d) have higher cost-effectiveness ratio than those containing nevirapine (1a and 1c). Table 4.5.8 summarises the cost-effectiveness ratios in the commonly used regimens and information comes from the tables 4.5.1, 4.5.2, 4.5.3, 4.5.6 and 4.5.7.

Table 4.5.8 Summary of cost-effectiveness ratio amongst the regimens

Antiretroviral regimens	Cost-effectiveness ratio
1a	R 2253.80/ 239.2 = **R9.42 /1cell per mm^3**
1b	R 4621.1/ 226.4 = **R20.41 /1cell per mm^3**
1c	R 2509.90/ 192.1 = **R13.07 /1cell per mm^3**
1d	R 6315.50/ 198.8 = **R31.77 /1cell per mm^3**

Incremental cost-effectiveness ratio is high between regimens 1c and 1 d and low between 1a and 1c. The information can be used when deciding on which regimens to switch to as less money is needed to gain the same benefit in CD4 cell count increase, as opposed to a more expensive regimen with the same benefit in terms of CD4 cell count increase. Table 4.5.9 shows incremental cost-effectiveness between the antiretroviral regimens.

Table 4.5.9 Determination of incremental cost-effectiveness ratio between average cost of antiretroviral regimens and average CD4 cell count increase

Antiretroviral Regimen	1a	1b	1c	1d
1a		R184.96 /1cell per mm^3	R4.26 /1cell per mm^3	R 92.10 /1cell per mm^3
1b	R184.96 /1cell per mm^3		R61.55 /1cell per mm^3	R61.39 /1cell per mm^3
1c	R4.26 /1cell per mm^3	R61.55 /1cell per mm^3		R 568.00 /1cell per mm^3
1d	R 92.10 /1cell per mm^3	R61.39 /1cell per mm^3	R 568.00 /1cell per mm^3	

R4.26 is spent in order to get additional benefit of 1 cell /mm^3 of incremental cost-effectiveness ratio, this means that between regimen 1a and 1c differences, in terms of benefit and cost are smaller when compared to R568/1cell/mm^3, required between regimen 1c and 1d. This information is useful for financial planning and control purposes. Additional cost must compare with the expected benefits for the patient.

4.10.3 A comparison of the costs of HIV/AIDS treatment, based on body weight increase of the patient as an outcome of antiretroviral treatment.

The study shows that the average body weight increase is higher for regimen 1b and about the same for regimen 1a, 1d and 1s. The least average body weight increase is observed to occur for regimen 1c. Table 4.6.1 shows the average body weight increase for different regimens.

Table 4.6.1 Average body weight increase in kg according to different regimens

Antiretroviral regimens	Number of patients in the regimen	Body weight increase in kg		
		Mean and standard deviation	Maximum	Median
1a	527	5.78±8.04	48	5
1b	437	6.17±6.90	30	5
1c	109	2.53±8.88	38	2
1d	89	5.31±7.53	32	4
1s	262	5.28±8.00	35	4

Table 4.6.2 demonstrates the cost-effectiveness ratio for regimens 1a and 1b using body weight against cost. Regimen 1a has lower cost-effectiveness ratio.

Table 4.6.2 Cost-effectiveness calculation using average body weight increase as an outcome of treatment in regimens 1a and 1b

Regimen	average cost	Outcome – average body weight increase kg	Cost - effectiveness ratio
1a	R 2253.8	5.78	R 2253.8/ 5.78= **R 389.93 /1kg**
1b	R 4621.1	6.17	R 4621.1/ 6.17= **R 748.96 /1 kg**

Incremental cost-effectiveness ratio
= R 4621.1– R 2253.8= R2367.30 = R6070.00/ 1kg body weight
6.17- 5.78 (-)0.39

Interpretation

R389.93 is spent for regimen 1a to increase body weight by 1 kg, while for regimen 1d to increase body weight by 1 kg, R748.96 is spent. Incremental cost-effectiveness was R6070 / 1kg. The interpretation made from this situation is that to get benefit of additional body weight increase of 1 kg, R6070.00 is supposed to be spent.

Table 4.6.3 shows the cost-effectiveness ratio for regimens 1a and 1c using body weight against cost. It points out that regimen 1a has lower cost-effectiveness ratio.

Table 4.6.3 Cost-effectiveness calculation using average body weight increase as an outcome of treatment in regimens 1a and 1c

Regimen	Mean cost	Outcome – mean body weight increase kg	Cost-effectiveness ratio
1a	R 2253.8	5.78	R 2253.8/ 5.78**= 389.93 /1kg**
1c	R 2509.9	2.53	R 2509.9/2.53 **= 992.06 /1 kg**

Incremental cost-effectiveness ratio
= R 2509.9 – R 2253.8= R256.1 = **R78.80 / 1kg** body weight
2.53- 5.78 (-)3.25

Interpretation

For regimen 1a to increase body weight by 1 kg, Lesotho has to spend R389.93. It spends R992.06 for regimen 1c to increase body weight by 1 kg. Incremental cost-effectiveness is R78.80/1kg. Therefore, to get additional body weight increase of 1kg, the country has to spend

R 78.80.

Table 4.6.4 shows the cost-effectiveness ratio for regimens 1b and 1d using body weight against cost. It demonstrates that regimen 1b has lower cost-effectiveness ratio.

Table 4.6.4 Cost-effectiveness calculation using average body weight increase as an outcome of treatment in regimens 1b and 1d

Regimen	Mean cost	Outcome – mean body weight increase kg	Cost - effectiveness ratio
1b	R 4621.1	6.17	R 4621.1/ 6.17= **748.96 /1 kg**
1d	R 6315.5	5.31	R 6315.5/5.32 = **1187.12 /1 kg**

Incremental cost-effectiveness ratio
= $\frac{\text{R 6315.5- 4621.1}}{\text{5.31-6.17}} = \frac{1694.4}{(-)\ 0.86}$ = **R1693.54 / 1kg** body weight

Interpretation

For regimen 1a to increase body weight by 1 kg, R748.96 is spent, and R1187.12 is spent for regimen 1d to increase body weight by 1 kg. Incremental cost-effectiveness is R1693.54/1kg. This means that to get additional benefit of body weight increase of 1 kg, R1693.54 is spent.

Table 4.6.5 demonstrates the cost-effectiveness ratio for regimens 1a and 1d using body weight against cost, it shows that regimen 1a has lower cost-effectiveness ratio.

Table 4.6.5 Cost-effectiveness calculation using average body weight increase as an outcome of treatment in regimens 1a and 1d

Regimen	Mean cost	Outcome – mean body weight increase kg	Cost - effectiveness ratio
1a	R 2253.8	5.78	R 2253.8/ 5.78= **389.93 /1kg**
1d	R 6315.5	5.31	R 6315.5/5.32 = **1187.12 /1 kg**

Incremental cost-effectiveness ratio
= $\frac{\text{R 6315.5 – R 2253.8}}{\text{5.31 – 5.78}} = \frac{\text{R4061.4}}{(-)0.47}$ = **R 8 641.28 / 1kg** body weight

Interpretation

For regimen 1a to increase body weight by 1 kg, R389.93 is spent. For regimen 1d to increase body weight by 1 kg, R1187.12 is spent. Incremental cost-effectiveness is R 8 641.28/1kg. This

means that to get additional benefit of body weight increase of 1 kg, R8 641.28 supposed to be spent.

