Medicine prescribing patterns in HIV/AIDS and non HIV/AIDS children: A comparative study in the private health care sector of South Africa.

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ABSTRACT

TITLE: Medicine prescribing patterns in HIV/AIDS and non-HIV/AIDS children: A comparative study in the private health care sector of South Africa

KEYWORDS: HIV/AIDS, antiretroviral drugs (ARVs), drug utilization review, opportunistic infections, private health care sector, South Africa, prescribed daily doses (PDDs), pharmacy benefit management company.

Background: According to the United Nations AIDS Reference Group (2010) and World Health Organization (2010:2), approximately 33 million people in the world had HIV/AIDS in 2009 of which 2.6 million were children. More than 30 million of these individuals resided in low- and middle-income countries. South-Africa had the highest prevalence of HIV/AIDS in the world with an estimated 5.2 million patients in 2009 (Statistics South Africa, 2010:2). Although the prevalence of human immunodeficiency virus (HIV) infection among children is reported to be high, little is known about other medication administrated concomitantly with their antiretroviral drugs.

Objective: The general objective of this study was to investigate possible changes in the medicine prescribing patterns of HIV/AIDS and non-HIV/AIDS children.

Methods: A quantitative, retrospective drug utilisation review was performed utilising medicine claims data of a South African pharmacy benefit management company. Data for a four-year period (Jan 1, 2005 to Dec 31, 2008) were analysed. The study population consisted of all children ≤12 years divided into those receiving ARVs (designated HIV positive) and those without (designated HIV negative).

Descriptive statistics such as average mean, standard deviation, *t*-test, *d*-values, and two way frequency tables were used to describe the results. Data were analysed using the Statistical Analysis System ® SAS 9.1 ® programme.

Results: The study population (children ≤ 12 years) represented 16.2% (n = 197 323) of the total population in 2005, 15.4% (n = 193 346) in 2006, 15.6% (n = 142 049) in 2007 and 13.3% (n = 98 939) in 2008. Children with HIV/AIDS represented 0.2% (n = 197 323) of the study population in 2005 and increased to 0.4% (n = 98 939) in 2008, whereas the percentage of children without HIV/AIDS decreased from 99.8% (n = 197 323) in 2005 to 99.6% (n = 98 939) in 2008. The total number of HIV/AIDS children that also received other medication concomitantly with their ARVs increased from 96.5% (n = 402) in 2005 to 97.2% (n = 427) in 2008. Males with HIV/AIDS who used other medication represented 52.6%

(n = 388) in 2005 and increased to 53.3% in 2008 while female HIV/AIDS patients represented 47.4% in 2005 and decreased to 46.7% in 2008.

Prescriptions containing three ARV items represented 69.5% (n = 2 969) of the total number of prescriptions received by HIV/AIDS patients in 2005 and decreased to 67.7% in 2008. The combination of lamivudine, nevirapine and stavudine were the three products that appeared most frequently on prescriptions for HIV/AIDS children in the age group 0 ≤ 1 years and 1 ≤ 5 years from 2005 to 2008. In the age group 5 ≤ 12 years the combination most frequently prescribed was lamivudine, nevirapine and zidovudine.

HIV positive children received 6.2 ± 4.62 prescriptions for other medication (non-ARVs) per year during 2005 compared to HIV negative children with 3.9 ± 3.71 ($p < 0.0001$, $d = 0.5$). In 2008 HIV positive children received 6.4 ± 5.02 prescriptions per year compared to HIV negative patients who received 4.36 ± 4.05 prescriptions ($p < 0.0001$, $d = 0.5$) in 2008.

HIV negative children received more central nervous system items, endocrine items and autacoids than HIV positive children, whereas HIV positive children received more respiratory system agents, dermatological, ear, nose throat and antimicrobials items.

Conclusion: The study showed that HIV positive children received significantly more prescriptions for other medication per year compared to their HIV negative counterparts. The top pharmacological groups mostly prescribed to both groups were respiratory agents, antimicrobials, analgesics, dermatological and ear, nose and throat items.

OPSOMMING

TITEL: Patrone vir die voorskryf van medisyne vir kinders met en sonder MIV/VIGS: ‘n vergelykende studie in die privaat gesondheidsorgsektor in Suid-Afrika

SLEUTELWOORDE: MIV/VIGS, antiretrovirale middels (ARM’s), oorsig oor gebruik van medisyne, opportunistiese infeksies, privaat gesondheidsorgsektor, Suid-Afrika, voorgeskrewe daaglikse dosisse (VDD’e), apteekvoordele bestuursorganisaie.

Agtergrond: Volgens die VIGS-studiegroep van die Verenigde Nasies (2010) en die Wêreldgesondheidsorganisasie (2010:2) het ongeveer 33 miljoen mense in die wêreld in 2009 MIV/VIGS gehad waarvan 2.6 miljoen kinders was. Meer as 30 miljoen van hierdie mense het in lande met lae of gemiddelde inkomste gewoon. Suid-Afrika het die hoogste voorkoms van MIV/VIGS in die wêreld gehad met ‘n beraamde 5.2 miljoen gevalle in 2009 (Statistics South Africa, 2010:2). Hoewel gemeld is dat die voorkoms van infeksie deur die menslike immuniteitsgebrekvirus (MIV) onder kinders hoog is, is min bekend oor ander medisyne wat saam met hulle antiretroviral middels toegedien word.

Doel: Die oorhoofse doel van hierdie studie was om moontlike veranderinge in die patrone vir die voorskryf van medisyne vir kinders met en sonder MIV/VIGS te ondersoek.

Metodes: ‘n Kwantitatiewe, retrospektiewe studie van die gebruik van medisyne is gedoen deur data van medisyne-eise van ‘n Suid-Afrikaanse apteekvoordele bestuursorganisaie. Data vir ‘n periode van vier jaar (1 Jan 2005 tot 31 Des 2008) is ontleed. Die studiepopulasie was alle kinders van 12 jaar en jonger verdeel in dié wat ARM’s ontvang het (MIV-positief) en die daarsonder (MIV-negatief).

Beskrywende statistiek soos gemiddeld, mediaan, standaard afwyking, *t*-toets, *d*-waardes en tweerigting frekwensietabelle is gebruik om die resultate te beskryf. Data is met die Statistical Analysis System ® SAS 9.1 ®-program verwerk.

Resultate: Die studiepopulasie (kinders $\leq$ 12 jaar) het in 2005 16.2% (n = 197 323) van die totale populasie uitgemaak, in 2006 was dit 15.4% (n = 193 346), in 2007 15.6% (n = 142 049) en in 2008 was dit 13.3% (n = 98 939). Kinders met MIV/VIGS het in 2005 0.2% (n = 197 323) van die studiepopulasie uitgemaak, wat in 2008 tot 0.4% (n = 98 939) gestyg het, terwyl die persentasie kinders sonder MIV/VIGS van 99.8% (n = 197 323) in 2005 tot 99.6% (n = 98 939) in 2008 gedaal het. Die totale aantal kinders met MIV/VIGS wat saam met hulle ARM’s ook ander medisyne gekry het, het van 96.5% (n = 402) in 2005 tot 97.2% (n = 427) in 2008 toegeneem. Manlikes met MIV/VIGS wat ander medikasie gekry het, het in

2005 52.6% (n = 388) uitgemaak wat in 2008 tot 53.3% gestyg het, terwyl vroulike pasiënte met MIV/VIGS in 2005 47.4% uitgemaak het wat in 2008 tot 46.7% gedaal het.

Voorskrifte wat ARM's bevat het, was in 2005 69.5% (n = 2 969) van die totale aantal voorskrifte vir MIV/VIGS-pasiënte en dit het in 2008 tot 67.7% gedaal. Lamivudien, nevirapien en stavudien was die kombinasie wat van 2005 tot 2008 die meeste op voorskrifte vir kinders met MIV/VIGS in die ouderdomsgroep $0 \leq 1$ en $1 \leq 5$ jaar voorgekom het. In die ouderdomsgroep $5 \leq 12$ jaar, was lamivudien, nevirapien en sidovudien die kombinasie wat die meeste voorgeskryf is.

MIV-positiewe kinders het in 2005 6.2 ± 4.62 voorskrifte per jaar vir ander medikasie (nie-ARM's) gekry vergeleke met 3.9 ± 3.71 ($p < 0.0001$, $d = 0.5$) vir MIV-negatiewe kinders. In 2008 het MIV-positiewe kinders 6.4 ± 5.02 voorskrifte per jaar ontvang vergeleke met 4.36 ± 4.05 voorskrifte aan MIV-negatiewe kinders ($p < 0.0001$, $d = 0.5$).

MIV-negatiewe kinders het meer items vir die sentrale senustelsel en endokrienstelsel asook outokoïede as MIV-positiewe kinders gekry, terwyl MIV-positiewe kinders meer items vir die respiratoriese stelsel, vel, ore neus en keel asook antimikrobiese middels gekry het.

Gevolgtrekking: Die studie het getoon dat MIV-positiewe kinders per jaar beduidend meer voorskrifte vir ander medikasie kry as hulle MIV-negatiewe eweknieë. Die farmakologiese groepe middels wat die meeste aan albei groepe voorgeskryf was, was antimikrobiese middels, analgetika en items vir die vel, ore, neus en keel.

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CHAPTER 1:

NATURE AND SCOPE OF THE STUDY

1.1 INTRODUCTION

Chapter 1 reflects on the general layout of this study which includes a problem statement, research objectives, and research methods.

1.2 PROBLEM STATEMENT

The Mayo Clinic (2008:2) defines AIDS (acquired immune deficiency syndrome) as a chronic serious condition caused by HIV. HIV/AIDS is a retrovirus that infects cells of the immune system, destroying or impairing their function (Guitierrez, 2008:499; Burke & Paterson., 1997:134). As the infection progresses, the immune structure becomes weaker, and the person becomes more at risk to infections (World Health Organization, 2010:1).

HIV 1 infections have developed into a worldwide epidemic over the past 30 years (Chakraborty, 2008:496). Approximately 33 million people in the world have HIV/AIDS of whom more than 30 million lived in low- and middle-income countries in 2009 (UNAIDS, 2010; World Health Organization, 2010:2). In 2009 an estimated 2 million people died as a result of HIV/AIDS, and 2,6 million people including 370 000 children were newly infected globally (UNAIDS, 2010). Africa represents 68% of the global total, while Africa's number of newly infected children cases represent 69% of the global total (UNAIDS, 2010). An estimated 5.2 million people were living with HIV/AIDS in South Africa in 2008, more than in any other country (Statistics South Africa, 2008:2). The first pediatric case of HIV/AIDS was reported in 1982, only one year after the first reports in adults (*CDC*, 1982:665).

According to Colvin (2010:359), HIV positive patients have more contact with health care services than HIV negative patients and HIV positive patients have increased hospital admissions, leading to ward overcrowding and have a dramatic effect on the mortality of the population (Zaba *et al.*, 2004:S1). Every minute of every day a child under the age of 15 years dies because of an AIDS associated illness worldwide (CDC, 2006:18.) It is believed that in 2008, over 250,000 South Africans died of HIV/AIDS (Statistics South Africa, 2008:2).

HIV/AIDS may have an important impact on individuals and community structures such as families (Frohlich, 2010:373). The cause of death and illnesses of HIV/AIDS infected persons leads to misery and high poverty because of the cost of the illness and death of HIV/AIDS patients that may cause a decline in economic growth (Zaba *et al.*, 2004:S4).

The immune response system is complex and involves many innate and adaptive components. In most cases, the immune response is insufficient to eradicate the virus, and the infection eventually results in a gradual decline of CD4 cell count from both memory and naïve cell compartments. This can be quantitatively reversed by the institution of Highly Active Antiretroviral Therapy (HAART) (Guitierrez, 2008:499). HAART is the treatment, composed of several antiretroviral drugs, that is prescribed to many HIV-positive patients (Alberta Reappraising AIDS society, 2011:1) (refer to Paragraph 2.8).

When the immune system is compromised by HIV infection, many people begin to experience some mild HIV/AIDS disease symptoms, such as skin rashes, fatigue, night sweats, slight weight loss, mouth ulcers, and fungal skin and nail infections (Beers *et al.*, 2006:1629; Guitierrez, 2008:499). Typical problems include chronic oral or vaginal thrush, recurrent herpes blisters on the mouth or genitalia, ongoing fevers, persistent diarrhoea, and significant weight loss (Beers *et al.*, 2006:1629; Plante & Lemon, 2010:8; Guitierrez, 2008:499).

When immune system damage is more severe, HIV-positive individuals may experience opportunistic infections (ASHA, 2011; Beers *et al.*, 2006:1628; Guitierrez, 2008:500; Myers & Kaemmerer, 2008:1328). An opportunistic infection is “an infection caused by a normal non pathogenic organism in a host whose resistance has been decreased by disorders such as HIV/AIDS”. Opportunistic infections are common in children with HIV/AIDS (Myers & Kaemmerer, 2008:1328) and are a major cause of morbidity and mortality in HIV infections (ASHA, 2011). Some of the most common opportunistic infections in children include *Pneumocystis carinii* pneumonia (PCP), *Mycobacterium avium* complex (MAC) disease, cytomegalovirus (CMV), toxoplasmosis, and candidiasis (Plante & Lemon, 2010:8; Guitierrez, 2008:500). The treatment of opportunistic infections is discussed in Section 2.7.

According to Hall *et al.* (2008:523), the use of antiretroviral medications has reduced mother-to-child transmission of HIV dramatically in the United States of America (USA) and other high resource countries. HAART including at least three drugs are recommended (refer to section 2.8). HAART has been associated with improved survival, decreased opportunistic infections, and improved growth and neurocognitive function, and better quality of life in children (Cotton *et al*, 2009:35).

The virological successes of HAART certainly promise a longer lifespan for HIV-infected children, but the long-term metabolic consequences [lipodystrophy, dyslipidemia, insulin resistance, hyperlactatemia, and decreased bone mineral density (BMD)] are of serious concern (Engelkirk & Burton, 2007:125). The use of ART in children is a highly specialised field and may cause some adverse effects such as lactic acidosis, haematological toxicity, rashes, hypersensitivity syndrome, hepatotoxicity and hyperlipidaemia (Cotton *et al*, 2009:35). Treatment failure can occur because of vomiting or spitting out antiretroviral drugs and not receiving medication on time (Cotton, 2009:32).

The goal of antiretroviral treatment in HIV/AIDS infected children is to reduce HIV/AIDS related morbidity and mortality, and increase survival (Department of Health, 2010a:29). HIV/AIDS patients who received antiretroviral medication are less hospitalised (Hellinger, 2006:631), and there may be a decrease in the number of HIV/AIDS related deaths (CDC, 2009:1).

An estimated 84 billion rand per year is spent on HIV/AIDS, support prevention and care programs in the low and middle income countries (UNAIDS, 2007). A study done in the public sector in South Africa indicate that the average cost over a twelve month period for first line ARV treatment was R 4355.28, and the average cost for second line ARV treatment per patient was R 8586.36 (Long *et al.*, 2010:918).

The following research questions can be formulated on the basis of the above-mentioned discussion.

- Are there any differences in the medicine prescribing patterns, excluding antiretroviral drugs, for HIV/AIDS and non-HIV/AIDS children, in terms of prevalence?
- Do gender and age play a role in the medicine prescribing patterns for HIV positive and HIV negative children?
- Do prescribers follow the HIV/AIDS treatment guidelines for children in South Africa?

1.3 RESEARCH OBJECTIVES

This research project includes general as well as various specific objectives.

1.3.1 General research objective

The general research objective was to compare the medicine prescribing patterns for HIV positive and HIV negative children in the South African private health care setting for the period 2005 to 2008 by using a medicine claims database.

1.3.2 Specific research objectives

The research project consisted of two phases, namely a literature review and an empirical investigation. The research objectives of the two phases included the following:

1.3.2.1 Phase 1: Literature review

The specific research objectives of the literature review included the following:

- To conceptualise HIV/AIDS in children.
- To describe the prevalence of HIV/AIDS, nationally as well as internationally, with specific reference to children.
- To describe opportunistic infections associated with HIV/ AIDS with specific reference to children.
- To describe the HIV/AIDS treatment guideline(s) for children with specific reference to those applicable to South Africa.

1.3.2.2 Phase 2: Empirical investigation

The specific research objectives of the empirical investigation phase of the study were:

- To investigate possible changes in medicine prescribing patterns, (including ART) based on gender and age, in HIV/AIDS children, during the selected four-year period, 2005-2008.
- To assess whether HIV/AIDS treatment guidelines were followed in the private health care sector of South Africa.
- To compare the medicine prescribing patterns, (excluding ARV drugs) in HIV/AIDS and non-HIV/AIDS children based on age and gender.

1.4 RESEARCH METHODOLOGY

The research consisted of two phases, namely a literature review and an empirical investigation.

1.4.1 Phase one: Literature review

The literature review focused on the most recent publications regarding the prevalence of HIV/AIDS in children, opportunistic infections associated with HIV/AIDS and the HIV/AIDS treatment guidelines for children with specific reference to those applicable to South Africa.

1.4.2 Phase two: Empirical investigation

A retrospective drug utilisation review was done on data provided by the database of a pharmaceutical benefit management company (PBM). The study period ranged from 1 January 2005 to 31 December 2008.

The total database consisted of all medicine claims during the period 1 January 2005 to 31 December 2008. The study population were extracted from the total database, and divided in two groups: children ≤ 12 years with HIV/AIDS and children ≤ 12 years without HIV/AIDS. Medication used by children ≤ 12 years with HIV/AIDS were divided in two groups: the ARV medication they used and the other medication they used.

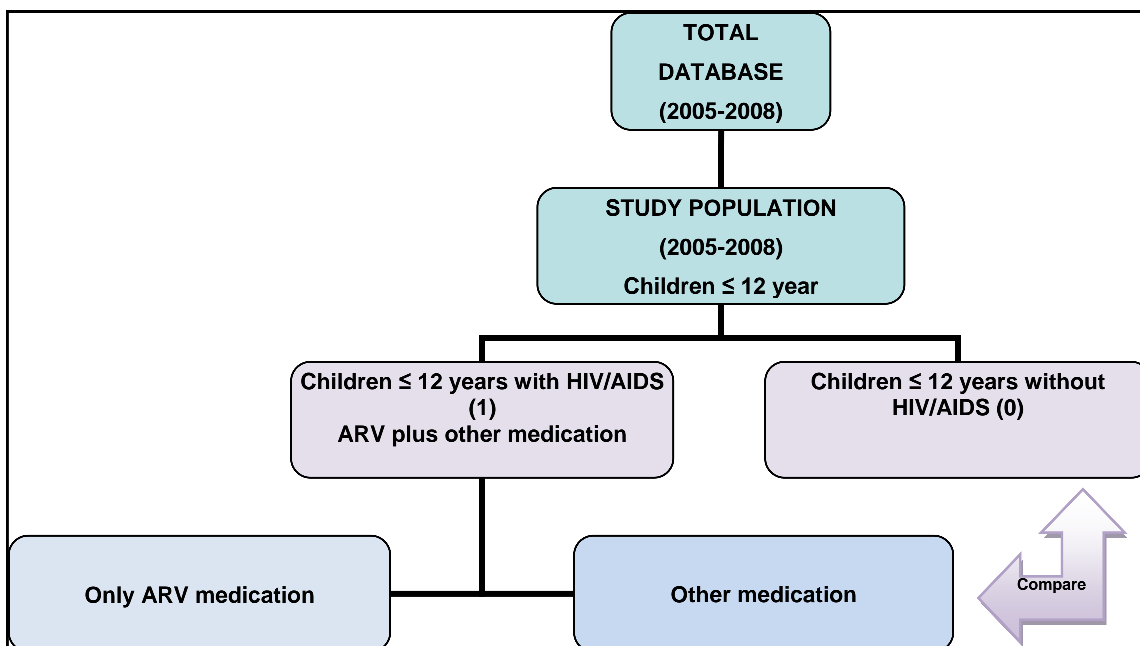


Figure 1.1: Organogram illustrating the different data subsets and the selection of the study population

1.5 ETHICAL CONSIDERATIONS

None of the patients, medical practices, pharmacies or medical scheme information could be identified and the study was concluded anonymously through the medicine claim database. Permission to conduct this study was granted by the PBM's board of directors as well as the Ethical Committee of the North-West University. The Ethical Committee of the North-West University granted the study with the following permission number: NWU – 0046-08-S5.

1.6 DIVISION OF CHAPTERS

The chapters are divided as follows:

Chapter 1: Nature and scope of study

Chapter 2: Opportunistic infections and antiretroviral treatment of HIV/AIDS children

Chapter 3: Empirical Investigation

Chapter 4: Results and Discussion

Chapter 5: Conclusion and Recommendations

1.7 LIST OF ABBREVIATIONS

The following abbreviations and acronyms were used for the purpose of this study.

ABC:	Abacavir
AIDS:	Acquired immunodeficiency syndrome
ART:	Antiretroviral therapy
ARVs:	Antiretroviral drugs
AZT:	Zidovudine
DDI:	Didanosine
DNA:	Deoxyribonucleic acid
DUR:	Drug utilisation review
D4T:	Stavudine
EFV:	Efavirenz
HAART:	Highly Active Antiretroviral Therapy
HIV:	Human immunodeficiency syndrome
IDV:	Indinavir
LPV/r:	Lopinavir/ritonavir

NFV: Nelfinavir

NRTI: Nucleoside reverse transcriptase inhibitor

NNRTI: Non-nucleoside reverse transcriptase inhibitor

NVP: Nevirapine

PBM: Pharmaceutical benefit management organization

PDD: Prescribed daily dose

PI: Protease inhibitor

R: Rand value

RNA: Ribonucleic acid

RTV: Ritonavir

SA: South Africa

SBI: Serious bacterial infections

SD: Standard deviation

TB: Tuberculosis

3TC: Lamivudine

1.8 TERMS AND DEFINITIONS

ARV: Antiretroviral treatment is all the medication used to achieve durable suppression of replication; this is generally achieved by using a combination of three or more antiretroviral items (Gibbon, 2008:218).

ART regimen: In this study it refers to one or more antiretroviral item that a patient used.

Child: According to the Pediatric Dosage Handbook (Taketomo *et al*., 2000:15), a child is a person 1 to 12 years of age. For the purpose of this study a child age will be 1 to 12 years of age, and divided into 3 groups, ≤ 12 months, 1 < 6 years and 6 to ≤ 12 years of age (Chakraborty, 2008:497; Taketomo, 2000:1129).

HAART: Highly Active Antiretroviral Therapy includes a combination of antiretroviral drugs that achieves virological suppression (Gibbon 2008:218).

HIV (+), HIV positive, HIV/AIDS patients: In the context of this study it includes every child who received one or more antiretroviral drugs during the study period.

HIV (-), HIV negative, non-HIV/AIDS patients: In the context of this study it includes every child who is possible HIV negative and who do not received antiretroviral medicine.

Prodrug: According to the Mosby Dictionary (Myers & Kaemmerer, 2008:1520) a prodrug is an "inactive or partially active drug that is metabolically changed in the body to an active drug".

OTHER MEDICATION: Other medication refers to all the medication HIV (+) patients received, ARVs excluded.

1.9 CHAPTER SUMMARY

This chapter served as an introduction to the rest of the dissertation. The problem statement, research questions and objectives, research methods, and division of chapters have been outlined. In the next chapter an overview of the HIV/AIDS disease will be given.

CHAPTER 2:

OPPORTUNISTIC INFECTIONS AND ANTIRETROVIRAL TREATMENT OF HIV/AIDS CHILDREN

2 INTRODUCTION

The aim of this chapter is to provide an overview of opportunistic infections and treatment protocols of HIV/AIDS in children.

2.1 DEFINITION OF HIV AND AIDS

The World Health Organization (2010) has defined human immunodeficiency virus (HIV), the cause of acquired immune deficiency syndrome (AIDS), as a retrovirus, belonging to the *Lentiviridae* subfamily acting on cells of the immune system that can impair or destroy their function (Burke *et al.*, 1997:134, Guitierrez, 2008:499).

HIV infection can be divided into two subgroups, namely HIV-1 and HIV-2. HIV-1 is mainly responsible for the global epidemic (Williamson & Martin, 2008:109), whereas HIV-2 is largely limited to West Africa (Wilson *et al.*, 2004:15). HIV-1 can be classified in three groups, called major, outlier and "non-major and non-outlier". The HIV-1 major group can be divided into subtypes A, B, C, D and E (Williamson & Martin, 2008:109). In South Africa, HIV-1 subtype C is responsible for more than 90% of cases (Wilson *et al.*, 2004:15). According to Beers *et al.* (2006:2341), the HIV-1 retrovirus leads to opportunistic infections and weakening of the immune system. A reverse transcriptase enzyme is produced by the retrovirus, allowing the DNA inside the host cell to be transcribed from the RNA genome (Myers & Kaemmerer, 2008:893). The retrovirus undergoes an abnormal biological process in which the genetic material, in the form of single stranded RNA, is converted to double stranded DNA (Evian, 2003:4). The lymphocyte genome integrated the viral DNA, and for HIV infection this is the basic process (Mortimer & Loveday, 2002:6). After the initial stage of the infection there is an extensive spreading of the virus and a quick decrease of the number of CD4 T-cells in peripheral blood (Pugh *et al.*, 2000:825). The helper T-cells are targeted by the circular shaped AIDS virus (Evian, 2003:4) and subsequently destroyed, causing an infection with an average incubation period of 10 years (Myers & Kaemmerer, 2008:893).

The syndrome described as AIDS refers to the last stage of an HIV infection, characterised by severe immunodeficiency (Mayo Clinic, 2008:2; Nester *et al.*, 2001:742). During this period, people living with AIDS already have serious infections or cancers (Plante & Lemon, 2010:8). A patient can

also be diagnosed with AIDS when infected with HIV and have a CD4 cell count of less than 200 to 500 cells/mm^3 (Myers & Kaemmerer, 2008:24).

2.2 EPIDEMIOLOGY

The first reported case of HIV was recognised in a 31 year-old homosexual male in June 1981 in the United States (Stine, 2009:1; Alcamo, 2002:3), whilst the first South African case of HIV/AIDS was reported in 1983. At this stage (1982-1987), HIV/AIDS was mainly associated with recipients, blood transfusion patients, haemophiliacs and homosexuals (Karim, 2005:33).

In the past 30 years HIV-1 infections have increased to develop into a worldwide epidemic (Chakraborty, 2008:496). Worldwide an estimated 14 000 people are being infected daily (Chakraborty, 2008:496). According to Coffee *et al.* (2007:345), South Africa is the country with the highest incidence of HIV cases in the world, with Gauteng and Kwazulu-Natal being the provinces where the most new HIV-infections occurred in 2005.

The incidence of HIV/AIDS is nine times lower in other race groups than in black race groups (South Africa, 2007:1). The highest incidence rate of HIV/AIDS is among persons in urban informal settings, with a prevalence of 25.8% twice as high than the 13.9% in urban formal areas (South Africa, 2007:1).

In 2005, 60% of deaths in South African hospitals were HIV/AIDS related (South Africa, 2007:1). In the 1990s there were 65 HIV/AIDS related deaths per 1 000 births compared to 75 HIV/AIDS related deaths per 1 000 births in 2006. In 2006, 71% of all deaths in people between the ages of 15 to 49 years were related to HIV/AIDS (South Africa, 2007:1). Table 2.1 depicts the incidence of HIV/AIDS in South Africa and worldwide.

Table 2.1: The incidence of HIV/AIDS in South Africa

Demographic data	In the year	Age and gender	Estimate	Reference
People living with HIV/AIDS worldwide	2009	Total	33.3 million (31.4 million–35.3 million	UNAIDS, 2010
	2009	Children under 15 years	2,55 million (1.7 million–3.4 million)	UNAIDS, 2010
HIV/AIDS related deaths worldwide	2009	Total	1.8 million (1.6 million–2.1 million)	UNAIDS, 2010
	2009	Children under 15 years	260 000 [150 000–360 000]	UNAIDS, 2010
People newly infected with HIV worldwide	2009	Total	2.6 million (2.3 million–2.8 million)	UNAIDS, 2010
	2009	Children	370 000 (230 000–510 000)	UNAIDS, 2010
People newly infected with HIV in South Africa	2009	Adults	340 000 (300 000–400 000)	UNAIDS, 2010
	2009	Adults and Children	390 000 (340 000–440 000)	UNAIDS, 2010
Number of people with HIV/AIDS in South Africa	2009	Adults and Children	5,6 million (5, 4 million–5,9million)	UNAIDS, 2010
	2009	Adults 15 + years	5,3 million (5,1 million–5,5 million)	UNAIDS, 2010
	2009	Orphans (0-17 year)	1 900 000 (1 600 000–2 400 000]	UNAIDS, 2010
HIV/AIDS related deaths in South Africa	2009	Adults and Children	310 000 [260 000–390 000]	UNAIDS, 2010
Number of people in the world with HIV/AIDS	2008	Total	33,4 million (31,1-35,8 million)	WHO/UNICEF, 2009
	2008	Adults	31,3 million (29,2-33,7 million)	WHO/UNICEF, 2009
	2008	Women (aged 15 and above)	15,7 million (14,2-17,2 million)	WHO/UNICEF, 2009
	2008	Children under 15 years	2,1 million (1,2-2,9 million)	WHO/UNICEF, 2009
People newly infected with HIV worldwide	2008	Total	2,7 million (2,4-3,0 million)	WHO/UNICEF, 2009
	2008	Adults	2,3 million (2,0-2,5 million)	WHO/UNICEF, 2009
	2008	Children under 15 years	430 000 (240 000-610 000 million)	WHO/UNICEF, 2009
HIV/AIDS-related deaths worldwide	2008	Total	2,0 million (1,7-2,4 million)	WHO/UNICEF, 2009
	2008	Adults	1,7 million (1,4-2,1 million)	WHO/UNICEF, 2009
	2008	Children under 15 years	280 000 (150 000-410 000 million)	WHO/UNICEF, 2009
People newly infected with HIV/AIDS in South Africa	2008	Adults	380 000	DOH, 2009
	2008	Paediatric	56 000	DOH, 2009
Number of people in South Africa with HIV/AIDS	2008	Adults and children	5,3 million (4,7 million-5,7 million)	UNAIDS,2010
	2008	Adults 15+	5,0 million (4,5 million-5,4 million)	UNAIDS,2010
	2008	Children	220 000 (130 000-300 000)	UNAIDS,2010

Table 2.1: The incidence of HIV/AIDS in South Africa (continue)

Demographic data	In the year	Age and gender	Estimate	Reference
HIV/AIDS-related deaths in South Africa	2008	Total	250 000	UNAIDS, 2010
	2007	Total	350 000	UNAIDS, 2009
HIV/AIDS related deaths in South Africa	2006	Women	7893	Statistics South Africa, 2008:24
	2006	Men	6854	Statistics South Africa, 2008:24
	2006	Children under 15 years	1235	Statistics South Africa, 2008:25
	2006	Children 1-4 year	348	Statistics South Africa, 2008:27

The statistics in Table 2.1 indicate that HIV/AIDS creates health challenges, not only in South Africa, but also in the rest of the world. According to Statistics South Africa (2008:31), a total number of 607 184 people died during 2006 of which 14 783 deaths were HIV/AIDS related. Furthermore, more women died due to HIV/AIDS when compared to death in men. According to UNAIDS (United Nations AIDS reference group) (2010:5), there was a decline in HIV/AIDS-related deaths between 2007 (350 000 deaths) and 2008 (250 000 deaths) in South Africa due to more patients receiving antiretroviral treatment. In spite of this decline in deaths, there were still many new infections, seen in 2009 as well as an increased number of people worldwide living with HIV/AIDS (UNAIDS, 2010:16).

According to Dorrington (2010:11), the decline in HIV/AIDS related deaths between 2006 and 2008, was due to the fact that more infected people received antiretroviral therapy (ART), which extended the life of these patients. The increased access to antiretroviral drugs (ARV) treatment has lead to a 19% decline in HIV/AIDS-related deaths between 2004 and 2009 (UNAIDS, 2010:8). A worldwide decline in HIV/AIDS-related deaths occurred between 2008 (estimated 2 million) and 2009 (estimated 1.8 million) (UNAIDS, 2010:16) (refer to Table 2.1).

2.3 BURDEN OF HIV/AIDS

HIV/AIDS has a huge impact on individuals or community structures such as families (Frohlich, 2010:373). HIV positive children are more prone to neglect by their families and friends; for example, according to Nattrass (2004:80), there is a growing number of HIV-positive neglected children in shelters, state-funded and private funded hospices in South Africa. Most of the responsibility for the care of these children living with HIV/AIDS falls onto family members in particular women who are actively involved in the care-giving process, leading to an over burdening

with responsibilities in the form of care and support roles (Kipp *et al*., 2006:2). The impact of HIV/AIDS on children includes deepening poverty and psychosocial defects in the family. Family members are often traumatised and have a variety of psychological reactions to illness and death of a family member, including stigmatisation in the family, and separation from associates and siblings (Richter, 2001:13).

According to Colvin (2010:359), HIV positive patients have more contact with health care services than HIV negative patients (Colvin, 2010:359). The current HIV/AIDS epidemic in South Africa affects the health system mainly in the form of low staff morale, and loss of staff due to illness (South Africa Department of Health, 2003:130). HIV/AIDS infection increases hospital admissions, leading to ward overcrowding (Colvin, 2010:359). This burden of HIV/AIDS is felt more in the public sector than in the private sector as the private sector seems to have more room to absorb the impact because of its low rate in bed residence in hospitals (South Africa Department of Health, 2003:133). According to a study done in Soweto, HIV positive children were hospitalised for an average of eight days compared to an average of six days in HIV negative children (Colvin, 2010:363).

HIV/AIDS has a dramatic effect on the mortality of the population (Zaba *et al*., 2004:S1). According to Frohlich (2010:375), the number of orphans resulting in AIDS related deaths in South Africa is predicted to rise over five million by 2014. A child under 15 years dies of an AIDS associated illness every minute of every day worldwide (CDC, 2006:18) The cause of death and illnesses of HIV/AIDS infected persons leads to misery and high poverty in households that may cause a decline in economic growth. Households' incomes are affected because of the cost of illness and death of HIV/AIDS patients in the family. Medical and funeral expenses are increased, and households' savings are affected because of increased financial needs, leading to deep poverty and increased borrowing (Zaba *et al*., 2004:S4). Poverty in households sometimes leads to alcoholism, poor access to health care, prostitution, limited access to education (with money for school fees used for other basic requirements instead) (Richter, 2001:11), low literacy levels, violence, fatalism, cultural and traditional disintegration (Evian, 2003:21), and loss of families' homes due to sale of belongings and land in an attempt to survive (Richter, 2001:11).

An estimated 84 billion rand per year is spent on HIV/AIDS, support prevention and care programmes in the low and middle income countries (UNAIDS, 2007). In a study done over a 3-year period (2005-2007) in South Africa, the average cost per participant during a twelve month period for first line ARV treatment was R 4 355.28, and the average cost for second line ARV treatment per patient was R 8 586.36 (Long *et al*., 2010:918). More patients received second line therapy than first line. This second line therapy was 2.4 times more expensive than first line therapy (Long *et al*., 2010:919). Rosen (2011:5) furthermore determined that the average cost per patient in care and

responding in the first year was R 6 056.40 per patient and for the second year was R 5 880.00 per patient, according to a study done in the Leratong Hospital (Rosen *et al.*, 2011:5). In a similar study done in an Academic referral hospital in Johannesburg with 8 000 HIV/AIDS patients, the average cost per patient for care and responding in the first year was R 5 180.00 and the second year was R 4 897.20 (Rosen *et al.,* 2011:5).

2.4 TRANSMISSION OF HIV/AIDS IN CHILDREN

HIV can be transmitted via a number of mechanisms, for instance, with the sharing of needles to inject drugs of abuse, sexual fluids, breast milk, during pregnancy and delivery in HIV-infected patients (Plante & Lemon, 2010:9; Wilson *et al.*, 2004:61). If a single drop of any of these fluids enters the body/bloodstream a person can be infected with HIV (American Social Health Association, 2011).

In the following section the different transmission types will be discussed.

2.4.1 Mother to child transmission (MTCT) of HIV

When a woman becomes infected with HIV, just before or during pregnancy, she has a high HIV viral load, symptomatic HIV disease, and a low CD4 cell count. It seems that it is more expected for a woman to transmit the virus to her baby during pregnancy (Evian, 2003:16; Tudor-Williams & Gibb, 2002:74).

The possibility of intrapartum transmission is 10% to 20% and the rate of intrauterine transmission is 5% to 10% (Spencer, 2005:231). In utero transmission of HIV-1 mainly occurs transplacentally, during labour and delivery or by maternofoetal transfusion (Chakraborty 2008:496; Wilson *et al.*, 2004:359). Intrapartum transmission of HIV-1 occurs when the virus is transmitted via maternal secretions to which the infant is exposed in the birth canal of throughout (Burke *et al.*, 1997:134).

Post partum transmission occurs via breast milk when breastfeeding (Wilson *et al.*, 2004:359).

According to Stine (2009:169), an estimated 90% of paediatric HIV/AIDS cases, are due to MTCT. An HIV-positive woman can infect her child with HIV during pregnancy, delivery or through breastfeeding (South African Department of Health, 2010). Breast milk transmission of HIV-1 is the most frequent and extended contact of an infant’s mouth, oesophageal and gastrointestinal tract to infected milk. The rate of infants infected through breastfeeding and not at birth is expected to be between 12% to 14% (Chakraborty, 2008:496). If the child is not breastfed the risk is reduced of by 20% (Muko *et al.*, 2004:133).

In 2008 the HIV/AIDS prevalence under pregnant women in South Africa was an estimated 200 000 (110 000-280 000) (UNAIDS, 2008:1). According to UNAIDS/UNICEF/WHO (2008), in 2007, an

estimated 57% of pregnant females who had HIV/AIDS globally received ARV treatment to prevent mother to child transmission. According to UNAIDS (2010:18), during the prenatal and breastfeeding stage an expected 370 000 (220 000-520 000) women were HIV positive in 2009 worldwide. Elective caesareans are suggested for HIV positive mothers, and breastfeeding must be avoided in newborns (Wilson *et al.*, 2004:361).

2.4.2 Other forms of transmission in children

The main route of transmission of HIV/AIDS in children younger than 10 years is mother to child transmission, in a few cases children have also been infected with HIV/AIDS through contaminated needles and blood transfusions (Muko, 2004:132). Blood to blood transmission can occur during the transfusion of blood, or blood products (Alcamo, 2002:41), but is unusual when blood of donors are carefully screened (Department of Health, 2010c:9; McFarland, 2009:1113). Blood to blood transmission can also occur by health care workers if they sustain accidental percutaneous needlestick injury contaminated with blood (Alcamo, 2002:41). In a very small number of children transmission can also be possible through contaminated equipment used by drug users (Alcamo, 2002:41), breast milk was given to the wrong baby in health facility, surrogate breastfeeding (Regensberg & Makiwane, 2009:74) and also because of sexual abuse and sexual activity in children in a few cases (Richter, 2001:12).

2.5 CLINICAL FEATURES OF HIV INFECTION IN CHILDREN

Table 2.2 illustrates the signs and conditions commonly found in HIV infected and non-HIV children.

Table 2.2: Signs and conditions that appear usually in HIV-infected children but not in uninfected children (Adapted from Department of Health, 2010:12)

Signs and conditions usually appearing in HIV-infected children, and uncommon in uninfected children	Signs and conditions in uninfected but also in HIV-infected children	Signs and conditions very specific to HIV infection
Herpes Zoster	Marasmus	Lymphoma
Neurologic dysfunction	Failure to thrive	Kaposi's sarcoma
Continuing fever	Bronchiectasis	Herpes zoster
Hepatosplenomegaly	Tuberculosis	Salmonella infection
Generalized lymphadenopathy	Severe pneumonia	Extrapulmonary cryptococcosis
Parotid swelling	Recurrent diarrhoea	Oesophageal candidiasis
Recurrent oral thrush	Chronic ear infection	*Pneumocystis jiroveci* pneumonia (PCP)
Severe bacterial infection	Anaemia	-
Severe pneumonia	-	-
Generalised dermatitis	-	-

2.6 CLASSIFICATIONS OF HIV/AIDS INFECTION IN CHILDREN

The paediatric dosage handbook (Taketomo *et al.*, 2000:15) defines a neonate as a newborn 1 to 4 weeks of age, and an infant as one month to one year of age. A child is then defined as 1 year to 12 years of age. According to Meyers and Kaenmmerer (2009:357), a child may also include a person between the neonates and infants. For the purpose of this study a child is regarded as a person from birth to 12 years of age.

An essential determination of the infection of HIV/AIDS is the stage of the infection (Mortimer & Loveday, 2002:6). The revised classification system for HIV-1 infection in children less than 13 years of age is presented in the Table 2.3 (Chakraborty, 2008:497; Taketomo, 2000:1129).

Table 2.3: Immunologic categories based on age-specific CD4 cell count and percentage of CD4+ T-lymphocyte

Immunologic Category	Age of child					
	≤12 months		1<6 years		6 to ≤12 years	
	CD4 cell count cells/mm^3	%	CD4 cell count cells/mm^3	%	CD4 cell count cells/mm^3	%
Category 1 Asymptomatic						
No evidence of suppression	>1500	>25	1000	>25	>500	>25
Category 2 Mildly symptomatic						
Moderate suppression	750-1499	15-24	500-999	15-24	200-499	15-24
Category 3						
Severe Suppression	<750	<15	<500	<15	<200	<15

Table 2.3 illustrates the CD4 cell count for children below the age of 13 years determined relative to their age. These counts are expressed as a percentage of the total amount of the lymphocytes (Chakraborty, 2008:497; Taketomo, 2000:1129). The CD4+ T-lymphocyte percentage serves as staging criteria for HIV/AIDS infection in children. The criteria incorporate the clinical symptoms ranging from no symptoms, to mild, moderate and severe suppression. Children born with HIV/AIDS are asymptomatic and classified in Category 1. During physical examination children often present with unexplained physical conditions such as those specified in Category 2 e.g. splenomegaly, hepatomegaly, lymphadenopathy, weight loss, unexplained low birth weight and fever of unknown reason (Wells *et al.*, 2009:438). Category 3 immune statuses refer to severe suppression, the last and final stage of HIV infection, AIDS (Evian, 2003:26).

The CDC (Centers for Disease Control and Prevention) (1993:3) and McFarland (2009:1174) refer to the following clinical categories:

- Category N: Asymptomatic, children who have just one of the conditions listed in category A (refer to Annexure A) or who have no signs and symptoms.
- Category A: Mildly symptomatic, children who have none of the conditions listed in categories B and C or two or more of the conditions listed in category A (refer to Annexure A).
- Category B: Moderately symptomatic, children who have none of the conditions in categories A and C or one of the conditions listed in category B (refer to Annexure A).
- Category C: Severe, children who have symptoms of one the conditions stated in Category C (refer to Annexure A).

Categories N, A, B, and C (Annexure A) are the classification for HIV in children. For example, a child with parotitis (category A) and nocardiosis, should be categorised as category B. A child with Kaposi's sarcoma will be classified as category C (Beers *et al.,* 2006:2345).

Category N is also referred to as the window period (Ajayi, 2003:19). An infected patient can remain without any symptoms from 6 months to a time of 11 years. In the asymptomatic phase, the HIV in the blood drops to a lower level, but continues to destroy the T-cells within the lymph nodes. An asymptomatic person will therefore be in good health and live a normal life, when the virus is latent (Stine, 2009:154). Category A, the mild symptomatic stage, represents the time immediately after the window period (Ajayi, 2003:20). This phase may last for months or years before the patient actually develops AIDS (Stine, 2009:155). During this stage of the infection, symptoms and signs start to develop because of biological attacks on the immune system, caused by viruses, parasites, and bacteria. During the moderate symptomatic phase (i.e. Category B), the viral load increases rapidly, and the immune system continues to deteriorate, and symptoms and signs of more severe HIV/AIDS related disease develop (Evian, 2003:30). Category C, the severe infection phase, is the last and fatal stage of the disease (Ajayi, 2003:20). Severe HIV infection is associated with a very high viral load, a low lymphocyte count, and a CD4 cell count below 200 cells/mm^3 (Evian, 2003:31).

The World Health Organization (2006:19) staging system of HIV/AIDS (refer to Appendix A) infection and disease in children differ from the Centers for Disease Control and Prevention (CDC), and other reference books on the Current Diagnosis and Treatment (McFarland, 2009:1174), in that, the WHO refers to no signs and symptoms or one sign listed in Category A, for Clinical Stage 1 infection, whereas the CDC refers to no signs and symptoms or persistent lymphadenopathy. The WHO refers furthermore only to the Herpes Zoster in Category B immune status, whereas the CDC includes this in Clinical stage II or Category A.

2.7 OPPORTUNISTIC INFECTIONS ASSOCIATED WITH HIV/AIDS IN CHILDREN

An opportunistic infection is “an infection caused by a normal non pathogenic organism in a host whose resistance has been decreased by disorders such as HIV/AIDS” (Myers & Kaemmerer, 2008:1328). Opportunistic infections are common in children with HIV/AIDS (Myers & Kaemmerer, 2008:1328). Opportunistic infections occur when the immune system functions are not effective; it is a major cause of morbidity and mortality in HIV infections and mycobacterial infections (ASHA, 2011). Opportunistic infections commonly occurring in children, include *inter alia Mycobacteruim Avium Complex*, *Mycobacteruim tuberculosis*, Salmonellosis, Candidiasis, Coccidiomycosis, Cryptococcal Meningitis, Histoplasmosis, Kaposi’s sarcoma, Systemic Non-Hodgkin’s Lymphoma, Hodgkin’s disease, Cryptosporidiosis, Isosporiasis, Microsporidiasis, *Pneumocystis carinii* Pneumonia, Toxoplasmosis, Cytomegalovirus, Hepatitis, Herpes simplex virus, Molluscum

Contagiosum, Oral hairy leukoplakia, Progressive Multifocal Leukoencephalopathy, Neurological conditions, Diarrhoea, Lymphadenopathy, warts, weight loss and wasting syndrome.

2.7.1 Mycobacterium Avium Complex (MAC)

Mycobacteruim Avium Complex (MAC) is caused by two related types of bacteria; i.e. *Mycobacterium intracellulare* and *Mycobacterium avium* (Nester *et al*., 2001:761). MAC usually affects the respiratory tract, although respiratory symptoms are not always HIV/AIDS related MAC (AEGIS, 2001:1). *Mycobacterium tuberculosis* are the most common type of mycobacterium infection; others include *Mycobacterium avium-intracellulare, Mycobacterium chelonei, Mycobacterium fortuitum, Mycobacterium kansasii, Mycobacterium leprae, Mycobacterium marinum, Mycobacterium ulcerus,* and *Mycobacterium xenopi* (Beers et al., 2006:2914).

In general the symptoms for MAC include fever, weight loss, diarrhoea, night sweats, unusually low levels of white and red blood cells, high blood levels of the liver enzyme alkaline phosphatise and painful intestines (AEGIS, 2001:1).

The transmission of MAC infections usually occurs through ingestion, inhalation, and inoculation through respiratory or gastrointestinal tract portals of entry (Benson *et al*., 2005:18). Localised enlargement of lymph nodes may develop in children (Nester *et al*., 2001:762).

The treatment protocol for children with MAC is clarithromycin, 7.5 -15 mg/kg body weight, with a max of 500 mg/dose twice daily orally, combined with ethambutol 15-25 mg/kg body weight (max 1 g/day) once daily orally, followed by chronic suppressive therapy, rifabutin 10-20 mg/kg which can be added for severe disease (CDC, 2009).

Table 2.4: Summary of the treatment protocol for children with MAC (CDC, 2009).

Drug	Weight	Max dosage
Clarithromycin	7.5-15 mg/kg	500 mg/dose
Ethambutol	15-25 mg/kg	2,5 g/day
Rifabutin	10-20 mg/kg	-

2.7.2 Mycobacterium tuberculosis

In developing countries, tuberculosis is one of the main opportunistic infections associated with HIV infection (Shearer & Hanson, 2003:174). Tuberculosis (TB) is the primary cause of death among HIV/AIDS infected Africans (Churchyard & Corbet, 2005:433). Tuberculosis is caused by the *Mycobacterium tuberculosis* organism (Webber, 2009:138). The primary infection is caused by the

tubercle bacilli. The primary infection is most of the time asymptomatic and is followed by a latent (dormant) phase (Beers *et al.,* 2006:1509).

Primary tuberculosis in children often spreads to the highly vascular epiphyses (Beers et al., 2006:1516). Lymphohematogenous dissemination through the lungs to extra pulmonary sites, including meninges and brain, skeleton, eyes, joints, lymph nodes, kidneys, intestines, larynx and skin, usually occur in infants (Hay *et al*., 2009:498). The main symptoms and signs of *Mycobacterium tuberculosis* includes chronic cough (lasting longer than 2 weeks), weight loss or failure to gain weight, anorexia, fever and night sweats (Harrison, 2002:357).

According to Hay *et al*. (2009:499), the most common risk factor for tuberculosis in children is exposure to a *Mycobacterium tuberculosis* infected adult. Tuberculosis is the result of inhalation of airborne particles containing *Mycobacterium tuberculosis* bacilli through singing, coughing, and other enforced respiratory exercises (Beers *et al.,* 2006:1510).

Tuberculosis is treated similarly in HIV negative and HIV positive persons. There are interactions between antituberculosis and ARV treatment; caution should be taken when treating HIV/AIDS patients with concurrent TB (Churchyard & Corbet, 2005:433). Rifamycins have drug interactions with indinavir, nelfinavir, and ritonavir and may decrease their serum concentration and the pharmacological effects of zidovudine (Tatro, 2004:768,975,1170).

According to Harrison (2002:362), the standard treatment regimen for tuberculoses in children is a four-month supervised regimen five times a week. For an uncomplicated primary disease rifampicin, isoniazid, and pyrazinamide are given for a period of eight weeks, followed by isoniazid and rifampicin only for eight more weeks. Isoniazid and rifampicin are given for four months in severe cases of tuberculosis. When these drugs are used individually the standard doses are isoniazid (10 to 15 mg/kg per day in two divided doses, maximum of 300 mg/24 hours), or rifampicin (10 to 20 mg/kg per day in two divided doses) or pyrazinamide (20 to 40 mg/kg per day in two divided doses, maximum of 2 g/24 hours) or ethambutol (15 to 25 mg/kg per day once daily) (Fox, 2002:744).

According to the standard treatment guidelines for hospitals of the South African Department of Health (2010:96), HIV/AIDS patients should be treated as follows:

- When a patient's CD4 cell count is <200 cells/mm^3, first start with the TB treatment. As soon as the TB treatment is tolerated (usually between 2-8 weeks of TB treatment) start with the ART.
- If a patient's CD4 cell count is between 200-350 cells/mm^3, start with the TB treatment and then start with ART after 8 weeks (intensive phase) of TB treatment.

- When a patient's CD4 cell count is >350 cells/mm^3, start with the TB treatment and defer ART.

- If the CD4 cell count is not available, start with the TB treatment and after 2-8 weeks of TB treatment, and the patient has severe disease or other clinical indications of advanced immune deficiency, start with ART.

In Table 2.5 the treatment regimen for tuberculosis in children is adapted from the Department of Health (2008:292).

Table 2.5: Treatment regimen for tuberculosis in children

Body weight of children	Intensive phase (Treatment given 7 days a week for 2 months)	Continuation phase (Treatment given 7 days a week for 4 months)
	Rifampicin, Isoniazid and Pyrazinamide (60 mg, 30 mg, 150 mg)	Rifampicin and Isoniazid (60 mg,30 mg)
2-2.9 kg	30 mg, 15 mg, 75 mg	30 mg, 15 mg
3-5.9 kg	60 mg, 30 mg, 150 mg	60 mg, 30 mg
6-8.9 kg	90 mg, 45 mg, 225 mg	90 mg, 45 mg
9-11.9 kg	120 mg, 60 mg, 300 mg	120 mg, 60 mg
12-14.9 kg	150 mg, 75 mg, 375 mg	150 mg, 75 mg
15-19.9 kg	180 mg, 90 mg, 450 mg	180 mg, 90 mg
20-24.9 kg	240 mg, 120 mg, 600 mg	240 mg, 120 mg
25-29.9 kg	300 mg, 150 mg, 750 mg	300 mg, 150 mg
30-35.9 kg	360 mg, 180 mg, 900 mg	360 mg, 180 mg
36-40 kg	420 mg, 210 mg, 1050 mg	420 mg, 210 mg

The treatment regimen for new cases of tuberculosis in children above 8 years of age is adapted from the Department of Health (2008:293).

Table 2.6: Treatment regimen for new cases of tuberculosis in children above 8 years of age

Patient body weight	Initial phase (Treatment given 7 days a week) for two months	Continuation phase (Treatment given 7 days a week for four months)	
	Rifampicin, Isoniazid, Pyrazinamide and Ethambutol (150 mg, 75 mg, 400 mg, 275 mg)	Rifampicin and Isoniazide (150 mg, 75 mg)	Rifampicin and Isoniazide (300 mg, 150 mg)
20-24 kg	225 mg, 112,5 mg, 600 mg, 412,5 mg	225 mg, 112, 5 mg	-
25-29 kg	225 mg, 112.5 mg, 600 mg, 412.5 mg	300 mg, 150 mg	-
30-37 kg	300 mg, 150 mg, 800 mg, 550 mg	300 mg, 150 mg	-
38-54 kg	450 mg, 225 mg, 1200 mg, 825 mg	450 mg, 225 mg	-
55-70 kg	600 mg, 300 mg, 1200 mg, 1100 mg	-	600 mg, 300 mg
> 71 kg	750 mg, 375 mg, 2000 mg, 1375 mg	-	600 mg, 300 mg

The above treatment should be given with pyridoxine 25 mg daily for the duration of the therapy (Department of Health, 2008:293).

2.7.3 Salmonellosis

Salmonellosis is caused by the bacteria *Salmonella* genus (Nester *et al*., 2005:604) and members of the *Enterobacteriaceae* family (Engelkirk & Burton, 2007:317). There are two species of Salmonella, i.e. *Salmonella enterica* and *Salmonella bongori* (Nester *et al*., 2005:604) and are members of the *Enterobacteriaceae* family. The bacteria are gram-negative bacilli that attack intestinal cells, discharge endotoxin, and form cytotoxins and enterotoxins (Engelkirk & Burton, 2007:317). Salmonellosis occurs 20 times more regularly in HIV positive individuals than in HIV negative ones (AEGIS, 2001:1). Disease caused by *Salmonella* can be divided into four categories, i.e. bacteremia, extraintestinal localised infection, acute gastroenteritis and eneteric fever (paratyphoid and typhoid fever) (Wells *et al*., 2009:431).

The symptom of salmonellosis includes fever, vomiting, diarrhoea, abdominal pain and weight loss (Nester *et al*., 2005:604). Salmonellosis occurs mostly in infants, children and adolescents (Wells *et al*., 2009:431).

Transmission of salmonella in patients is usually *via* ingestion, contaminated food (unpasteurised milk, raw fruits and vegetables, meats and poultry) and contaminated water (Engelkirk & Burton, 2007:317).

Ceftriaxone 25 - 37.5 mg/kg may be used in children intramuscular or intravenous for 7 to 10 days for severe salmonella disease (Beers et al., 2006:1470). Fluid and electrolyte replacement are furthermore important in the management of salmonellosis (Wilson *et al.*, 2004:124).

2.7.4 Fungal infections

Fungal infections usually occur in HIV-infected individuals with severe immune suppression (CD4 cell count < 100 cells/mm^3) (CDC, 2009). These fungal infections can be divided in candidiasis, coccidioidomycosis, cryptococcal meningitis, and histoplasmosis. A brief discussion of these infections follows in subsequent paragraphs.

2.7.4.1 Candidiasis

Candidiasis is caused by the *Candida albicans* organism (Harrison, 2002:242). Candidiasis involving the mouth (oral i.e. thrush) and oesophagus is one of the most common problems in patients with HIV/AIDS (Colvin, 2010:338), occurring in 50%-58% of patients, similar to the prevalence patterns of dermatitis in these children (CDC, 2009:2). Symptoms of oral candidiasis are adherent flaky plaques covering all or part of the tongue, lips, gums and buccal mucous membranes (Harrison, 2002:243). Mucocutaneous candidiasis may involve any mucous or cutaneous surface of the body (Guitierrez, 2008:321).

Therapy depends on the severity of the disease (Guitierrez, 2008:322). Oral thrush candidiasis in children can be treated with nystatin suspension (1 mL of 100,000 IU/mL suspension) after meals for 7 days; fluconazole 3-6 mg/kg daily for 7 to 14 days, pain may be relieved with paracetamol (Department of Health in South Africa, 2010:53). Esophageal candidiasis may be treated with fluconazole, 3 mg/kg/day for up to 21 days (AEGIS, 2001:1; Department of Health in South Africa, 2010:53). Amphotericin is used for severe illness (Beers *et al.*, 2006:988).

2.7.4.2 Coccidiomycosis

Coccidiomycosis is caused by the fungus *Coccidioides immitis.* Infection results from inoculation or inhalation of arthrospores (Wilson & Fairall, 2007:492).

The general signs and symptoms of acute pulmonary coccidiomycosis include headaches, fatigue, fever, arthralgias, and dry cough, dyspnea, and pleuritic and chest pains. Chronic progressive pulmonary coccidioidomycosis symptoms are sub-acute and include fever, productive cough, hemoptysis, pleuritic chest pain and weight loss (Proia, 2003:389).

In endemic areas of HIV-infected patients, coccidioidomycosis is a common opportunistic infection. The disease manifestations range from focal pulmonary infiltrates to widespread military disease with multiple organ involvement and meningitis (McPhee, 2009:1361).

The preferred therapy for non-menigeal coccidiomycosis infection in the acute phase (disseminated disease or diffuse pulmonary) in children is amphotericin B deoxycholate 0.5 to 1.0 mg/kg body weight intravenously once daily continued until clinical improvement is obtained (CDC, 2009:2). In the acute phase of meningeal infection, fluconazole, (5 to 6 mg/kg body weight intravenously once daily) can be used or twice daily in an oral dose (maximum of 800 mg per day) (CDC, 2009:3; Benson *et al.,* 2005: 50).

2.7.4.3 Cryptococcal meningitis

According to Wilson and Fairall (2005:493), *Cryptococcus neoformans* is the fungus that causes cryptococcal meningitis.

The transmission of the Cryptococcus organism is through inhalation. *Cryptococcus* may spread commonly to the brain and meninges, typically manifesting as microscopic multifocal intracerebral lesions. Bigger focal brain lesions and meningeal granulomas may be evident. Cryptococcal meningitis is fatal and requires aggressive therapy (Beers *et al*., 2006:1531).

The first symptoms of cryptococcal meningitis are usually headaches, vomiting, and nausea, with fever that can develop over days continuing for months (McPhee & Papadakis., 2009:1363). Papilledema and meningeal signs generally are seizures, and cranial nerve dysfunction may also occur (Hay *et al.,* 2007:1217).

For cryptococcal meningitis in children, the standard treatment regimen to start with is amphotericin B (1.0 mg/kg, intravenously, once daily) for 14 days or longer. Thereafter the treatment regimen can change to fluconazole (12-15 mg/kg per day, maximum 400 mg) for a period of 8 to 10 weeks. Relapse episodes can be treated with amphotericin B for a period of 4 to 8 weeks (Department of Health, 2010:58; Shelburne & Hamil, 2009:1363).

2.7.4.4 Histoplasmosis

According to Beers *et al. (2006:1534*) histoplasmosis is a hematogenous and pulmonary infection cause by *Histoplasma capsulatum*. It generally follows an asymptomatic primary infection and is regularly chronic.

The transmission of Histoplasmosis is through inhalation of condia. The inhalation of the condia converts into budding cells that are engulfed by phagocytic cells in the lungs according to Dominguez *et al.* (2009:1219).

Progressive disseminated histoplasmosis generally occurs among patients with a CD4 cell count of less than 150 cells/mm^3. Localised pulmonary histoplasmosis may occur in patients with a CD4 cell count >300 cells/mm^3 (Benson *et al.,* 2005:57).

Symptoms of primary pulmonary histoplasmosis include dry cough, dyspnea, myalgias, fever, chills and pleurisy. Immune-mediated rheumatological syndromes may also develop in patients with primary infection. Patient with HIV/AIDS is usually associated with progressive disseminated histoplasmosis signs, include cough, dyspnea, diarrhoea, weight loss, mucosal ulcerations and fever (Proia, 2003:385).

Effective use of ART may reduce the incidence of histoplasmosis (Benson *et al*., 2005:56). The severity of infection and the immune status of the host, however, play a role in the decision to treat histoplasmosis (Proia, 2003:386). For example, for mild disseminated histoplasmosis in children itraconazole oral solution can be used, starting with a dose of 2 to 5 mg/kg body weight per dose (maximum 200 mg), needed to be taken 3 times a day for 3 days, followed by 2 to 5 mg/kg body weight (maximum 200 mg) per dose needed twice daily for 12 days. For severe disseminated histoplasmosis Amphotericin B, 3 mg/kg body weight is needed intravenously once daily for 7 to 14 days. This is followed by chronic suppressive therapy with itraconazole, started with a dose of 2 to 5 mg/kg body weight per dose (maximum 200 mg), taken 3 times a day for 3 days, followed by 2 to 5 mg/kg body weight (maximum 200mg) per dose twice daily for 12 days (CDC, 2009:6).

2.7.5 Kaposi's Sarcoma (Human Herpes virus 8)

The Human Herpes virus type 8 causes Kaposi's sarcoma. Kaposi's sarcoma is a tumour of vascular neoplasm (Daniel & Levy, 2003:282).

The signs of Kaposi's sarcoma are purple or red plaques, macules or nodules on cutaneous or mucous membranes. Marked oedema may occur with a small amount of or no skin lesions. The symptoms of pulmonary Kaposi's sarcoma are shortness of breath, hemoptysis, and cough or chest pain (Berger, 2009:131).

The in vitro activity of cidofovir, foscarnet, and ganciclovir against Human Herpes virus type 8, are associated with reduced disease progression. Effective antiretroviral treatment suppresses HIV-1 replication and reduced Kaposi's sarcoma in infected children (Benson *et al*., 2005: 75). ART and radiotherapy can be used for a tumour with local oedema (Spencer, 2005:214).

2.7.6 Lymphoma

Lymphoma is the malignant proliferation of lymphoid cells, arising from and associated with the spleen, lymph nodes and thymus (Maloney *et al.,* 2009:863*).* There are two basic forms of Lymphoma, i.e. Systemic Non-Hodgkin's Lymphoma, and Hodgkin's disease. A short discussion on these types of lymphoma follows subsequently.

2.7.6.1 Systemic Non-Hodgkin's Lymphoma (NHL)

Paediatric Non-Hodgkin's lymphoma can be sub-divided in a few groups, i.e., non-cleaved cell, lymphoblastic lymphomas, large B-cell lymphoma and anaplastic large cell lymphoma. (Maloney, 2009:867). About 10% of HIV infected patients are infected with Non-Hodgkin's lymphoma, and can be associated with the Epstein-Barr virus, a herpes virus (AEGIS, 2001:12).

The symptoms and signs at presentation are determined by the position of lesions and the level of dissemination. The signs of lymphoma in children with HIV/AIDS include weight loss, fever, extranodal manifestation of hepatomegaly, and abdominal distension. Non-Hodgkin's Lymphoma can involve the central nervous system or bone marrow (McClain, 2003:338).

Systemic chemotherapy is the choice of treatment used mostly in Non-Hodgkin's lymphoma, unless the entire tumour can be removed; surgical resection is not used (Maloney *et al*., 2009:867). Non-Hodgkin's lymphoma in low grade can be treated with fludarabine, rituxmab, and ibritumomab. Tiuxetan or tositumomab can be used for relapsed or refractory disease. Non-Hodgkin's lymphoma in high grade combination therapy can be depending on the histologic classification, but usually include vincristine, cyclophosphamide, doxorubicin and prednisone (Rugo, 2009:1467).

2.7.6.2 Hodgkin's disease

Hodgkin's disease is present at earlier stages than Non-Hodgkin's disease (McClain, 2003:345). Overall, about 4% of HIV/AIDS infected patients develop Hodgkin's disease (Spencer, 2005:21).

The symptoms and signs of Hodgkin's disease in children usually presents with painless cervical adenopathy. The lymph nodes have a rubbery texture and regularly feel firmer than inflammatory nodes. Hodgkin's disease arises in lymph nodes and reach the nodal groups. Splenomegaly and hepatomegaly are symptoms of the advanced disease. Symptoms of fever greater than 38ºC, unintentional weight loss and nights sweats can also be present (Maloney, 2009:864).

The treatment protocol depends on the different stages of the disease. The stages of Hodgkin's disease in general can be treated with a combination of chemotherapeutic agents (doxorubicin, vinblastine, bleomycin, and dacarbazine) plus radiation therapy or a longer course of chemotherapy alone. Low risk Hodgkin's disease in children can be treated for a period of nine weeks with AV-PC (adriamycin [doxorubicin], vincristine, prednisone, and cyclophosphamide) (Maloney *et al*., 2009:864). For intermediate risk children, etoposide and bleomycin are added to the treatment for low risk patients for 4 to 6 months (Beers *et al.,* 2006:1168). A combination of chemotherapy and irradiation is used in advanced stages of the disease (Maloney *et al*., 2009:865).

2.7.7 Protozoal infections

A brief discussion of these infections follows in subsequent paragraphs.

2.7.7.1 Coccidiosis (Cryptosporidiosis, Isosporiasis) and Microsporidiosis

The causes of coccidiosis are *Cryptosporiduim* species, *Isospora belli, Cyclosporacayetanensis*, and S*arcocystis species*. Microsporidiosis is caused by at least 14 species, *Enterocytozoon bieneusi* and *Encephalitozoon intestinalis* are the most usual ones (Rosenthal, 2009:1336). A discussion of cryptosporidiosis, isosporiasis and microsporidiosis follows in the subsequent paragraphs.

- **Cryptosporidiosis**

Cryptosporidiosis is caused by *Cryptosporidium* species, and infects the small bowel mucosa, and the extraintestinal sites and the large bowel mucosa in immunosuppressed patients (Benson *et al.*, 2005:16).

The symptoms and signs in paediatric patients include abdominal cramping, watery diarrhoea, accompanied by nausea, vomiting and fever. In patients with HIV/AIDS, cryptosporidiosis is a well characterised cause of diarrhoea. Extra intestinal disease with HIV/AIDS is also caused by *Cryptosporidium* (Rosenthal, 2009:1336).

The treatment of patients with cryptosporidiosis in HIV/AIDS individuals are HAART with nitazoxanide (Beers *et al.*, 2006:1566; Dominguez *et al.*, 2009:1201). Children 1 to 3 years of age may be treated with 100 mg nitazoxanide twice daily. Children aged 4 to 11 years may be treated with 200 mg nitazoxanide twice daily whereas those older than 12 years may be treated with 500 mg twice daily for treatment duration of a maximum of 14 days (CDC, 2009:12).

- **Isosporiasis**

Isosporiasis is caused by *Isospora belli.* The infection is the result of contaminated food and water (Benson *et al.*, 2005:105). The usual symptoms and signs of isosporiasis include diarrhoea anorexia, abdominal cramps, malaise, vomiting, weight loss and headache. Fever in patients is unusual (Benson *et al.*, 2005:105; Rosenthal, 2009:1338).

Isosporiasis is effectively treated with trimethoprim (160 mg) and sulphametoxazole (800 mg) four times daily for a period of ten days. For improved adherence and tolerability trimethoprim (320 mg) plus sulfamethoxazole (1600 mg) can be given twice daily for ten to fourteen days (Benson *et al.*, 2005:105). Higher doses can be used in HIV/AIDS patients (Rosenthal, 2009:1338).

- **Microsporidiosis**

Microsporidiosis is an infection with microsporidia (Beers *et al.,* 2006:1569). In HIV/AIDS patients the infection is commonly associated with *E. bieneusi* and *E. intestinalis* (Rosenthal, 2009:1336).

The disease is mainly contracted through ingestion (Webber, 2009:270), and also through direct inoculation of the eyes (Rosenthal, 2009:1336). The disease causes chronic diarrhoea, disseminated infection and corneal disease (Beers *et al.,* 2006:1569).

Microsporidia treatment is usually complex (Rosenthal 2009:1338). In children, albendazole treatment of 7.5 mg/kg body weight (maximum dose of 400 mg) twice daily orally can be used until immune reconstitution, after starting with HAART (CDC, 2009) HAART in HIV/AIDS patients may also lead to improvement of symptoms (Beers *et al.,* 2006:1570).

2.7.8 Pneumocystis Pneumonia

Pneumocystis jiroveci is the infection that causes Pneumocystis Pneumonia (Wilson *et al.,* 2005:493). *Pneumocystis jiroveci* refers to the different species that infect humans whereas *Pneumocystis carinii* refers to pneumocystis that infects rodents (Benson *et al.,* 2005:5).

The incidence of *Pneumocystis pneumonia* has increased dramatically since the beginning of HIV/AIDS. In patients with HIV/AIDS, *Pneumocystis pneumonia* is one of the most common pulmonary opportunistic infections (Engelkirk & Burton, 2007:302). The mode of transmission is airborne, and most of the cases occur when the patient's CD4+ count is below 200 cells/mm^3 (Shelburne, 2009:1361).

The signs and symptoms of *Pneumocystis Pneumonia* includes a shortness of breath, non-productive cough developing over a time, bilateral pulmonary pacification, hypoxia (Wilson *et al.,* 2005:493*),* fever and dyspnoea (Wells *et al*., 2009:444; Shelburne *et al.,* 2009:1361). Cotrimoxazole can be used orally as initial dose treatment (Department of Health, 2008:286). Table 2.7 summarises the initial treatment for *Pneumocystis Pneumonia* (Adapted from Department of Health, 2008:286).

Table 2.7: The initial dose treatment (before referral) for Pneumocystis Pneumonia

Cotrimoxazole treatment can be used for Pneumocystis Pneumonia given four times daily.			
Weight (kg)	**Age** (Month/Years)	**Select between one of the following**	
		Suspension (mL)	**Tablets** (80/400 mg)
≥ 2.5-3.5 kg	Birth to 1 month	2,5 mL	-
≥ 3.5-7 kg	≥ 1 to 6 months	5 mL	-
≥ 7-11 kg	≥ 6 to 18 months	7,5 mL	-
≥ 11-17.5 kg	≥ 18 months to 5 years	10 mL	-
≥ 17.5 -25 kg	≥ 5 to 7 years	15 mL	120/600 mg
≥ 25 -35 kg and above	≥ 7-11 years	20 mL	160/800 mg

According to the Department of Health (2010:44), the preferred hospital treatment for children with Pneumocystis Pneumonia is paracetamol 10 to 15 mg/kg/dose 6 hourly, ampicillin intravenously 100 mg/kg/day, and gentamicin intravenously. For patients 10 years and younger, 8 mg/kg of gentamicin can be used immediately and then 6 mg/kg per day after that. For patients older than 10 years 7 mg/kg immediately, and after that 5 mg/kg, the total duration of the therapy is 7 to 10 days (Department of Health, 2010:44).

2.7.9 Toxoplasmosis

Toxoplasmosis is caused *by Toxoplasma gondi* (Beers *et al.,* 2006:1584*).* Intracellular replication of the tachyzoites causes cell lysis and spread of the infection to adjacent cells or to other tissues via the blood stream. *Toxoplasma gondi* in chronic infection appears as bradyzoite containing tissue cysts that do not trigger an inflammatory reaction (Dominguez, 2009:1196).

The primary infection of toxoplasmosis is characterised by lymphadenopathy, headache, malaise, fever and a sore throat. The congenital infection presents as an acute infection and leads to central nervous system abnormalities and retinochoroiditis. In HIV (+) patients infected with toxoplasmosis, toxoplasmosis can lead to miocarditis, retinochoroiditis, pneumonitis and encephalitis following acute infection (Rosenthal, 2009:1330).

For the treatment of congenital toxoplasmosis pyrimethamine can be used. A dosage of 2 mg/kg body weight is needed once daily for a period of 2 days, there after 1 mg/kg body weight is needed once daily for a period of 2 to 6 days. After that 1 mg/kg body weight is needed orally 3 times a week, added with folic acid, 10 mg orally with each dose of pyrimethamine, plus dapsone 50 mg/kg body weight needed twice daily (CDC, 2009:16).

The treatment for acquired toxoplasmosis infections in children is pyrimethamine 2 mg/kg body weight (maximum dose of 50 mg daily) needed daily for a period of 3 days. After that 1 mg/kg body

weight (maximum dose of 25 mg daily) is needed once daily, plus sulfadiazine, 25 to 50 mg/kg body weight (maximum dose of 1,0 to 1,5 g/dose) needed orally 4 times a day, plus leucovorin 10 to 25 mg orally once daily, followed by chronic suppressive therapy, the duration of the therapy is for 6 weeks and longer (CDC, 2009:17). In patients who cannot tolerate sulphonamides, clindamycin can be used (Dominguez, 2009:1197).