Table 4.6.6 shows results of the cost-effectiveness ratio for regimen 1c and 1d, and it is observed that regimen 1c has lower cost-effectiveness ratio, and the incremental cost-effectiveness ratio is R1 463.69 for 1 kg of body weight to be gained as an additional benefit.

Table 4.6.6 Cost-effectiveness calculation using average body weight increase as an outcome of treatment in regimens 1c and 1d

Regimen	Mean cost	Outcome – mean body weight increase kg	Cost effectiveness ratio
1c	R 2509.9	2.53	R 2509.9/2.53 = **992.06 /1 kg**
1d	R 6315.5	5.31	R 6315.5/5.32 = **1187.12 /1 kg**
Incremental cost-effectiveness ratio = $\frac{\text{R 6315.5- 2509.9}}{\text{5.13 -2.53}} = \frac{\text{R 3805.6}}{\text{2.6}}$ = **R1463.69 / 1kg** body weight			

Interpretation

For regimen 1c to increase body weight by 1 kg, R992.06 is spent, while for regimen 1d to increase body weight by 1 kg, R1187.12 is spent. Incremental cost-effectiveness is R1 463.69/ 1kg. For a benefit of additional body weight increase of 1 kg, R1463.69 is spent.

Table 4.6.7 shows the cost-effectiveness ratio between regimens 1b and 1c, results show that regimen 1b has lower cost-effectiveness ratio with incremental cost-effectiveness ratio of R580.00 for additional benefit of 1 kg to be gained.

Table 4.6.7 Cost-effectiveness calculation using average body weight increase as an outcome of treatment in regimens 1b and 1c

Regimen	Mean cost	Outcome – mean body weight increase kg	Cost-effectiveness ratio
1b	R 4621.1	6.17	R 4621.1/ 6.17= **748.96 /1 kg**
1c	R 2509.9	2.53	R 2509.9/2.53 = **992.06 /1 kg**
Incremental cost-effectiveness ratio = $\frac{\text{R 4621.1- 2 509.9}}{\text{6.17 – 2.53}} = \frac{\text{R 2 111.2}}{\text{3.64}}$ = **R580.00 / 1kg** body weight			

In summary, it costs the clinics more to increase body weight of the patient by 1kg using regimens containing zidovudine, and less for regimens containing stavudine. The differences are due to the probable fact that stavudine has metabolic side effects that lead to lipodystrophy. However, body weight increase is not only directly due to antiretroviral treatment. Dietary supplement that are provided, opportunistic infection reduction, HIV/AIDS patients‟ ability to eat properly and other reasons also result in body weight increase. The major aim of antiretroviral treatment is to increase patients‟ survival rate and to reduce morbidity and mortality.

Table 4.6.8 shows the summary of the cost-effectiveness ratios between the regimens with regimen 1d having the highest ratio and 1a has the lowest. Information comes from tables 4.6.2, 4.6.3, 4.6.4, 4.6.5, 4.6.6, 4.6.7.

Table 4.6.8 Summary of cost-effectiveness ratios for regimens where treatment was not switched according to body weight increase.

Antiretroviral regimens	Cost-effectiveness ratio
1a	R 2253.8/ 5.78**= 389.93 /1kg**
1b	R 4621.1/ 6.17**= 748.96 /1 kg**
1c	R 2509.9/2.53 **= 992.06 /1 kg**
1d	R 6315.5/5.32 **= 1187.12 /1 kg**

Comparison between the use of regimen 1a and 1c shows the lowest incremental cost-effectiveness ratio while the ratio is the highest between 1a and 1d. However the cost of antiretroviral regimen costs for body weight increase seems to be too high. A lot of money is required to increase body weight by 1 kg. The positive fact is that antiretroviral drug combination does not increase body weight. If it did, body weight would increase out of proportion because they are a lifetime treatment.

Table 4.6.9 demonstrates the incremental cost-effectiveness ratio between the regimens, with 1a and 1d having the largest incremental cost effectiveness ratio. Incremental cost-effectiveness ratio is found to be the smallest between regimens 1a and 1c. Information comes from tables 4.6.2, 4.6.3, 4.6.4, 4.6.5, 4.6.6, 4.6.7.

Table 4.6.9 Incremental cost-effectiveness ratio between mean cost of antiretroviral regimens and mean body weight increase

Antiretroviral Regimen	1a	1b	1c	1d
1a		R6070.00 / 1kg	R78.80 / 1kg	R 8 641.28 / 1kg
1b	R6070.00 / 1kg		R580.00 / 1kg	R1693.54 / 1kg
1c	R78.80 / 1kg	R580.00 / 1kg		R1463.69 / 1kg
1d	R 8641.28 / 1kg	R1693.54 / 1kg	R1463.69 / 1kg	

The incremental cost-effectiveness ratio of cost between various regimens means that switching of regimens from 1a to 1d must be carefully considered as the benefit of increasing body weight by 1 kg costs the highest which is R8 641.28, whereas switching between regimens 1a and 1c requires the least amount (R 78.80) to raise body weight by 1kg.

4.10.4 Comparison of cost-effectiveness ratio between the antiretroviral regimens and treatment outcome which are CD4 cell count and body weight

It is deduced from table 4.6.10 that when regimens cost is compared with treatment outcome of CD4 cell count and body weight, the cost effectiveness ratios for CD4 cell count increase are much lower that the cost-effectiveness ratios for body weight increase. Information comes from tables 4.5.8 and 4.6.8.

Table 4.6.10 Comparison of cost-effectiveness ratio between the antiretroviral regimens and treatment outcome which are CD4 cell count and body weight

Antiretroviral regimens	Cost-effectiveness ratio using CD4 cell count as outcome	Cost-effectiveness ratio using body weight as outcome
1a	R 2253.80/ 239.2 = **R9.42 /1cell per mm^3**	R 2253.8/ 5.78= **R 389.93 /1kg**
1b	R 4621.1/ 226.4 = **R20.41 /1cell per mm^3**	R 4621.1/ 6.17= R **748.96 /1 kg**
1c	R 2509.90/ 192.1 = **R13.07 /1cell per mm^3**	R 2509.9/2.53 = R **992.06 /1 kg**
1d	R 6315.50/ 198.8 = **R31.77 /1cell per mm^3**	R 6315.5/5.32 = R **1 187.12 /1 kg**

Assessment of cost–effectiveness of antiretroviral regimens used in the treatment of HIV/AIDS shows that stavudine-based regimens cost less than zidovudine based. A higher CD4 cell count increase is a response for antiretroviral treatment. The stavudine-based regimen is given to the majority of patients and results in cost saving, but a high benefit for HIV/AIDS patients. This information may be used for the decision to continue use of stavudine in Lesotho. The cost of

drugs is deciding factor for the CD4 cell count increase and for the cost-effectiveness ratio. Zidovudine-based regimens especially one with Nevirapine, also have a lower cost effectiveness ratio. Cost-effectiveness ratios for both stavudine and zidovudine-based regimens with efavirenz as well as the cost/prevalence index, and *d* value are higher than those with nevirapine,. This information may be used in major public health decisions on antiretroviral regimens that the country decides to use, bearing in mind that Lesotho has the third highest HIV/AIDS prevalence and is one of the least developed countries. It depends heavily on foreign assistance, especially for HIV/AIDS management.

4.11 Chapter summary

The total number of HIV/AIDS patients who receive antiretroviral treatment in the study was 1424, of which 62 percent are females and 38 percent. All of them are between the ages of 19 and 70 years with the majority (75 percent) of them between the ages of 25 and 45 years. The study finds that almost half of the patients are employed.

About 68 percent of the patients are on stavidine-based regimens with 31 percent of those on efavirenz. The rest receive nevirapine. About 14 percent of the study sample receives zidovudine-based regimens with efavirenz for half of them. The remaining half receives nevirapine. Antiretroviral treatment started as far back as 2004. However, the majority of the patients were initiated on HAART between 2006 and 2007. Some patients switched to other regimens due to the initial lack of response or toxicities from original antiretroviral drugs in the regimens.

The majority of the patients do not experience opportunistic infection because they are on opportunistic infections prophylaxis. About 10 percent of the study sample is treated for TB. The 71 percent of patients on stavudine-based regimens experience antiretroviral side effects. On the other hand 84 percent of patients on zidovudine-based regimens experience side effects, although only a fewer of them are actually exposed to zidovudine.

The cost of antiretroviral regimen is lower for stavudine-based regimen than that of zidovudine - based regimen. There are more stavudine regimens containing efavirenz than those containing nevirapine. The same applies for zidovudine-based regimen. Switched regimens are more costly because they contained second line antiretroviral drugs. The latter are more expensive.

Assessing the response of patients to antiretroviral treatment regimens shows a better response, in terms of both CD4 cell count increase as well as in terms of body weight increase. These positive effects are observed from the stavudine-based regimens, more than from the zidovudine-based regimens.

In terms of cost-effectiveness, stavudine-based regimens with nevirapine (1a) show the lowest cost-effectiveness ratio of R9.42 /1cell per mm^3, while zidovudine-based regimens with efavirenz (1d) show the highest R31.77 /1cell per mm^3.

CHAPTER 5

Conclusions and recommendations of the study

In this chapter major conclusions are drawn, based on the specific objectives of the study, and recommendations are made in line with the findings and conclusions.

5.1.1 Main objective

The main objective of the study was to assess the cost of antiretroviral medication treatments. This is achieved by specifically assessing the cost of antiretroviral regimens, antiretroviral drug side effects, the cost of drugs used for prophylaxis and treatment of opportunistic infections as well as the cost of monitoring laboratory tests and dietary supplements.

5.1.2 Specific literature objectives

Chapter 2 of the study discussed all the specific literature objectives, and all of them are met in the shown paragraphs.

They were as follows:

- To define origin of HIV/AIDS, its diagnosis, and goals of treatment (see chapter 2, par. 2.1.1, 2.1.3 and 2.2.2).
- To classify and briefly describe antiretroviral drugs (see chapter 2, par. 2.2.3, 2.2.3.1, 2.2.3.2, and 2.2.3.3).
- To familiarize the researcher with the local antiretroviral treatment guidelines in order to assess whether antiretroviral prescribing was in accordance with the guidelines (see chapter 2 par. 2.2.5, 2.2.6, 2.2.7, 2.2.7.1, 2.2.7.2, 2.2.7.3, 2.2.7.3 and 2.2.7.6).
- To identify antiretroviral side effects and their treatment (see chapter 2 par. 2.2.10 and 2.2.11).
- To assess hospitalization of HIV/AIDS patients (see chapter 2 par. 2.2.13.)
- To define opportunistic infections, their prophylaxis and treatment (see chapter 2 par. 2.2.14, 2.2.14.1 and 2.2.14.2).
- To determine the reasons for switching antiretroviral drugs in a regimen (see chapter 2, par. 2.2.9).
- To critically evaluate CD4 cell count and its role in HIV and evaluate CD4 cell count as an outcome of HIV/AIDS treatment (see chapter 2, par. 2.3.1).

- To evaluate implications of body weight in HIV/AIDS and its role in disease development and evaluate body weight as an outcome of HIV/AIDS treatment (see chapter 2, par. 2.3.2).
- To evaluate studies that determined the cost of HIV/AIDS treatment in terms of drugs and related monitoring laboratory tests (see chapter 2, par. 2.6).
- To evaluate studies that assessed cost effectiveness of antiretroviral regimen (see chapter 2 par. 2.6.1).

5.1.3 Specific research objectives

Specific research objectives of the empirical study were divided into antiretroviral treatment, treatment outcome, treatment cost and economic evaluation

The study had the following objectives concerning the treatment of HIV/AIDS:

- To determine if the antiretroviral prescribing followed National Antiretroviral Treatment Guidelines of Lesotho (2004).
- To assess retention of antiretroviral treatment to first line treatment.
- To assess if switching of antiretroviral therapy from one regimen to another followed recommended policy by the National Antiretroviral Treatment Guidelines of Lesotho (2004).
- To investigate the prescribing patterns of medicines used for the treatment of opportunistic infection and if that was according to National Antiretroviral Treatment Guidelines (2004).
- To determine if side effects of antiretroviral were treated according to National Antiretroviral Treatment Guidelines of Lesotho (2004).

Cost of antiretroviral treatment

The study had the following objectives concerning the cost of antiretroviral treatment:

- To compare the medicine treatment costs of different HAART regimens.
- To assess impact of additional cost imposed by associated monitoring laboratory tests, dietary supplements as well as treatment of side effects at different ART clinics.
- To assess cost implication of antiretroviral regimen switching on overall cost of HIV/AIDS treatment.
- To compare prophylaxis and treatment cost of opportunistic infections in different ART clinics.

- To compare if second line antiretroviral treatment cost implied with first line treatment.
- To assess total cost of HIV/AIDS treatment in private and public clinics.

Economic evaluation of antiretroviral

The study had the following objectives concerning the economic evaluation of antiretroviral treatment:

- To determine cost to effectiveness ratio between two antiretroviral regimens using CD4 cell count as the main measure of outcome.
- To determine cost to effectiveness ratio between two antiretroviral regimens using body weight increase as the subsidiary measure of outcome.
- To calculate the incremental cost effectiveness ratio between the antiretroviral regimens.

5.2 Treatment of HIV/AIDS

Objective: One objective of the study was to determine the antiretroviral prescribing patterns, and whether they followed the National Antiretroviral Treatment Guidelines of Lesotho (2004 & 2007)

Conclusion

The study concludes that prescribing of antiretroviral drugs followed Antiretroviral Treatment Guidelines of Lesotho both 2004 and 2007. Therefore it was concluded that both public and private ART clinics follow the guidelines provided for prescribing. Following treatment guidelines is a good practice and that also affects the cost containment as well as incidence of antiretroviral medicines resistance. Not only that but also the reliable supply of medicines as medicines remain the same for a long time.

Objective: To assess retention of treatment to first line treatment

Conclusion

The study concludes that most HIV/AIDS patients (81.5 percent) are retained in their original antiretroviral regimen in the Maseru ART clinics. Retention of the same regimen also affects reliable supply of medicines as they do not often change. This will help with quantification in order to have enough quantities of medicines at all times in the clinics. Particularly because

patients on antiretroviral are not supposed to run out of medicines, more so, the switching of antiretroviral regimen cannot be a result of out of stock of a certain medicine in the triple therapy.

Objective: To assess whether the switching of antiretroviral therapy from one regimen to another follows the recommended switching as outlined in the National Antiretroviral Treatment Guidelines of Lesotho (2004).

Conclusion

It is concluded that antiretroviral switching is carried out also in accordance to antiretroviral treatment guidelines. Switching of antiretroviral medicines is always a decision that needs to be taken from time to time, using scientific, medical reasons and patient response to treatment. The purpose of treatment guidelines is to guide all activities relating to HIV/AIDS treatment and that is why switching when following guidelines becomes appropriate. Therefore, appropriate and available medicines are prescribed.