2.7.10 Viral infections

A brief discussion of these infections follows in subsequent paragraphs.

2.7.10.1 Cytomegalovirus

Infection with the Cytomegalovirus is a main cause of death and morbidity in immunocompromised persons (Beers *et al.*, 2006:1605). It usually occurs in patients with a CD4 count below 50-100 cells/mm^3 (Spencer, 2005:153).

The Cytomegalovirus can be transmitted through body fluids, blood or transplanted organs (Beers *et al.,* 2006:1605) and is usually transmitted in utero. The cytomegalovirus spread during reactivated or primary maternal infection, occurring in 1-4 % of pregnancies, with a transplacental transmission rate of 40%. Cytomegalovirus can be asymptomatic in the newborn stage (Thilo *et al.,* 2009:51).

The Cytomegalovirus retinitis is therefore one of the main clinical manifestations and usually occurs as a unilateral disease (Benson *et al.*, 2005: 34). Peripheral retinitis may be asymptomatic or presents with floaters or peripheral visual field defects (Benson *et al.*, 2005:34).The cytomegalovirus affects the retina, throat and colon, and can also affect almost any other internal organ.

Cytomegalovirus encephalitis includes signs and symptoms of headache and fever. Symptoms of chest pains, difficulty in swallowing and hiccups are signs of cytomegalovirus esophagitis. Signs of cytomegalovirus colitis and gastritis include diarrhoea, weight loss, abdominal pain, and rectal spasms (AEGIS, 2001:4).

The cytomegalovirus in children is treated with an induction treatment of ganciclovir (5 mg/kg every twelve hours intravenously for a period of fourteen to twenty one days) followed by a lower dose of maintenance treatment (5 mg/kg intravenously every 24 hours) 5 to 7 days a week, continued until improvement of symptoms are obtained (CDC, 2009:18; Department of Health, 2010:59; Shandera, 2009:1216).

2.7.10.2 Hepatitis

Hepatitis refers to the inflammation of the liver characterised by diffuse or patchy necrosis (Beers *et al.*, 2006:218). Hepatitis viruses can be divided in five types, i.e. A, B, C, D and E viruses: Hepatitis A virus, Hepatitis B virus, Hepatitis C virus, Hepatitis D virus and Hepatitis E virus. (Beers *et al.*, 2006:218). For the diagnosis and treatment of Hepatitis it is important to make sure which type of Hepatitis is present (Webber, 2009:92).

The Hepatitis A virus is a RNA picornavirus (single stranded) (Beers *et al.*, 2006:221) causing symptoms of fever, abdominal discomfort, lethargy, vomiting and diarrhoea (Webber, 2009:92). The transmission is usually through contaminated food and water (AEGIS, 2001:15). There is no specific treatment for the infection with this type of virus, however, but fatty foods must be avoided (Sokol *et al.*, 2009:622).

The Hepatitis B virus is a double stranded DNA genome, with an outside surface coat and internal core protein (Friedman, 2009:586). Hepatitis B infection is more severe than Hepatitis A (Webber, 2009:92) and is usually transmitted through infected blood and blood products (Friedman, 2009:586). Bed rest and a nutritious diet are recommended for patients with active symptomatic Hepatitis B (Hay, 2009:622). For children with chronic hepatitis B, Interferon-α is recommended, a dose of (5-6 million U/m^2 body surface areas injected 3 times a week subcutaneously) (Sokol *et al.*, 2009:624). In children lamivudine (3 mg/kg/d up to 100 mg/d orally for twelve months) is usually successful in 25% of children (Sokol *et al.,* 2009:624; Webber, 2009:174).

The Hepatitis C virus is a *flavivirus* with single standard RNA (Beers *et al.*, 2006:222). Similar to Hepatitis B, Hepatitis C is transmitted through contact with infected blood. The high incidence of mildly symptomatic or asymptomatic appearance is not usually recognised in acute Hepatitis C infected patients (Benson *et al.* 2005:87). Interferon α (3 million U/m^2 for six to twelve months three times a week) and ribavirin (15 mg/kg daily) in combination can be used for chronic Hepatitis C in children (Sokol *et al.*, 2009:627).

The Hepatitis D virus can only replicate in the presence of the Hepatitis B virus and is a defective RNA virus (Beers *et al.*, 2006:222). Hepatitis D in combination with Hepatitis B can cause acute hepatitis. Chronic Hepatitis B can also cause chronic Hepatitis D. The treatment of Hepatitis D is the same as for Hepatitis B (Sokol *et al.,* 2009:626; Webber, 2009:174).

The Hepatitis E virus is similar to hepatitis A infection, and is most commonly found in young adults. The signs and symptoms of the infection include fever, nausea, vomiting, anorexia, and jaundice. Transmission is through water and can also be asymptomatic in children (Webber, 2009:94). There is no specific therapy for Hepatitis E (Sokol *et al.*, 2009:626).

2.7.11 Herpes viruses

2.7.11.1 Herpes simplex virus

Herpes simplex virus infection can be sub-divided into Herpes simplex type 1 and Herpes simplex type 2 (Shandera *et al*., 2009:1205). Herpes simplex type 1 causes cold sores and is sometimes associated with systemic lesions in infants (Webber, 2009:268) and respiratory tract infection (National Department of Health, 2008:94). The usual manifestation of Herpes simplex type 2 is genitalis (Benson *et al*., 2005: 50).

In patients with a CD4 cell count less than 100 cells/mm^3, ulceration may occur in the perineum and buttocks (Benson *et al*., 2005:70).

Based on the treatment guidelines for Herpes simplex virus according to the National Department of Health (2008:94), acyclovir is needed for patients younger than two years of age, 200 mg three times daily for a period of 5 days, and for those 2 years and older, 400 mg acyclovir can be used 3 times daily for a period of 5 days. If super infections occur, flucloxacillin 12-25 mg/kg per dose (maximum of 500 mg per dose) is needed four times a day, with amoxicillin 10-25 mg/kg, 3 times a day for secondary bacterial infections (Department of Health, 2010:54).

2.7.11.2 Varicella and Herpes Zoster viruses

HIV-1 infected persons are fifteen to twenty five times more at risk for Herpes Zoster infection than general persons. Herpes Zoster can occur at any CD4 cell count in HIV-1 infected patients (Benson *et al.* 2005:72).

Varicella Zoster infection occurs in HIV-1 infected patients with a CD4 cell count <50 cells/mm^3 (Benson *et al.,* 2005:72). Varicella Zoster virus is a Human herpes type 3 virus (Benson *et al*., 2005:162). The Varicella Zoster virus causes chickenpox, and is an acute systemic virus infection generally found during childhood (Department of Health, 2008:190). This infection usually consists of mild symptoms with vesicles that are followed by crops and papules becoming crusted (Beers *et al*., 2006:1603; Department of Health, 2010:54) and containing a cloudy fluid (Department of Health, 2008:189).

According to the Department of Health (2010:54), the treatment guideline for Varicella Zoster is acyclovir 80 mg/kg orally every 6 to 8 hours for a period of 7 to 14 days. Flucloxacillin 12-25 mg/kg per dose (maximum of 500 mg per dose) is added 4 times daily, with amoxicillin 10-25 mg/kg, 3 times daily for secondary bacterial infection in children. For the treatment of Herpes Zoster in children, acyclovir 10 to 20 mg/kg/dose 3 to 6 times daily is required (Department of Health, 2010:54).

2.7.11.3 Molluscum Contagiosum

Molluscum Contagiosum is caused by a poxivirus that induces the epidermis to reproduce, and form bumps, and are usually seen in paediatric children as well as sexually active adolescents (Moreli, 2009:386).

Molluscum is usually spread through direct contact with lesions or through sexual contact (Webber, 2009:270). Molluscum lesions can appear any place on the body except the soles and palms (Beers *et al.,* 2006:998) and usually occur on the face or upper trunk (AEGIS, 2001:20).

Patients with a T-helper cell count less than 100 cells/mm^3 are usually at risk for Molluscum contagiosum infection. In patients with HIV/AIDS it is usually difficult to remove molluscum unless the immunity improves. Intergeneral highly active antiretroviral treatment in HIV/AIDS patients helps to clear molluscum spontaneously (Berger, 2009:128). Iodine tincture can be used with an applicator (Department of Health, 2010:55), topical cantharidien, cryotherapy with liquid nitrogen, and curettage can be used additionally (Moreli *et al*., 2009 386).

2.7.11.4 Oral hairy leukoplakia

The Epstein-Barr virus is the cause of oral hairy leukoplakia (Beers *et al*., 2006:1631). The symptoms are usually white, thickened, corrugated patches with an adherent shaggy or hairy surface on the tongue (Flaitz *et al*., 2003:258), that cannot be removed from the mucosal surface. The leukoplakia can range in diameter (Lustig *et al*., 2009:194). Oral leukoplakia can occur at any CD4+ range, but usually occur in those with CD4+ count under 200 cells/mm^3 and can be treated with acyclovir; the dose of acyclovir for patients 3 months to 2 years is 100 mg 4 times daily, and over 2 years 200 mg 4 times daily and topical podophyllin (AEGIS, 2001:2).

2.7.11.5 Progressive Multifocal Leukoencephalopathy

Progressive multifocal leukoencephalopathy is caused by a polyomavirus called JC virus. It usually appears in patients with HIV/AIDS because of their impaired cell-mediated immunity. The signs and symptoms include hemiplegia, hemiparesis, ataxia, aphasia, mental dysfunction and visual field disturbances (Shandera *et al.,* 2009:1231).

Some individuals may experience neurological improvement, whereas others might become neurologic stable with antiretroviral treatment when the CD4 cell count rises in progressive multifocal leukoencephalopathy patients (Benson *et al*., 2005:77).

2.7.12 Neurological conditions

Neurological conditions refer to impairment of the peripheral and central nervous system (Evian, 2003:151). The AIDS dementia complex is a chronic cognitive deterioration due to the brain

infection, and might be seen at later stages of HIV infection (Beers *et al.,* 2006:1818) where the CD4 cell count is below <100 cells/mm^3, and highly active antiretroviral therapy is not used (Spencer, 2005:181). The symptoms and signs in the early stage of AIDS dementia is slow thinking and expressing, difficulty in concentrating, manifestation of depression and apathy (Beers *et al.*, 2006:1818; Spencer, 2005:181). Treatment of AIDS dementia complex with highly active antiretroviral therapy usually improves the cognitive function and CD4 cell counts (Beers *et al.*, 2006:1819; Spencer, 2005:181).

2.7.13 Other conditions and complications

2.7.13.1 Diarrhoea

During the mild form of HIV infection, diarrhoea usually occurs (Evain, 2003:130) and may be a sign of systemic or intestinal infection (Spencer, 2006:150) leading to dehydration and weight loss. Children must be treated for dehydration (Evain, 2003:130), with oral rehydration fluids (Department of Health, 2008:22) and a replacement of optimal nutritional therapy, with an additional dose of Vitamin A (1 capsule of Vitamin A 100 000 IU for infants 6-11 months is needed daily, and 2 capsules for 12 months and older) (Department of Health, 2008:22). Children still being breastfed, requires more frequent and longer breastfeeds daily. Small meals are furthermore required at least 6 times a day for infected children (Department of Health, 2010:52).

2.7.13.2 Lymphadenopathy

Lymphadenopathy occurs in the advanced stage of HIV/AIDS infection and is characterised by night sweats, fevers, weight loss, local pain and signs of obstruction to local lymphatic circulation (Spencer, 2005:88); symptoms of chronic cough or an enlarged liver can also appear. Lymphadenopathy may persist for months (Evian, 2003:146).

2.7.13.3 Warts

Warts are caused by Human papillomavirus (HPV) infection (Spencer, 2005:47) and are benign epidermal lesions (in particular the mucosal- and cutaneous squamous epithelium) occurring frequently in HIV-infected children (Beers *et al.*, 2006:999). The HPV can be divided in more than a 100 distinct types (CDC, 2009:24). The signs and symptoms and HIV-infection includes a smooth, flat, skin-coloured or slightly pigmented surface occurring particularly on the face, backs of the hands and knees (Department of Health, 2008:95). The warts are usually asymptomatic but may sometimes cause pain, especially when the warts are located on a weight bearing surface areas, for example, under the feet. The main therapy for HPV-infection in children is liquid nitrogen, and for flat warts topical retinoid gel may be used. An application of 50% trichloroacetic acid once monthly is further recommended (Department of Health, 2010:56).

2.7.13.4 Weight loss and wasting syndrome

HIV/AIDS has a direct effect on the gastro-intestinal tract. Weight loss and wasting syndrome may occur because of chronic diarrhoea (two or more loose stools daily for thirty or more days) (Department of Health, 2010:60) or secondary opportunistic infections (such as bacteria and viruses) (Evian, 2003:166). Weight loss and wasting syndrome is significant to the morbidity and mortality of HIV/AIDS patients (Wilson *et al.*, 2004:124) and refer to advanced HIV/AIDS infection (Department of Health, 2010:60).

2.8 TREATMENT OF HIV/AIDS

HIV/AIDS infection is currently regarded as a chronic condition rather than a terminal illness (Hellinger *et al.*, 2006:631). The aim of antiretroviral treatment is therefore to improve the quality of life of HIV/AIDS infected children as long as possible (Department of Health, 2010:28; Tudor-Williams, 2000:4).

The use of antiretrovirals for the treatment of HIV/AIDS has been proven beneficial over years in those patients receiving ART and they are less hospitalized than before on earlier drug therapy (Hellinger *et al.*, 2006:631), and there is a decrease in the number of deaths (CDC, 2009:1). The goal of antiretroviral treatment in HIV/AIDS infected children is to reduce HIV/AIDS related morbidity and mortality, and increase survival (Department of Health, 2010:29).

Virologic, immunologic and clinical criteria should be considered when deciding to initiate antiretroviral treatment in children (Beers *et al.*, 2006:2350). For example, it is not recommended to initiate antiretroviral treatment in asymptomatic children (Department of Health, 2010:28), those with CD4 counts above 350 cells/mm^3 (Wells *et al.*, 2009:436) or when the immune system is irreversibly changed (Department of Health, 2010:28). Antiretroviral treatment should, however, be initiated in asymptomatic patients with a CD4 cell count of 250 cells/mm^3 or less, or those with a progressive drop in the CD4 cell count and a high viral load (Evian, 2003:82). In symptomatic children, ART should be initiated with the first clinical signs and symptoms related to immune-deficiency (Evian, 2003:82) (Refer to section 2.6).

2.8.1 First-line antiretroviral treatment regimen

According to the WHO (2010:29) and the South African Department of Health (2010:28), there are a selected number of first-line and second-line treatment regimes for children with HIV/AIDS. Approaches to support adherence is essential for the effectiveness and stability of any first-line treatment regimen (WHO, 2010:29). Unless contraindicated, all children can use the first-line treatment indicated in Table 2.8 and Table 2.9.

Table 2.8 suggests a list of paediatric first-line therapy (Department of Health, 2010:30; Department of Health, 2008:196, South African Medical Association Guidelines (Cotton *et al.*, 2009:38).

Table 2.8: Suggested paediatric first-line therapy

Indicator	Therapy
1.Starting at age under 3 years or less than 10 kg	• Abacavir or Stavudine (1 mg/kg/dose 12 hourly stavudine) • Lamivudine (4 mg/kg/dose 12 hourly) • Lopinavir/ritonavir (80/20 mg, 230 mg/m^2/dose of lopinavir component 12 hourly)
2. Starting at age over 3 years or more than 10 kg	• Abacavir or Stavudine 1 mg/kg/dose 12 hourly of stavudine • Lamivudine, (4 mg/kg/dose 12 hourly) • Efavirenz (350 mg/m^2/dose 12 hourly as a single daily dose)

All children under 3 years of age or weighing less than 10 kg with HIV/AIDS should be started with treatment as listed in Table 2.8. Children older than 3 years and weighing more than 10 kg should be started with the treatment regimen also as listed in Table 2.8. Stavudine may be continued if the HIV/AIDS children use it with no side effects. Abacavir should be substituted when lipodystrophy is suspected (Department of Health, 2010:30; Department of Health, 2008:196).

Table 2.9 suggested the recommended first-line ARV treatment for infants and children (WHO, 2010:36).

Table 2.9: Recommended first-line ARV treatment for infants and children

Infants	Children
Infant or a child younger than 24 months not exposed to ARV's start with Nevirapine and 2 NRTI*.	Children 24 months to 3 years start with Nevirapine and 2 NRTI
Infant or a child younger than 24 months exposed to NNRTI during maternal treatment, start with lopinavir/ritonavir + 2 NRTI.	Children older than 3 years start with Nevirapine or Efavirenz and 2 NRTI
Infant or child younger than 24 months with unknown ARV exposure start with Nevirapine + 2 NRTI.	

***Note: Nucleoside reverse transcriptase inhibitors (NRTI) are lamivudine or stavudine or zidovudine or abacavir.**

The recommended first-line treatment regimen, according to the WHO (2010:30) for HIV/AIDS infected infants and children are listed in Table 2.9. Efavirenz should be avoided in children younger than 3 years of age because of a lack of dosing information (WHO, 2010:36).

2.8.2 Second-line antiretroviral treatment regimens

The second-line treatment regimen in children is used when there is a failure with the first-line treatment regimen (Kambugu *et al.*, 2008:559; Department of Health, 2010:31). Failures of treatment may be the result of the development of drug resistance, non-adherence to medication, intolerance to one or more medications, adverse drug-drug interactions, or pharmacokinetic-pharmacodynamic variability (Wells *et al.*, 2009:436). Table 2.10 summarises the suggested second-line treatments in children (Department of Health, 2008:196).

Table 2.10: Suggested second-line treatments in children

Previous regimen	Second-line antiretroviral treatment
Children younger than 3 years or weighing less than 10 kg	**Children younger than 3 years or weighing less than 10 kg**
• **Stavudine** PLUS • **Lamivudine** PLUS • **Lopinavir/ritonovir**	• **Zidovudine** 180-240 mg/m^2/dose, twice daily PLUS • **Didanosine** Smaller than 8 months 100 mg/m^2/dose or 8 months and older 120 mg/m^2/dose two times daily, orally PLUS • **Nevirapine** 120 mg/m^2/dose, orally once daily
Children 3 years and older or 10 kg and bigger	**Children 3 years and older or 10 kg and bigger**
• **Stavudine** PLUS • **Lamivudine** PLUS • **Efavirenz**	• **Zidovudine** 180-240 mg/m^2/dose, twice daily, orally PLUS • **Didanosine** 120 mg/m^2/dose two times daily, orally PLUS • **Lopinavir/ritonavir** (80/20) 230 mg/m^2/dose twice daily, orally

- **Didanosine must be administered 2 hours before or after other antiretroviral treatment.**
- **Lopinavir/ritonavir must be administered with food, a high fat meal will increase absorption of lopinavir/ritonavir.**
- **Didanosine must be taken with food.**

Table 2.8 illustrates the change from a first-line regimen to a second-line antiretroviral treatment regimen; for example, children younger than 3 years or < 10 kg receiving stavudine, lamivudine, and the combination, should be initiated with lopinavir/ritonavir, zidovudine, didanosine and a combination of lopinavir/ritonavir. Children 3 years or older or ≥ 10 kg treated with the first-line consists of stavudine, lamivudine and efavirenz, should be changed to zidovudine, didanosine and a combination of lopinavir/ritonavir. Children previously treated with a regimen consisting of stavudine, lamivudine and lopinavir/ritonavir should be changed to zidovudine, didanosine and efavirenz. Table 2.11 summarises the second-line ARV treatment regimens for infants and children with treatment failure (Adapted from the WHO, 2010:57).

Table 2.11: Recommended second-line ARV treatment regimens for infants and children with treatment failure

Infants and children younger than 24 months	**Preferred second line regimen**
Infant or a child younger than 24 months not exposed to ARV's	Lopinavir/ritonovir plus 2 NRTI
Infant or a child younger than 24 months exposed to NNRTI during maternal treatment	NNRTI's plus 2 NRTI
Infant or a child younger than 24 months with unknown ARV exposure	Lopinavir/ritonavir plus 2 NRTI
Children 24 months and older	Boosted Protease inhibitor component plus 2 NRTI

- **Didanosine must be administered 2 hours before or after other antiretroviral treatment.**
- **Lopinavir/ritonavir must be administered with food; a high fat meal will increase absorption of lopinavir/ritonavir**
- **Didanosine must be taken with food**

2.8.3 Classification of ARVs

ARVs can be divided in three groups, namely nucleoside and nucleotide reverse transcriptase inhibitors (NRTIs), non-nucleoside reverse transcriptase inhibitors (NNRTI), and protease inhibitors (PIs) (Cotton *et al.*, 2009:39).

2.8.3.1 Nucleoside and nucleotide reverse transcriptase inhibitors (NRTIs)

The NRTIs was of the first drugs developed against HIV (Evian, 2003:81; Adler, 2002:54). The NRTI's are used to terminate the DNA chain which act as false substrates for enzyme reverse transcriptase (Adler, 2002:54, Stine, 2009:72). Current available NRTIs are abacavir (ABC), didanosine (DDL), lamivudine (3TC), stavudine, zalcitabine, zidovudine and tenofovir (Rossiter, 2010:333-336; MIMS, 2010:298-304). All NRTIs are considered prodrugs (Guitierrez, 2008:501).

Tenofovir may not be used in children under the age of 18 years (Snyman, 2010:292; Beers *et al*., 2006:2347).

The fixed dose combinations of abacavir plus lamivudine, and zidovudine plus lamivudine are used as second-line regimes (Katz & Zolopa, 2009:1196). One of the most common side-effects of NRTIs is hypersensitivity reactions in patients (Guitierrez, 2008:501). Trimethoprim-sulphamethoxazole increases lamivudine serum levels (Guitierrez, 2008:496).

Anti-acids decrease the bioavailability of zalcitabine (Baxter, 2008:792). Valproate increases the biovailability of zidovudine (Baxter, 2008:792). The pharmacological effects of zidovudine may be decreased by rifabutin, rifampicin, rifapentine (Tatro, 2004:1498). Alcohol, clotrimazole, diuretics and pentamidine increase the risk of pancreatic toxicity with the use of didanosine (Guitierrez, 2008:496). Paracetamol increases the risk of bone marrow suppression when used with zidovudine (Baxter, 2008:820). Table 2.12 suggests the dosage for children, special instructions, potential drug interactions and side effects of NRTIs.

Table 2.12: The recommended dosage, special instructions, drug interactions and side effects associated with NRTIs

NRTIs Generic name Trade name® (Rossiter, 2010:333-336; MIMS, 2010:298-304)	**Recommended child dosage** (Rossiter, 2010:333-336; MIMS, 2010:298-304, Fox, 2002:806-808)	**Special instructions** (Wilson *et al.,* 2004:333-334)	**Drug interactions** (Fox, 2002:807; MIMS, 2010:298-304)	**Side effects** (Beers *et al.*, 2006:2347-2348; MIMS, 2010:300-303; Rossiter 2010: 332-334; Spencer, 2004: 14-18)
Abacavir (ABC) Ziagen®	< 13 years, 8 mg/kg 12 h, up to maximum of 600 mg per day	Alcohol, etanol and ethyl alcohol increase abacavir level, (Tatro, 2004:1, Guitierrez, 2008:505)	No significant interactions between (ABC) and (3TC)	Hypersensitivity reaction (2-5%) fever, rash, fatigue, asthma-like symptoms, myalgias and gastro-intestinal symptoms
Didanosine (DDI) Videx® Aspen Didanosine® Sonke-Didanosine®	Oral dose, 240 mg/m^2 daily or 120 mg/m^2 twice daily[A,], 200 mg/m^2/day[B]	Take dose on an empty stomach one hour before or two hours after food, because food reduce the absorption of didanosine	Didanosine decrease the gastric absorption of dapsone, fluoroquinolones, itraconazole, ketoconazole and tetracycline (Guitierrez, 2008:496)	Pancreatitis, lipodystrophy, peripheral neuropathy
Lamivudine (3TC) 3TC® Adco Lamivudine® Aspen Lamivudine® Auro-Lamivudine® Sonke-Lamivudine®	Oral dose, 4 mg/kg twice daily max. daily dose of 300 mg, neonates younger than 30 days, 2 mg/kg twice daily	None	Trimetoprim increase plasma concentration	Nausea, vomiting, lactic acidosis', fatigue, headache, rash, peripheral neuropathy
Stavudine (d4T) Zerit® Aspen Stavudine® Auro-Stavudine® Sonke-Stavudine® Stavir®	Oral dose > 3 months and ≤ 30 kg, 1 mg/kg 12 hourly; > 30 kg, 30 mg 12 hourly	None	zidovudine and doxorubicin inhibitate antiviral effects	Lactic acidosis, pancreatistis, lipodystrophy, gastrointestinal disturbances, rash, hepatitis
Zidovudine (AZT) Retrovir® Aspen Zidovudine® Auro-Zidovudine® Cipla-ZIdovudine® Sonke-Zidovudine®	3 months - 12 years, 180 mg/m^2 12 hourly; maximum 800 mg/day, newborn: 2 mg/kg 6 hourly start within 12 hours after birth and continue until 6 weeks old.	Suspension may be given with food for children (Rossiter, 2010:334)	Increased toxic effects may occur with potent nephrotoxic ganciclovir, interferon, and TMP-SMX. acyclovir. probenecid, atovaquone, methadone and valproic acid may increase zidovudine concentration	Anemia, neutropenia, nausea, headache, insomnia, myopathy, gastrointestinal disturbances, lactic acidosis

Note*

There is a difference in the dosage of didanosine between Rossiter, and the MIMS. According to Rossiter (2010:333), the dosage for didanosine is an oral dose, of 240 mg/m^2 daily or 120mg/m^2 twice daily, and according to the MIMS, (2010:301) it is an oral dose of [b]200 mg/m^2/daily

MAX=maximum

TMP-SMX=Trimetoprim-Sulphametoksasool

2.8.3.2 Non-nucleoside reverse transcriptase inhibitors (NNRTI)

NNRTIs inhibit reverse transcriptase activity thereby suppressing replication of the human immunovirus (Adler, 2002:54, Katz, 2009:1199; Stine, 2009:74). These agents are generally used in combination (Cotton *et al.*, 2009:21) typically with two NRTIs, to prevent the development of resistance (Rossiter, 2010:336). The current available NNRTIs is efavirenz, nevirapine, and delavirdine. Delavirdine is not registered in South Africa (Snyman, 2010:355). Efavirenz used with ergot derivatives, midazolam, triazolam and alprazolam can cause prolonged sedation and respiratory depression (Tatro, 2004:217). Alcohol and psychoactive drugs cause additive central nervous system depression (Guitierrez, 2008:496). Table 2.13 summarises the child dosage, special instructions, drug interactions and side effects of the NNRTIs.

Table 2.13: Suggested child dosage, special instructions, drug interactions and side-effects of NNRTIs

NNRTI	Recommended child dosage	Special instructions	Drug interactions	Side effects
Generic name Trade name® (Rossiter, 2010:336-337; MIMS, 2010:298-304)	(Rossiter, 2010:336-337; MIMS, 2010:298-304)	(Rossiter, 2010:336-337, Wilson *et al.*, 2004:333	(Rossiter, 2010:336-337; MIMS, 2010:298-304, Wilson *et al.*, 2004:333)	(Beers *et al.*, 2006:2348; Rossiter, 2010:336-337, Wilson *et al.*, 2004:333)
Efavirenz (EFV) Stocrin® Adco Efavirenz® Aspen-Efavirenz® Auro-Efavirenz® Cipla-Efavirenz®	Administered once daily: 13 -1 5 kg: 200 mg; 15 - 20 kg: 250 mg; 20 - 25 kg: 300 mg; 25-32,5 kg: 350 mg; 32,5 -40 kg:400 mg; 40 kg or over, 600 mg	Not used in children under 3 years or less than 13 kg. Bedtime dosage is recommended. Avoid taking with high fatty meals.	Induce or inhibit metabolism of hepatically metabolized drugs, when given with rifampicin possibly effective at normal dose	Skin rash, central nervous system dysfunction, nausea, vomiting, diarrhoea
Nevirapine (NVP) Viramune® Aspen Nevirapine® Auro-Nevirapine® Cipla Nevirapine® Sonke-Nevirapine®	2 months to 8 years, oral dose of 4 mg/kg once daily for a period of two weeks, then 7 mg/kg twice daily, ≥ 8 years, 4 mg/kg once daily for 2 weeks, then 4 mg/kg twice daily. MAX 400 mg/day	None	Induces plasma concentration of protease inhibitors, Rifampicin decreases levels of nevirapine	Life-threatening hepatitis, nausea, skin reactions

2.8.3.3 Protease inhibitors (PIs)

Protease inhibitors bind to the substrate of the viral protease enzyme, inhibiting the enzyme (Adler, 2002:54; McFarland, 2009:1119) thereby causing suppression in HIV replication (Stine, 2009:74; Rossiter, 2010:338). The PIs are always used in combination with other medications (Rossiter, 2010:338) and it is important to adjust the protease inhibitor dosage as needed (Tatro, 2004:1123). Current available protease inhibitors include amprenavir, atazanavir, indinavir, lopinavir/ritonavir, nelfinavir, ritonavir, and saquinavir. Atazanavir and saquinavir are not indicated for children under 13 years of age (Beers *et al.*, 2006:2349), and amprenavir is not available in South Africa (Rossiter, 2010:338; MIMS, 2010:298-304). The cytochrome P450 isoenzyme system metabolises the protease inhibitors (Baxter, 2008:772). Drugs that induce P450 isoenzyme reduce plasma concentration of the PIs (Guitierrez, 2008:506).

The primary adverse effects of PIs are gastro-intestinal and include diarrhoea, constipation, abdominal cramps, flatulence, acid reflux nausea and vomiting (Guitierrez, 2008:505). Ritonavir is more likely than nelfinavir to cause severe diarrhoea, and dyslipidaemia associated with the use of PIs is a risk factor for premature atherosclerosis (Guitierrez, 2008:505). Delavirdine increases the levels of PIs whereas nevirapine and efavirenz decrease the levels of protease inhibitors (Baxter, 2008:784). The metabolism of PIs is increased by phenobarbital and other barbiturates (Baxter, 2008:785). Itraconazole increases the levels of indinavir, lopinavir/ritonavir (Baxter, 2008:814). Rifampicin decreases the levels of lopinavir and indinavire (Cotton *et al.*, 2009:38). Table 2.14 summarises the child dosage, special instructions, drug interactions and side effects of PIs.

Table 2.14: Suggested child dosage, special instructions, drug interactions and side effects of PIs

PIs	Recommended child dosage	Special instructions	Drug interactions	Side effects
Generic name Trade name® (Rossiter, 2010:336-337; MIMS	(Rossiter, 2010:336-337; Beers *et al*., 2006:2349; MIMS, 2010:298-304)	(Rossiter, 2010:336-337, Wilson *et al*., 2004:333, Fox 2002:813)	(Rossiter, 2010:336-337; MIMS, 2010:298-304, Wilson *et al*., 2004:333)	(Beers *et al*., 2006:2348; Rossiter, 2010:336-337, Wilson *et al*., 2004:333)
Indinavir (IDV) Crixivan®	4 to 17 years: 500 mg/m^2, max of 800 mg, every 8 hours[A]	Take on an empty stomach	Inhibits cytochrome P450 Omeprazole decreases Indinavir level (Baxter 2008:816)	Lipodystrophy, Gastrointestinal side-effects, crystalluria
Lopinavir/ritonavir (LPV/r) Aluvia® Kaletra®	[B]7 kg to less than 15 kg: 12/3 mg/kg twice daily, 15 to 40 kg: 10/2,5 mg/kg twice daily, greater than 40 kg: Up to max of 400/100mg twice daily [C] , < 13 years: 10-12 mg/kg lopinavir twice daily, [D]lopinavir 230 mg + ritonavir 57,5 mg/m^2, twice daily max. Of 400 LPV and 100 mg ritonavir.	Take with a meal	Inhibits cytochrome P450, and also induces some P450 isoenzymes Reduced lamotrigine and phenytoin plasma levels (Baxter 2008:784)	Gastrointestinal side-effects, lipid abnormalities, fat redistribution
Nelfinavir (NFV) Viracept®	Over 2 years , 20 to 30 mg/kg 8 hourly	Administrate with a meal	Inhibits cytochrome P450 Reduced Phenytoin levels (Baxter 2008:784)	Lipid abnormalities, diarrhoea, gastrointestinal side-effects
Ritonavir (RTV) Norvir®	Over 2 years, 250 mg/m^2, 12 hourly, increased over a week to 350 mg/m^2 12 hourly, up to max. of 600mg[E], < 13 years 400 mg/m^2, 12 hourly	Food increase tolerability	Inhibits cytochrome P450, and also induces certain P450 isoenzymes Carbamazepine levels and toxicity are increased by ritonavir (Baxter, 2008:785).	Lipid abnormalities, fat redistribution, gastrointestinal side-effects

Note*

[a] The MIMS does not indicate the dose for a child, only Rossiter and Beers *et al*. indicates the dose in children.

The MIMS[B], Rossiter[C] and Beers *et al*.[D] differ in their treatment of (LPV/r) for children.

Rossiter[E] and Beers *et al*.[F] differ in their treatment of ritonavir for children, and the MIMS does not indicate a dose for ritonavir in children.

2.9 CHAPTER SUMMARY

In this chapter HIV/AIDS as a disease was discussed, as well as the main methods of HIV transmission, the stages of the HIV disease, opportunistic infections associated with HIV/AIDS and treatment of HIV/AIDS. The empirical investigation will be discussed in chapter 3.

CHAPTER 3:

EMPIRICAL INVESTIGATION

3 INTRODUCTION

In this chapter the research objectives and empirical research methodology that was followed in the study, and database employed will be discussed.

3.1 SPECIFIC OBJECTIVES OF THE EMPIRICAL INVESTIGATION

The general aim of this study was to determine the medicine prescribing patterns in HIV positive children compared with HIV negative children in the private health care sector of South Africa.

The specific research objectives of the empirical investigation phase of the study were:

- To compare the medicine prescribing patterns (prevalence), (excluding ARV drugs) in HIV positive and HIV negative children, based on age and gender.
- To investigate possible changes in the medicine prescribing patterns, (including ART) based on gender and age in HIV positive children, during the selected four-year period, 2005-2008.
- To assess whether HIV/AIDS treatment guidelines were followed in the private health care sector.

3.2 RESEARCH METHODOLOGY

3.2.1 Research Design

A drug utilisation review (DUR) study was defined by the World Health Organization (WHO) in 1977 as "*the marketing, distribution, prescription, and use of drugs in a society, with special emphasis on the resulting medical, social and economic consequences*" (WHO, 2003:2). The main goal of a drug utilisation review is to facilitate the rationale behind the usage of drugs and it forms part of investigational studies (Sjöqvist & Birkett, 2003:78). Drug utilisation studies can be performed in three different ways i.e. prospective, concurrent, or retrospective, depending during which stage the data is collected (Sachdeva & Patel, 2010:11).

Prospective DUR is the type of review that takes place before a patient receives their medication, at the time the dispensing claim is set. Concurrent DUR is the type of review that takes effect in intervening while the patient is receiving the medication (Peterson *et al.*, 2007:219-220).

A retrospective drug utilization review is performed after the drug has been dispensed and used by the patient, with the main goal of establishing inappropriate or suboptimal drug use (Fulda *et al.*, 2004:434) and to design interventions with providers and consumers to prevent inappropriate prescribing and unfavorable medication usage (Thomas *et al.*, 2004:434). This study is based on a retrospective drug utilisation review.

A retrospective drug utilisation review was conducted on data provided by a pharmaceutical benefit management company (PBM) in South Africa.

3.2.2 Data source

The data used in this study were obtained from a medicine claims database of a PBM company for the study period of 1 January 2005 to 31 December 2008. The PBM managed the administration of 38 medical schemes and four capitation provider clients (overall 1.5 million South Africans) in 2009.

The following data fields were obtained from the PBM: birth date, gender, prescription number, prescription date, active ingredient, amounts prescribed, total medicine cost, scheme contribution and patient contribution.

The total database for all 4 years (1 January 2005 to 31 December 2008) consisted of all the medicine claims data available on the database. For the purpose of this study, children 12 years and younger were used as the study population. The study population were extracted from the total population, and divided in two groups namely, children ≤ 12 years with HIV/AIDS and children ≤ 12 years without HIV/AIDS. Medication used by children ≤ 12 years with HIV/AIDS were further sub-divided in two groups, namely the ARV medication they used and the “other” medication. The other medications used by the HIV/AIDS children were compared to the medication for children 12 years and younger without HIV/AIDS. Figure 3.1 displays the different data subsets and selection of study population.

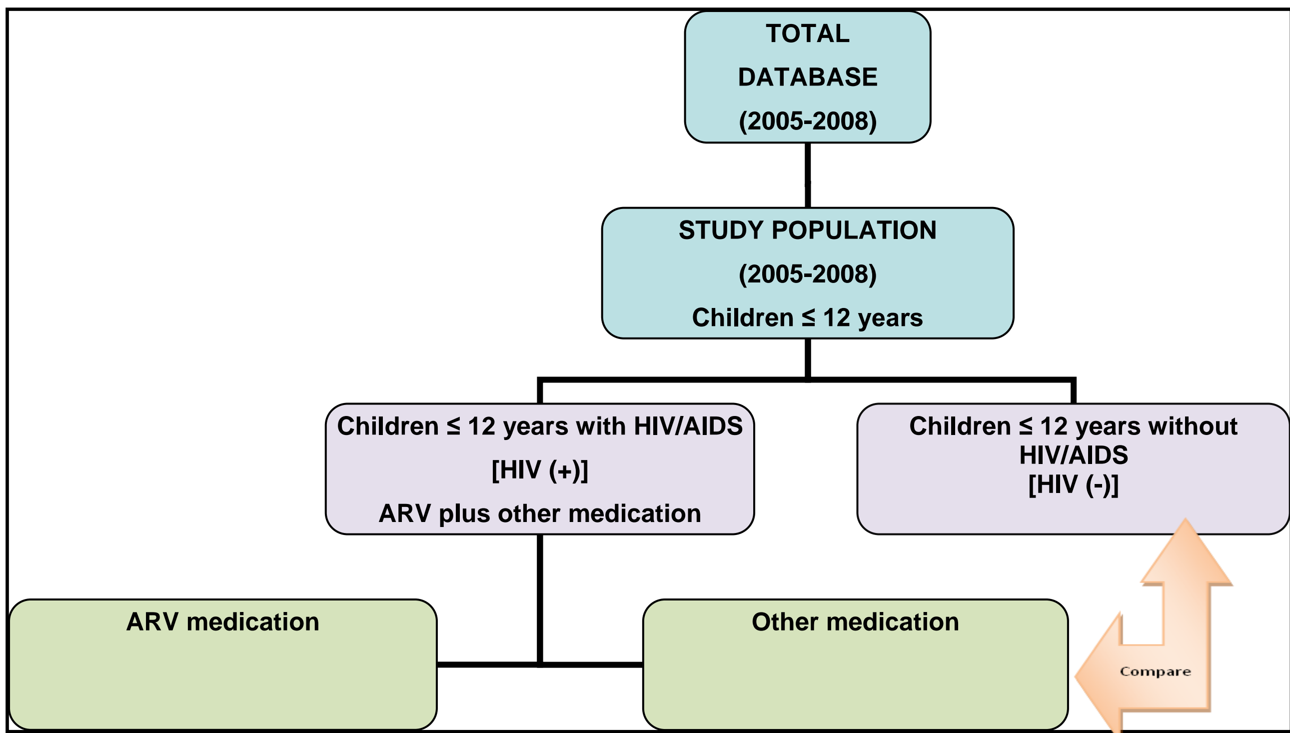


Figure 3.1: Organogram illustrating the different data subsets and the selection of the study population

3.3 STUDY MEASURES

The following criteria were selected as study measures: age, gender, number of prescriptions dispensed, number of medicine items dispensed, and the cost of medicine.

3.3.1 Age

Age is referred to as a period of time that has passed since the time of birth (Pugh, 2000:34). The age of the person was calculated on the database from 1 January of the year following the date that the prescription was dispensed.

For the purpose of this study the total study population was divided into five age groups, i.e.:

- Age group 1: ≤ 12 years
- Age group 2: >12, ≤ 18 years
- Age group 3: >18, ≤ 30 years
- Age group 4: >30, ≤ 60 years
- Age group 5: > 60 years

The study population (children ≤ 12 years) was divided into the following three age groups as described by the paediatric dosage handbook (Taketomo *et al*., 2000:15):

- Age group 1.1: >0, ≤ 1 years
- Age group 1.2: >1, ≤ 5 years
- Age group 1.3: >5, ≤ 12 years

3.3.2 Gender

Gender is defined by the Cambridge Advanced Learner's Dictionary (2010) as "*the physical and social condition of being male or female*." The WHO (2011) defines gender as the biological and physiological characteristics, behaviour activities and attributes in a "*given society considered appropriate for men and women."* For the purpose of this study, gender was divided in three categories namely, female, male and unknown. The unknown category was used when the patient's gender was not indicated.

3.3.3 Number of prescriptions dispensed

According to the Mosby Dictionary (Myers & Kaemmerer, 2008:1357), prescriptions are an "*order for medication, therapy, or therapeutic device given by a properly authorized person."* The number of prescriptions per patient was calculated per year, and can be used as a measure of the medicine usage.

3.3.4 Prescribed daily dosage

The WHO (2003:4) defines the PDD as "the average daily dose prescribed, as obtained from a representative sample or prescription". For the purpose of this study, the PDD was calculated as the milligrams of a specific active ingredient dispensed per day. This was calculated using the following formula:

$$PDD = \frac{STRENGTH * QUANTITY}{DAYS\ SUPPLY}$$

Where:

Strength = Strength per table, capsules or ml

Quantity = The number of tablets, capsules or ml

Days supply = The number of days supply dispensed

The PDD was compared to an "optimal" dosage range. The optimal dosage range was determined for indications from use as set out in the following references, namely SAMF (Gibbon, 2008, 316-317), the MIMS (Snyman, 2011:298-312) and Martindale (Sweetman, 2011). These references recommended the calculation of dosages based on weight or body surface area.

Because of a lack of clinical data (such as weight or length) on the database the growth charts for children of the CDC and monograms for the average body surface area by age groups was used to calculate these optimal doses. The 50th percentile on the average weight-for-age growth charts of the CDC, and the mean surface area (m^2) by age was used as standard criteria.

The optimal age dosage range for medicine items, were calculated using the 50th percentile on the average weight for age or body surface area per age group charts (Center for Disease Control and Prevention, 2000(b):5; Trouilloud, 2008:234). The optimal daily dosage of the active ARV ingredients in children with HIV/AIDS, were divided in the three age groups. For each age group there was a minimum or a maximum weight or body surface area per patient (refer to Table 3.1).

Based on the 50th percentile of the growth charts and the minimum weight or body surface area for the:

- age group >0, ≤ 1 years, was 3.55 kg or 0.23 m^2 and the maximum of 10.25 kg or 0.47 m^2.
- age group >1,≤ 5 years the minimum weight or body surface area was 10.26 kg or 0.471 m^2 and maximum was 18 kg or 0.73 m^2.
- age group >5, ≤ 12 years, the minimum weight or body surface area was 18.1 kg or 1.25 m^2 and maximum was 41 kg 1.25 m^2.

For example:

Based on the indications set by SAMF (Gibbon, 2008:316-317), the MIMS (Snyman, 2011:298-312) and Martindale (Sweetman, 2011), the optimal dosage range for lamuvidine for patients in the age group (>5, ≤ 12 years) was 4 mg/kg twice daily to a maximum dose of 300 mg per day. The minimum dose was therefore calculated as 144.8 mg [4 mg *18.1 kg *2 times daily] whereas the maximum dose was 300 mg per day. The optimal dosage range for zidovudine for patients in the age group (>5, ≤ 12 years) was 360 mg/m^2/day in 3 to 4 divided doses to a maximum of 800 mg/day. Based on calculations using the nomograms for average body surface area, a minimum dose of 262.8 mg was calculated [360 mg*0.731 m^2 per day] with a maximum dose of 800 mg per day.

Table 3.1: Optimal dosage ranges for age and weight/body surface area.

Optimal dosage range of prescribed active ARV ingredients in children with HIV/AIDS						
	>0 ≤ 1 year		>1 ≤ 5 year		>5 ≤ 12 years	
	Min (3.55 kg) or (0.23 m^2)*(mg)	Max (10.25 kg) or (0.47m^2)*(mg)	Min (10.26 kg) or (0.471 m^2)* (mg)	Max (18 kg) or (0.73m^2)*(mg)	Min (18.1 kg) or (0.731m^2)*(mg)	Max (41 kg) or (1.25 m^2)*(mg)
ABACAVIR	56.8	82	82.08	144	144.8	328
DIDANOSINE	46.0	112.8	112.81	175.2	175.21	300
EFAVIRENZ	-	-	-	250	250	600
INDINAVIR	-	-	-	584	584.1	1000
LAMIVUDINE	28.4	82	82.1	144	144.8	300
LOPINAVIR	85.2	246	246.2	432	434.4	800
NELFINAVIR	-	-	918	1620	1629	3690
NEVIRAPINE	49.7	143.5	143.6	252	253.4	400
RITONAVIR	-	-	329	511	511.1	875
STAVUDINE		20.5	20.52	36	36.2	2460
ZIDOVUDINE		169.2	169.21	262.8	262.81	800

Efavirenz is not indicated in children under 3 years or 13 kg.
Indinavir is not indicated for children under 4 years.

3.3.5 Number of medicine items dispensed

According to the Mosby Dictionary (Myers & Kaemmerer, 2008:1328) "*medicine is a drug or a remedy for illness.*" The Medicines and Related Substances Control Act (101/1965) of South Africa defines medicine as "*any substance or mixture of substances used or purporting to be suitable for use or manufactured or sold for use in the diagnosis, treatment, mitigation, modification or prevention of disease, abnormal physical or mental state or the symptoms thereof in man*". The number of medicine items as well as the average number of medicine items dispensed per prescription per patient, and the average number of medicine items dispensed per patient for other medication were calculated, and can be used as a measure of the medicine usage.

3.3.6 Cost of medicine

The Merriam-Webster dictionary (2011a) defines cost as monetary value paid or charged for something, for this study it refers to the medicine items. The cost of medicine items will be determined for the following categories and expressed in rand-value (R).

- The total cost of all medicine items claimed during the four study years from 1 January 2005 to 31 December 2008 for the total population according to patient age and gender.
- The total cost of all medicine items claimed during the four study years from 1 January 2005 to 31 December 2008 for the study population according to the patient age and gender
- The total cost of all medicine items claimed during the four study years from 1 January 2005 to 31 December 2008 for the study population with HIV/AIDS according to the patient age and gender.

- The total cost of all medicine items claimed during the four study years from 1 January 2005 to 31 December 2008 for the study population without HIV/AIDS according to the patient age and gender.

The total cost per prescription consisted of the total patient's contribution and the total amount paid by the medical aid scheme.

- The average cost per item per patient for total cost, patient's contribution and scheme contribution.
- The average cost per prescription for total cost, patient's contribution and scheme contribution.
- The average cost per prescription per patient for total cost, patient's contribution and scheme contribution.

3.3.7 Classifications systems

The different classification systems that were used to classify the medicine claimed through the database was the Monthly Index of Medical Specialties (MIMS).

The MIMS® classification system is based on classifying medication according to pharmacological action (Snyman, 2010:10a). For the purpose of this study, main pharmacological and sub pharmacological groups were used

The antiretroviral agents can be divided in the following sub pharmacological groups (refer to Table 3.1.)

Table 3.2: Illustration of the categories of the antiretroviral agents

Nucleoside and nucleotide reverse transcriptase inhibitors (NRTIs)	**Non - nucleoside reverse transcriptase inhibitors (NNRTI)**	**Protease inhibitors (PIs)**
Abacavir	Efavirenz	Indinavir
Didanosine	Nevirapine	Lopinavir/ritonavir
Lamivudine		Nelfinavir
Stavudine		Ritonavir
Zidovudine		Lopinavir

3.4 STATISTICAL ANALYSIS

The statistical analysis was carried out with the help of the Statistical Analysis System®,(SAS 9.1®) programme. The analysis consisted of four parts.

- The first part of the analysis was performed on all medicine items on the database from 2005 to 2008.
- The second part of the analysis was performed on all the medicine items prescribed for children 12 years and younger from 2005 to 2008.
- The third part of the analysis was performed on all HIV/AIDS medicine items for children 12 years and younger.
- The fourth part was performed on all the other medicine items for children 12 years and younger with HIV/AIDS.

3.4.1 Descriptive statistics

The following descriptive statistics were used to investigate the data:

3.4.1.1 Frequency

According to Martin and Pierce (1999:13), the number of items of which a particular value occurs in a set of data, or the number of times a particular category occurs can be defined as frequency. The Merram Webster Dictionary defines, *"Frequency is the number of times that a periodic function repeats the same sequence of values during a unit variation the independent variable of the independent variable, which include the number, proportion, or percentage of items in a particular category in a set of data"* (Merriam-Webster, 2011b.).

Frequency as measurements was used to calculate the number of items and prescriptions.

3.4.1.2 Average value (mean)

The average value or arithmetic mean is the sum of all the values making up a set of observations divided by the number of observations (Banerjee, 2003:3; Samuals & Witmer, 1999.32). The following equation is used for the calculation of the population mean:

$$\bar{x} = \frac{\sum x_i}{n}$$

Where:

$\bar{x}$ = mean

$\sum x_i$ = sum of all given x values

n = number of observations in the population

For the purpose of the analysis of the data the average value (mean) was used to determine the following:

- Average number of prescriptions per patient per year.
- Average number of medicine items per prescription.
- Average total cost per prescription.
- Average cost per item.

3.4.1.3 Standard deviation

The standard deviation is the difference between observations or data entries and the sample mean (Samuels & Witmer, 1999:103) and is a good descriptive measure of variability, although it can be strongly affected by outliers (Banerjee, 2004:5). The population standard deviation is calculated as follows:

$$s = \sqrt{\frac{\sum (x_i - \bar{x})^2}{n - 1}}$$

Where:

s = standard deviation

x_i = any value in the dataset

$\bar{x}$ = arithmetic mean (average)

n = number of observations

For the purpose of the study the standard deviation was used to determine the following:

- The standard deviation of the number of prescriptions per patient per year.
- The standard deviation of the number of medicine items per prescription.
- The standard deviation of the total cost per prescription.
- The standard deviation of the cost of all medicine items.

3.4.2 Inferential statistics

The following inferential statistics were used to investigate the data:

3.4.2.1 The *t*- test

The paired *t*-test "tests if the population means estimated by two dependent samples differ significantly"; the test can be used on two groups that are matched on one or more characteristics (Banerjee, 2003:59).

The *t*-test was used to observe the difference between the means of prescriptions, medicine items, and number of prescriptions per patient. The *p*-value is statistically significant if ($p \leq 0.05$) (Cohen & Lea, 2004:37).

3.4.2.2 Two-way frequency tables

Two-way frequency table is tables with intervals of values and corresponding frequencies, these tables indicated how the observed data is distributed over the different classes (Swanepoel *et al.*, 2010:32).

The *Phi*-coefficient is the "measure that reflects the relative proportions in two-way frequency tables and is not affected by the total sample size" (Cohen & Lea, 2004:211). The *phi-coefficient* can be interpreted as a measure of practical significance. Guidelines for the interpretation of it is 0.1 for a small effect; 0.3 for a medium effect and 0.5 for a large effect (Cohen & Lea, 2004:211).

3.4.2.3 Effect sizes/ d-values

According to Cohen (1988:24), the (*d*) value is a "*degree with which the phenomenon is present in the population".* Cohen and Lea (2004:60) define the *d*-value as the difference between two means divided by the largest standard deviation of the two means. The following formula can be used for the calculation of Cohen's *d* value:

$$d = \frac{\bar{x}_a - \bar{x}_b}{s_{max}}$$

Where:

d = effect size

$\bar{x}_a$ = average cost value of a

$\bar{x}_b$ = average cost value of b

s_{max}= the maximum standard deviation of two averages

The *d*-value can be interpreted as follow (Cohen, 1988:3):

IdI = 0.2 small effect with no significant difference

IdI = 0.5 medium effect which is observable and may be significant

IdI = 0.8 large effect with a significant and practical importance

The *d*-value was used during data analysis to determine whether the differences between averages are practically significant, for example, to determine whether the average number of prescriptions of HIV (+) patients, and other medication is practically significantly higher than that for HIV (-) patients.

3.5 RELIABILITY AND VALIDITY OF THE RESEARCH DATA

The data for the analysis were obtained from the medical claims database. There was no direct manipulation of the data done by the researcher. The research done was performed from the perspective that all the data from the database were precise and correct. Data for the four years were obtained from one database only, thus limiting external validity, implying that the results can be generalised to the specific database and study population only.

3.6 ETHICAL CONSIDERATIONS

None of the patients, medical practices, pharmacies or medical scheme information could be identified and the study was concluded anonymously through the medicine claim database. Permission to conduct this study was granted by the PBM's board of directors as well as the Ethical Committee of the North-West University. The Ethical Committee of the North-West University granted the study with the following permission number: NWU – 0046-08-S5.

3.7 CHAPTER SUMMARY

This chapter focused on the research methodology. The general and specific objectives, research design, data source, study population, and ethical aspects were discussed.

The results from the empirical investigation will be discussed in chapter 4.

CHAPTER 4:

RESULTS AND DISCUSSION

4 Introduction

In this chapter the results of the empirical study will be discussed. This discussion entails a comparison between the medicine prescribing patterns of HIV/AIDS [HIV(+)] and non-HIV/AIDS [HIV(-)] children in the private health care sector of South Africa for the period from 1st of January 2005 to 31st December 2008.

ARV medication was identified from the medicine claims database of a pharmaceutical benefit management company (PBM) according to the MIMS® classification system (refer to Paragraph 3.3.7.1). The focus of this study was on children 12 years and younger. Figure 4.1 depicts the order in which the results of the study will be presented.

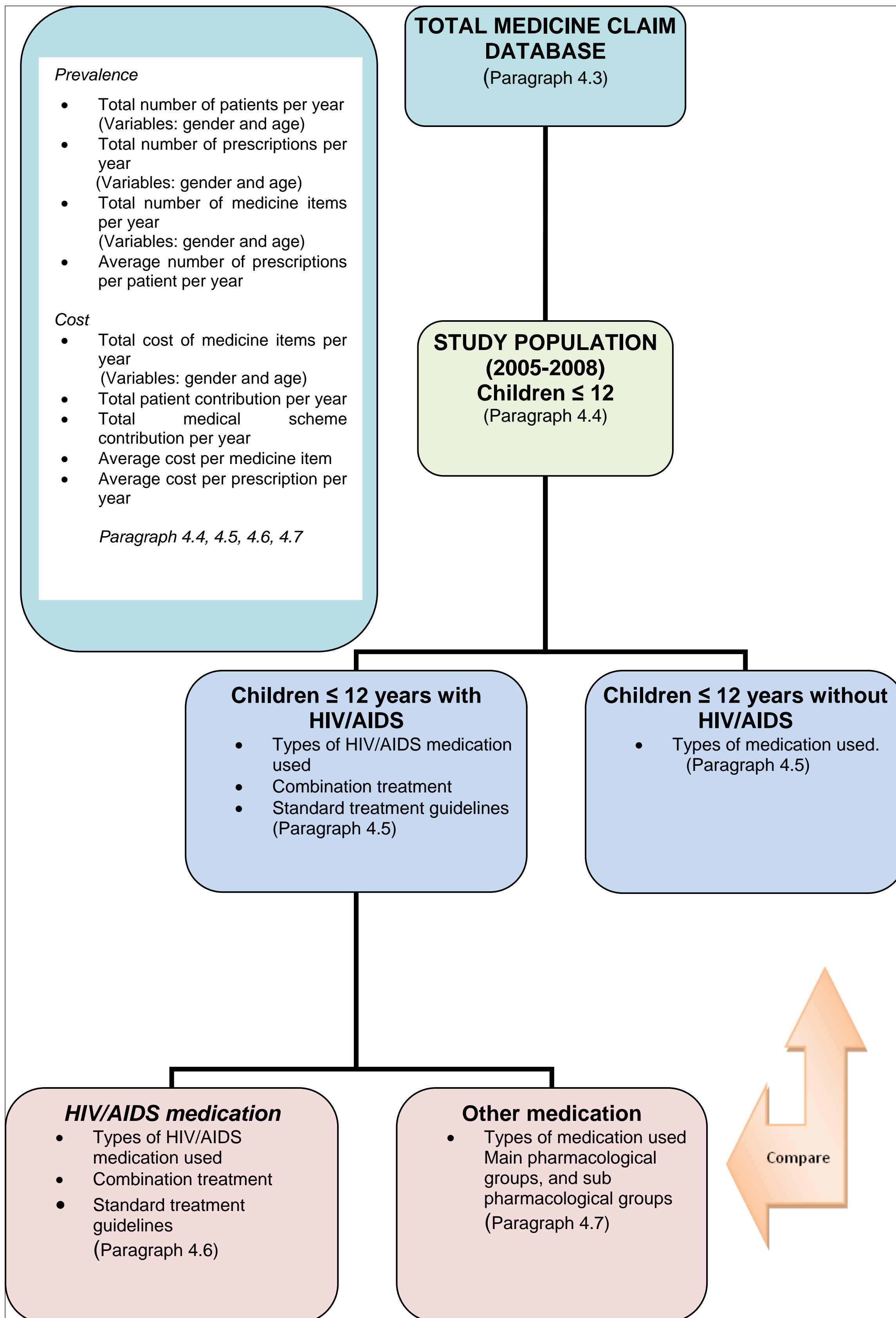


Figure 4.1: Schematic representation of the general data analysis

The total population (medicine claims database) HIV (+) vs. HIV (-) consisted of all medicine claims data on the database from the 1st January 2005 to 31st December 2008. The study population were extracted from the total population and consisted of all patients ≤ 12 years. The study population was divided into two groups: patients ≤ 12 years with HIV/AIDS and patients in the same age group without HIV/AIDS. The medicine of the HIV/AIDS patients in the study population (≤ 12 years) was sub-divided in two further groups based on medicine treatment, namely in ARVs and other medication (refer to Figure 4.2).

4.1 ANNOTATIONS REGARDING THE INTERPRETATION OF THE RESULTS

Percentages may not always add up to 100%, because of rounding.

Gender was not indicated on some of the prescriptions; these are indicated by “gender unknown”.

4.2 GENERAL ANALYSIS OF THE TOTAL DATABASE

This section provides a general analysis of the complete medicine claim database (refer to Table 4.1). The data used for this study represents a section of the private health care sector of South Africa.

4.3 OVERVIEW OF THE TOTAL POPULATION

Table 4.1 provides the general information of the total database from 1 January 2005 to 31 December 2008. A discussion on the total number of patients, the total number of prescriptions, the total number of medicine items claimed and associated costs follows in subsequent paragraphs.

Table 4.1: The total number of patients, prescriptions, medicine items and cost of the total population

Total population				
	2005	2006	2007	2008
Total number of patients	1 218 357	1 259 093	911 211	759 192
Female	675 813	698 475	502 071	415 332
Male	540 874	559 531	408 733	343 860
Unknown gender	1 670	1 087	407	0
≤ 12 years	197 323	197 323	142 047	98 939
>12 ≤ 18 years	103 279	103 279	84 776	66 911
>18 ≤ 30 years	163 989	163 989	127 762	100 784
>30 ≤ 60 years	565 966	565 966	408 484	351 891
> 60 years	187 800	187 800	148 142	140 667
Total number of prescriptions	8 292 790	8 808 953	7 824 989	6 701 792
Female	4 979 024	5 279 031	4 704 039	4 018 665
Male	3 306 649	3 525 108	3 119 132	2 683 127
Unknown gender	7 117	4 814	1 818	0
≤ 12 years	764 918	790 184	652 869	435 452
>12 ≤ 18 years	347 931	367 516	320 639	257 151
>18 ≤ 30 years	696 025	750 681	651 715	511 361
>30 ≤ 60 years	4 158 947	4 444 499	3 886 099	3 317 625
> 60 years	2 324 969	2 456 073	2 313 667	2 180 203
Average number of prescriptions per patient (SD) per year	6.8 (7.65)	7.0 (7.87)	8.6 (8.46)	8.8 (8.70)
Total number of medicine items	19 500 774	21 113 422	19 075 724	16 439 253
Female	11 750 190	12 699 707	11 509 346	9 893 928
Male	7 734 461	8 403 158	7 562 466	6 545 325
Unknown gender	16 123	10 557	3 912	0
≤ 12 years	1 916 485	2 005 1 07	1 658 615	1 085 511
>12 ≤ 18 years	817 362	882 991	766 228	602 822
>18 ≤ 30 years	1 515 393	1 664 776	1 460 354	1 127 045
>30 ≤ 60 years	9 554 373	10 419 400	9 294 102	7 974 978
> 60 years	5 697 161	6 141 148	5 896 425	5 648 897
Average number of medicine items per prescription (SD)	2.4 (1.54)	2.4 (1.57)	2.4 (1.62)	2.5 (1.66)
Total patients contribution per year (R)	217 417 602.20	261 028 782.73	303 277 143.74	307 322 784.93
Total medical scheme contribution (R)	99 059 421.71	1 698 709 951.36	1 615 007 032.92	1 478 548 228.92
Total cost of all items per year (R)	1 819 865 251.63	1 959 738 734.09	1 918 284 176.66	1 785 871 013.85
Female (R)	1 084 626 865.29	1162254536.29	1 138 188 990.86	1057274453.63
Male (R)	733 769 633.85	796360401.04	779 508 488.81	728 596 560.22
Unknown Gender (R)	1 468 752.49	1123796.76	586 696.99	0
≤ 12 years (R)	109 274 025.64	113 854 950.76	98 699 796.11	70 776 260.18
>12 ≤ 18 years (R)	57 432 463.39	61 197 176.43	56 085 634.71	47 616 435.55
>18 ≤ 30 years (R)	118 696 627.07	127 030 861.51	116 836 805.48	99 956 243.85
>30 ≤ 60 years (R)	860 104 284.97	929 170 57.83	892 506 955.74	823 506 542.62
> 60 years (R)	674 357 850.57	728 485 227.56	754 154 984.62	744 015 531.65
Average cost per prescription (SD) (R)	219.5 (344.41)	222.(397.41)	245.2 (603.55)	266.5 (793.43)
Average cost per medicine item (SD) (R)	93.3 (166.36)	92.8 (196.42)	100.6 (324.11)	108.6 (436.75)

R: Rand value

SD: Standard deviation

4.3.1 Number of patients

According to the reports from the South African Council of Medical Schemes (CMS, 2007:51; CMS, 2008:123), 6 835 612 persons were registered as members or beneficiaries in South Africa in 2005, increasing to 7 127 343 in 2006, 7 605 236 in 2007, and 7 784 826 in 2008. The total number of patients on the database used in this study therefore represented 17.8% of these beneficiaries in 2005, decreasing to 9.8% in 2008 (refer to Table 4.1).

4.3.2 Gender distribution of patients

Female patients represented 55.5% of the total number of patients on the total database in both 2005 (n = 675 813) and 2006 (n = 698 475), thereafter decreasing to 55.1% in 2007 (n = 502 071) and 54.7% in 2008 (n = 415 332). Males subsequently represented the smaller portion of the total number of patients on the database, at 39.9% in 2005, 40.1% in 2006, 39.9% in 2007, and 40.0% in 2008. These results are similar to findings from reports published by the Council for Medical Schemes regarding patients registered as medical aid schemes' beneficiaries in South Africa, with females representing from 51.1% of beneficiaries in 2005, to 51.3% in 2006, 51.8% in 2007 and decreasing to 48.2% in 2008 (CMS, 2008:30, CMS 2009:125).

4.3.3 Age distribution of patients

According to the reports from the South African Council of Medical Schemes (CMS, 2008:28), the average age of medical scheme beneficiaries in South Africa for 2006 was 31.6 years, with a growth trend in those aged 25 to 29 years. In 2007, the average age for beneficiaries was 31.4 years, and 31.5 years for 2008 (CMS, 2009:125). In line with this, the majority of patients used in this study were in the age group 30 to 60 years (Table 4.1).

4.3.4 Number of prescriptions, medicine items and associated medicine treatment cost

Table 4.1 also shows the number of prescriptions, the total number of medicine items, and total cost of all prescriptions per year. From 2005 to 2006 the total number of prescriptions, the total number of medicine items and costs increased by an average of 6.2%, 8.3% and 7.7% respectively. From 2006 to 2008, however, there was a decrease in the total number of prescriptions per year, medicine items per year and total cost of all medicine items per year on the database of 23.9%, 22.1% and 17.3% respectively. This decrease might be explained by a decrease in the number of medical scheme beneficiaries administrated by the PBM's database or the number of medical schemes claimed through the PBM.

Female patients claimed the largest number of medicine items from the total database with a percentage of 60.3% (n =19 500 774) in 2005, 60.2% (n = 21 113 422) in 2006, 60.3% (n = 19 075 724) in 2007 and 60.2% (n = 16 439 253) in 2008 respectively.

The largest proportion of the medicine items, prescriptions, and cost were claimed for patients between the ages of 30 and 60 years. The total number of medicine items in this age group increased from 29.2% (n = 19 500 774) in 2005 to 34.36% (n = 16 439 253) in 2008. The total number of prescriptions for this age group decreased from 46.7% (n = 8 292 790) in 2005 to 32.5% (n = 6 701 792) in 2008. The cost of all medicine items per year for patients between the ages of 30 and 60 years increased from 37.1% (n = R 674 357 850.57) in 2005 to 41.7% (n = R 744 015 531.65) in 2008 (refer to Table 4.1).

The average number of prescriptions per patient per year for the total population increased from 2005 (6.8 ± 7.62) to 2008 (8.8 ± 8.70) with a small effect size therefore a practically significant difference ($d = 0.2$) (refer to Table 4.1). The average cost per medicine item for the total population increased from (R 93.32 ± 166.36) in 2005 to (R 108.63 ± 436.75) in 2008 ($d = 0.04$). The average cost per prescription for the total population increased from (R 219.45 ± 344.44) in 2005 to (R 266.48 ± 793.43) in 2008 ($d = 0.05$). Based on Cohen's (1988:3) interpretation of *d*-values, these are of no practical significance.

4.3.5 Summary of the total population

There was an increase in the average number of medicine items per prescription, the average number of prescriptions per patient, and the cost per prescription from 2005 to 2008. Patients in the age group 30 to 60 years represented with the largest portion of medicine items, prescriptions and associated medicine item costs. There may be a decrease in the total number of medical scheme patients administrated by the PBM database from 2007 to 2008. It might be because of a decreased number of medical schemes that are administrated by the PBM.

4.4 OVERVIEW OF THE STUDY POPULATION

The study population was extracted from the total population, and divided in two groups: children ≤ 12 years with HIV/AIDS and children ≤ 12 years without HIV/AIDS.

Table 4.2 provides the general information of the study population from 1 January 2005 to 31 December 2008. A discussion on the study population, prescriptions and medicine items claimed and associated costs follows in subsequent paragraphs. The n-values in Table 4.1 were used as denominator for calculations in this section.

The study population was further sub-divided into the following three age groups as described by the paediatric dosage handbook (Taketomo *et al*., 2000:15):

- >0, ≤ 1 years
- >1, ≤ 5 years
- >5, ≤ 12 years

Table 4.2: Total number of patients, prescriptions, medicine items and costs of the study population

Study population (> 0 ≤ 12 years)				
	2005	**2006**	**2007**	**2008**
Total number of patients	197 323	193 346	142 049	98 939
Female	95 510	93 983	68 999	48 094
Male	101 519	99 192	73 008	50 845
Unknown gender	294	171	42	0
>0 ≤ 1 years	9 441	8 912	2 047	18
>1 ≤ 5 years	69 502	678 84	48 478	29 034
>5 ≤ 12 years	118 380	116 550	91 524	69 887
Total number of prescriptions	764 918	790 184	652 869	435 452
Female	363 937	375 281	309 380	206 243
Male	400 190	414 475	343 396	229 209
Unknown gender	791	428	93	0
>0 ≤ 1 years	30 826	30 171	11 501	68
>1 ≤ 5 years	318 126	330 051	275 223	156 307
>5 ≤ 12 years	415 966	429 962	366 145	279 077
Average number of prescriptions per patient (SD) per year	3.9 (3.75)	4.1 (3.90)	4.6 (4.15)	4.4 (4.12)
Total number of medicine items	1 916 485	2 005 107	1 658 615	1 085 511
Female	914 353	957 597	791 593	517 962
Male	1 000 150	1 046 485	866 833	567 549
Unknown gender	1 982	1 025	189	0
>0 ≤ 1 years	69 859	69 768	26 841	144
>1 ≤ 5 years	811 320	854 762	714 530	400 340
>5 ≤ 12 years	1 035 306	1 080 577	917 244	685 027
Average number of medicine items per prescription (SD)	2.5 (1.36)	2.5 (1.38)	2.5 (1.39)	2.5 (1.39)
Total patient contribution per year (R)	10 214 603.93	13 788 253.74	15 968 130.96	12 536 365.95
Total medical scheme contribution (R)	99 059 421.71	100 086 527.97	82 731 665.15	58 248 798.32
Total cost of all items per year (R)	109 274 025.64	113 874 781.71	98 699 796.11	70 785 164.27
Female (R)	50 222 300.79	51 936 901.23	44 840 497.73	31 851 057.64
Male (R)	58 947 971.96	6 1854 692.71	53 839 148.53	38 934 106.63
Unknown gender (R)	103 752.89	83 187.77	20 149.85	0
>0 ≤ 1 years (R)	4 091 890.80	4 260 160.82	1 857 953.54	4 826.07
>1 ≤ 5 years (R)	43 005 378.16	44 588 753.71	38 659 235.38	23 232 499.57
>5 ≤ 12 years (R)	62 176 756.68	65 025 867.18	58 182 607.19	47 547 838.63
Average cost per medicine item (SD) (R)	57.02 (74.75)	56.79 (84.52)	59.51 (111.26)	65.21 (97.52)
Average cost per prescription per year (SD) (R)	142.86 (147.25)	144.11 (165.64)	151.18 (151.18)	162.56 (192.86)

R: Rand value
SD: Standard deviation

4.4.1 Demographic profile of patients

The study population represented 16.2% (n = 197 323) of the total population in 2005, 15.4% (n = 193 346) in 2006, 15.6% (n = 142 049) in 2007 and 13.3% (n = 98 939) in 2008. The total number of patients from the study population therefore decreased with more than a half from 2005 to 2008. Male patients represented 18.8% (n = 101 519) of all male patients

in 2005, and decreased to 14.8% (n = 50 845) in 2008. Female patients represented between 14.1% (n = 95 510) in 2005 and 11.6% (n = 48 094) of the female patients in 2008.

Patients aged >0, ≤ 1 years represented 4.8% of the total study population in 2005 (n = 9 441), decreasing to 0.02% (n = 18) in 2008. Patients aged >1 ≤ 5 years represented 35.2% of the study population in 2005 (n = 69 502) decreasing to 29.3% (n = 29 034) in 2008, whereas patients aged >5 ≤ 12 years represented 59.9% (n = 118 380) in 2005 and increasing to 70.6% (n= 69 887) in 2008.

4.4.2 Number of prescriptions

The total number of prescriptions from the study population (children ≤ 12 years) decreased from 9.2% (n = 764 918) in 2005 to 6.5% (435 452) in 2008. Prescriptions for males represented 12.1% (n = 400 190) of all prescriptions on the total database in 2005, decreased to 8.5% (n = 229 209) in 2008. Prescriptions for female patients represented between 7.3% (n = 363 937) in 2005 and decreased to 5.1% (n = 206 243) of prescriptions of the total population's females in 2008.

The number of prescriptions for patients aged >0 ≤ 1 year represented 4.0% (n = 764 918) of the total database's prescriptions in 2005 and decreased to 0.02% (n = 36) in 2008. Prescriptions for patients aged >1 ≤ 5 year represented 41.6% (n = 318 126) in 2005 of the total database prescriptions, and increased to 42.2% (n = 275 223) in 2007 and decreased to 35.90% (n = 156 307) in 2008. Prescriptions for patients aged >5 ≤ 12 years represented 54.4% (n = 415 966) of the total database prescriptions in 2005 and increased to 60.1% (n = 279 077) in 2008.

4.4.3 Number of medicine items

The number of medicine items in the study population in relation to the total database can be observed in (Table 4.2). The presentation of the medicine items showed the same trend as the number of prescriptions.