Objective: To identify the prescribing patterns of opportunistic infection treatment and prophylaxis and whether that was according to National Antiretroviral Treatment Guidelines (2004).

Conclusion

Study concludes that (see par. 4.2.5.3) prescribing patterns for treatment and prophylaxis of opportunistic infections followed antiretroviral treatment guidelines (2004). Opportunistic infections are treated as they are treated in other counties as indicated in the literature. Their treatment is however, not stipulated in National Antiretroviral Treatment Guidelines 2004. This gives the prescribers in the ART clinics freedom to prescribe according to other sources of literature as well as liberty to prescribe non- generic medicines. As it is observed from the results (see table 4.3.10) that affected the cost of treating opportunistic infections. This increases the total cost of treatment of HIV/AIDS and may affect the financial planning of the provider of services. This calls for review of the guidelines.

Objective: To determine whether antiretroviral side effect are treated according to the National Antiretroviral Treatment Guidelines of Lesotho.

Conclusion

It is concluded that the treatment of antiretroviral side effects (see par. 4.2.9), opportunistic infections treatment and prophylactic drugs follows the norm. In the cases where the treatment does not follow the Lesotho antiretroviral treatment guidelines, it does follow some form of reference material such as South African Medicines Formulary or British National formulary. However, this leads to unnecessary freedom in prescribing as more expensive medicines are chosen instead of what the guidelines says. This increases to cost of treating HIV/AIDS in the clinics as observed in table 4.3.10. However this was later corrected in 2007 and 2010 antiretroviral treatment guidelines of Lesotho.

5.3 Outcome of HIV/AIDS treatment

This section will draw conclusion mainly on the outcome of antiretroviral treatment.

Objective: To determine CD4 cell count changes brought about by antiretroviral therapy.

Conclusion

The study concludes that the average overall CD4 cell count increase is 235.70 cell/mm^3 ± 216.93 in all the ART clinics in the study (see par.4.7.3.1). This is an important outcome in the treatment of HIV/AIDS, as it shows disease progression or treatment success. It may also indicate when treatment needs changing. It indicates immunologic treatment failure or treatment success that leads to retention on the same regimen for prolonged periods as well as cost containment and savings. Cost increase that emanates from switching antiretroviral regimens to second or third line which has higher cost implications can be avoided. It is mentioned that higher CD4 cell count enables the body to fight against opportunistic infections and related cancers, hence increased wellness of the patient.

Objective: To assess whether there were any average body weight changes brought about by treatment provided.

Conclusion

Average weight gain is 5.53kg ± 7.78 in all the ART clinics in the study (see par. 4.7.3.3). Wasting is one of major the causes of mortality in HIV/AIDS, and most patients come to the clinics severely under-weight. However, with antiretroviral treatment most patients gain weight

as an indirect measure of treatment success. Gaining of body weight forms an important part in the management of HIV/AIDS. Patients themselves gain confidence on the treatment when they gain weight especially those with severe wasting initially.

Objective: To identify incidences of antiretroviral side effects and how they impact on overall treatment of HIV/AIDS.

Conclusion

The study concludes that there is generally high incidence of antiretroviral side effects (see par. 4.7.6.1). The impact of antiretroviral side effects treatment leads to patients being retained on the same antiretroviral regimen. It also improves the comfort of care for the patient. The outcome of treatment of antiretroviral side effects improves patients‟ adherence to medicines as it is found out that antiretroviral side effects may impact on medicine taking behavior of the patient. The antiretroviral side effects can be a predictor of switching of a certain drug in the regimen depending on its severity.

5.4 Cost of antiretroviral treatment

In this section conclusion will be drawn from cost of antiretroviral treatment.

Objective: To compare the medicine cost of different HAART regimens.

Conclusion

Several assessment instruments were used, namely, cost/prevalence index to assess how expensive the regimen is and the *d*-value to compare differences in cost between the two regimens. From paragraph 4.7.6.1 it is concluded that regimens 1b, 1d which contain efavirenz and 1s are relatively more expensive than regimens 1a and 1c which contain nevirapine. Regimen 1s includes second line drugs which are more costly. The use of the *d*-value shows practical differences in the cost of regimens between regimens 1b and 1a, 1d and 1c, 1d and 1a. Their *d*-value is above 0.8. There are also nearly practical differences between regimens 1c and 1b on one hand, and 1s and 1a on the other hand. There is no significant difference between the cost of other regimens. The situation leads to the conclusion that regimens that include efavirenz (1b and1d) are more expensive as well as 1s that includes the cost of second line drugs. This information may be used when a new ART clinic is opened to guide prescribing

of antiretroviral treatemnt if cost is a concern. The study futher concludes that the decision to start on any regimen depends heavily on HIV/AIDS patient, including the patients medical history, stage of the disease, other diseases present, as well as other drugs that the patient is taking.

Objective: To assess the impact of additional cost imposed by associated monitoring laboratory tests, dietary supplements as well as treatment of side effects at different ART clinics.

Conclusion

Taking the cost of the other drugs (that is medicines for the treatment of antiretroviral drugs side effects, opportunistic infections prophylaxis and treatment) dietary supplements and laboratory tests into account**,** it is concluded that additional cost adds up to 16 percent of the total cost of the treatment of HIV/AIDS patients. The largest cost comes from laboratory test. The second largest cost comes from medicines used for the treatment of opportunistic infections. Some of the laboratory tests are more costly than stavudine-based regimen with nevirapine (1a) in one year (see figure 4.6.2). The study shows the difference in the treatment of side-effect that leads to cost increase for the management of HIV between the clinics.

Objective: To assess the cost implication of ART regimen-switching on the cost of HIV/AIDS treatment.

Conclusion

The study concludes that switching of antiretroviral regimen impacts on the cost of treatment both positively and negatively, depending on which regimen the patient is put on. Switching of regimens moves patients into cheaper or more expensive antiretroviral regimens. However, in Lesotho switching is not based on cost, but on antiretroviral toxicities, pregnancy status, TB and antiretroviral drug interactions and other reasons (See par. 4.2.4 and 4.6.2.1).

Switching to cheaper antiretroviral regimens leads to cost saving in the management of HIV, and the saved money can be used for HIV/AIDS prevention efforts of the country, or for increased access to HIV/AIDS treatment. On the other hand switching to more costly antiretroviral regimens increases the cost of treatment of HIV/AIDS and there is no saving of monetary resources. This may lead to budgets not covering the whole population on treatment.

Objective: to compare prophylaxis and treatment cost of opportunistic infections in different ART clinics.

Conclusion:

The conclusions are drawn from both prophylaxis and treatment of opportunistic infections.

Opportunistic infection treatment

Treatment of opportunistic infections contributes 0.02 percent of the total cost of treating HIV/AIDS patients; it is because incidence of opportunistic infection is relatively low (see figure 4.6.2). This piece of information is relevant for budgeting purposes. It means that low budget for treatment of opportunistic infections can be made, and this is cost saving and the money can be channeled for other important issues in the management of HIV/AIDS, such as prevention efforts. Between the clinics it is clear that use of generic medicines lowers the cost further, therefore, use of generic medicines is highly recommended for the treatment of opportunistic infections. Some medicines that are used for treatment of opportunistic infections are donated, therefore proper budgeting for them is still necessary to avoid expiry.

Opportunistic infection prophylaxis

The study concludes that more resources are spent on prophylaxis of opportunistic infection in the public clinics than in private clinics. The amount of money spent is not proportional to the number of patients on prophylaxis. St. Joseph‟s and Qoaling ART clinics have fewer patients, who are on prophylaxis for a prolonged period (cost/prevalence index of 2.8 and 1.9), (see par. 4.7.6.2 and Table 4.3.3.

Fewer resources are used in both Senkatana and Khanya ART clinics yet they have higher patient population. This means that the clinics use prophylaxis for as long as it is needed, and stop when CD4 cell count reaches 200cells/mm^3. WHO antiretroviral treatment guidelines recommend that cotrimoxazole prophylaxis, when the patient reaches CD4 cell count of 200 cell/mm^3 should be discontinued. However Goldie, *et al.,* (2002: 921) observes that stopping of prophylaxis is more cost effective if carried out at the first observed CD4 cell count of above 300 cell/mm^3.

Objective: To identify whether the implied second line antiretroviral cost is more than that of first line treatment.

Conclusion

The study concludes that second line antiretroviral regimens cost more than the first line regimens. However, the conclusion may need to be confirmed through a further study because fewer patients are on second line (1s) as most switching of antiretroviral regimens is still within first line regimens (82 percent). However, second line regimens are found to be more costly than first line regimens when theoretical costs are used (see figure 4.6.1). Putting more patients on second line regimens can increase the cost tremendously to a point where the government of Lesotho may not afford to treat HIV/AIDS anymore.

Objective: To assess the total cost of HIV treatment in private and public clinics.

Conclusion

It is concluded that some antiretroviral regimens cost more than others. Regimens that contain efavirenz cost more than regimens containing nevirapine.

It is also concluded that first line regimens cost less than second line antiretroviral. Additional to antiretroviral regimen costs, is the cost of treating antiretroviral drugs side effects; the cost of opportunistic infections treatment and prophylaxis. These costs increase the total cost of antiretroviral treatment significantly.

The annual laboratory tests cost is higher than some of the antiretroviral regimens" cost. The cost of laboratory tests is more in the public clinics because more tests are carried out, whereas they cost less in the private clinics as fewer tests are carried out. The dietary supplements cost increase is insignificant. Some private clinics prescribe more costly dietary supplements while public clinics prescribe standard and relatively low cost dietary supplements. Some public clinics spend more resources on prophylaxis than other (see par.4.7.4.1 and table 4.2.5).

5.5 Economic evaluation

Economic evaluation is carried out to assess cost-effectiveness between the regimens

Objective:

- To determine cost to effectiveness ratio between two antiretroviral regimens using CD4 cell count increase as the main measure of outcome.

Conclusion

The study concludes that when CD4 cell count increase is used as an outcome measure regimen 1a is the most cost-effective, followed by 1b which are the stavudine-based regimens. This means that it cost less to gain more benefit from the antiretroviral treatment.

Objective

- To determine cost to effectiveness ratio between two antiretroviral regimens using body weight increase as the subsidiary measure of outcome

Conclusion

The study finds regimen 1a and 1b to be more cost-effective than regimens 1c and 1d when body weight increase is an outcome of antiretroviral treatment.

Objective

- To calculate the incremental cost effectiveness ratio between the antiretroviral regimens

Conclusion

Additional costs must produce additional benefits in the management of HIV/AIDS, the study finds moving patients from regimen1a to 1c requires R4.26 to be spent in order to get additional benefit of 1 cell /mm^3 of incremental cost-effectiveness ratio, in terms of benefit and cost are smaller when compared to R568/1cell/mm^3, that is required to move patients from regimen 1c to 1d for the same effectiveness of 1 cell/mm^3. This information is useful for financial planning and control purposes. Switching of regimens can in some way be based on the cost of alternative regimens in order to minimise unnecessary spending of financial resources.

5.6 Recommendations of the study

The study makes the following recommendations

5.6.1 Treatment of HIV/AIDS

- Similar research should be carried out based on the new World Health Organisation antiretroviral treatment guidelines 2010.

- Review of local antiretroviral treatment guidelines for better prescribing guidance.

- Use of generic medicines for treatment of opportunistic infections and antiretroviral side effects is recommended.

- Prolonged prophylaxis of opportunistic infections must be discouraged as unnecessary cost is spent on cotrimoxazole prophylaxis.

- When initiating antiretroviral treatment to patients with wasting syndrome regimen 1d should be considered.

5.6.2 Outcome of treatment of HIV/AIDS

- CD4 cell count, a routine laboratory test should be used as a guide of how many people need certain drugs for prophylaxis for country-wide budgeting. For example the overall patients CD4 cell count can be obtained from the HIV/AIDS population to see how many patients whose CD4 cell count is below 200cells/mm^3. The next step could be to draw up a budget for medicines used for commonly occurring opportunistic infections, and for medicines used for opportunistic infection prophylaxis. In this way budgeting would be more. In addition, stock-outs and expiration of medicines intended for opportunistic infection would be avoided.
- Body weight could also be used to determine the number of patients who require dietary supplements. This would lead to accurate budgeting and avoidance of stock-out. Expiration of dietary supplements would also be avoided.

5.6.3 Other recommendations

- It is recommended that Lesotho computerize the medical records. This is observed as a serious limitation of the studies (similar to the present one) carried out in Lesotho.

- It is further recommended that ART clinics be supervised so that they may adhere to antiretroviral treatment guidelines and receive advice on when to start and stop prophylaxis

5.6.4 Recommendations for further research

- It is recommended that a prospective cohort study be carried out to assess the cost of antiretroviral regimens and prophylaxis and treatment of opportunistic infections in order to get a comparative picture of the cost of HIV treatment.

- A pharmacovigilance study should be carried out to obtain further details about adverse effects of antiretroviral drugs and appropriate prescribing patterns be obtained.

5.7 Chapter summary

All the research objectives of the study are met. Literature objectives are met in chapter two of the study while empirical objectives are met in chapter five. Study conclusions are drawn in line with empirical research objectives. The important conclusions related to the cost of antiretroviral regimens and associated costs are that first line regimens containing stavudine are relatively less expensive than those containing zidovudine. CD4 cell count increase is higher with the former type of treatment. The same can be said about first line antiretroviral combinations containing nevirapine. They are less expensive than those containing efavirenz. The former increase CD4 cell count more. Recommendations of the study are further made.

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APENDICES

In appendices, information that helps clarify or add to existing information in the main chapters is further described and tables to provide additional information is laid out according to how chapters are formulated. Therefore naming of the tables and subtopics follows the format of the chapters where appendix 1 is information in chapter 1, and appendix 2 is additional information for chapter 2 and so on and so forth.