The total number of medicine items from the study population decreased from 9.8% (n = 1 916 485) in 2005 to 6.6% (n = 1 085 511) in 2008. Medicine items for males represented 12.9% (n = 1 000 150) of all medicine items on the database in 2005 thereafter decreased to 8.7% (n = 567 549) in

2008. Medicine items of female patients represented between 7.8% (n = 914 353) in 2005 and decreased to 5.2% (n = 517 962) of all medicine items in 2008.

Medicine items for patients aged >0, ≤ 1 year represented 3.6% (n = 69 859) of the total database medicine items in 2005 and decreased to 0.01% (n = 144) in 2008. Patients aged >1, ≤ 5 years represented 42.3% (n = 811 320) of the total database medicine items in 2005 and increased to 43.1% (n = 714 530) in 2007. It decreased to 36.9% (n = 400 340) in 2008. Medicine items for patients aged >5 ≤ 12 years represented the majority of medicine item claims 54.0% (n = 1 080 577) in 2005 and increased to 63.1% (n = 685 027) in 2008 of the total database's medicine items.

An average of (2.5 ± 1.36) medicine items were claimed per prescription from the study population in 2005, compared to (2.5 ± 1.38) in 2006, (2.5 ± 1.39) in 2007 and (2.5 ± 2.39) in 2008. Calculated *d*-values showed no practically significant difference from 2007 to 2008, (*d* = 0.02) and between 2005 and 2008 (*d* = 0.008).

4.4.4 Total cost of all medicine items per year

In Table 4.2 the total medicine cost of the study population in relation of the total database will be presented.

The total medicine cost of the study population represented 6.0% (n= R 109 274 025.6) of the total medicine cost on the database in 2005 and decreased to 4.0% (n = R 70 785 164.0) in 2008 (refer to Table 4.2). Medicine items for males represented 8.0% (n = R 58 947 971.96) of the total cost of all medicine items in 2005, thereafter decreased to 5.3% (n = R 38 934 106.6) in 2008. Medicine items for female patients represented between 4.6% (n = R 50 222 300.8) in 2005 and 3.0% (n = R 31 851 057.6) of the total cost of all medicine items in 2008.

Medicine cost for patients aged >0 ≤ 1 years represented, 3.7% (n = R 4 091 890.8) of the total database's medicine cost in 2005 and decreased to 0.01% (n =R 4 826.07) in 2008. Medication for patients aged >1 ≤ 5 years represented, 39.4% (n= R 811 320) of the total database medicine items in 2005 and decreased to 32.8% (n = R 23 232 500) in 2008. Medication for patients aged >5 ≤ 12 years represented 56.9% (n = R 62 176 756.68) in 2005, of the total database medicine items and increased to 67.2% (n = R 47 547 839) in 2008.

The average cost per medicine item for the study population increased from (R 57.02 ± 74.75) in 2005 to (R 65.21 ± 97.52) in 2008 with no practical significant difference (*d* = 0.1). The average cost per prescription for the study population increased from R 142.86 ± 147.25 in 2005 to R 162.56 ± 192.86 in 2008 with no practical significant difference (*d* = 0.1).

4.4.5 Summary of the study population

The total number of patients in the study population decreased with more than a half from 2005 to 2008 (refer to Paragraph 4.5.1). The total number of prescriptions in the study population (children ≤ 12 years) subsequently also decreased with 3% from 2005 to 2008. The presentation of the medicine items showed the same trend as the number of prescriptions. The reason for the decreasing in medicine items, and prescriptions over the four-year period might be because of medical schemes that are not administrated by the PBM anymore. The total cost of the medicine items from the study population decreased from 6.0% in 2005 to 4.0% in 2008.

4.5 OVERVIEW OF THE PATIENTS WITH HIV/AIDS, AND PATIENTS WITHOUT HIV/AIDS

Table 4.3 provides the general information of the study population divided in patients with HIV/AIDS, and patients without HIV/AIDS from 1 January 2005 to 31 December 2008. A discussion on the prescriptions and medicine items claimed and associated costs follows in subsequent paragraphs.

Table 4.3: The total number of patients, prescriptions, medicine items and costs of the study population with HIV/AIDS and without HIV/AIDS

	Study population							
	Children WITH HIV/AIDS				**Children WITHOUT HIV/AIDS**			
	2005	**2006**	**2007**	**2008**	**2005**	**2006**	**2007**	**2008**
Total number of patients	402	496	464	427	196 921	192 850	141 585	98 512
Female	191	242	217	200	95 319	93 741	68 782	47 894
Male	211	254	247	227	101 308	98 938	72 761	50 618
Unknown gender	0	0	0	0	294	171	42	
>0 ≤ 1 years	10	15	5	0	9 431	8 897	2 042	18
>1 ≤ 5 years	157	191	160	124	69 345	67 693	48 318	28 910
>5 ≤ 12 years	235	290	299	303	118 145	116 260	91 225	69 584
Total number of prescriptions	5 033	7 150	7 129	6 309	759 885	783 034	141 585	429 143
Female	2 416	3 349	3 385	2 965	361 521	371 932	305 995	203 278
Male	2 617	3 801	3 744	3 344	397 573	410 674	339 652	225 865
Unknown gender	0		0		791	428	93	0
>0 ≤ 1 years	66	98	58	0	30 760	30073	11 443	68
>1 ≤ 5 years	1 979	2 750	2 454	1 842	316 147	327 301	272 769	154 465
>5 ≤ 12 years	2 988	4 302	4 617	4 467	412 978	425 660	361 528	274 610
Average number of prescriptions per patient per year (SD)	12.5 (7.49)	14.4 (7.69)	15.4 (6.68)	14.8 (7.01)	3.9 (3.71)	4.1 (3.85)	4.6 (4.09)	4.4 (4.05)
Total number of medicine items	17 475	2 4934	25 472	22 920	1 899 010	1 980 173	1633143	1062591
Female	8 289	11 580	11 879	10 780	906 064	946 017	779 714	507 182
Male	9 186	13 354	13 593	12 140	990 964	1 033 131	853 240	555 409
Unknown gender	0	0	0	0	1 982	1 025	189	0
>0 ≤ 1 years	254	296	167	0	69 605	69 472	26 674	144
>1 ≤ 5 years	6 779	9 456	8 557	6 648	804 541	845 306	705 973	393 692
>5 ≤ 12 years	10 442	15 182	16 748	16 272	1 024 864	1 065 395	900 496	668 755
Average number of medicine items per prescription (SD)	3.5 (1.36)	3.5 (1.42)	3.6 (1.3)	3.6 (1.30)	2.5 (1.35)	2.5 (1.37)	2.5 (1.39)	2.5 (1.37)
Total patient contribution per year (R)	24 946.39	52 194.30	52 740.88	56854.63	10 189 657.54	1 373 6059.44	52 740.88	12 479 511.32
Total medical scheme contribution (R)	2 159 729.66	2 558 487.27	2 704 466.85	2 68 4128.06	96 899 692.05	97 528 040.70	80 027 198.30	55 564 670.26 3
Total cost of all items per year (R)	2 184 676.05	2 610 681.57	2 757 207.73	2 740 982.69	107 089 349.59	111 264 100.14	95 942 588.38	6 804 4181.58
Female (R)	1 076 238.60	1 253 472.95	1 306 099.94	1 253 173.07	49 146 062.19	50 683 428.28	43 534 397.79	30 597 884.57
Male (R)	1 108 437.45	1 357 208.62	1 451 107.79	1 487 809.62	57 839 534.51	60 497 484.09	52 388 040.74	37 446 297.01
Gender unknown (R)	0	0	0	0	103 752.89	83 187.77	20 149.85	0
>0, ≤ 1 years (R)	13 976.44	21 312.59	12 550.97	0	4 077 914.36	4 238 848.23	1 845 402.57	4 826.07
>1 ≤ 5 years (R)	935 928.62	1 041 730.09	878 015.33	688 675.20	42 069 449.54	43 547 023.62	37 781 220.05	22 543 824.37
>5, ≤ 12 years (R)	1 234 770.99	1 547 638.89	1 866 641.43	2 052 307.49	60 941 985.69	63 478 228.29	56 315 965.76	45 495 531.14
Average cost per medicine item (SD) (R)	125.02 (159.46)	104.70 (125.69)	108.24 (120.30)	119.59 (137.38)	56.39 (73.23)	56.19 (83.69)	58.75 (110.94)	64.04 (96.14)
Average cost per prescription (SD) (R)	434.07 (373.58)	365.13 (292.60)	386.71 (281.05)	434.46 (314.52)	140.93 (142.61)	142.09 (162.65)	148.58 (220.13)	158.56 (187.58)

R: Rand value

SD: Standard deviation

4.5.1 Demographic profile of patients

The general prevalence of children with HIV/AIDS in relation to the number of children without HIV/AIDS is portrayed in (Table 4.3). The total number of HIV/AIDS children in relation to the study population (children ≤ 12 years) increased from 0.2% (n = 197 323) in 2005 to 0.4% (n = 98 939) in 2008, whereas the number of children without HIV/AIDS in relation to the study population (children ≤ 12 years) decreased from 99.8% (n = 197 323) in 2005 to 99.6% in 2008 (n = 98 939) (refer to Table 4.3).

Male HIV/AIDS patients represented 0.2% (n = 101 519) of the males in the study population in 2005 (n = 101 519) and increased to 0.5% (n = 50 845) in 2008. Male patients without HIV/AIDS represented 99.8% (n = 101 519) of the male study population in 2005 and decreased to 99.6% (n = 50 845) in 2008. In a similar fashion the prevalence of HIV/AIDS in females in the female study population increased from 0.2% (n = 95 510) in 2005 to 0.4% (n = 48 094) in 2008, whereas females without HIVAIDS in the female study population decreased from 99.8% (n = 95 510) in 2005 to 99.6% (n = 48 094) in 2008 (refer to Table 4.3).

The following deduction can be made from (Table 4.3) regarding the age group distribution of patients.

- Age group 1 (>0, ≤ 1 years):

HIV/AIDS patients represented 0.1% (n= 9 441) of the total population in this age group in 2005 and increased to 0.2% (n = 2 047) in 2007 and decreased with only 18 patients in 2008. Children without HIV/AIDS in this age group increased from 99.9% (n= 9 441) in 2005 to 100% (n = 18) in 2008.

- Age group 2 (>1, ≤ 5 years):

HIV/AIDS patients represented 0.2% (n = 69 502) of the total population in this age group in 2005 and increased to 0.4% (n = 29 034) in 2008. Patients without HIV/AIDS represented 99.8% (n = 69 502) of the total population in this age group in 2005 and decreased to 99.6% (n = 29 034) in 2008.

- Age group 3 (>5 ≤ 12 years):

HIV/AIDS patients represented 0.2% (n = 118 380) in 2005 and increased to 0.4% (n = 69 887) in 2008 of the total population in this age group, whereas patients without HIV/AIDS represented 99.8% (n = 118 380) in 2005 and decreased to 99.6% (n =69 887) in 2008 of the total population in this age group (refer to Table 4.3).

4.5.2 Number of prescriptions

The total number of prescriptions for HIV/AIDS patients in relation to those prescriptions for patients without HIV/AIDS can be observed in (Table 4.3). The prescriptions for HIV/AIDS patients included in this analysis consisted of both the ARV medication as well as the other medication prescribed to those patients (Table 4.3). The total number of prescriptions for patients with HIV/AIDS in relation to the study population in 2005 was 0.7% (n = 764 918) and increased to 1.5% in 2008 (n = 435 452), whereas the total number of prescriptions for patients without HIV/AIDS in relation to the study population in 2005 was 99.3% (n = 764 918) and decreased to 98.6% in 2008 (n = 435 452) (refer to Table 4.3).

Prescriptions for male patients with HIV/AIDS represented 0.6% (n = 363 937) of the male study population prescriptions in 2005 and increased to 1.5% in 2008 (n = 206 243), whereas prescriptions of male patients without HIV/AIDS represented 99.4% (n = 400 190) of the male prescriptions study population in 2008 and decreased to 98.5% (n = 229 209) in 2008. In a similar fashion from 2005 to 2008 prescriptions for female HIV/AIDS patients in female study population increased from 0.7% (n = 363 937) in 2005 to 1.4% (n = 206 243) in 2008. Prescriptions of females without HIV/AIDS represented 99.3% (n = 363 937) in 2005 of the female study population and decreased to 98.6% (n = 206 243) in 2008 (refer to Table 4.3).

- Age group 1 (>0, ≤ 1 years):

Prescriptions prescribed to HIV/AIDS patients represented 0.2% (n= 30 826) in 2005 and increased to 0.5% (n = 11 501) in 2007 of the total number of prescriptions in this age group and after that it decreased with 68 prescriptions in 2008. Prescriptions for patients without HIV/AIDS represented 99.8% (n= 30 826) in 2005 of the study population in this age group and increased to 100% (n = 68) in 2008.

- Age group 2 (>1, ≤ 5 years):

Prescriptions for HIV/AIDS patients represented 0.6% (n = 318 126) of the study population's prescriptions in this age group in 2005 and increased to 1.2% (29 034) in 2008. Prescriptions for patients without HIV/AIDS represented 99.3% (n = 318 126) in 2005 and decreased to 98.8% (n = 29 034) in 2008.

- Age group 3 (>5, ≤ 12 years):

Prescriptions for HIV/AIDS patients represented 0.7% (n = 415 966) of the study population's prescriptions in this age group in 2005 and increased to 1.6% in 2008. Prescriptions for patients without HIV/AIDS represented 99.3% (n = 118 380) of the study population's prescriptions in this age group and decreased to 98.4% in 2008 (refer to Table 4.3).

The average number of prescriptions per patient per year for HIV/AIDS patients increased from (12.5 ± 7.52) in 2005 to (15.4 ± 6.74) in 2007 and a medium effect (*d* = 0.4) was found. It decreased further to (14.78 ± 7.01) (*d* = 0.8) in 2008. The calculated *d*-value of (*d* = 0.8) illustrated a practically significant difference with regard to the average number of prescriptions per patient per year between 2007 and 2008. The average number of prescriptions per patient per year for children without HIV/AIDS increased from (3.9 ± 3.71) in 2005 to (4.6 ± 3.82) in 2007. A small effect *d*-value (*d* = 0.2) was noticeable. It decreased further to (4.36 ± 4.05) with a *d*-value (*d* = 0.05) of no practically significant importance during 2008.

4.5.3 Number of medicine items

The number of medicine items claimed for HIV/AIDS children in relation to those without HIV/AIDS can be observed in Table 4.3. The total number of medicine items for HIV/AIDS children in relation to the study population was 0.9% (n = 1 916 485) in 2005 and increased to 2.1% (n = 1 085 511) in 2008, whereas the total number of medicine items for patients without HIV/AIDS in relation to the study population was 99.9% (n = 1 916 485) in 2005 and decreased to 97.9% (n = 1 085 511) in 2008 (refer to Table 4.3).

Medicine items prescribed for males with HIV/AIDS represented 0.9% of the total number of medicine items prescribed to the males in the study population (n = 914 353) in 2005 and increased to 2.14% (n = 206 243) in 2008. Medicine items for male patients without HIV/AIDS represented 99.1% (n = 1 000 150) of the total number of medicine items prescribed to males in 2005; and decreased to 97.8% (n = 567 549) in 2008. In a similar fashion medicine items for HIV/AIDS females in the female study population increased from 0.9% (n = 914 353) in 2005 to 2.1% (n = 517 962) in 2008. Medicine items for females without HIVAIDS decreased from 99.1% (n = 914 353) in 2005 to 97.9% (n = 567 549) in 2008 of the total number of medicine items prescribed to females (refer to Table 4.3).

- Age group 1 (>0, ≤ 1 years):

Medicine items prescribed for patients with HIV/AIDS represented 0.4% (n = 69 859) in 2005 of all medicine items prescribed to the study population in this age group and increased to 0.6% (n = 26 841) in 2007 and decreased to 0.0% in 2008. Medicine items for children without HIV/AIDS represented 99.6% (n = 69 859) of medicine items prescribed in 2005 and increased to 100% (n = 144) in 2008.

- Age group 2 (>1, ≤ 5 years):

Medicine items prescribed for HIV/AIDS patients represented 0.8% (n = 811 320) of all medicine items prescribed to the study population in this age group in 2005 and increased to 1.7% (n = 29 034) in 2008, whereas medicine items for patients without HIV/AIDS represented 99.2% (n = 811 320) of all medicine items prescribed to the study population in this age group in 2005 and decreased to 98.3% (n = 400 340) in 2008.

- Age group 3 (>5, ≤ 12 years):

Medicine items prescribed for HIV/AIDS patients in this age group represented 1.0% (n = 1 035 306) of all medicine items prescribed for the study population in this age group in 2005 and increased to 2.4% in 2008. Patients without HIV/AIDS medicine items represented 98.9% (n = 1 035 306) of all the medicine items prescribed to the study population in this age group in 2005 and decreased to 97.6% in 2008 (n = 685 027) (refer to Table 4.3).

The average number of medicine items per prescription for the HIV/AIDS patients increased from (3.5 ± 1.41) in 2005 to (3.6 ± 1.41) in 2008 (d = 0.07). The average number of medicine items for patients without HIV/AIDS increased from (2.5 ± 1.35) in 2005 to (2.5 ± 1.39) in 2007 and thereafter decreased to (2.5 ± 1.37) in 2008 (d = 0.02). The above d-values have no practically significant difference.

4.5.4 Total medicine cost

The total cost of all medicine items in patients with HIV/AIDS in relation to those without HIV/AIDS can be observed in Table 4.3. The total medicine cost of HIV/AIDS patients represented 2.0% (n = R 109 274 025.60) of the total medicine cost of the study population in 2005 and increased to 3.9% (n = R 70 785 164.27) in 2008. Medicine cost of patients without HIV/AIDS represented 98.0% (n = R 113 874 782) of the total medicine cost of the study population in 2005 and decreased to 96.1% (n = R 1 085 511) in 2008 (refer to Table 4.3).

The total cost of all medicine items for male HIV/AIDS patients represented 1.9% of the male study population medicine cost in 2005 (n = R 58 947 971.96) and increased to 3.8% in 2008 (n = R 38 934 106.63), whereas the cost of all medicine items of male patients without HIV/AIDS represent 98.1% (n = R 58 947 972) of the male cost of all the medicine items of the study population in 2008 and decreases to 96.0% (n = R 38 9341 06.63) in 2008. In a similar fashion from 2005 to 2008 the total cost of all medicine items per year in HIV/AIDS females in the female study population increased from 2.1% (n = R 50 222 300.79) in 2005 to 3.9% (n = R 31 851 057.64) in 2008; the cost of the medicine items of the females without HIV/AIDS per year in the female study population decreased from 97.8% (n = R 50 222 301) in 2005 to 96.07% (n = R 31 851 058) in 2008 (refer to Table 4.3).

- Age group 1 (>0, ≤ 1 years):

The total medicine cost of HIV/AIDS patients in this age group represented 0.3% (n = R 4 091 890.80) of the total medicine cost of the study population in 2005 and increased to 0.7% (n = R 1 857 953.54) in 2007. It furthermore decreased to 0.0% (n = 0) in 2008. The total medicine cost of children without HIV/AIDS represented 99.7% (n = R 4 091 890.8) of the total medicine cost of the study population in 2005 and increased to 100% (n = R 4 826.07) in 2008.

- Age group 2 (>1, ≤ 5 years):

The total cost of HIV/AIDS patients' medicine items in this age group represented 2.2% (n = R 43 005 378.16) of the medicine cost of the study population in 2005 and increased to 3.0% (n = R 23 232 499.57) in 2008. Medicine cost of patients without HIV/AIDS in this age group represented 97.8% (n = R 43 005 378) of the medicine cost of the study population in 2005 and decreased to 97.0% (n =R 23 232 500) in 2008.

- Age group 3 (>5, ≤ 12 years):

The total medicine of HIV/AIDS patients in this aged group represented 2.0% (n = R 62 176 756.68) of the study population medicine cost in this age group in 2005 and increased to 4.3% (n = R 47 547 838.63) in 2008. However, the total medicine cost of patients without HIV/AIDS in this age group, represented 98.0% (n = R 1 035 306.00) of the total medicine cost of the study population in the same age group in 2005 and decreased to 95.7% in 2008 (n = R 4 7547 839.00) (refer to Table 4.3).

The average cost per medicine item for HIV/AIDS patients decreased from (R 125.02 ± 159) in 2005 (R 104.70 ± 125.69) (d = 0.1) in 2006 and thereafter increased to (R 119.59 ± 137.38) (d = 0.1) in 2008. The average cost per medicine item for patients without HIV/AIDS decreased from (R 56.39 ±

73.23) in 2005 to (R 56.19 ± 83.69) in 2006 and thereafter increased to (R 64.04 ± 96.14) (*d* = 0.1) in 2008. The above *d*-value*s* have no practically significant importance.

The average cost per prescription of patients with HIV/AIDS decreased from (R 434.07 ± 373.58) (*d = 0.2*) in 2005 to (R 365.13 ± 292.60) in 2006 and increased after that to (R 434.46 ± 314.5) (*d* = 0.2) in 2008. The average cost per prescription per year for patients without HIV/AIDS increased from (R 140.93 ± 142.09) in 2005 to (R 158.56 ± 187.58) (*d* = 0.09) in 2008; the above *d*-value*s* have no practically significant difference.

4.5.5 Summary of children with HIV/AIDS and without HIV/AIDS

The total number of children with HIV/AIDS in relation to the study population increased from 0.2% in 2005 to 0.4% in 2008 whereas the number of children without HIV/AIDS in relation to the study population decreased from 99.8% in 2005 to 99.6% in 2008. The total number of prescriptions for HIV/AIDS patients in relation to the study population in 2005 was 0.7% and increased to 1.5% in 2008, whereas the total number of prescriptions for patients without HIV/AIDS in relation to the study population in 2005 was 99.3% and increased to 98.6% in 2008. The total medicine cost for HIV/AIDS patients in relation to the study population increased from 2005 to 2008, whereas the total cost of all medicine items for patients without HIV/AIDS in relation to the study population decreased from 2005 to 2008.

4.6 OVERVIEW OF HIV/AIDS PATIENTS ARVS AND OTHER MEDICATION

Table 4.4 provides the general information of the study population with HIV/AIDS, of the ARVs they used as well as their other medication from 1 January 2005 to 31 December 2008.

Table 4.4: The total number of patients, prescriptions, medicine items and costs of the study population ARV medication and other medication

Study population with HIV/AIDS								
	Only ARV				Other medication			
	2005	2006	2007	2008	2005	2006	2007	2008
Total number of patients	402	496	463	427	388	477	458	415
Female	191	242	216	200	184	229	216	194
Male	211	254	247	227	204	248	242	221
>0 ≤ 1 years	10	15	5	0	8	13	4	0
>1 ≤ 5 years	157	191	159	124	151	181	159	121
>5 ≤ 12 years	235	290	299	303	229	283	295	294
Total number of prescriptions	2 969	4 363	4 498	4 149	4 467	6 309	6 347	5 587
Female	1 486	2 047	2 145	1 985	2 077	2 944	2 973	2 631
Male	1 483	2 316	2 353	2 164	2 390	3 365	3 374	2 956
>0 ≤ 1 years	25	50	25	0	62	90	57	0
>1 ≤ 5 years	1 123	1 666	1 439	1 177	1 844	2 522	2 286	1 695
>5 ≤ 12 years	1 821	2 647	3 034	2 972	2 561	3 697	4 004	3 892
Average number of prescriptions per patient per year	7.4 (4.72)	8.8 (4.93)	9.71 (4.31)	9.72 (4.54)	11.5 (7.17)	13.2 (7.56)	13.8 (6.91)	13.4 (7.13)
Total number of medicine items	9 058	13 505	14 196	13 224	8 417	11 429	11 276	9 696
Female	4 495	6 249	6 635	6 290	3 794	5 331	5 244	4 490
Male	4 563	7 256	7 561	6 934	4 623	6 098	6 032	5 206
>0 ≤ 1 years	66	144	73	0	188	152	94	0
>1 ≤ 5 years	3 260	4 845	4 235	3 555	3 519	4 611	4 322	3 093
>5 ≤ 12 years	5 732	8 516	9 888	9 669	4 710	6 666	6 860	6 603
Average number of medicine items per prescription (SD)	3.05 (0.71)	3.1 (0.72)	3.2 (0.71)	3.05 (0.73)	1.9 (1.34)	1.8 (1.33)	1.8 (1.31)	1.7 (1.32)
Total patient contribution per year (R)	5 178.61	12 412.82	4 283.47	5 595.01	19 767.78	39 781.48	48 457.41	51 259.62
Total medical scheme contribution (R)	1 856 716.20	2 165 033.20	2 332 189.97	2 329 284.40	303 013.46	393 454.07	372 276.88	354 843.66
Total cost of all items per year (R)	1 861 894.81	2 177 446.02	2 336 473.44	2 334 879.41	322781.24	433 235.55	420 734.29	406 103.28
Female (R)	937 153.73	1 057 050.77	1 108 430.20	1 075 095.01	139 084.87	196 422.18	197 669.74	178 078.06
Male (R)	924 741.08	1 120 395.25	1 228 043.24	1 259 784.40	183 696.37	236 813.37	223 064.55	228 025.22
>0 ≤ 1 years (R)	8 726.48	16 685.32	9 562.47	0	52 49.96	4 627.27	2 988.50	0
>1 ≤ 5 years (R)	810 650.26	884 104.67	716 435.53	580 603.28	125 278.36	157 625.42	161 579.80	108 071.92
>5 ≤ 12 years (R)	1 042 518.07	1 276 656.03	1 610 475.44	1 754 276.13	192 252.92	270 982.86	256 165.99	298 031.36
Average cost per prescription (SD) (R)	627.11 (334.09)	499.07 (258.20)	519.45 (227.37)	562.76 (262.76)	72.26 (121.11)	68.67 (108.39)	66.29 (113.48)	72.69 (136.24)
Average cost per medicine item (SD) (R)	178.10 (205.55)	161.23 (178.10)	164.59 (127.31)	176.56 (144.96)	38.35 (64.54)	37.91 (54.70)	37.31 (57.11)	41.88 (74.11)

R: Rand value

SD: Standard deviation

4.6.1 Overview of HIV/AIDS patients' other medication

A discussion of the prescriptions and medicine items claimed for other medication HIV/AIDS patients received and their associated costs follows in subsequent paragraphs. HIV/AIDS patients received. The n-values in Table 4.3 were used as denominator for calculations in this section.

4.6.1.1 Demographic profile of patients

The total number of HIV/AIDS children that received also other medication concomitantly with their ARVs increased from 96.5% (n = 402) in 2005 to 97.2% (n = 427) in 2008. Males with HIV/AIDS who used other medication represented 52.6% (n = 388) in 2005 while female HIV/AIDS patients represented 47.4% (n = 388) in 2005. The male HIV/AIDS patients increased to 53.3% (n = 415) in 2008 and female HIV/AIDS patients decreased to 46.7% (n = 415) in 2008 (refer to Table 4.4).

Other medication were mostly prescribed to HIV/AIDS patients in the > 5 ≤ 12 years age group during 2005 representing 59.0% (n = 388) and increased to 71% (n = 415) of all HIV/AIDS patients during 2008. HIV/AIDS patients in the age group > 5 ≤ 12 years who received other medication represented 97.4% (n = 235) in 2005 and decreased to 97.0 % (n = 303) of all the HIV/AIDS patients in this age group in 2008.

4.6.1.2 Number of prescriptions

The total number of prescriptions of other medication for HIV/AIDS patients decreased from 88.8% (n = 5 033) in 2005 to 88.6% (n = 6 309) in 2008. Prescriptions for other medication in HIV/AIDS males increased from 2005 to 2008. This correlated with the patterns seen with the prescriptions for other medication for female patients.

Prescriptions of other medication for HIV/AIDS males form the largest portion with 53.5% (n = 4 467) of all the other medication prescribed to HIV/AIDS children in 2005 and decreased to 52.9% (n = 5 587) in 2008. Prescriptions of other medication prescribed to female HIV/AIDS patients represented 46.5% (n = 4 467) in 2005 and increased to 47.1% (n = 5 587) in 2008 of all prescriptions for other medication prescribed to HIV/AIDS patients.

Prescriptions prescribed to HIV/AIDS patients in the age group >5, ≤12 years represented most of the prescriptions from 2005, 57.3% (n = 4 467) to 2008, 69.7%. (n = 5 587). Prescriptions for HIV/AIDS patients in this age group >0 ≤ 1 years represented the least of the prescriptions for other medication. The average number of prescriptions for HIV/AIDS patients per year for other medication was (11.5 ± 7.14) in 2005 and increased (13.8 ± 6.92) in 2007. It decreased further to

(13.4 ± 7.12) in 2008. These decreases between the different years were not practically significant (*d* = 0.2).

4.6.1.3 Number of medicine items

The total number of other medicine items prescribed to HIV/AIDS patients in relation to all medicine items prescribed to HIV/AIDS patients decreased with 48.2% (n = 17 475) in 2005 to 42.3% (n = 22 920) in 2008. Other medication items prescribed to males with HIV/AIDS represented 59.6% (n = 4 467) in 2005 and decreased to 53.0% (n = 5 587) in 2008. Other medicine items prescribed to HIV/AIDS females increased from 46.5% (n = 4467) in 2005 to 47% (n = 5 587) in 2008.

HIV/AIDS patients in the age group >5 ≤ 12 years represented most of the other medication items between 2005, 56% (n = 8 417) and in 2008, 68.1% (n = 9 696). HIV/AIDS patients in the age group >0 ≤ 1 year represented the least number of other medicine items. The average number of medicine items of other medication per prescription decreased from 2005 (1.9 ± 1.34) to 2008 (1.7 ± 1.32). No practically significant differences between 2005 and 2008 could be found (*d* = 0.1).

4.6.1.4 Medicine cost of medication

Medication cost for other medication for HIV/AIDS patients in relation to the total medicine cost of HIV/AIDS patients represented 14.8% (n = R 2 184 676.05) in 2005 and 14.8% (n = R 2 740 982.69) in 2008. The total patient contribution for HIV/AIDS patients other medication in relation to the total patients contribution for all the medication HIV/AIDS patients received was 79.2% (n = R 24 946.39) in 2005 and increased to 90.2% (n = R 56 854.63) in 2008. The total medical scheme contribution for HIV/AIDS patients other medication was 14.0% (n = R 2 159 729.66) in 2005 and decreased to 13.2% (n = R 2 684 128.06) in 2008 of the total medicine cost of HIV/AIDS patients.

Medication cost of other medication in males with HIV/AIDS represented 57% (n = R 322 781.24) in 2005 of the total medication cost for HIV/AIDS patients decreased to 56.1 % (n = R 406 103.28) in 2008, whereas the total cost of all medicine items of other medication for female patients in 2005 were 43.1% (n = R 303 013.46) and increased to 44.0% (n = R 406 103.28) in 2008.

HIV/AIDS patients in the age group >5, ≤ 12 years represented most of the cost of the other medication with 15.6% (n = R 1 234 770.99) in 2005, and decreased to 14.5% (n = R 2 052 307.49) in 2008. HIV/AIDS patients in the age group >5, ≤ 12 years represented the largest cost of medicine items of the other medication with 56% (n = R 322 781.24) in 2005 and increased to 73.4% (n = R 406 103.28) in 2008. HIV/AIDS patients in the age group >0, ≤ 1 year represent the least cost of medicine items the other medication.

The average cost per prescription for other medication in HIV/AIDS patients was (R 72.26 ± 121.11) and decreased to (R 66.29 ± 113.48) in 2007, with no practically significant difference (*d* = 0.05). It increased from 2007 to 2008 to (R 72.69 ± 136.24), with no practically significant differences (*d* = 0.05).

The average cost per medicine item for the other medication in HIV/AIDS patients was (R 38.35 ± 64.54) in 2005 and decreased to (R 37.11 ± 57.11) in 2007, with no practically significant differences (*d* = 0.02). It increased from 2007 to 2008 to (R41.88 ± 74.11). The calculated (*d* = 0.02) illustrated no practically significant difference with regard to the average cost per medicine item between 2007 and 2008.

4.6.1.5 Summary of HIV/AIDS patients other medication

The majority of HIV/AIDS patients received other medication (refer to Paragraph 4.6.1.1) HIV/AIDS patients in the age group > 5 ≤ 12 years, and male patients received mostly other medication.

There was a decrease in the percentage of HIV/AIDS patients who received prescriptions for other medication from 2005 to 2008. The total number of other medication medicine items claimed for HIV/AIDS patients in relation to all their medicine items also decreased from 2005 to 2008 (refer to Paragraph 4.6.1.3).

The total cost of HIV/AIDS patients' other medication in relation to the total medicine cost of HIV/AIDS patients received, stayed the same from 2005 to 2008 with 14.8%.

4.6.2 Overview of ARV usage in HIV/AIDS patients

Table 4.4 provides the general information of the study population divided in ARVs and other medication of HIV/AIDS patients from 1 January 2005 to 31 December 2008. A discussion of the HIV/AIDS patients' ARV medication prescriptions and medicine items claimed and associated costs follow in subsequent paragraphs. The n-values in Table 4.3 were used as denominator for calculations in this section.

4.6.2.1 Number of prescriptions

ARV prescriptions represented 59.1% (n = 5 033) of all prescriptions received by HIV/AIDS children in 2005 and increased to 65.7% (n =6 309) in 2008. The average number of prescriptions per patient per year containing ARVs increased from (7.4 ± 4.72) in 2005 to (9.7 ± 4.51) in 2008. The results reveal a medium effect (*d* = 0.5) may be practically significant. This increase in the number of prescriptions may be practically significant based on Cohen's (1988:3) effect size.

4.6.2.2 Number of medicine items

The ARVs medication for HIV/AIDS children represented 51.8% (n = 17 475) of all the items prescribed to these children in 2005 and increased to 57.7% (n = 22 920) in 2008. Males received more ARV medicine items prescribed than females. The average number of ARV medicine items per prescriptions increased from 3.47 ± 1.36 in 2005 to 3.63 ± 1.30 in 2008 with no practically significant ($d = 0.1$) between 2005 and 2008 .

4.6.2.3 Total cost of ARVs medicine items per year

The total ARV medication cost in relation to the medicine cost of all medication prescribed to HIV/AIDS patients was 85.2% (n = R 2 184 676.05) in 2005 and increased to 87.0% (n = R 268 4128.06) in 2008. The total patients' contribution per year for ARV medication in relation to the total patients' contribution of all medication HIV/AIDS patients received was 20.8% (n = R 24 946.39) in 2005 and decreased to 9.8% (n = R 56 854.63) in 2008. The total medical scheme contribution to ARV medication in relation to the total medical scheme contribution for all the medication HIV/AIDS patients used was 86.0% (n = R 2 159 729.66) in 2005 and increased to 86.9% (n = R 2 684 128.06) in 2008 (refer to Table 4.3).

The average cost per prescription for ARV medication decreased from (R627.11 ± 334.09) in 2005 to (R 499.07 ± 258.20) in 2006 (with a medium effect *d*-value). From 2006 it increased to 2008 with (R 562.76 ± 262.76) with a small effect size with no practically significant difference ($d = 0.2$).

The average cost per ARV medicine items was (R 178.10 ± 205.55) in 2005 and decreased to (R 161.23 ± 178.10) in 2006, with no practically significant *d*-value ($d = 0.08$). It increased to (R176.56 ±144.96) from 2006 to 2008. The calculated ($d = 0.08$) illustrated no practically significant difference with regard to the average cost per medicine item per year between 2007 and 2008.

Table 4.5 illustrates the ARVs according to the active ingredient.