Appendix A

1. Letter of permission form the Ministry of Health and Social Welfare Ethics Committee.

Appendix B Clinical staging by WHO

World Health Organization Clinical Staging
Clinical Stage 1 1. Acute retroviral infection 2. Asymptomatic 3. Persistent generalized lymphadenopathy
Clinical Stage 2 1. Unintentional weight loss –(less than 10% of body weight) 2. Minor mucocutaneous manifestations, prurigo, fungal nail infections, recurrent oral ulcerations, angularcheilitis. 3. Herpes zoster 4. Recurrent upper respiratory tract infections
Clinical stage 3 1. Weight loss (more than 10% body weight) 2. Unexplained diarrhoea > 1 month 3. Unexplained prolonged fever - > 1 month 4. Oral candidiasis

5. Vulvo vaginitis candidiasis, chronic >1 month, poorly responding to treatment
6. Oral hairy Leukoplakia
7. Pulmonary tuberculosis
8. Severe bacterial infection e.g pneumonia

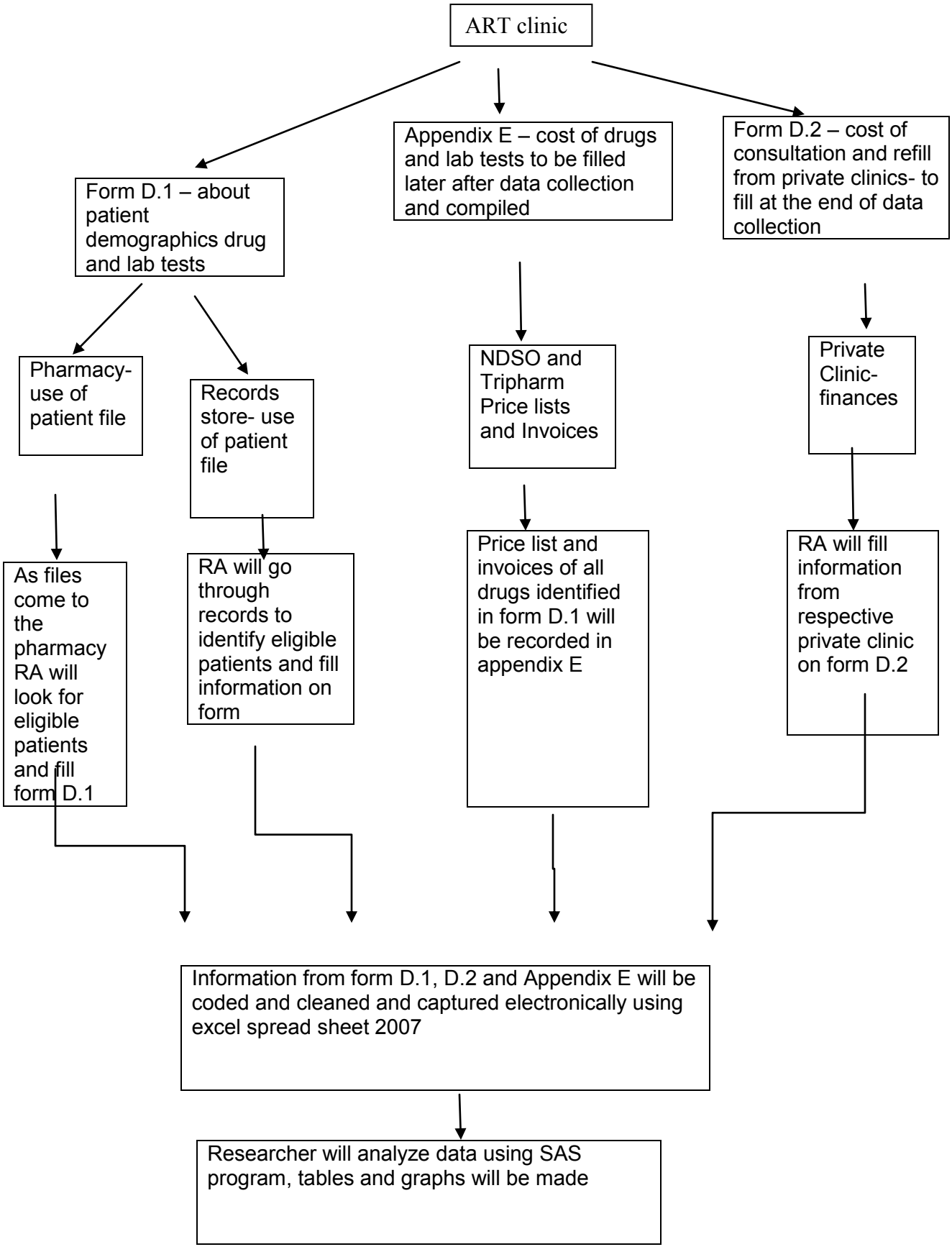
Clinical stage 4

1. HIV wasting syndrome
2. Pneumocystis Cariini pneumonia
3. Toxoplasmosis
4. Cryptosporidiosis with diarrhoea >1 month
5. Cryptosporidiosis extra-pulmonary
6. Cytomegalovirus
7. Herpes simplex virus infection, muco-cuteneous> 1 month
8. Progressive multifocal leuko-encephalopathy
9. Any disseminated endemic mycosis
10. Oesophageal candidiasis
11. Extra-pulmonary TB
12. Lymphoma
13. Kaposi Sarcoma
14. HIV encephalopathy
15. Invasive cervical carcinoma

Appendix C Clinics descriptions including type, functions and population enrolled and initiated on ART until August 31 2008

In Maseru – total no of patients enrolled is 57 210 and on ART is 24 218								
Item	Senkatana ART Centre	Healthy Lifestyle and Diabetes Centre	Khanya medical centre	Medicare Family Clinic	Thusong St. Joseph Hospital	Qoaling Filter clinic	Bophelong Adult clinic	Mabote Filter Clinic
Date opened	2004	2001	February 2005	March 2004	August 2005	June 2006	January 2005	June 2006
Type	Government	Private	Private	Private	CHAL	Government	Government	Government
Number of patients enrolled	9016	995	708	404	1500	1217	5032	667
Number of Patients on ART	2816	904	500	220	550	289	1839	168
Main Function	ART	ART	ART	ART	ART	ART	ART	ART
Other Functions	-	Diabetes and other chronic illnesses	Treatment of other diseases	Treatment of other diseases	-	Treatment of other diseases	-	Treatment of other disease
Vicinity	Attached to MDR-TB Hospital	Next to the bus-stop	Next to bus-stop	In the city centre	Attached to St. Joseph hospital Roma	Filter clinic for QE II Hospital	Attached to QE II hospital	Filter clinic for QE II Hospital
Total no of patients enrolled is – 19539, and on ART is – 6 476								

Appendix D shows a pictogram of how data was collected


ART clinic
Form D.1 – about patient demographics drug and lab tests
Appendix E – cost of drugs and lab tests to be filled later after data collection and compiled
Form D.2 – cost of consultation and refill from private clinics- to fill at the end of data collection
Pharmacy- use of patient file
Records store- use of patient file
NDSO and Tripharm Price lists and Invoices
Private Clinic- finances
As files come to the pharmacy RA will look for eligible patients and fill form D.1
RA will go through records to identify eligible patients and fill information on form
Price list and invoices of all drugs identified in form D.1 will be recorded in appendix E
RA will fill information from respective private clinic on form D.2
Information from form D.1, D.2 and Appendix E will be coded and cleaned and captured electronically using excel spread sheet 2007
Researcher will analyze data using SAS program, tables and graphs will be made

Appendix D.1 data collection form for individual patients in the ART clinics

Study title: A review of antiretroviral medicines cost in primary health care clinics in Lesotho

Name of clinic _____ patient number _____ Age ___ gender ___ occupation _____ Date of first visit _____1st CD4 Count _____Date of first rapid test _____ ARV initiation date: _____

Pre-HAART drugs (include dates and drugs given)

_____
_____
_____
_____
_____

Date of visit												
ARV therapy												
Prophylaxis												
Other conditions												
Other drugs												
CD4 count												
Body wt												
Adherence %												
A- D4T/3TC/NVP, B- D4T/3TC/EFV, C- AZT/3TC/NVP, D- AZT/3TC/EFV, E- D4T/3TC/KAL, F- AZT/3TC/KAL, G- ABC/DDI/KAL												

Appendix D.2 shows methods of payment in the private clinics

Private Clinic
Name of clinic: _____
Consultation fee: _____
Refill fee: _____

Appendix E Copy of excel spread sheet 1 – summarizing each patient's full details all the HIV/AIDS patients were captured here for viewing of how the spread sheet look like.

Facility	Type of fac	Age	Gender	Occupatior	Date_Visit1	Date_Tx_Start
Bophelong	Public	26	F	NW	5/11/2006	6/27/2006
Bophelong	Public	28	F	NW	11/13/2006	2/20/2007
Bophelong	Public	24	F	NW	10/17/2005	11/29/2005
Bophelong	Public	42	M	W	12/13/2006	3/27/2006
Bophelong	Public	33	F	NW	1/12/2006	2/2/2006
Bophelong	Public	37	F	W	11/14/2006	12/7/2006
Bophelong	Public	42	F	W	10/20/2006	11/20/2006
Bophelong	Public	39	F	NW	1/26/2006	2/28/2006
Bophelong	Public	34	F	NW	2/16/2006	3/24/2006

Appendix F Copy of excel spread sheet (2007) for prices used – Data instrument 3.2.2

Item	amount	Unit cost	cost		
ENSURE		40.19			
Feso4		0.01	0		
prenatal		0.9	0		
centrum		1.65	0		
Mvt		0.02	0		
Folic acid		0.02	0		
power meal		2.14	0		
Instameal		42	0		
Calcium		0.046	0		
FBC		6	25	150	150
HB		3	10	30	10
U&E, Cr	3	2	45		45
Viral Load		3	433.2	1299.6	1300
Tramadol		50	1.9	95	2.2
KETOCONAZOLE	OT17	21	1.9	39.9	39.9
TEGRETOL			2.56	0	6.7
stavudine 30mg	60	19	17.24	327.56	327.56
Lamivudine 150mg	60	19	21.89	415.91	415.91
Nevirapine 200mg	60	19	24.15	458.85	

Appendix G Antiretroviral substitution for specific side effects

Regimen	Toxicity	Substitution
Stavudine/lamivudine/efavirenz	Stavudine-related neuropathy or pancreatitis Efavirenz- related persistent CNS toxicity	Switch stavudine to zidovudine Switch efavirenz to nevirapine
Stavudine/lamivudine/nevirapine	Stavudine-related neuropathy or pancreatitis Nevirapine-related severe hepatotoxicity Nevirapine – related severe rash but not life threatening Nevirapine- life threatening rash (Steven Johnsons Syndrome) Lactic acidosis	Switch stavudine to zidovudine Switch nevirapine to efavirenz for non life threatening rash (except for early pregnancy) Switch nevirapine to Lopinavir/retonavir for life threatening rash. Consult expert
Zidovuidne/didanosine/lopinavir-ritonavir	Zidovudine –related anaemia and neutropenia Didanosine- related GI effects Didanosine- related pancreatitis or hepatitis Lopinavir/ritonavir- related GI symptoms Lopinavir/ritonavir- related hypercholesterolaemia Lipodystrophy, Impaired glucose tolerance	Switch zidovudine to stavudine Switch didanosine formulation to enteric coated one Consult expert Consult expert Consult expert Consult expert Consult expert Consider hypoglycaemic agent except metformin

Source: National Antiretroviral Treatment Guidelines 2004:85

Appendix H Excel spread sheet (2007) 3 for calculation for switched regimen

1a					
Triomune 30/200/150 2008	6	52.08	312.48	Lamivir 30/150 2008	3
Triomune 30/200/150 2007	13	52.84	686.92	kal 2006	3
Triomune 30/200/150 2006	14	106.78	1494.92	Lamivir 30/150 2007	10
Triomune 30/200/150 2005	12	175.89	2110.68	kal 2007	10
Triomune 30/200/150 2004	18	106.98	1925.64	Lamivir 30/150 2007	2
tenofovir/3TC 300/300MG 2007/8		132.60	0	efavirenz 600mg	2
efavirenz 600mg 2008	6	99.19	595.14	Lamivir 30/150 2008	8
1b				efavirenz 600mg 200	8
Lamivir 30/150 2008	6	31.29	187.74		

Appendix I Grading of antiretroviral drug side effects

Symptom	Grade 1	Grade 2	Grade 3	Grade 4
Painful feet (stavudine)	Mild, does not need treatment	Moderate, bothers the patient – paracetamol, pyridoxine	Symptoms day + night - amitriptyline	Functional impairment – switch d4T
Abdominal pain stavudine	Mild + transient – no treatment	Food intake decreased – small meals + meticlopramide	Minimal food intake – stop ARVs	Patient too sick for OPD treatment - hospitalise
Vomiting stavudine	Once /day lasting for 3 days - metoclopramide	4 episodes /day not dehydrated – metoclopramide + ORT assess in 3 days	3 episodes dehydrated- metoclopramide stos ARVs	Dehydrated and too sick- hospitalise
Psychological efavirenz	Dizziness- reassure patient	Vivid dreams- reassure patient	Mood changes persistent disturbing dreams- chlorpromazine	Acute psychosis, hallucinations confused behaviour- stop ARVs hospitalise
Skin rash nevirapine	Red itchy - chlorpheniramine	Macula-popular rash or dry scales – aqueous creanm betamethasone, chlorphaniramine	Blisters or moist loss of skin- stop all ARVs, chlorpheniramine	Rash involves mucous membranes + eyes – stop all ARVs hospitalise

Source:National Antiretroviral Treatment Guidelines 2007: 131

Appendix J Comparison of treatment of antiretroviral side effects in practice and in literature.

Side effect	ARV	Treatment at clinics	Treatment at National Antiretroviral Treatment Guidleines 2007
Rash	Nevirapine	Prednisone, hydrocortisone cream, betomathasone cream, mepyramine cream, calamine lotion, allergex	Betamethasone, chlorpheniramine,
Peripheral pneuropathy	Stavudine	Carbamazepine, amitryptyline, diclofenac, vit B complex, phenytoin	Amitryptyline, pyridoxine, paracetamol
Pancreatitis	Stavudine	Hyoscine	
Gastritis	Zidovudine	Myogel, cimetidine, omeprazole, ranitidine	
Anaemia	Zidovudine	Folic acid, ferrous sulphate	
Nausea and vomiting	stavudine, nevirapine	Stemetil, hyoscine	Metoclopramide (stemetil)
Constipation		Dalcolux	
Cough and nasal symptoms	Lamivudine	DPH, alcophylline, clear cough, pholcodiene	
Headache	Zidovudine	Panado, panacod	
CNS effects	Efavirenz	Diazepam, librium, amitryptyline	Chlopromazine

Appendix K
Data Summary and analysis

Results and analysis

1. **Demographics**

a) Facility (column A) and its type (column B) – i.e. whether it is public or private or CHAL *(column A and B from excel spreadsheet)*

b) Age distribution(Column C) by facility (A) with the following categories 20-29, 30-39, 40-49, 50-59, 60-69, 70-79, 80-89 *(column A and C)*

c) Gender distribution(column D) by facility (A) and also by age distribution (C) above *(column A, C and D)*

d) Occupation status distribution (Column E) by facility (A) and gender(D) distribution *(column A, D and E)*

e) Cost-to-patient distribution (AD) by facility (A) and type of facility (B) *(column A,B and AD)*

f) Adherence to treatment (AC) by facility (A), regimen (I) and incidence of side effect (M). *(column A, I, AC, and M)*

g) Incidence of opportunistic infections (P) by facility (A) by regimen(I) *(column A, I and P)*

h) Incidence of OI in patients (P) receiving prophylaxis (K) by facility (A) *(column A, K and P)*

i) No. of patients given dietary supplements (W) given by facility(A) *(column A and W)*

j) TB incidence (S) by facility (A) and age (C) distribution *(column A, C and S)*