Table 4.5: ARV medication according to active ingredient

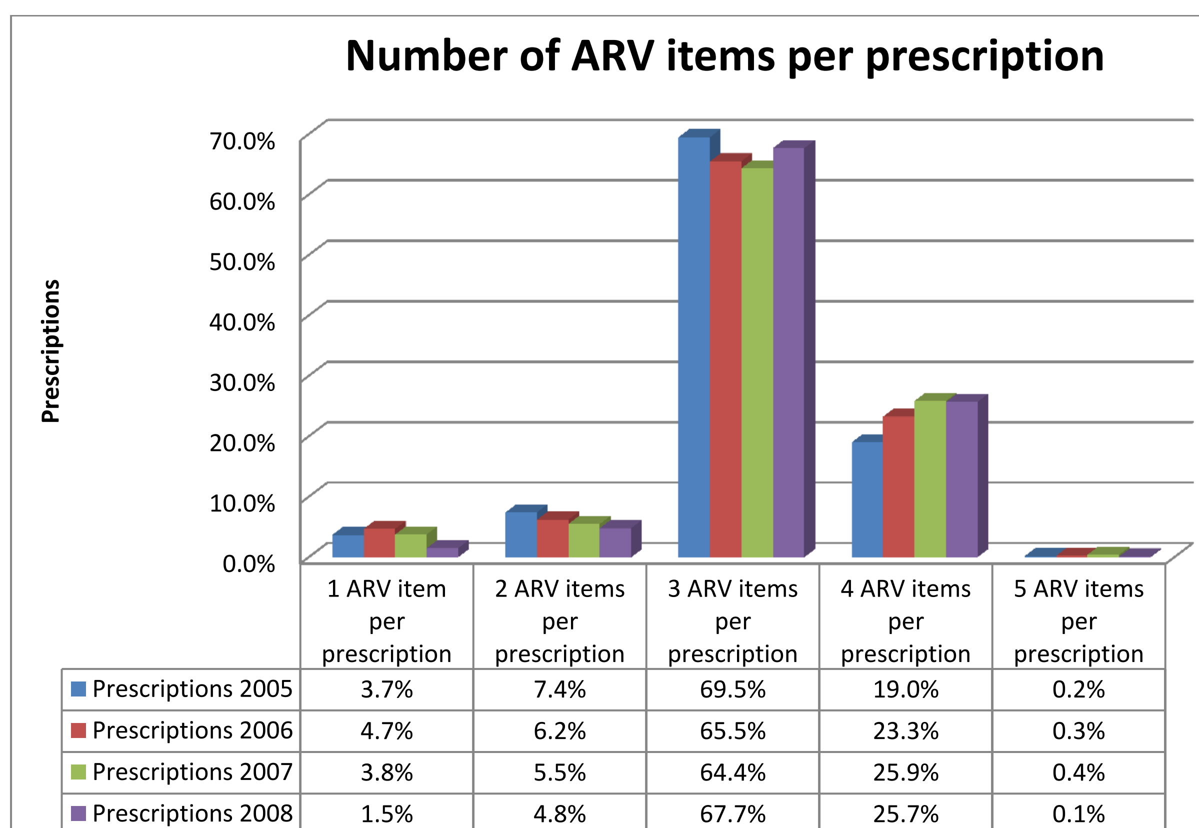
Active ingredient of ARV's	Number of medicine items 2005 (N)	% Medicine items	Number of medicine items 2006(N)	% Medicine items	Number of medicine items 2007 (N)	% Medicine items	Number of medicine items 2008 (N)	% Medicine items
LAMIVUDINE (NRTI)	2615 (1)	28.2	3 854 (1)	28.2	4 123 (1)	28.4	3 859 (1)	28.6
NEVIRAPINE (NNRTI)	1563 (2)	16.9	1 922 (4)	14.1	1 782 (4)	12.3	1 467 (4)	10.9
STAVUDINE (NRTI)	1400 (3)	15.1	2 379 (2)	17.4	2 618 (2)	18.1	2 518 (2)	18.7
ZIDOVUDINE (NRTI)	1382 (4)	14.9	1 655 (5)	12.1	1 619 (5)	11.2	1 421 (5)	10.5
EFAVIRENZ (NNRTI)	1278 (5)	13.8	2357 (3)	17.3	2 609 (3)	18.0	2 449 (3)	18.2
LOPINAVIR/RITONAVIR (PI)	465 (6)	5.0	856 (6)	6.3	1 087 (6)	7.5	1330 (6)	9.9
DIDANOSINE (NRTI)	294 (7)	3.2	323 (7)	2.4	300 (7)	2.1	172 (7)	1.3
RITONAVIR (PI)	98 (8)	1.2	84 (9)	0.6	112 (9)	0.8	56 (9)	0.4
ABACAVIR (NRTI)	71 (9)	0.8	106 (8)	0.8	148 (8)	1.0	165 (8)	1.2
LAMIVUDINE/ZIDOVUDINE (NRTI)	55 (10)	0.6	60 (10)	0.4	36 (10)	0.3	43 (10)	0.3
NELFINAVIR (PI)	32 (11)	0.4	41 (11)	0.3	20 (12)	0.1	-	-
INDINAVIR (PI)	17 (12)	0.2	5 (13)	0.04	30 (11)	0.2	-	-
SAQUINAVIR (PI)	-	-	12 (12)	0.09	16 (13)	0.1	9 (11)	0.1

% Medicine items are calculated by dividing the number of the medicine items (N) by the sum of the medicine items for each active ingredient multiplied by 100.

Lamivudine was the most frequently prescribed active ingredient representing 28.2% (n = 2 615) of the total number of ARV medicine items in 2005 and increased to 28.6% (n = 3 859) in 2008. From 2006 to 2008 the order of the top 5 active ingredients based on prevalence changed (refer to Table 4.5). Stavudine moved up to second place and showed an increase in prescribing prevalence from 17.4% (n = 2 379) in 2006 to 18.7% (n = 2 518) in 2008. Efavirenz moved up to third place from 2006 to 2008 from fifth place in 2005. Nevirapine dropped two positions to fourth place from 2005 to 2006, decreasing in prevalence from 16.9% (n = 1 563) in 2005 to 10.9% (n = 1 467) in 2008. Zidovudine dropped one place from 2005 to 2006 and decreased from 14.9% (n = 1 382) in 2005 to 10.5% (n = 1 421) in 2008. Saquinavir was only prescribed from 2006 to 2008 whereas nelfinavir and indinavir were not prescribed during 2008. Lopinavir/ritonavir and didanosine stayed in the sixth and seventh positions over the four year period. Ritonavir moved down to the ninth position from 2005 to 2006-2008 and abacavir moved up to the eighth position from 2005 to 2006. Lamivudine/Zidovudine stayed in the tenth position. The eleventh, twelfth, and thirteenth positions varied between nelfinavir, indinavir and saquinavir.

4.6.3 Prescribing patterns of ARV medication according to age group for prevalence

The aim of antiretroviral treatment is to improve the quality of life of HIV/AIDS infected children for as long as possible (Department of Health, 2010:28; Tudor-Williams, 2000:4). Unless contraindicated, all children should be treated with the first-line treatment as indicated (refer to Paragraphs 2.8.1.1 and 2.8.1.2). Figure 4.1 illustrates the total number of ARV items per prescription per year. According to this figure, three ARV items per prescription were the most frequently prescribed over the study period. In the subsequent paragraph the total number of ARV items per prescription is discussed.



	1 ARV item per prescription	2 ARV items per prescription	3 ARV items per prescription	4 ARV items per prescription	5 ARV items per prescription
Prescriptions 2005	3.7%	7.4%	69.5%	19.0%	0.2%
Prescriptions 2006	4.7%	6.2%	65.5%	23.3%	0.3%
Prescriptions 2007	3.8%	5.5%	64.4%	25.9%	0.4%
Prescriptions 2008	1.5%	4.8%	67.7%	25.7%	0.1%

Figure 4.2: Number of ARV items per prescription per year

Prescriptions containing one ARV item represented 3.7% (n = 2 969) in 2005, 7.4% (n = 4 363) in 2006, 3.8% (n = 4 498) in 2007 and 1.5% (n = 4 149) in 2008 of all prescriptions HIV/AIDS patients received per year. Prescriptions containing of two ARV items decreased from 7.4% (n = 2 969) in 2005 to 4.8% (n = 4 149) in 2008, whereas prescriptions containing three ARV items represented 69.5% (n = 2 969) in 2005, 65.5% (n = 4 363) in 2006, 64.4% (n = 4 498) in 2007 and 67.7% (n = 4 149) in 2008. Prescriptions containing four ARV items increased from 19.0% (n = 2 969) in 2005 to 25.9% (n = 4 498) in 2007, and decreased to 25.7% (n = 4 149) in 2008. Prescriptions consisted with five ARV items increased from 0.2% (n = 2 969) in 2005, to 0.4% (n = 4 498) in 2007, and decreased to 0.1% (n = 4 149) in 2008.

4.6.3.1 One and two antiretroviral items per prescription in the study population

The prescribing of only one or two antiretroviral drugs are not allowed, according to the National Treatment Guidelines for HIV/AIDS of South Africa (refer to Paragraph 2.8.11). Antiretroviral treatment in the form of one or two drug regimes is now regarded as obsolete because of severe problems with resistance that cause treatment failure (WHO's Guidelines Modules on Antiretroviral Treatments, 2011:2). Of great concern is the transmission of resistant viruses which would cause existing ARVs to become redundant (Martinson *et al.*, 2003:249). Appendix B (Table B1 and B2) indicates the number of prescriptions with one or two ARV medicine items. Prescriptions with only one ARV consisted mostly of lamivudine containing products and prescriptions with two ARVs consisted mostly of lamivudine and stavudine containing products.

4.6.3.2 More than two medicine items per prescription in the study population

The triple regimes of ARVs using three or more antiretrovirals have shown impressive short-term results, and successfully undertakes virological suppression (WHO's Guidance Modules on Antiretroviral Treatments, 2011:2; Gibbon, 2008:318). Approaches to support adherence is essential for the effectiveness and stability of any first line treatment regimen (WHO, 2010:29).

Table 3.1 refers to the prescribed daily dosage (PDD) of ARVs in children with HIV/AIDS. The PDD was calculated as the number of milligrams dispensed per day or per body surface area per age group, per prescription multiplied by the average kilogramme mass of the patient (CDC, 2000b:5, Trouilloud 2008:234). The optimal age dosage range for abacavir, didanosine efavirenz, indinavir, lamivudine, lopinavir, nevirapine, stavudine and zidovudine were calculated using the 50th percentile on the average weight for age or body surface area per age group charts (CDC, 2000b:5, Trouilloud 2008:234). The following reference manuals were used to identify the prescribed daily doses: SAMF (Gibbon, 2008:316-317), the MIMS (Snyman, 2011:298-312) and Martindale (Sweetman, 2011).

4.6.3.2.1 Three products per prescription (> 0 ≤ 1 years of age)

The combination of lamivudine, nevirapine and stavudine are the three combination products that appeared most frequently in the age group for > 0 ≤ 1 years for 2005, 2006, 2007 and 2008 respectively (refer to Appendix B Table B.3). This combination is the recommended first line ARV treatment for children, according to the World Health Organization (2010:36), the South African Medical Association Guidelines (Cotton *et al.*, 2009:38) and the Department of Health (2010:30). The prescribed daily doses of these products were – most of the time – correct, according to the SAMF (Gibbon, 2008, 316-317), the MIMS (Snyman, 2011:298-312) and Martindale (Sweetman, 2011). The PDD calculated for nevirapine (187 mg/day) (n = 1) and (360 mg/kg) (n = 1) in 2005,

(153 mg/day) (n = 3) and (267 mg/day) (n = 3) in 2006, (260 mg/day) (n = 6) in 2007 were higher than the recommended daily dosage of maximum 143.5 mg/day for patients in this age group. These PDDs were calculated using the CDC growth charts on the 50th percentile interval. PDDs of 153 mg/day would be suitable for a patient on the 70th percentile interval. Patients that received 187 mg/day would also be suitable for a patient at the 90th percentile for weight; doses of 260 mg/day, 360 mg/day and 267 mg/day as received by patients aged >0 ≤ 1 years were not recommended (refer to Table 3.1). The PDD for efavirenz of 600 mg/day in 2005 in the age group of >0 ≤ 1 years is higher than the recommended PDD for that age group; 600 mg is the maximum dosage recommended for children more than 40 kg (refer to Table 3.1). The standard treatment guidelines were followed in all the other prescriptions.

4.6.3.2.2 Three products per prescription (> 1 ≤ 5 years of age)

The combination of three products in children aged > 1 ≤ 5 years can be seen in Appendix B (Table B.3). The products that occur most were lamivudine, nevirapine and stavudine. This combination is the recommended first line ARV treatment for children, according to the World Health Organization (2010:36), South African Medical Association Guidelines (Cotton *et al.*, 2009:38) and the Department of Health (2010:30). According to SAMF (Gibbon, 2008:316-317), the MIMS (Snyman, 2011:298-312) and Martindale (Sweetman, 2011), the PDD for nevirapine (4800 mg/day) (n = 26) in 2006, and in 2008 (n = 64) was higher than the recommend daily dose of 143.6 mg/day-252 mg/day, and the maximum daily dose of 400 mg/day for adults. This may refer to a fault in the data when the data were typed in by the Pharmaceutical benefit management organization, but if this is not the problem nevirapine is over prescribed. The standard treatment guidelines were followed in all the other prescriptions.

4.6.3.2.3 Three products per prescription (> 5 ≤ 12 years of age)

Appendix B (Table B.3) displays the combination of three medications for each year in the study period for the > 5 ≤ 12 years age group. The type of combination that was most frequently prescribed was lamivudine, nevirapine and zidovudine. This combination is the recommended first line ARV treatment for children, according to the World Health Organization (2010:36), South African Medical Association Guidelines (Cotton *et al.*, 2009:38) and the Department of Health (2010b:30). The PDD calculated for nevirapine (6400 mg/day) (n = 125) in 2008, again much higher than the recommended daily dose of 253.4 mg/day (minimum) to 400 mg/day (maximum) (refer to Table 3.1). The standard treatment guidelines were followed in all the other prescriptions.

4.6.3.2.4 Four products per prescription

In Appendix B (Table B.4.) the combination of four products prescribed for the study population can be seen. The combination of lamivudine, lopinavir, ritonavir and stavudine were mostly prescribed

together. The PDD calculated for lopinavir (800 mg/day) (n = 34) in 2005, 2006 and 2007 was higher than the recommended dose of 246.2 mg/day (minimum) to 432 mg/day (maximum) for lopinavir (refer to Table 3.1) in the age group of (> 1 ≤ 5 year). The PDD of lamivudine prescriptions was 160 mg/day (n = 110) in 2006, 2007 and 2008 was higher than the recommended dose of (82.1 mg/day- 144 mg/day) (refer to Table 3.1). These doses were calculated on the average mass of the 50th percentile of the CDC growth charts for children. A dose of 160 mg/day, would be suitable for a child at his/her 90th percentile for weight and age.

4.6.3.2.5 Five products per prescription

Appendix B (Table B.5) displays the combination of five products per prescription for the study population. The combination of abacavir, didanosine, lopinavir, ritonavir and stavudine were mostly prescribed together. Calculated PDDs were higher for lopinavir (800 mg/day) (n = 56) in 2005, 2006 and 2007 for the age group > 1 ≤ 5 year than the recommended dose of 246.2 mg/day- 432 mg/day. The dose of lamivudine (160 mg/day) (n = 1) in 2006 was also much higher than the recommended daily dose of maximum (82 mg/day) (refer to Table 3.1) for the age group > 0 ≤ 1 years of age.

4.6.3.3 Summary of the number of ARV items per prescription

By studying the information in Appendix B (Table B.1.to B.5), prescriptions with one or two ARV items on are not allowed (refer to Paragraph 4.6.3.1).Three, four and five products per prescription have shown successfully short-term results (refer to Paragraph 4.6.3.2). On most of the prescriptions the standard treatment guidelines were followed with prescribed daily dosages within the range of treatment of what is recommended and the combination of treatment.

4.7 A COMPARISON BETWEEN “OTHER MEDICATION” USED BY HIV (+) AND HIV (-) PATIENTS

Other medication refers to all the medication HIV (+) patients received, ARVs excluded, in comparison to all the medication HIV (-) patients received. In the subsequent paragraphs a discussion follows on the general prescribing patterns of “other medication” used by HIV (+) and all the medication used in HIV (-) patients.

4.7.1 General prescribing patterns

The t-test procedure and effect sizes (*d*- values) were used to determine whether there were statistical and practically significant differences between the prescribing patterns of other medication used by HIV (+) and HIV (-) patients based on gender and age.

The following measurements were compared between HIV (+) and HIV (-) patients:

- Cost of medicine therapy of “other” medication. These were divided into the total cost, scheme contribution, and patient contribution.
- Number of medicine items per prescription.
- Number of prescriptions per patient per year.

Table 4.6 to 4.8 represent a comparison of the average cost per medicine item per patient, average cost per prescription per patient, and the average number of medicine items per prescription per patient between HIV (+) and HIV (-) patients.

Table 4.6: The average cost per medicine item per patient according to total cost

Average cost per medicine item per patient (R)							
	N	**Mean**	**Standard deviation**	**Standard error**	**95% CI Mean**	***p* > ItI**	***d*-value**
Total cost							
2005							
HIV (-)	196 921	56.1	50.4	0.1	55.8-56.3	< 0.0001	0.4
HIV (+)	388	36.7	27.8	1.4	33.7-33.9		
2006							
HIV (-)	192 850	55.0	57.5	0.1	54.8-55.3	< 0.0001	0.3
HIV (+)	477	36.5	32.5	1.5	33.6-39.45		
2007							
HIV (-)	141 584	56.2	70.3	0.2	53.8-54.5	<0.0001	0.3
HIV (+)	458	35.6	29.2	1.4	38.3-29.2		
2008							
HIV (-)	98 512	56.9	58.3	0.2	56.5-57.3	< 0.0001	0.4
HIV (+)	415	35.8	33.8	1.7	32.5-39.0		
Scheme contribution							
2005							
HIV (-)	196 921	51.3	47.7	0.1	51.1-51.5	< 0.0001	0.4
HIV (+)	388	34.6	27.6	1.4	31.9-37.4		
2006							
HIV (-)	192 850	48.65	53.3	0.1	48.4-48.9	< 0.0001	0.3
HIV (+)	477	33.1	29.1	1.3	30.5-35.7		
2007							
HIV (-)	141 584	44.8	56.6	0.2	44.6-45.2	< 0.0001	0.2
HIV (+)	458	31.7	27.5	1.3	29.2-34.3		
2008							
HIV (-)	98 512	46.0	50.3	0.2	45.7-46.3	< 0.0001	0.3
HIV (+)	415	31.6	31.1	1.6	28.6-34.6		
Patient contribution							
2005							
HIV (-)	196921	4.8	14.3	0.03	4.7-4.8	< 0.0001	0.2
HIV (+)	388	2.1	4.6	0.2	2.1-1.6		
2006							
HIV (-)	192 850	6.4	17.8	0.04	6.3-6.5	< 0.0001	0.3
HIV (+)	477	3.4	8.7	0.4	2.6-4.2		
2007							
HIV (-)	141 584	9.3	30.0	0.1	9.2-9.5	< 0.0001	0.2
HIV (+)	458	3.9	6.2	0.3	3.3-4.7		
2008							
HIV (-)	98 512	10.9	21.7	0.1	10.8-11.0	< 0.0001	0.3
HIV (+)	415	4.1	6.0	0.3	3.6-4.7		

Table 4.7: The average cost per prescription per patient according to total cost, scheme contribution and patient contribution

Average cost per prescription per patient (R)							
	N	**Mean**	**Standard deviation**	**Standard error**	**95% CI Mean**	***p* > ltl**	***d*-value**
Total cost							
2005							
HIV (-)	196 921	128.8	98.7	0.2	128.8-129.2	< 0.0001	0.6
HIV (+)	388	74.2	70.7	3.6	67.2-81.3		
2006							
HIV (-)	192 850	127.2	108.4	0.2	126.7-127.6	< 0.0001	0.5
HIV (+)	477	71.3	62.3	2.9	65.7-76.9		
2007							
HIV (-)	141 584	129.5	126.9	0.3	128.9-130.2	< 0.0001	0.5
HIV (+)	458	69.1	66.7	3.1	62.9-75.2		
2008							
HIV (-)	98 512	133.9	118.7	0.3	133.2-134.6	< 0.0001	0.5
HIV (+)	415	69.53	79.3	3.9	61.9-77.2		
Scheme contribution							
2005							
HIV (-)	196 921	117.9	93.7	0.2	117.5-118.4	< 0.0001	0.5
HIV (+)	388	69.9	69.1	3.5	63.0-76.8		
2006							
HIV (-)	192 850	112.5	100.1	0.2	112.1-113.0	< 0.0001	0.5
HIV (+)	477	64.4	57.0	2.6	59.2-69.5		
2007							
HIV (-)	141 584	108.2	104.1	0.3	107.7-108.8	< 0.0001	0.5
HIV (+)	458	61.3	61.8	2.9	55.6-66.9		
2008							
HIV (-)	98 512	109.3	103.5	0.3	108.7-110.0	< 0.0001	0.5
HIV (+)	415	60.9	71.2	3.5	54.0-67.7		
Patient contribution							
2005							
HIV (-)	196 921	10.8	28.4	0.1	10.7-11.0	< 0.0001	0.2
HIV (+)	388	4.3	12.2	0.6	3.1-5.6		
2006							
HIV (-)	192 850	14.6	35.8	0.1	14.5-14.8	< 0.0001	0.2
HIV (+)	477	6.9	18.3	0.8	5.3-8.6		
2007							
HIV (-)	141 584	21.3	56.0	0.1	21.0-21.6	< 0.0001	0.2
HIV (+)	458	7.8	14.8	0.7	7.8-6.4		
2008							
HIV (-)	98 512	24.6	43.5	0.2	24.3-24.9	< 0.0001	0.2
HIV (+)	415	86.7	15.0	0.7	7.2-10.11		

Table 4.8: The average number of medicine items per prescription per patient from 2005 to 2008

Average number of medicine items per prescription per patient							
	N	**Mean**	**Standard deviation**	**Standard error**	**95% CI Mean**	***p*** **> ltl**	***d*-value**
2005							
HIV (-)	196 921	2.6	1.1	0.002	2.5-2.6	< 0.0001	0.6
HIV (+)	388	1.9	0.7	0.03	1.8-1.9		
2006							
HIV (-)	192 850	2.6	1.1	0.002	2.6-2.6	< 0.0001	0.7
HIV (+)	477	1.8	0.7	0.03	1.8-1.9		
2007							
HIV (-)	141 548	2.6	1.0	0.002	2.6-2.7	< 0.0001	0.7
HIV (+)	458	1.8	0.6	0.03	1.7-1.9		
2008							
HIV (-)	98 512	2.6	1.0	0.003	2.6-2.6	< 0.0001	0.8
HIV (+)	415	1.8	0.7	0.03	1.7-1.8		

Tables 4.6 to 4.8 reveal that there were statistically significant differences ($p < 0.0001$) between HIV (+) and HIV (-) patients with regard to the following measurements:

- Average cost per medicine item per patient.
- Average cost per prescription (divided into scheme contribution and patient contribution).
- Average number of medicine items per prescription.

Effect sizes (*d*-values) with a value of 0.2 or less have a small effect with no practical significance. A *d*-value of 0.5 has a medium effect with an observable effect and may be practically significant and the *d*-value of 0.8 has a large effect with a practical and significant importance (refer to Paragraph 3.4.2.1). According to Table 4.8, the differences in the average number of medicine items per prescription per patient for HIV (+) and HIV (-) for 2005, 2006, 2007 and 2008 is practically and statistically significant ($p < 0.0001$; $d = 0.6$ for 2005, $d = 0.7$ for 2006 and 2007, and $d = 0.8$ for 2008).

The results in Appendix C (Tables C1 to C14) reveal no statistical significant differences between HIV (+) and HIV (-) patients based on gender and age group for the following measurements:

- Average cost per medicine items per patient.

- Average cost per prescription (divided into total cost, scheme contribution and patient contribution).

- Average number of medicine items per prescription per patient.

Table 4.9 displays the average number of prescriptions per patient (sulphonamides included); whereas Table 4.11 shows the average number of prescriptions per patient where the sulphonamides were excluded from the analysis.

Table 4.9: The average number of prescriptions per patient receiving sulphonamides

Average number of prescriptions per patient (sulphonamides included)							
	N	**Mean**	**Standard deviation**	**Standard error**	**95% CI Mean**	***p* > ltl**	***d*-value**
2005							
HIV (-)	196 921	3.9	3.7	0.008	3.8 -3.9	< 0.0001	1.2
HIV (+)	388	11.5	7.2	0.4	10.8 - 12.2		
2006							
HIV (-)	192 850	4.1	3.9	0.009	4.0 - 4.1	< 0.0001	1.3
HIV (+)	477	13.2	7.5	0.3	12.5 - 13.9		
2007							
HIV (-)	141 584	4.6	4.1	0.01	4.5 - 4.6	< 0.0001	1.4
HIV (+)	458	13.9	6.9	0.3	13.2 - 14.5		
2008							
HIV (-)	98 512	4.4	4.0	0.01	4.3 - 4.4	< 0.0001	1.4
HIV (+)	415	13.5	7.1	0.4	12.8 -14.2		

According to the South African Medical Association Guidelines (Cotton *et al*., 2009:48) and Martinson *et al*. (2003:238), sulphonamides (co-trimoxazole) is used as preventive therapy for *Pneumocystis jirovei* in patients with HIV/AIDS; therefore, for the purpose of this study sulphonamides (co-trimoxazole) are seen as part of the patients' chronic treatment.

Table 4.10: The average number of prescriptions without sulphonamides

Average number of prescriptions per patient (sulphonamides excluded)							
	N	Mean	Standard deviation	Standard error	95% CI Mean	*p* > ltl	d-value
2005							
HIV (-)	196 851	3.9	3.7	0.008	4.3 - 4.4	< 0.0001	0.5
HIV (+)	343	6.2	4.6	0.2	5.9 -6.7		
2006							
HIV (-)	192 780	4.1	3.8	0.008	4.0 - 4.1	< 0.0001	0.5
HIV (+)	439	7.0	5.4	0.3	6.5 -7.5		
2007							
HIV (-)	141 560	4.6	4.1	0.01	4.5 -4.6	< 0.0001	0.5
HIV (+)	430	6.6	5.0	0.2	6.2 -7.1		
2008							
HIV (-)	98 494	4.4	4.0	0.01	4.3 -4.4	< 0.0001	0.5
HIV (+)	374	6.4	5.0	0.3	5.9 - 6.9		

HIV (+) patients received more prescriptions than HIV (-) patients per year (refer toTable 4.9 and 4.10). Based on (Table 4.10), HIV (+) patients received more prescriptions than HIV (-) patients, with a (p < 0.0001) and a (d =0.5) that has a medium effect that may be practically significant. The difference between the average number of prescriptions per HIV (+) and HIV (-) patients for 2005, 2006, 2007 and 2008 was practically and statistically significant.

4.7.2 Prescribing patterns of the different pharmacological groups

The prevalence of main pharmacology groups and sub-pharmacological groups will be discussed below.

4.7.2.1 Prevalence of the main pharmacology groups in HIV (+) and HIV (-) patients

Appendix D summarises the prevalence of the main pharmacological groups prescribed for children with HIV/AIDS and those without HIV/AIDS for the period 2005 to 2008. All medicine items (excluded ARVs) were divided based on the main pharmacological groups as described in the MIMS (Snyman, 2010:14-16) for the period from 2005 to 2008.

Appendix D (Tables D.5, D.6, D.7 and D.8) portrays the complete list of the main pharmacological groups according to prevalence in HIV (+) and HIV (-) patients from 2005 to 2008.

According to the South African Medical Association Guidelines (Cotton *et al*., 2009:48) and Health System Trust: South Africa Health review (Martinson *et al*., 2003:238), co-trimoxazole is used as preventive therapy for *Pneumocystis jirovecii* in HIV/AIDS children.

Based on Appendix D (Tables D1 – D4), sulphonamides represented an overall average percentage of 47.3%, for antimicrobials when sulphonamides were included over the four years whereas where

sulphonamides were excluded the overall average percentage was 20.6% from 2005 to 2008; for this reason, in the following section the sulphonamides (co-trimoxazole) are seen as preventive therapy for *Pneumocystis jirovecii* in HIV/AIDS and are not part of HIV/AIDS children's other medication.

The summary of the ten main pharmacological groups for HIV (+) and HIV (-) are illustrated in Figure 4.3, 4.4, 4.5 and 4.6.

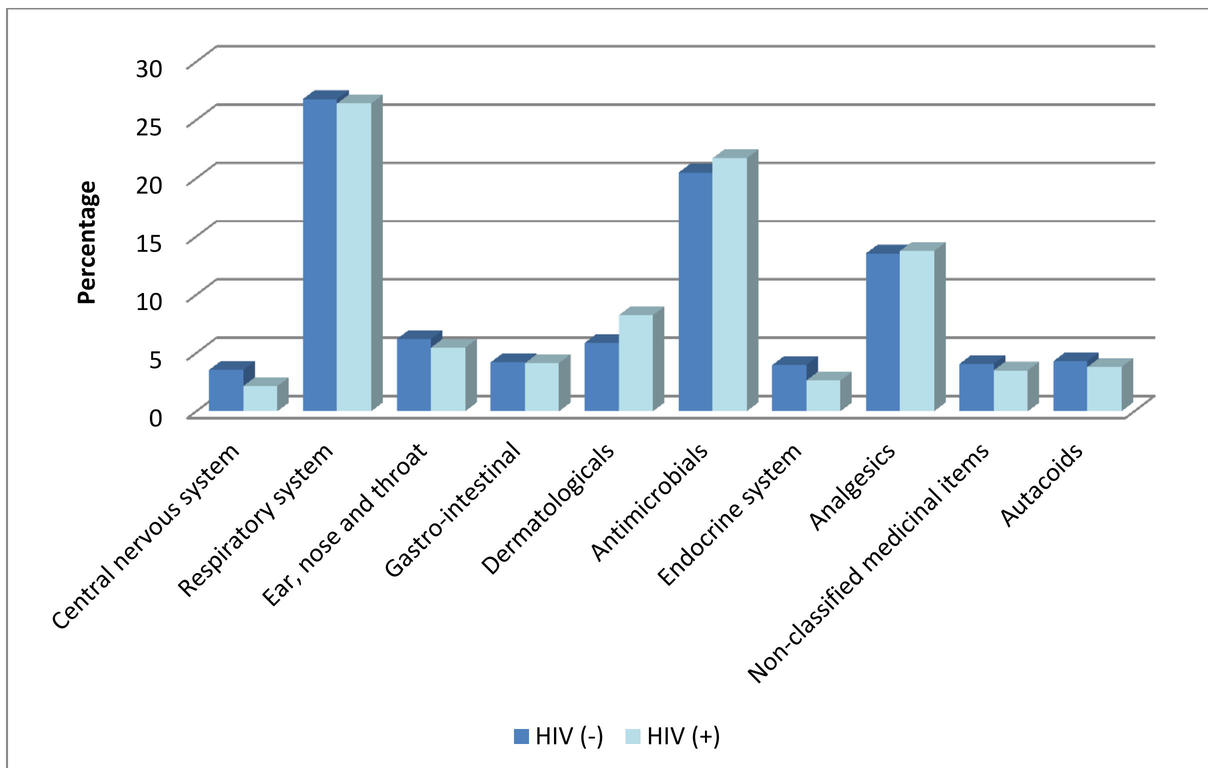


Figure 4.3: The top ten main pharmacological groups for 2005

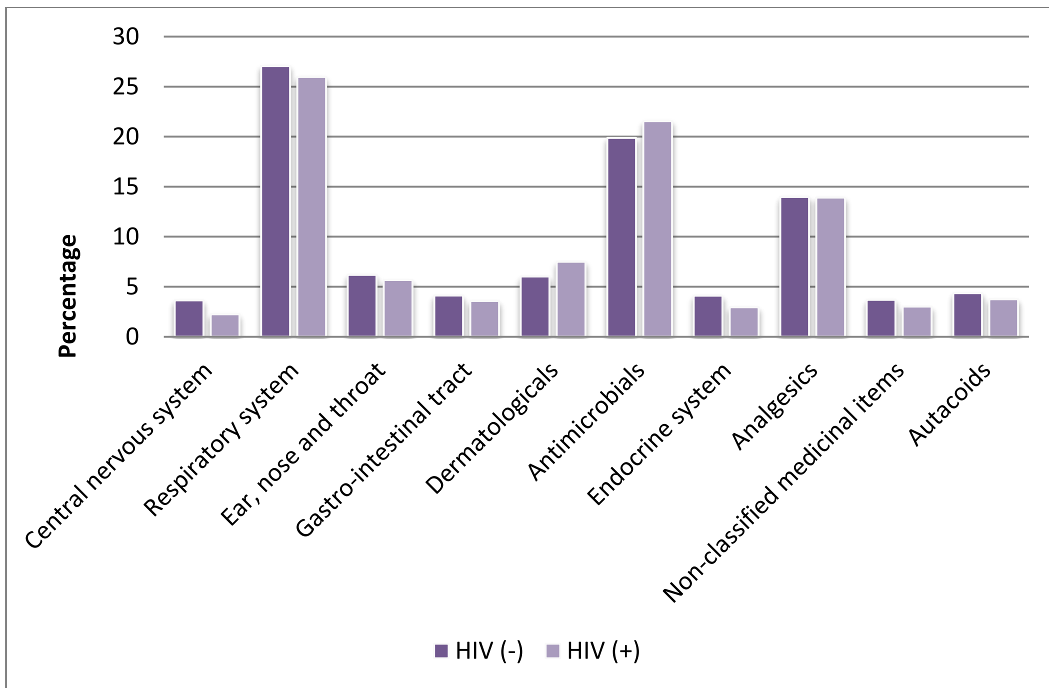


Figure 4.4: The top ten main pharmacological groups for 2006

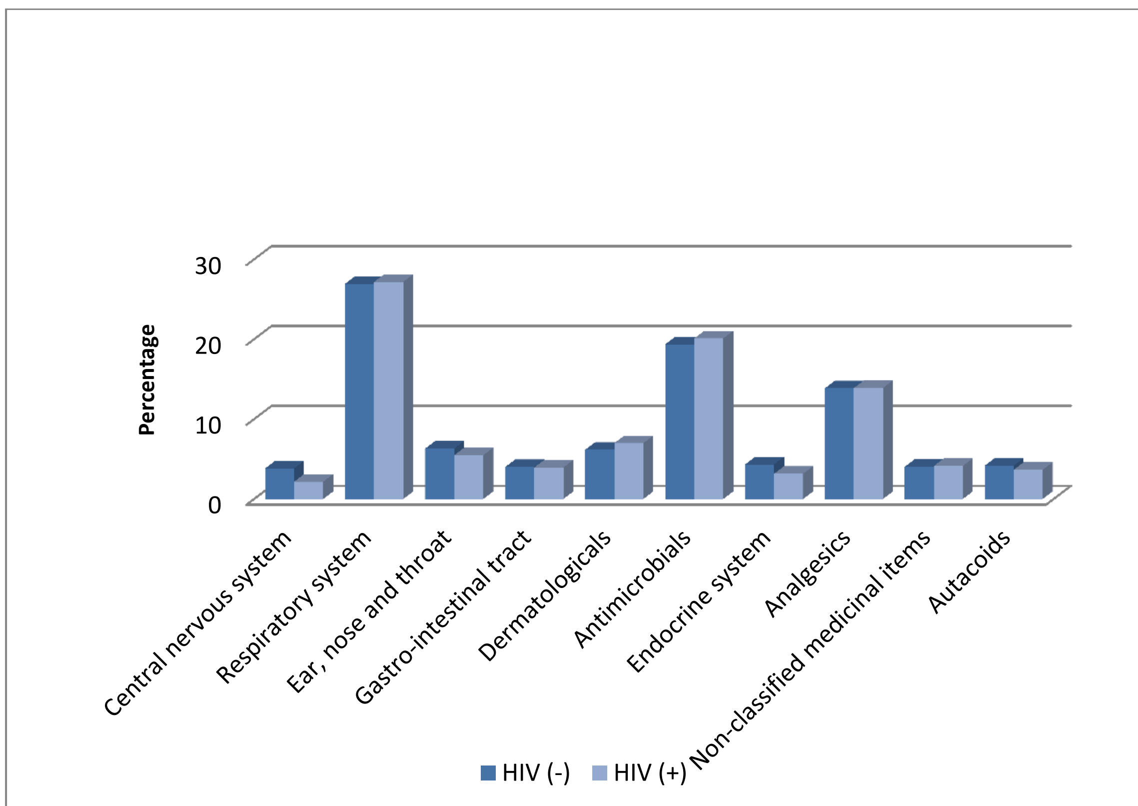


Figure 4.5: The top ten main pharmacological groups for 2007

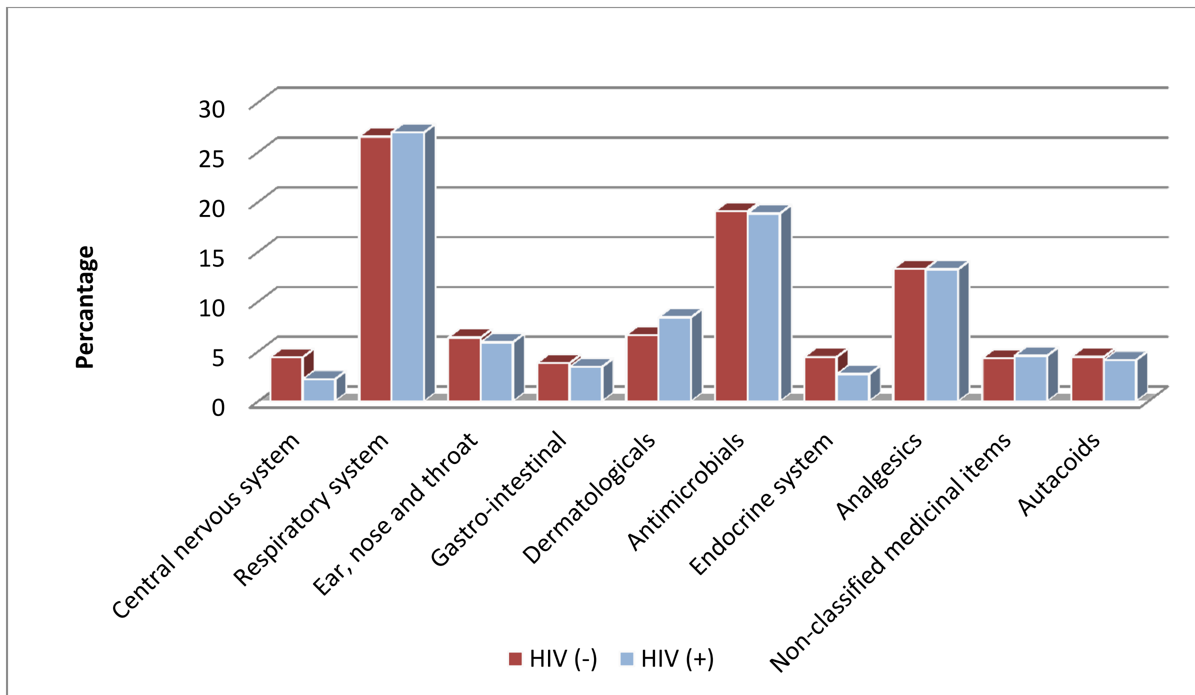


Figure 4.6: The top ten main pharmacological groups for 2008

There were non-remarkable changes in the prevalence of the main pharmacological groups in Figure 4.3, 4.4, 4.5, 4.6 for HIV (+) and HIV (-) patients.

The top ten main pharmacological groups based on prevalence consisted of the respiratory system agents, antimicrobials, analgesics, dermatological products, ear, nose and throat items, autacoids, non-classified medication items, endocrine system, gastro-intestinal and central nervous system items (refer to Figure 4.3, 4.4, 4.5 and 4.6 and appendix D Table D5, D6, D7 and D8).

HIV (-) patients received more central nervous system items, endocrine items and autacoids than HIV (+) patients. HIV (+) patients received more respiratory system, dermatological, ear, nose and antimicrobials items than HIV (-) patients. Amino-acids, cytostatics, special foods and immunological items are the items that are less received by both groups.

The prevalence of the sub pharmacological groups of the top five main pharmacological groups in HIV (+) and HIV (-) patients will be discussed in the subsequent section.

4.7.2.2 The prevalence of the sub pharmacological groups of the top five main pharmacological groups in HIV (+) and HIV (-) patients

The top five pharmacological groups that appear most was the respiratory system agents, antimicrobial agents, analgesics, dermatological and ear, nose and throat items. The sub-groups will be discussed below.

4.7.2.2.1 Respiratory system agents

Medicine from the main pharmacological group of respiratory system agents were prescribed the most to both HIV (+) and HIV (-) patients (refer to Figures 4.3, 4.4, 4.5, and 4.6). Within this pharmacological group the sub-group cough and cold were mostly prescribed to both HIV (+) and HIV (-) patients from 2005 to 2008 (Table 4.11). The percentage of HIV (-) patients who received cough and cold medication decreased from 64.8% (n = 507 570) in 2005 to 61.1% (n = 282 186) in 2008 and for HIV (+) patients it decreased from 68.7% (n = 1 552) in 2005 to 66.8% (n = 1 688) in 2008. HIV (+) patients received more cough and colds medication than HIV (-) patients over the four year period (refer to Table 4.12). A larger percentage of HIV (-) patients received anti-asthmatics than HIV (+) patients over the four year period with 6.9% (n = 507 570) in 2005 and 9.8% (n = 282 186) in 2008 for HIV (-) patients compared to 3.5% (n = 1 552) in 2005 to 5.7% (n = 1 688) in 2008 for HIV (+) patients. Bronchodilators were positioned second in sub pharmacological groups for the respiratory system and occurred more in HIV (+) patients than HIV (-) patients with 25.4% (n = 507 570) in 2005 compared to 25.5% (n = 282 186) in 2008 for HIV (-) compared to 26.6% (n = 1 552) in 2005 declining to 25.8% (n = 1 688) in 2008 for HIV (+) patients. Mycolytics occur more in HIV (-) patients than HIV (+) patients over the four year study period with 2.9% (n = 507 570) in 2005 escalating to 3.7% (n = 282 186) in 2008 for HIV (-) patients compared to 1.2% (n = 1 552) in 2005 to 1.6 (n = 1 688) in 2008 for HIV (+) patients.

The results for the respiratory system was practical and statistically significant with a small effect over the four year period [(p <.0001) and a (*Phi Coefficient* = 0.1)].

Table 4.11 Respiratory medication and their sub-groups for 2005 to 2008

Respiratory system agents												
	2005			2006			2007			2008		
Frequency Column %	**HIV (-)**	**HIV (+)**	**Total**	**HIV (-)**	**HIV (+)**	**Total**	**HIV (-)**	**HIV (+)**	**Total**	**HIV (-)**	**HIV (+)**	**Total**
Cough and colds	328 994 64.8	106 6 68.6	330 060 64.8	341 484 63.8	1 409 69.2	342 893 63.8	277 321 63.1	1 445 70.9	278 766 63.2	172 265 61.1	1128 66.8	173 393 61.1
Bronchodilators	128 848 25.4	413 26.6	129 261 25.4	137 099 25.6	529 26.0	137 628 25.6	108 628 24.7	471 23.1	109 099 24.7	71 824 25.5	436 25.8	72 260 25.5
Mucolytics	14 690 2.9	18 1.2	14 708 2.9	16 044 3.0	28 1.4	160 72 2.9	14 641 3.3	29 1.4	14 670 3.3	10 430 3.7	27 1.6	10 457 3.7
Anti-asthmatics	35 006 6.9	55 3.5	35 061 6.9	406 60 7.6	69 3.4	40 729 7.6	38 724 8.8	93 4.6	38 817 8.8	27 661 9.8	97 5.8	27 758 9.8
Others	32 0.01	0 0.00	32 0.01	16 0.00	0 0.00	16 0.00	9 0.00	0 0.00	9 0.0	6 0.00	0 0.00	6 0.00
Total	507 570 99.7	1 552 0.30	509 122 100.00	535 303 99.6	2035 0.4	537 338 100.00	439 323 99.5	2 038 0.5	441 361 100.0	282 186 99.4	1 688 0.6	283 874 100.00
Statistic	**Value**			**Value**			**Value**			**Value**		
***p*-value**	<.0001			<.0001			<.0001			<.0001		
Phi Coefficient	0.01			0.01			0.01			0.01		

4.7.2.2.2 Antimicrobials

Medicine from the main pharmacological group of antimicrobials were positioned in second place in both groups of the study population (refer to Table 4.12). Within this class, the beta-lactams were prescribed the most to both sub-groups; however, at a higher rate in HIV (-) patients with 79.8% (n =387 952) in 2005 to 78.2% (n = 202 536) in 2008 compared to HIV (+) patients with 66.9% (n = 1 276) in 2005 to 70.2% (n = 1 180) in 2008. HIV (+) patients received more antifungal agents than HIV (-) patients with 9.8% (n = 1 276) in 2005 to 6.6% (n = 1 180) in 2008 for HIV (+) patients compared to HIV (-) patients with 3.1% (n =387 952) in 2005 to 3.3% (n = 202 536) in 2008.

In the second position for HIV (+) and HIV (-) patients the sub pharmacological group were erythromycin and other macrolides. HIV (+) patients received more erythromycin and other macrolides than HIV (-) patients over the four year period with 12.6% (n =387 952) in 2005 to 13.5% (n = 202 536) in 2008 for HIV (-) patients compared to HIV (+) patients with 13.4% (n = 1 276) in 2005 to 14.5% (n = 1 180) in 2008. Within this class the antifungal items were prescribed the third most to both groups of the study population, however, at a higher prevalence in HIV (+) patients with 9.8% (n = 1 276) in 2005 to 6.6% (n = 1 180) in 2008 compared to HIV (-) patients with 3.1% (n =387 952) in 2005 to 3.3% (n = 202 536) in 2008. Larger percentages of HIV (-) patients received aminoglycosides, tetracyclines and chloramphenicols than HIV (+) patients in 2005. In 2006 HIV (-) patients received more tetracyclines, and chloramphenicols than HIV (+) patients. In 2007 HIV (-) patients received more aminoglycosides and chloramphenicals than HIV (+) patients. A larger percentage of HIV (-) patients received antiprotozoal agents than HIV (+) patients in 2008. The antimicrobials sub-group that were received less by HIV (+) and HIV (-) patients in the study population over the four year period were the chloramphenicols with 0.1% (n = 389 228) in 2005, 0.02% (n = 394 966) in 2006, 0.02% (n = 317 268) in 2007 and 0.3% (n = 203 716) in 2008.

Opportunistic infections are common in children with HIV/AIDS (Myers & Kaemmerer, 2008:1328). This might be the reason why HIV (+) patients received more antifungal and antiprotozoal agents than HIV (-) patients. Fungal infections usually occur in HIV-infected individuals (CDC, 2009).

The results for the antimicrobials were practical and statistically significant with a small effect over the four year period [(p <.0001) and a (*Phi Coefficient* = 0.1) in 2005, (*Phi Coefficient* = 0.1) in 2006, (*Phi Coefficient* = 0.1) in 2007 and (*Phi Coefficient* = 0.1) in 2008].

Table 4.12: Antimicrobials and their sub-groups for 2005 to 2008

Antimicrobials												
	2005			2006			2007			2008		
Frequency Column %	**HIV (-)**	**HIV (+)**	**Total**	**HIV (-)**	**HIV (+)**	**Total**	**HIV (-)**	**HIV (+)**	**Total**	**HIV (-)**	**HIV (+)**	**Total**
Beta-lactams	309 757 79.84	854 66.93	310 611 79.80	312 464 79.45	1 116 66.07	313 580 79.39	248 400 78.67	1 020 67.68	249 420 78.61	158 453 78.23	828 70.17	159 281 78.19
Antifungal agents	12 166 3.14	125 9.80	12 291 3.16	12 804 3.26	146 8.64	12 950 3.28	10 284 3.26	110 7.30	10 394 3.28	6 581 3.25	78 6.61	6 659 3.27
Antiprotozoal agents	7 815 2.01	47 3.68	7 862 2.02	7 761 1.97	44 2.61	7 805 1.98	6 507 2.06	38 2.52	6 545 2.06	4 481 2.21	22 1.86	4 503 2.21
Antiviral agents	4 269 1.10	37 2.90	4 306 1.11	4 532 1.15	47 2.78	4 579 1.16	4415 1.40	51 3.38	4 466 1.41	2 888 1.43	47 3.98	2 935 1.44
Erythromycin and other macrolides	48 956 12.62	171 13.40	49 127 12.62	51 046 12.98	249 14.74	51 295 12.99	42 169 13.35	248 16.46	42 417 13.37	27 319 13.49	171 14.49	27 490 13.49
Aminoglycosides	1 214 0.31	3 0.24	1 217 0.31	1 276 0.32	6 0.36	1282 0.32	1 152 0.36	2 0.13	1 154 0.36	883 0.44	6 0.51	889 0.44
Tetracyclines	614 0.16	1 0.08	615 0.16	489 0.12	1 0.06	490 0.12	406 0.13	3 0.20	409 0.13	252 0.12	2 0.17	254 0.12
Chloramphenicols	345 0.09	1 0.08	346 0.09	88 0.02	0 0.00	88 0.02	93 0.03	0 0.00	93 0.03	32 0.02	1 0.08	33 0.02
Quinolones	1 810 0.47	12 0.94	1 822 0.47	1 819 0.46	9 0.53	1 828 0.46	1 518 0.48	8 0.53	1 526 0.48	989 0.49	9 0.76	998 0.49
Mycobacteria	225 0.06	22 1.72	247 0.06	196 0.05	69 4.09	265 0.07	170 0.05	27 1.79	197 0.06	156 0.08	12 1.02	168 0.08
Other antibacterial agents	781 0.20	3 0.24	784 0.20	802 0.20	2 0.12	804 0.20	647 0.20	0 0.00	647 0.20	502 0.25	4 0.34	506 0.25
Total	387 952 99.67	1276 0.33	389 228 100.00	393 277 99.57	1 689 0.43	394 966 100.00	315 761 99.53	1 507 0.47	317 268 100.00	202 536 99.42	1180 0.58	203 716 100.00
Statistic	**Value**			**Value**			**Value**			**Value**		
***p*-value**	<.0001			<.0001			<.0001			<.0001		
Phi Coefficient	0.1			0.1			0.1			0.1		

4.7.2.2.3 Analgesics

Analgesics were prescribed third most in HIV (+) and HIV (-) patients, according to prevalence (refer to Table 4.13). Within this pharmacological group analgesics and antipyretics were the sub-group that was prescribed most too both groups; however, at a higher frequency in HIV (-) patients with 50.9% (n =256 625) in 2005 declining to 44.7% (n = 140 963) in 2008 compared to HIV (+) patients with 48.1% (n = 808) in 2005 to 41.3% (n = 828) in 2008. A larger percentage of HIV (+) patients received combination therapy than HIV (-) with 49.0% (n =256 625) in 2005 to 55.11% (n = 140 963) in 2008 in HIV (-) patients compared to HIV (+) patients with 51.8% (n = 808) in 2005 to 58.5 % (n = 828) in 2008. The use of analgesics and antipyretics items decreased in both groups with 50.8% (n = 257 433) in 2005 going down to 41.4% (n = 141 791) in 2008. Narcotic analgesics were the less used in HIV (+) and HIV (-) patients in the study population with 0.1% (n = 257 433) in 2005 to 0.12% (n = 141 791) in 2008.

The results for the pharmacological sub-groups for analgesics items were not practical or statistically significant over the four year period.

Table 4.13: Analgesics and their sub-groups for 2005 to 2008

Analgesics												
	2005			2006			2007			2008		
Frequency Column %	**HIV (-)**	**HIV (+)**	**Total**	**HIV (-)**	**HIV (+)**	**Total**	**HIV (-)**	**HIV (+)**	**Total**	**HIV (-)**	**HIV (+)**	**Total**
Narcotic analgesics	260 0.10	0 0.00	260 0.10	230 0.08	0 0.00	230 0.08	216 0.10	0 0.00	216 0.10	138 0.10	1 0.12	139 0.10
Analgesic and antipyretics	130 497 50.85	389 48.14	130 886 50.84	131 341 47.50	486 44.59	131 827 47.49	102 925 45.54	444 42.65	103 369 45.53	63 076 44.75	343 41.43	63 419 44.73
Combination	125 829 49.03	419 51.86	126 248 49.04	144 900 52.40	603 55.32	145 503 52.41	122 775 54.33	597 57.35	123 372 54.34	77 685 55.11	484 58.45	78 169 55.13
Others	39 0.02	0 0.00	39 0.02	49 0.02	1 0.09	50 0.02	75 0.03	00 0.00	75 0.03	64 0.05	0 0.00	64 0.05
Total	256 625 99.69	808 0.31	257 433 100.00	276 520 99.61	1090 0.39	277 610 100.00	225 991 99.54	1041 0.46	227 032 100.00	140 963 99.42	828 0.58	141 791 100.00
Statistic	**Value**			**Value**			**Value**			**Value**		
***p*-value**	0.3			0.04			0.1			0.2		
Phi Coefficient	0.004			0.005			0.005			0.005		

4.7.2.2.4 Dermatologicals

From the class of dermatologicals the cortico-steroids were prescribed most from 2005 with 41.4% (n = 111 737) to 2008 with 34.6% (n = 71 035) in both groups. HIV (-) patients received more antibacterial dermatologicals in 2005 than HIV (+) patients with 18.6% (n = 111 253) for HIV (-) patients compared to 9.2% (n = 484) for HIV (+) patients in 2005. HIV (+) patients received more antibacterial antiseptic agents than HIV (-) patients from 2006 to 2008 with 18.7% (n = 588) in 2006 to 19.5 % (n = 527) in 2008 for HIV (+) patients, compared to 17.0% (n = 119 271) in 2006 to 16.15% (n = 70 508) in 2008 for HIV (-) patients. A larger percentage of HIV (-) patients received psoriasis and acne treatment than HIV (+) patients. There was a higher prevalence fungicides in HIV (+) patients with 19.2% (n = 484) in 2005 to 19.7% (n = 527) in 2008 compared to HIV (-) patients with 17.8% (n = 111 253) in 2005 to 15.9% (n = 70 508) in 2008. Emollients and protectives are the sub-pharmacological group that occurred the least over the four year study period in HIV (+) and HIV (-) patients, with 0.3% (n = 111 737) in 2005 to 0.3% (n = 71 035) in 2008. HIV (+) patients are immune-compromised patients and that might be the reason why they received most of the times more antibacterial antiseptic agents, antiparasitics and fungicides agents than HIV (-) patients.

The results for the pharmacological sub-groups for dermatological items were not practical or statistically significant over the four year period.

Table 4.14: Dermatologicals and their sub-groups for 2005 to 2008

Dermatologicals 2007												
	2005			2006			2007			2008		
Frequency Column %	HIV (-)	HIV (+)	Total	HIV (-)	HIV (+)	Total	HIV (-)	HIV (+)	Total	HIV (-)	HIV (+)	Total
Antibacterial antiseptic agents	20 698 18.60	93 9.21	20 791 18.61	20 271 17.00	110 18.71	20381 17.00	16966 16.90	103 19.66	17069 16.91	11389 16.15	103 19.54	11492 16.18
Antiparasitics	3 715 3.34	20 4.13	3 735 3.34	3530 2.96	27 4.59	3557 2.97	1834 1.83	8 1.53	1842 1.83	1247 1.77	13 2.47	1260 1.77
Fungicides	19 842 17.84	93 19.21	19 935 17.84	21403 17.94	115 19.56	21518 17.95	16981 16.91	115 21.95	17096 16.94	11247 15.95	104 19.73	11351 15.98
Corticosteroids	46 070 41.41	219 45.25	46 289 41.43	47451 39.78	238 40.48	47689 39.79	37433 37.29	189 36.07	37622 37.28	24388 34.59	179 33.97	24567 34.58
Psoriasis	9 627 8.65	15 3.10	9 642 8.63	14684 12.31	38 6.46	14722 12.28	17643 17.57	62 11.83	17705 17.54	15779 22.38	73 13.85	15852 22.32
Acne	920 0.83	1 0.21	921 0.82	805 0.67	4 0.68	809 0.67	696 0.69	0 0.00	696 0.69	557 0.79	3 0.57	560 0.79
Melanin inhibitors and stimulants	1 0.00	0 0.00	1 0.00	5 0.00	0 0.00	5 0.00	11 0.01	0 0.00	11 0.01	6 0.01	0 00.00	6 0.01
Emolients and protectives	333 0.30	0 0.00	333 0.30	365 0.31	5 0.85	370 0.31	336 0.33	2 0.38	338 0.33	210 0.30	4 0.76	214 0.30
Others	10047 9.03	43 8.88	10 090 9.03	10757 9.02	51 8.67	10808 9.02	8491 8.46	45 8.59	8536 8.46	5685 8.06	48 9.11	5733 8.07
Total	11 1253 99.57	484 0.43	111 737 100.00	119271 99.51	588 0.49	119859 100.00	100391 99.48	524 0.52	100915 100.00	70508 99.26	527 0.74	71035 100.00
Statistic	Value			Value			Value			Value		
***p*-value**			0.0001			0.0003			0.0022			0.0021
Phi Coefficient			0.01			0.02			0.02			0.02

4.7.2.2.5 Ear, nose and throat

HIV (-) patients received more topical nasal preparations with 67.5% (n = 117 386) in 2005 to 65.9% (n = 103 382) in 2008 than HIV (+) patients with 51.7% (n = 321) in 2005 to 56.1% (n = 371) in 2008. A larger percentage of HIV (+) patients received ear drops, ointments and mouth and throat preparation with 11.8% (n = 321) in 2005 to 9.4% (n = 371) in 2008 than HIV (-) patients with 8.9% (n = 117 386) in 2005 to 8.4% (n = 67 869) in 2008. There was an increase in the used of mouth and throat preparations from 23.5% (n = 117 707) in 2005 to 25.6% (n = 68 240) in 2008.

The results of the pharmacological sub-groups for ear, nose and throat items was statistically significant with a (p <.0001) but not practical significant from 2005 to 2008.

Table 4.15: Ear, nose and throat items and their sub-groups for 2005 to 2008

Ear, nose and throat												
	2005			2006			2007			2008		
Frequency **Column %**	**HIV (-)**	**HIV (+)**	**Total**	**HIV (-)**	**HIV (+)**	**Total**	**HIV (-)**	**HIV (+)**	**Total**	**HIV (-)**	**HIV (+)**	**Total**
Topical nasal preparations	79 289 67.55	166 51.71	79 455 67.50	81 793 66.78	236 53.15	82 029 66.73	67 696 65.74	216 52.55	67 912 65.69	44 772 65.97	208 56.06	44 980 65.91
Ear drops and ointments	10 534 8.97	38 11.84	10 572 8.98	10 712 8.75	61 13.74	10 773 8.76	9 107 8.84	48 11.68	9 155 8.86	5 737 8.45	35 9.43	5 772 8.46
Mouth and throat preparations	27 563 23.48	117 36.45	27 680 23.52	29 981 24.48	147 33.11	30 128 24.51	26 168 25.41	147 35.77	26 315 25.45	17 360 25.58	128 34.50	17 488 25.63
Total	117 386 99.73	321 0.27	117 707 100.00	122 486 99.64	444 0.36	122 930 100.00	102 971 99.60	411 0.40	103 382 100.00	67 869 99.46	371 0.54	68 240 100.00
Statistic	**Value**			**Value**			**Value**			**Value**		
***p*-value**	<.0001			<.0001			<.0001			<.0001		
Phi Coefficient	0.02			0.02			0.02			0.02		

4.8 Summary

The top five main pharmacological sub-groups were respiratory system items, antimicrobials items, analgesics, ear nose and throat and dermatological items. The sub-group cough and cold medication occurred most for HIV (+) and HIV (-) patients from 2005 to 2008 in the main pharmacological group of the respiratory system. Beta-lactams were the antimicrobial that occurred most in the study population. Analgesics are the main pharmacological group in the third position according to prevalence, analgesics and antipyretics is the sub-group that occurred most during the study population.

HIV (-) patients received more central nervous system items, endocrine items and autacoids than HIV (+) patients. HIV (+) patients received more respiratory system, dermatologicals, ear nose and antimicrobials items than HIV (-) patients.

CHAPTER 5

CONCLUSIONS AND RECOMMENDATIONS

5 Conclusions

The conclusions of this study, based on the results of the literature review and empirical investigation are presented in this chapter. The limitations encountered during the study, as well as the recommendations for future studies, are also included in this chapter.

5.1.1 Conclusions based on the literature review

The following conclusions can be formulated with regard to the literature review.

- *The first specific objective of the literature review was to conceptualise HIV/AIDS in children:*

  Through the literature overview, the main concepts regarding HIV/AIDS were investigated (refer to Chapter 2). This research objective was achieved *via* a broad overview of HIV/AIDS, with specific focus in South Africa and in children. The extent of HIV epidemic, including the spread of the epidemic, burden of HIV/AIDS (impact of population growth, social and economic effects) was investigated (refer to Sections 2.2, & 2.3). From this review was found that in the past 30 years HIV-1 infection have increased to develop in a worldwide epidemic and has a large impact on the mortality of the population. HIV positive children have more contact with health care workers, increased hospital admissions and are more prone to be neglect by their families. The impact of HIV/AIDS on children includes deepening poverty and psychosocial defects in the family. An estimated 84 billion rand per year is spent on HIV/AIDS support prevention and care programmes in the low and middle income countries (refer to Section 2.3).

  Furthermore, the transmission of HIV, clinical features and classification of HIV/AIDS in children were discussed (refer to Section 2.4, 2.5 & 2.6). It was established from the literature that an estimated 90% of paediatric HIV/AIDS cases, and new born/infants were directly infected *via* mother to child transmission (refer to Section 2.4.1). The transmission of HIV-1 infection *via* breast milk is frequent in children (refer to Section 2.4.1). The immune response is insufficient to eradicate the virus, and the infection eventually results in a gradual decline of CD4 cell count (refer to Section 2.6). An essential determination of the infection of HIV/AIDS is the stage of the infection (refer to Section 2.6).

- *The second specific objective of the literature review was to describe the prevalence of HIV/AIDS, nationally as well as internationally, with specific reference to children:*

  This research objective was approach *via* a broad overview of the prevalence of HIV/AIDS nationally as well as internationally with specific reference to children (refers to Section 2.2). It was establish from the literature that approximately 33 million people in the world have HIV/AIDS of whom more than 30 million live in low- and middle-income countries in 2009 (refer to Section 1.2). South Africa is the country with the highest incidence of HIV cases in the world (Coffee *et al*., 2007:345). A child under 15 years dies of an HIV/AIDS associated illness every minute of every day worldwide (refer to Section 1.2). In 2009, an estimated 2 million people globally died as a result of HIV/AIDS, whilst 2.6 million people (including 370 000 children) were newly infected. Africa represented 68% of the total global infections; while Africa's number of newly infected children represents 69% of the global total (refer to Section 1.2).

- *The third specific objective of the literature review was to describe opportunistic infections associated with HIV/AIDS with specific reference to children:*

  Through the literature review, the opportunistic infections associated with HIV/AIDS with specific reference to children was investigated (refer to Section 2.7). Opportunistic infections are common in children with HIV/AIDS (refer to Section 2.7) and occurs when the immune system functions are compromised or function not properly. It is a major cause of morbidity and mortality in HIV infected children (refer to Section 2.7). Opportunistic infections that are usually occurring in children, include *inter alia mycobacterium avuim complex*, *mycobacterium tuberculosis,* salmonellosis, *candidiasis, coccidiomycosis, cryptococcal meningitis, histoplasmosis,* Kaposi's sarcoma, systemic non-Hodgkin's lymphoma, Hodgkin's disease, cryptosporidiosis, isosporiasis, microsporidiasis, *pneumocystis carinii pneumonia,* toxoplasmosis, cytomegalovirus, hepatitis, herpes simplex virus, molluscum contagiosum, oral hairy leukoplakia, progressive multifocal, leukoencephalopathy, neurological conditions, diarrhoea, lymphadenopathy, warts, weight loss and wasting syndrome (refer to Section 2.7).

- *The fourth specific objective of the literature review was to describe the HIV/AIDS treatment guideline(s) for children with specific reference to those ARV's applicable to South Africa:*

  This objective was approached via an appraisal of the literature of ARV's (refer to Section 2.8). The aim of antiretroviral treatment is therefore to improve the quality of life of HIV/AIDS infected children as long as possible and to reduce HIV/AIDS related morbidity and mortality.

The use of highly active antiretroviral therapy has been proven beneficial over years in those patients receiving the treatment and they are less hospitalised than before on earlier drug therapy, also there is a decrease in the number of HIV/AIDS related deaths (refer to Section 2.8).

Approaches to support adherence is essential for the effectiveness and stability of any first-line treatment regimen (refer to Section 2.8.1). Unless contraindicated, all children can use first-line treatment. The first-line treatment for an infant or a child younger than 24 months not exposed to ARVs, start with nevirapine and 2 NRTI's (nucleoside reverse transcriptase inhibitor).The first-line treatment for a infant or a child younger than 24 months exposed to NNRTI during maternal treatment, start with lopinavir/ritonavir and 2 NRTI's. The first line treatment for an infant or child younger than 24 months with unknown ARV exposure starts with nevirapine and 2 NRTI's. Children 24 months to 3 years have to start with nevirapine and 2 NRTI's. The first-line treatment for children older than 3 years is nevirapine or efavirenz and 2 NRTI's .The second-line treatment regimen in children is used when there was a failure with the first-line treatment regimen (refer to Section 2.8.2). Furthermore drug interactions, recommended doses in children, special instructions and side effects of these ARV's were discussed (refer to Section 2.8.3).

5.1.2 Conclusions based on the empirical investigation

The following conclusions can be formulated with regard to the empirical investigation.

- *The first specific objective of the empirical investigation was to investigate possible changes in the medicine prescribing patterns; (including ART) based on gender and age, in HIV/AIDS children, during the selected four-year period, 2005-2008:*

HIV/AIDS has a significant prevalence among children in the private health care sector (refer to Section 2.2). The study population (children ≤ 12 years) represented 16.2% of the total population in 2005 and decreased to 13.3% in 2008. The total number of prescriptions in the study population subsequently also decreased with 3% from 2005 to 2008. The reason for the decrease in medicine items, and prescriptions over the four year period might be because of a decrease in number of members that claimed as well as the number of medical schemes administrated by the PBM.

HIV/AIDS patients in the age group > 5, ≤ 12 years, and male HIV/AIDS children received mostly other medication (ARVs excluded) concomitantly with their ARVs. Other medication (ARVs excluded) represented 96.5% of all medication prescribed to HIV/AIDS children in 2005 and increased to 97.2% in 2008 (refer to Section 4.6.1).

ARV prescriptions and medicine items received by HIV/AIDS children increased from 2005 to 2008. The average number of ARV prescriptions per patient per year increased from 7.4 ± 4.72 in 2005 to 9.7 ± 4.51 in 2008.

Gender seems to have a small influence because the males received 50.4% of the ARV medicine items in 2005 and increased to 52.4% in 2008, while females received 49.6% of the total number of ARV items in 2005 and decreased to 47.6% in 2008 (refer to section 4.6.2). There were more male patients that received ARV's in the study population than females (refer to Table 4.4). The average number of ARV medicine items per prescriptions increased from 2005 to 2008 (refer to Section 4.6.2). The ARV medication cost indicated for HIV/AIDS children increased from 2005 to 2008 (refer to Section 4.6.3).

- *The second specific objective of the empirical investigation was to assess whether HIV/AIDS treatment guidelines were followed in the private health care sector of South Africa:*

Lamivudine was the most frequently prescribed antiretroviral active ingredient over the study periode. Lamuvidine prevalence increased from 2005 to 2008. Prescriptions containing three antiretroviral active ingredients were mostly prescribed over the four year study period. Prescriptions containing one ARV active ingredient are the least observed of all prescriptions prescribed to HIV/AIDS patients. The prevalence of prescriptions containing two ARV active ingredients decreased from 2005 to 2008. The prescribing of only one or two antiretroviral drugs are not allowed according to the National Treatment Guidelines for HIV/AIDS of South Africa (refer to Section 2.8.1). Prescriptions with only one ARV consisted mostly of lamuvidine containing products and those prescriptions with two ARV's contained mostly lamuvidine and stavudine containing products (refer to Section 4.6.3.1).

HAART have shown impressive short term results, and successfully undertakes virological suppression (WHO's Guidance Modules on Antiretroviral Treatments, 2011:2; Gibbon, 2008:318). Prescriptions containing three ARV active ingredients represented 69.5% in 2005, 65.5% in 2006, 64.4% in 2007 and 67.7% in 2008 of all the ARV prescrptions. Prescriptions with four or five ARV active ingredients increased from 2005 to 2007, and decreased to 2008 (refer to Section 4.6.3.2.5).

According to the World Health Organization (2010:36), the South African Medical Association Guidelines (Cotton *et al.*, 2009:38) and the Department of Health (2010b:30), the guidelines set for combination treatment in HIV/AIDS patients was two NRTI's and one NNRTI's. In agreement with these results the majority of the prescriptions complained to these guidelines (refer to section 4.6.3).

The prescribed daily doses of nevirapine, efavirenz, lopinavir and lamuvidine were higher than the recommended daily dosages in a number of cases (refer to section 4.6.3). The prescribed daily dosages indicated for individual active ingredients complied with the standard treatment guidelines on the majority of prescriptions.

- *The third specific objective of the empirical investigation was to compare the medicine prescribing patterns (prevalence), (excluding ARV drugs) in HIV/AIDS and non-HIV/AIDS children, based on age and gender:*

HIV (+) children received 6.2 ± 4.62 prescriptions for other medication (non-ARVs) per year during 2005 compared to HIV (-) (non-HIV/AIDS) children with 3.9 ± 3.71. In 2008 HIV (+) children received 6.4 ± 5.02 prescriptions per year compared to HIV (-) patients who received 4.36 ± 4.05 prescriptions in 2008. The average cost per prescription for the other medication for HIV (+) children decreased from 2005 to 2008, while the average cost per prescription for HIV (-) children increased from 2005 to 2008 (refer to Section 4.7.2). HIV (-) patients received more medicine items per prescription than HIV (+) patients over the four year period. The average number of medicine items per prescription for HIV (-) children stay the same over the four year period while HIV (+) patients number of medicine items deceased from 2005 to 2008 (refer to Section 4.7.2). The study showed that HIV (+) children received significantly more prescriptions for other medication per year compared to their HIV (-) counterparts (refer to Section 4.7.2). While HIV (-) patients cost per prescription and number of medicine items were higher than their HIV (+) counterparts (refer to Section 4.7.2).

The top ten main pharmacological groups claimed for HIV (+) and HIV (-) patients based on prevalence consisted of the respiratory system agents, antimicrobials, analgesics, dermatologicals, ear, nose and throat items, autacoids, non-classified medication items, endocrine system, gastro-intestinal and central nervous system items (refer to Figures 4.3, 4.4, 4.5 and 4.6)

HIV (-) patients received more central nervous system items, endocrine items and autacoids than HIV (+) patients. HIV (+) patients received more respiratory system, dermatologicals, ear, nose and throat medicine items and antimicrobials items than HIV (-) patients over the four year period (refer to Section 4.7.1).

From the main pharmacological group, respiratory system, the subgroup cough and cold medication occurred mostly in both HIV (+) and HIV (-) children during 2005 to 2008. The reason for this might be many of the cough and cold medication are OTC products (Vernacchio *et al.*, 2008:323) or many of the cough and cold products are used for respiratory tract infection and

allergic disease which appear regular in children according to the official journal of the American academic of paediatrics (Vernacchio *et al*., 2008:323).

Beta-lactams were the antimicrobial that occurred mostly in the study population. The main pharmacological group, analgesic was in the third position according to prevalence. In this main pharmacological group, the sub-group analgesics and antipyretics occurred most in the study population.

5.1.3 Recommendations

The following recommendations are proposed for future studies.

- Investigate the future medicine treatment cost of HIV/AIDS children in South Africa.
- Investigate the interactions between the other medication of patients and the patients ARV treatment.
- Further research should be done on the medicine prescribing patterns in HIV/AIDS children and non-HIV/AIDS children in the public health care sector of South Africa, adherence to ARV therapy medication use, prescribed daily dosage of ARV's, cost of their medication and hospital admission, and their clinical diagnosis can be investigated.

5.1.4 Limitations

Throughout the study there were certain limitations that influence the applicability.

- Only one PBM's data were used throughout the study, and made generalisation of results to the total private health care in South Africa difficult.
- The lack of detailed clinical data (*i.e.* stage of the disease, and weight of patients) limited the study for example, the weight of the children was unknown, therefore the average prescribed daily dosages were evaluated according to Center for Disease Control and Prevention growth charts (refer to Section 3.3.4).
- Certain patients were not classified in age groups and gender and were known as "unknown" patients that were excluded from the calculations.
- Although HIV (-) patients may have HIV infection, they do not used ARV's medication because they probably are at the early stage of HIV infection, and these information were not indicated on the database.

5.2 CHAPTER SUMMARY

In this chapter conclusions pertaining to the objectives of the literature review as well as empirical investigation were presented, recommendations made for future studies and factors that limited the scope of the study were also discussed.