2. Treatment

a) Duration (H) of treatment distribution by facility (A) and type of facility (B) with the following categories 10-19, 20-29, 30-39, 40-49, 50-59, 60-69 *(column A, B and H)*

b) Frequency of ARV regimen (I) by facility (A) *(column A and I)*

c) Number of drugs used for treating side effects (N) by facility (A) and by regimen (I) *(column A, I and N)*

d) No. of drugs for OI treatment (Q) by facility (A) and by regimen (I) *(column A, I and Q)*

e) Prophylaxis of OI (K) by facility (A) *(column A and K)*

f) TB treatment (S) by facility (A) *(column A and S)*

3. Monitoring

a) Number of lab test (U) by facility (A) by regimen (I) *(column A, I and U)*

b) Number of patients whose Viral load (AE) was measured by facility (A) by regimen (I) *(column A, I and AE)*

4. Outcome

a) CD4 count at the beginning of ARV treatment (Y) by facility (A) by regimen (I) [0-49, 50-99, 100-149, 150-199, 200-249, 250-299, 300-349, 350-399, 400-449, 450-499, above 500] *(column A, I and Y)*

b) CD4 count at the end of duration of treatment (Z) by facility (A) by regimen (I) [0-99, 100-199, 200-299, 300-399, 400-499, 500-599, 600-699, 700-799, 800-899, 900-999, above 1000] *(column A, I and Z)*

c) Weight at the beginning of ARV treatment (AA) by facility (A) and by regimen (I) [30-39,40-49, 50-59, 60-69, 70-79, 80-89, above 90] *(column A, I and AA)*

d) Weight after treatment duration (AB) by facility (A) by regimen (I) [30-39,40-49, 50-59, 60-69, 70-79, 80-89, above 90] *(column A, I and AB)*

e) Incidence of side effects (M) by facility (A) and by regimen (I) *(column A, I and M)*

5. Cost assessment

a) Cost of ARVs (J) by duration of treatment (H) by facility (A) by regimen(I) *(column A, H, I and J)*

b) Cost of prophylaxis (L) by facility (A), by duration of OI (K) by regimen (I) *(column A, I, K and L)*

c) Cost of side effects (O) by regimen (I), by facility(A), by incidence (M) by no. of drugs (N) for treatment of side effects *(column A, I, M, N and O)*

d) Cost of treatment of OI (R) by facility (A), by regimen (I), by incidence (P), and no of drugs for OI treatment (Q) *(column A, I, P,Q and R)*

e) Cost of TB treatment (T) by facility (A) by TB incidence (S) *(column A, S and T)*

f) Cost of dietary supplements (X) by facility (A) and by no, of items given (W) *(column A, W and X)*

g) Cost of Lab tests (V) by facility (A), by regimen (I) by no. of lab tests (U) *(column A, I, U and V)*

6. Comparisons

a) Compare CD4 increase (Y-Z) in different regimens (I) by facility (A) *(column A, I and {Z-Y})*

b) Compare weight increase (AB-AA) in different regimens (I) by facility (A) *(column A, I and {AB-AA})*

c) Compare cost of dietary supplements (V) by facility (A) by weight increase (AB-AA) *(column A, {AB-AA}, and V)*

d) Compare incidence of OI (P) in different facilities (A), type of facility (B) and duration of OI prophylaxis (K) *(column A, B, K and P)*

e) Compare cost of prophylaxis (L)and cost of treatment of OI"s (R) by facility (A) and its type (B) *(column A, B, L and R)*

f) Compare incidence of side effects (M) in different regimens (I) by facility (A) *(column A, I and M)*

g) Compare the number of drugs used to treat side effect (O) by facility (A), by regimen (I) by incidence of side effects (N) (*column A, I, N and O)*

h) Compare cost of ARV side effects treatment (P) by regimen, (I) by facility (A), by incidence of side effects(N) and number of drugs used for side effects treatment (0) *(column A, I, N, O and P)*

i) Compare cost of lab tests (V) in different regimens (I) by facility (A) and number of lab tests done (U) *(column A, I, U and V)*

j) Compare total cost of ARV regimens (J) with total cost of drugs for side effect (O), OI treatment cost (R), cost of OI prophylaxis (L), cost of lab tests (V), cost of TB treatment (T), and cost of dietary supplements (X) , by regimen (I) and by facility (A) *(column A, I, J, L, O, R, T, V, and X)*

k) Compare incidence of side effects (M) and adherence (AC) in different facilities (A) and in different ARV regimens (I) *(column A, I, M and AC)*

l) Compare weight increase (AB-AA) by OI incidence (P) and its treatment (Q) by facility (A) *(column A, {AB-AA}, P and Q)*

m) Compare weight increase (AB-AA) with dietary supplementation (W) and by facility (A) *(column A, {AB-AA} and W)*

n) Compare CD 4 count increase (Z-Y) with dietary supplementation (W) by facility (A) *(A, W, and {Z-Y})*

7. Calculations

a) Calculate the significance of cost differences of different ARV regimens (J) by facility (A) and by regimen (I) *(column A, I and J)*

b) Calculate the significance of cost of OI prophylaxis (L) with OI treatment cost (R) in different facilities (A) *(column A , L and R)*

c) Calculate the significance of ARV regimen cost (J) increase/decrease by changing original ARV regimen (I) in different facilities (A) *(column A, I and J)*

d) Calculate the significance of cost increase ARV regimens (J) in different ARV regimens (I) by additional cost of treating side effects (O) in different facilities (A). *(column A, I, J and O)*

e) Calculate the significance of cost increase of ARV regimens (J) in different ARV regimens (I) by additional cost of lab tests (V) in different facilities (A) *(column A, I, J, and V)*

f) Calculate the significance of CD count increase (Z-Y) in different regimens (I) by facility (A) *(column A, I, and {Z-Y})*

g) Calculate the significance of weight increase (AB-AA) in different facilities (A) by regimen (I) *(column A, I and {AB-AA})*

8. Pharmacoeconomic evaluation

a) Cost effectiveness analysis (total cost of regimen by % increase in CD count by 500 by facility and overall)

i. regimen A and B,

ii. regimen A and C,

iii. regimen A and D

iv. regimen A and regimen switch

Cost	**% outcome**	**Cost effectiveness ratio**
Cost of regimen A	**% CD 4 increase**	
Cost of regimen B	**% CD 4 increase**	

Incremental cost effectiveness analysis

Total cost of A- total cost of B = Outcome of A-outcome of B

b) add cost of dietary supplements (column X) to cost ARV regimen (column J) and outcome should be weight increase {AB-AA} for different regimen (column I) in different facilities (A) *(A, I, J, and {AB-AA})*

c) add cost of dietary supplements (column X) to cost ARV regimen (column J) and outcome should be CD count increase (Z-Y) for different regimen (column I) in different facilities (A) *(A, I, J, X and (Z-Y)*

d) add cost of treatment of side effects (column O) to individual ARV regimen (column I) and adherence percentage (AC) (I, O, AC)

e) add cost of monitoring lab tests (V) to cost of individual ARV regimen (J) and CD count increase (Z-Y)