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APPENDIX A

The following is the Clinical categories for children with human immunodeficiency virus (HIV) infection younger than 13 years of age (Adapted from Centers for Disease Control and Prevention, 1993:4-7, McFarland, 2009:1120)

Category N: Asymptomatic

Children who have just one of the conditions listed in category A or who have no signs and symptoms.

Category A: Mildly Symptomatic

Children who have none of the conditions listed in categories B and C and two or more of the following conditions:

- Parotitis
- Dermatitis
- Splenomegaly
- Hepatomegaly
- Lymphadenopathy (≥0.5 cm at more than two sites; bilateral one site)
- Continual upper respiratory infection, sinusitis, or otitis media

Category B: Moderately symptomatic

Children who have symptoms of one of the following conditions stated below belong in category B, other than those in category A and C.

- Varicella, disseminated (complicated chickenpox)
- Toxoplasmosis, onset before one month of age
- Persistent fever (lasting > 1 month)
- Nocardiosis
- Nephropathy
- Lymphoid interstitial pneumonia (LIP) or pulmonary lymphoid hyperplasia complex
- Leiomyosarcoma
- Herpes zoster
- HSV bronchitis, pneumonitis, or esophagitis with onset before one month of age

- Herpes simplex virus more than two times a year
- Hepatitis
- Diarrhea, chronic or frequent
- Cytomegalovirus infection
- Cadiomyopathy
- Candidiasis, oropharyngeal (thrush), persisting (>2 months) in children >6 months of age.
- Bacterial meningitis, pneumonia, or sepsis (single episode)
- Anemia (<8 gm/dl), neutropenia (< 1,000/mm^3) or thrombocytopenia (<100,000/mm^3) persisting ≥30 days

Category C: Severe

Children who have symptoms of one of the following conditions stated below belong in category C.

- Serious bacterial infections, several or frequent (i.e.any grouping of at least two culture-confirmed infections within a 2-year period), of the next types: septicemia, pneumonia, meningitis, bone or joint infection, or abscess of an internal organ or body cavity (except otitis media, superficial skin or mucosal abscesses, and indwelling catheter-related infections
- Candidiasis, esophageal or pulmonary (lungs, trachea, bronchi)
- Coccidioidomycosis, disseminated
- Cryptococcosis, extrapulmonary
- Cryptosporidiosis or isoporiasis with diarrhea persistent > 1 month
- Cytomegalovirus disease with beginning of symptoms at age > 1 month (at position other than liver, spleen, or lymph nodes)
- HIV encephalopathy
- Herpes simplex virus infection causing a mucocutaneous ulcer that persists for more than 1 month; or bronchitis, pneumonitis, or esophagitis for any duration affecting a child over 1 month of age
- Histoplasmosis, disseminated (at a site other than or in addition to lungs or cervical or hilar lymph nodes)
- Kaposi's sarcoma

- Lymphoma, primary, in brain
- Lymphoma, small, non cleaved cell (Burkitt's), or immunoblastic or large cell lymphoma of B-cell or unknown immunologic phenotype
- *Mycobacterium tuberculosis* infection, disseminated or extrapulmonary
- Mycobacterium, other species or unidentified species, disseminated (at a site other than or in addition to lungs, skin, or cervical or hilar lymph nodes)
- *Mycobacterium avium complex* or *Mycobacterium kansasii*, disseminated (at site other than or in addition to lungs, skin, or cervical or hilar lymph nodes)
- Pneumocystis carinii pneumonia
- Progressive multifocal leukoencephalopathy
- *Salmonella* (nontyphoid) septicemia, recurrent
- Toxoplasmosis of the brain with onset at greater than 1 month of age
- Wasting syndrome

Table A The following is the Clinical categories for children with human immunodeficiency virus (HIV) infection (Adapted from WHO, 2006:19)

Stage I
• No signs and symptoms in children (Asymptomatic)
• Persistent general lymphadenopathy (PGL)
Stage II
• Hepatosplenomegaly
• Papular pruritic eruptions
• General wart virus infection
• Molluscum contagiosum
• Fungal nail infections
• Oral ulcerations
• Parotid swelling
• Lineal gingival erythema
• Herpes zoster
• Upper respiratory tract infection
• Tonsillitis, sinusitis, otorrhoea, or otitis media
Stage III
• Unexplained moderate malnutrition not adequately responding to standard therapy
• Diarrhea (14 days or more)
• Constant fever (above 37.5°C > month)
• Persistent oral candidiasis (6 to 8 weeks after born)
• Oral hairy leukoplakia
• Acute necrotizing ulcerative gingivitis or periodontitis
• Tuberculosis of the lympnode
• Pulmonary tuberculosis
• Bacterial pneumonia
• Interstitial pneumonitis of the lymphnode
• Brochiectasis, chronic HIV/AIDS associated lung
• Anaemia (<8 g/dl), neutropenia (<0.5 × 109 per liter)
• Chronic thrombocytopenia (<50 × 109 per liter)
Stage IV
• Severe wasting, stunting or malnutrition not responding.
• *Pneumocystis pneumonia*
• Bacterial infections (such as empyema, pyomyositis)
• Bone or joint infection or meningitis but excluding pneumonia)
• Chronic herpes simplex infection
• Extrapulmonary tuberculosis
• Kaposi's sarcoma
• Oesophageal, trachea, bronchi or lung candidiasis
• Central nervous system toxoplasmosis (One month after born)
• HIV encephalopathy
• Cytomegalovirus infection
• Extrapulmonary cryptococcosis
• Endemic mycosis (coccidiomycosis, extrapulmonary histoplasmosis)
• Chronic cryptosporidiosis
• Chronic isosporiasis
• Non-tuberculosis *Mycobacterium* infection
• B-cell non-Hodgkin lymphoma
• Progressive multifocal leukoencephalopathy
• HIV-associated cardiomyopathy and HIV-associated nephropathy

APPENDIX B

Table B.1 A summarized table of the top five active ingredients prescribed with one antiretroviral item per prescription in each age group ranked according to prevalence

Age group	ARV medicine item 1	Average PDD of item	Number of Rx
2005			
1	Lamivudine	80	1
1	Zidovudine	33	1
1	Zidovudine	40	1
2	Lamivudine	80	8
2	Nevirapine	240	4
2	Stavudine	20	4
2	Ritonavir	480	3
2	Lamivudine	130	2
3	Lamivudine	150	12
3	Zidovudine	300	10
3	Stavudine	40	9
3	Lamivudine	160	4
3	Nevirapine	200	4
3	Zidovudine	400	4
2006			
1	Zidovudine	67	2
1	Zidovudine	100	1
1	Zidovudine	133	1
2	Lamivudine	80	6
2	Efavirenz	50	5
2	Lamivudine	40	5
2	Nevirapine	320	4
2	Lamivudine	100	3
3	Zidovudine	400	12
3	Nevirapine	320	11
3	Lamivudine	80	10
3	Lamivudine	160	10
3	Efavirenz	200	9
2007			
1	Zidovudine	143	1
2	Lamivudine	90	12
2	Abacavir	150	8
2	Lamivudine	160	6
2	Efavirenz	600	4
2	Stavudine	13	4
2	Lamivudine	80	12
3	Lamivudine	80	10
3	Lamivudine	160	10
3	Zidovudine	300	7
3	Ritonavir	720	5
3	Stavudine	40	5
2008			
2	Lamuvidine	80	6
2	Stavudine	40	3
2	Lamuvidine	140	3
2	Nevirapine	320	3
2	Lamuvidine	140	3
3	Efavirenz	400	5
3	Stavudine	30	4
3	Nevirapine	500	3
3	Zidovudine	266	3
3	Zidovudine	333	2

PDD-Prescribed daily dosage (mg)
Rx- Prescription
Age: 1 = > 0 ≤ 1 years
2 = > 1 ≤ 5 years
3 = > 5 ≤ 12 years

Table B.2 A summarized table of the top five active ingredient prescribed with two antiretroviral items per prescription in each age group ranked according to prevalence

Age	ARV medicine item 1	ARV medicine item 2	Average PDD of item 1	Average PDD of item 2	Number of Rx
2005					
1	Lamivudine	Nevirapine	60	126	1
1	Lamivudine	Nevirapine	66	360	1
2	Lamivudine	Stavudine	80	20	7
2	Ritonavir	Stavudine	240	7	6
2	Lamivudine	Ritonavir	160	480	5
2	Nevirapine	Zidovudine	80	133	4
2	Ritonavir	Stavudine	186	15	3
3	Didanosine	Stavudine	200	40	8
3	Lamivudine	Stavudine	150	40	8
3	Lamivudine	Zidovudine	116	300	6
3	Lamivudine	Zidovudine	160	266	6
3	Efavirenz	Lamivudine	200	80	5
3	Lamivudine	Zidovidine	300	600	5
2006					
2	Lamivudine	Stavudine	80	20	18
2	Nevirapine	Zidovudine	480	266	8
2	Lopinavir	Ritinovir	800	200	7
2	Lopinavir	Ritinovir	320	80	6
2	Lamivudine	Stavudine	100	33	4
2	Lamivudine	Stavudine	110	33	4
3	Lopinavir	Ritinovir	480	120	8
3	Lamivudine	Stavudine	300	60	7
3	Efavirenz	Zidovudine	200	100	5
3	Abacavir	Lamivudine	150	240	4
3	Efavirenz	Lamivudine	200	80	4
3	Lamivudine	Zidovudine	225	400	4
3	Lamivudine	Zidovudine	300	300	4
2007					
2	Lamivudine	Stavudine	80	20	7
2	Lamivudine	Zidovudine	160	200	5
2	Nevirapine	Stavudine	320	13	5
2	Lopinavir	Retinovir	320	80	5
2	Lamivudine	Zidovudine	146	286	4
	Lopinavir	Retinovir	800	200	4
3	Efavirenz	Zidovudine	200	100	11
3	Lopinavir	Ritinovar	480	120	9
3	Didanosine	Stavudine	250	60	6
3	Didanosine	Zidovudine	200	750	6
3	Lamivudine	Stavudine	160	33	4
3	Lamivudine	Stavudine	216	60	4
3	Lamivudine	Stavudine	225	40	4
2008					
2	Lamivudine	Stavudine	160	33	7
2	Lamivudine	Stavudine	80	20	5
2	Lamivudine	Stavudine	80	26.6	5
2	Nevirapine	Zidovudine	440	200	3
2	Lamivudine	Stavudine	160	40	2
3	Efavirenz	Zidovudine	200	100	28
3	Lamivudine	Zidovudine	150	333	10
3	Nevirapine	Stavudine	400	40	7
3	Abacavir	Lamivudine	480	240	5
3	Didanosine	Stavudine	250	60	5
3	Nevirapine	Zidovudine	400	300	5

PDD-Prescribed daily dosage (mg)
Rx- Prescription
Age: 1 = > 0 ≤ 1 years
2 = > 1 ≤ 5 years
3 = > 5 ≤ 12 years

Table B.3 A summarized table of the top five active ingredient prescribed with three antiretroviral items per prescription in each age group ranked according to prevalence

Age	ARV medicine item 1	ARV medicine item 2	ARV medicine item 3	Average PDD of item 1	Average PDD of item 2	Average PDD of item 3	Number of Rx
2005							
1	Lamivudine	Nevirapine	Stavudine	56.7	103	20	5
1	Lamivudine	Nevirapine	Stavudine	28	187	13	1
1	Efavirenz	Lamivudine	Zidovudine	600	300	600	1
1	Lamivudine	Nevirapine	Stavudine	28	187	13	1
1	Lamivudine	Nevirapine	Stavudine	66	360	20	1
2	Lamivudine	Nevirapine	Stavudine	80	140	20	25
2	Lamivudine	Nevirapine	Stavudine	80	146	20	14
2	Lamivudine	Nevirapine	Zidovudine	160	160	267	14
2	Lamivudine	Nevirapine	Zidovudine	120	120	200	13
2	Lamivudine	Nevirapine	Zidovudine	120	210	300	12
2	Lamivudine	Nevirapine	Zidovudine	160	240	333	12
3	Lamivudine	Nevirapine	Zidovudine	150	300	400	53
3	Lamivudine	Nevirapine	Zidovudine	150	300	300	45
3	Lamivudine	Nevirapine	Zidovudine	225	300	400	36
3	Lamivudine	Nevirapine	Stavudine	150	300	40	34
3	Lamivudine	Nevirapine	Zidovudine	150	200	400	18
2006							
1	Lamivudine	Nevirapine	Stavudine	20	153	7	3
1	Lamivudine	Nevirapine	Zidovudine	50	267	120	3
1	Lamivudine	Nevirapine	Zidovudine	80	103	133	2
1	Lamivudine	Nevirapine	Zidovudine	80	103	200	2
1	Lamivudine	Nevirapine	Stavudine	33	200	13	2
2	Lamivudine	Nevirapine	Stavudine	80	4800	20	26
2	Efavirenz	Lamivudine	Zidovudine	200	160	200	23
2	Lamivudine	Nevirapine	Stavudine	80	320	20	17
2	Lamivudine	Nevirapine	Zidovudine	107	440	200	17
2	Lamivudine	Nevirapine	Zidovudine	80	80	200	16
3	Lamivudine	Nevirapine	Zidovudine	150	300	300	90
3	Lamivudine	Nevirapine	Stavudine	150	300	40	74
3	Lamivudine	Nevirapine	Stavudine	225	300	40	28
3	Lamivudine	Nevirapine	Zidovudine	225	300	400	23
3	Efavirenz	Lamivudine	Stavudine	600	300	60	21
3	Lamivudine	Nevirapine	Zidovudine	150	300	400	21
3	Lamivudine	Nevirapine	Zidovudine	300	400	400	21
2007							
1	Lamivudine	Nevirapine	Stavudine	50	260	13	6
2	Lamivudine	Nevirapine	Stavudine	80	373	20	23
2	Efavirenz	Lamivudine	Stavudine	200	160	26	18
2	Lamivudine	Nevirapine	Stavudine	113	500	33	18
2	Lamivudine	Nevirapine	Stavudine	100	440	27	16
2	Lamivudine	Nevirapine	Stavudine	147	186	40	13
2	Lamivudine	Nevirapine	Zidovudine	107	453	203	13
3	Lamivudine	Nevirapine	Zidovudine	200	300	300	47
3	Lamivudine	Nevirapine	Zidovudine	150	300	300	46
3	Lamivudine	Nevirapine	Stavudine	150	300	40	33
3	Efavirenz	Lamivudine	Stavudine	600	300	60	32
3	Lamivudine	Nevirapine	Zidovudine	300	400	400	28
2008							
2	Lamivudine	Nevirapine	Stavudine	160	4800	33	34
2	Lamivudine	Nevirapine	Stavudine	160	480	26	30
2	Lamivudine	Nevirapine	Zidovudine	80	320	200	16
2	Lamivudine	Nevirapine	Stavudine	80	320	20	14
2	Lamivudine	Nevirapine	Stavudine	160	320	53	13
3	Lamivudine	Nevirapine	Zidovudine	160	6400	333	83
3	Lamivudine	Nevirapine	Stavudine	160	6400	30	42
3	Lamivudine	Nevirapine	Zidovudine	240	300	300	34
3	Lamivudine	Nevirapine	Zidovudine	240	400	400	33
3	Lamivudine	Nevirapine	Zidovudine	240	267	333	28

PDD-Prescribed daily dosage (mg)
Rx- Prescription
Age: 1 = $> 0 \le 1$ years
2 = $> 1 \le 5$ years
3 = $> 5 \le 12$ years

Table B.4 A summarized table of the top five active ingredient prescribed with four antiretroviral items per prescription in each age group ranked according to prevalence

Age	ARV medicine item 1	ARV medicine item 2	ARV medicine item 3	ARV medicine item 4	Average PDD of item 1	Average PDD of item 2	Average PDD of item 3	Average PDD of item 4	No. of RX
				2005					
1	Lamivudine	Lopinavir	Ritonavir	Stavudine	26	160	40	6	1
2	Lamivudine	Lopinavir	Ritonavir	Stavudine	80	320	80	20	19
2	Lamivudine	Lopinavir	Ritonavir	Stavudine	100	320	80	26	17
2	Lamivudine	Lopinavir	Ritonavir	Stavudine	50	320	80	13.3	10
2	Lamivudine	Lopinavir	Ritonavir	Stavudine	106	320	80	26	10
2	Lamivudine	Lopinavir	Ritonavir	Stavudine	80	800	200	20	9
2	Lamivudine	Lopinavir	Ritonavir	Zidovudine	100	320	80	180	9
3	Efavirenz	Efavirenz	Lamivudine	Stavudine	200	100	150	40	76
3	Efavirenz	Efavirenz	Lamivudine	Zidovudine	200	50	150	400	40
3	Efavirenz	Efavirenz	Lamivudine	Stavudine	200	50	150	40	39
3	Efavirenz	Efavirenz	Lamivudine	Zidovudine	200	100	150	400	36
3	Efavirenz	Efavirenz	Lamivudine	Zidovudine	200	150	225	400	35
				2006					
1	Lamivudine	Lopinavir	Ritonavir	Stavudine	40	160	40	13	11
1	Lamivudine	Lopinavir	Ritonavir	Zidovudine	40	160	40	106	6
1	Lamivudine	Lopinavir	Ritonavir	Zidovudine	50	320	80	120	5
1	Lamivudine	Lopinavir	Ritonavir	Stavudine	40	320	80	13	1
1	Lamivudine	Lopinavir	Ritonavir	Zidovudine	63	320	80	136	1
2	Lamivudine	Lopinavir	Ritonavir	Stavudine	80	320	80	20	60
2	Lamivudine	Lopinavir	Ritonavir	Stavudine	160	800	200	30	20
2	Lamivudine	Lopinavir	Ritonavir	Stavudine	80	800	200	20	17
2	Lamivudine	Lopinavir	Ritonavir	Stavudine	100	320	80	26	16
2	Lamivudine	Lopinavir	Ritonavir	Zidovudine	100	320	80	200	13
3	Efavirenz	Efavirenz	Lamivudine	Stavudine	200	100	150	40	102
3	Efavirenz	Efavirenz	Lamivudine	Stavudine	200	50	150	40	69
3	Efavirenz	Efavirenz	Lamivudine	Zidovudine	200	50	150	300	44
3	Efavirenz	Efavirenz	Lamivudine	Zidovudine	200	100	150	300	42
3	Efavirenz	Efavirenz	Lamivudine	Stavudine	200	150	225	60	33
				2007					
1	Lamivudine	Lopinavir	Ritonavir	Stavudine	80	320	80	13	6
1	Lamivudine	Lopinavir	Ritonavir	Stavudine	80	800	200	6	4
1	Lamivudine	Lopinavir	Ritonavir	Stavudine	80	800	200	13	4
1	Abacavir	Lamivudine	Lopinavir	Ritonavir	80	80	320	20	3
1	Lamivudine	Lopinavir	Ritonavir	Stavudine	28	96	24	6	1
2	Lamivudine	Lopinavir	Ritonavir	Stavudine	80	320	80	20	32
2	Lamivudine	Lopinavir	Ritonavir	Stavudine	90	320	80	26	27
2	Lamivudine	Lopinavir	Ritonavir	Stavudine	66	320	80	26	21
2	Lamivudine	Lopinavir	Ritonavir	Stavudine	160	320	80	26	20
2	Lamivudine	Lopinavir	Ritonavir	Stavudine	106	320	80	26	19
3	Efavirenz	Efavirenz	Lamivudine	Stavudine	200	50	150	40	80
3	Efavirenz	Efavirenz	Lamivudine	Stavudine	200	100	150	40	64
3	Efavirenz	Efavirenz	Lamivudine	Zidovudine	200	100	150	300	34
3	Efavirenz	Efavirenz	Lamivudine	Zidovudine	200	150	225	400	34
3	Efavirenz	Efavirenz	Lamivudine	Stavudine	200	100	225	40	33
				2008					
2	Lamivudine	Lopinavir	Ritonavir	Stavudine	160	320	80	33	36
2	Lamivudine	Lopinavir	Ritonavir	Stavudine	160	320	80	30	34
2	Efavirenz	Efavirenz	Lamivudine	Stavudine	200	50	160	30	33
2	Lamivudine	Lopinavir	Ritonavir	Stavudine	160	320	120	40	23
2	Lamivudine	Lopinavir	Ritonavir	Zidovudine	160	320	80	200	23
3	Efavirenz	Efavirenz	Lamivudine	Stavudine	200	100	240	40	86
3	Efavirenz	Efavirenz	Lamivudine	Stavudine	200	150	300	60	73
3	Efavirenz	Efavirenz	Lamivudine	Stavudine	200	100	160	40	45
3	Efavirenz	Efavirenz	Lamivudine	Stavudine	200	50	160	30	43
3	Efavirenz	Efavirenz	Lamivudine	Stavudine	200	50	150	40	42

PDD-Prescribed daily dosage (mg)
Rx- Prescription
Age: 1 = > 0 ≤ 1 years
2 = > 1 ≤ 5 years
3 = > 5 ≤ 12 years

Table B.5 A summarized table of the top five active ingredient prescribed with five antiretroviral items per prescription in each age group ranked according to prevalence

Age	ARV medicine item 1	ARV medicine item 2	ARV medicine item 3	ARV medicine item 4	ARV medicine item 5	Average PDD of item 1	Average PDD of item 2	Average PDD of item 3	Average PDD of item 4	Average PDD of item 5	No. of RX
2005											
2	Abacavir	Lamivudine	Lopinavir	Ritonavir	Stavudine	40	130	320	80	30	11
2	Abacavir	Lamivudine	Lopinavir	Ritonavir	Stavudine	100	80	320	80	40	3
2	Abacavir	Lamivudine	Lopinavir	Ritonavir	Stavudine	90	100	800	200	30	3
2	Abacavir	Lamivudine	Lopinavir	Ritonavir	Stavudine	110	113.	320	80	30	3
2	Didanosine	Didanosine	Efavirenz	Efavirenz	Stavudine	50	100	200	50	40	2
3	Didanosine	Didanosine	Lopinavir	Ritonavir	Stavudine	50	20	800	200	30	6
3	Didanosine	Didanosine	Lopinavir	Ritonavir	Stavudine	100	150	799	198	40	8
3	Didanosine	Didanosine	Lopinavir	Ritonavir	Stavudine	50	20	800	200	40	6
3	Didanosine	Didanosine	Lopinavir	Ritonavir	Stavudine	100	150	533	132	40	5
3	Abacavir	Efavirenz	Efavirenz	Lamivudine	Stavudine	150	200	100	160	40	4
3	Efavirenz	Efavirenz	Lamivudine	Stavudine	Stavudine	200	150	150	40	60	1
2006											
2	Abacavir	Lamivudine	Lopinavir	Ritonavir	Stavudine	100	100	800	200	30	7
2	Lamivudine	Lopinavir	Ritonavir	Ritonavir	Zidovudine	60	320	80	160	140	6
2	Lamivudine	Lopinavir	Ritonavir	Ritonavir	Stavudine	90	320	80	240	26	5
2	Abacavir	Efavirenz	Efavirenz	Lamivudine	Stavudine	100	200	50	133	30	3
2	Abacavir	Efavirenz	Efavirenz	Lamivudine	Stavudine	90	200	50	140	30	3
2	Lamivudine	Lopinavir	Ritonavir	Ritonavir	Stavudine	160	342	85	257	26	1
3	Didanosine	Didanosine	Lopinavir	Ritonavir	Stavudine	50	20	800	200	60	8
3	Didanosine	Didanosine	Efavirenz	Efavirenz	Stavudine	50	20	200	50	40	6
3	Didanosine	Didanosine	Lopinavir	Ritonavir	Stavudine	50	20	800	200	40	6
3	Abacavir	Efavirenz	Efavirenz	Lamivudine	Stavudine	145	200	150	300	60	3

PDD-Prescribed daily dosage (mg)
Rx- Prescription
Age: 1 = $> 0 \leq 1$ years
2 = $> 1 \leq 5$ years
3 = $> 5 \leq 12$ years

Table B.5 A summarized table of the top five active ingredient prescribed with five antiretroviral items per prescription in each age group ranked according to prevalence

Age	ARV medicine item 1	ARV medicine item 2	ARV medicine item 3	ARV medicine item 4	ARV medicine item 5	Average PDD of item 1	Average PDD of item 2	Average PDD of item 3	Average PDD of item 4	Average PDD of item 5	No. of RX
2007											
2	Abacavir	Efavirenz	Efavirenz	Lamivudine	Stavudine	200	50	140	30	2	7
2	Abacavir	Lamivudine	Lopinavir	Ritonavir	Stavudine	100	80	160	40	13.3	6
2	Lamivudine	Lopinavir	Ritonavir	Ritonavir	Stavudine	80	320	80	480	20	4
2	Abacavir	Lamivudine	Lopinavir	Ritonavir	Stavudine	120	80	320	80	20	3
2	Abacavir	Efavirenz	Efavirenz	Lamivudine	Stavudine	120	200	50	180	30	2
2	Abacavir	Efavirenz	Efavirenz	Lamivudine	Stavudine	100	200	50	200	40	2
3	Didanosine	Didanosine	Lopinavir	Ritonavir	Stavudine	50	100	800	200	40	13
3	Didanosine	Didanosine	Lopinavir	Ritonavir	Stavudine	25	10	800	200	40	8
3	Didanosine	Efavirenz	Efavirenz	Stavudine	Stavudine	250	200	100	20	30	4
3	Didanosine	Efavirenz	Efavirenz	Stavudine	Stavudine	200	200	100	20	30	2
3	Didanosine	Efavirenz	Efavirenz	Stavudine	Stavudine	400	200	100	20	30	1
2008											
2	Didanosine	Didanosine	Lopinavir	Ritonavir	Zidovudine	50	100	480	120	400	3
2	Abacavir	Lamivudine	Lopinavir	Ritonavir	Stavudine	160	80	320	80	20	2
3	Didanosine	Didanosine	Lopinavir	Ritonavir	Stavudine	25	10	800	200	60	16
3	Didanosine	Didanosine	Lopinavir	Ritonavir	Stavudine	25	10	800	200	40	15
3	Abacavir	Efavirenz	Efavirenz	Lopinavir	Ritonavir	320	200	100	480	120	10
3	Abacavir	Efavirenz	Efavirenz	Lamivudine	Stavudine	480	200	50	240	40	4
3	Abacavir	Efavirenz	Efavirenz	Lopinavir	Ritonavir	320	200	100	160	40	2
3	Didanosine	Didanosine	Lopinavir	Ritonavir	Stavudine	25	10	800	200	30	2

APPENDIX C

Table C.1 Average cost per medicine item per patient according to gender for total cost (R)

Average cost per medicine item per patient						
	N	Mean	Standard deviation	Standard error	95% CI Mean	*p* > F
Total cost						
2005*						
HIV (-)						
Female	95319	54.2	47.5	0.2	54.0-54.4	0.9
Male	101308	57.9	53.0	0.2	57.7-58.1	
HIV (+)						
Female	184	34.4	19.6	1.4	33.0-35	0.9
Male	204	38.8	33.5	2.3	36.5-41.1	
2006*						
HIV (-)*						
Female	93 741	53.0	57.7	0.2	52.8-53.2	0.8
Male	98 938	57.0	57.2	0.2	56.8-57.2	
HIV (+)						
Female	229	33.7	20.0	1.3	32.4-35.0	0.8
Male	248	39.1	40.7	2.6	36.5-41.7	
2007*						
HIV (-)						
Female	68 782	51.8	62.7	0.2	51.6-52.0	0.2
Male	72760	56.4	76.6	0.3	56.1-56.7	
HIV (+)						
Female	216	37.3	32.6	2.2	35.1-39.5	0.2
Male	242	34.1	25.7	1.7	32.4-35.8	
2008						
HIV (-)						
Female	47 894	54.2	52.8	0.2	54.0-54.4	0.5
Male	50 618	59.5	62.9	0.3	59.2-59.8	
HIV (+)						
Female	194	35.2	33.3	2.4	32.8-37.6	0.5
Male	221	36.3	34.3	2.3	34.0-3.8	

*Unknown 2007-42
*Unknown 2006-171
*Unknown 2005-294

Table C.2 Average cost per medicine item per patient according to gender for scheme amount (R)

Average cost per medicine item per patient						
	N	**Mean**	**Standard deviation**	**Standard error**	**95% CI Mean**	***p* > F**
Scheme amount						
2005*						
HIV (-)						
Female	95 319	49.6	45.2	0.1	49.4-49.7	0.8
Male	101 308	52.9	50.0	0.2	52.7-53.1	
HIV (+)						
Female	184	32.4	19.3	1.4	31.0-33.8	0.8
Male	204	36.6	33.3	2.3	34.3-38.9	
2006*						
HIV (-)						
Female	93 741	46.8	54.2	0.2	46.6-47.0	0.9
Male	98 938	50.4	52.3	0.2	50.2-50.6	
HIV (+)						
Female	229	40.0	19.2	1.3	38.7-41.3	0.9
Male	248	35.1	35.8	2.3	32.8-37.4	
2007*						
HIV (-)						
Female	68 782	42.9	47.4	0.2	42.7-50.1	0.2
Male	72 760	46.7	64.0	0.2	46.5-46.9	
HIV (+)						
Female	216	33.3	31.2	2.1	31.2-35.4	0.2
Male	242	30.3	23.6	1.5	28.8-31.8	
2008						
HIV (-)						
Female	47894	43.9	45.6	0.2	43.7-41.1	0.4
Male	50618	48.0	54.2	0.2	47.8-48.2	
HIV (+)						
Female	194	31.5	31.7	2.3	29.2-33.8	0.4
Male	221	31.7	30.7	2.1	29.6-33.8	

*Unknown 2007-42
*Unknown 2006-171
*Unknown 2005-294

Table C.3 Average cost per medicine item per patient according to gender for patient contribution (R)

Average cost per medicine item per patient						
	N	Mean	Standard deviation	Standard error	95% CI Mean	*p* > F
Patient contribution						
2005*						
HIV (-)						
Female	95319	4.6	12.8	0.04	4.6-4.6	0.9
Male	101308	4.9	15.6	0.05	4.9-4.9	
HIV (+)						
Female	184	2	4	0.3	1.7-2.3	0.9
Male	204	2.2	5.1	0.4	1.8-2.6	
2006*						
HIV (-)						
Female	93741	6.1	16.6	0.1	6.0-6.2	0.6
Male	98938	6.7	18.8	0.1	6.6-6.8	
HIV (+)						
Female	229	2.7	4.6	0.3	2.4-3.0	0.6
Male	248	4.1	11.2	0.7	3.4-4.8	
2007*						
HIV (-)						
Female	68782	8.9	33.2	0.1	8.8-8.9	0.7
Male	72760	9.7	26.8	0.1	9.6-9.8	
HIV (+)						
Female	216	4	6.8	0.5	3.5-4.5	0.7
Male	242	3.8	5.6	0.4	3.4-4.2	
2008						
HIV (-)						
Female	47894	10.3	20	0.1	10.2-10.4	0.8
Male	50618	11.5	23.3	0.1	11.4-11.6	
HIV (+)						
Female	194	3.7	5.2	0.4	3.3-4.1	0.8
Male	221	4.5	6.6	0.4	4.1-4.9	

*Unknown 2007-42
*Unknown 2006-171
*Unknown 2005-294

Table C.4 Average cost per prescription per patient according to gender for total cost (R)

Average cost per prescription per patient						
	N	**Mean**	**Standard deviation**	**Standard error**	**95% CI Mean**	***p* > F**
Total cost						
2005*						
HIV (-)						
Female	95 319	125.8	95.4	0.3	125.5-126.1	0.5
Male	101 308	131.6	101.6	0.3	131.3-131.9	
HIV (+)						
Female	184	67.8	53.2	4.0	63.8-71.7	0.5
Male	204	80.0	83.1	5.8	74.2-85.8	
2006*						
HIV (-)						
Female	93 741	124.0	102.7	0.3	123.7-124.3	0.8
Male	98 938	130.2	113.4	0.4	129.8-130.6	
HIV (+)						
Female	229	66.6	50.0	3.3	63.3-69.9	0.8
Male	248	75.6	72.0	4.6	71.0-80.2	
2007*						
HIV (-)						
Female	68 782	126.0	124.8	0.5	125.5-126.5	0.3
Male	72 760	132.8	128.8	0.5	132.3-133.3	
HIV (+)						
Female	216	72.6	77.3	5.3	67.3-77.9	0.3
Male	242	66.0	55.7	3.6	62.4-69.6	
2008						
HIV (-)						
Female	47 894	129.9	112.6	0.5	129.4-130.4	0.7
Male	50 618	137.7	124.0	0.5	137.2-138.2	
HIV (+)						
Female	194	68.0	80.1	5.8	62.2-73.8	0.7
Male	221	70.9	78.8	5.3	65.6-76.2	

*Unknown 2007-42
*Unknown 2006-171
*Unknown 2005-294

Table C.5 Average cost per prescription per patient according to gender for scheme amount

Average cost per prescription per patient (R)						
	N	**Mean**	**Standard deviation**	**Standard error**	**95% CI Mean**	***p* > F**
Scheme amount						
2005*						
HIV (-)*						
Female	95 319	115.3	90.7	0.2	115.1-115.5	0.4
Male	101 308	120.5	96.4	0.3	120.2-120.8	
HIV (+)						
Female	184	63.7	50.8	3.7	60.7-67.4	0.4
Male	204	75.5	81.9	5.7	69.8-81.2	
2006*						
HIV (-)*						
Female	93 741	109.8	95.7	0.3	109.5-110.1	0.9
Male	98 938	115.1	103.9	0.3	114.8-115.4	
HIV (+)						
Female	229	60.8	45.7	3.0	63.8-57.8	0.9
Male	248	67.7	65.6	4.2	63.5-71.9	
2007*						
HIV (-)						
Female	68 782	105.3	97.2	0.4	104.9-105.7	0.2
Male	72 760	111.0	110.2	0.4	110.6-11.4	
HIV (+)						
Female	216	64.6	73.0	5.0	64.1-65.1	0.2
Male	242	58.2	50.0	3.2	55.0-61.4	
2008						
HIV (-)						
Female	47 894	106.2	98.0	0.4	105.8-106.6	0.6
Male	50 618	112.3	108.4	0.5	111.8-112.8	
HIV (+)						
Female	194	60.5	74.8	5.4	55.1-65.9	0.6
Male	221	61.2	68.0	4.6	56.6-65.8	

*Unknown 2007-42
*Unknown 2006-171
*Unknown 2005-294

Table C.6 Average cost per prescription per patient according to gender for patient contribution (R)

Average cost per prescription per patient						
	N	**Mean**	**Standard deviation**	**Standard error**	**95% CI Mean**	***p* > F**
Patient contribution						
2005*						
HIV (-)						
Female	95 319	10.5	27.0	0.1	10.4-10.6	1.0
Male	101 308	11.1	29.7	0.1	10.9-11.2	
HIV (+)						
Female	184	4.1	10.2	0.8	3.3-4.9	1.0
Male	204	4.6	13.7	1.0	3.6-5.6	
2006*						
HIV (-)						
Female	93 741	14.2	34.3	0.1	14.1-14.3	0.7
Male	98 938	15.0	37.2	0.1	14.9-15.1	
HIV (+)						
Female	229	5.8	12.7	0.1	5.7-5.9	0.7
Male	248	8.0	22.3	1.4	6.6-9.4	
2007*						
HIV (-)						
Female	68 782	20.8	63.9	0.2	20.6-21.0	0.8
Male	72 760	21.8	47.2	0.6	21.2-22.0	
HIV (+)						
Female	216	7.9	16.0	1.1	6.8-9.0	0.8
Male	242	7.7	13.8	0.8	6.9-8.5	
2008						
HIV (-)						
Female	47 894	23.7	42.0	0.2	23.5-23.9	0.9
Male	50 618	25.4	45.0	0.2	25.2-25.6	
HIV (+)						
Female	194	7.5	11.9	0.9	6.6-8.4	0.9
Male	221	9.7	17.1	1.2	8.5-10.9	

*Unknown 2007-42
*Unknown 2006-171
*Unknown 2005-294

Table C.7 The average medicine items per prescription per patient for 2005 to 2008 (R)

Average medicine items per prescription per patient						
	N	**Mean**	**Standard deviation**	**Standard error**	**95% CI Mean**	***p* > F**
2005*						
HIV (-)*						
Female	95319	2.6	1.1	0.003	2.58-2.603	0.6
Male	101308	2.6	1.1	0.003	2.58-2.603	
HIV (+)						
Female	184	1.8	0.7	0.1	1.7-1.9	0.6
Male	204	1.9	0.7	0.04	1.86-1.94	
2006*						
HIV (-)						
Female	93 741	2.6	1.1	0.003	2.58-2.603	0.9
Male	98 938	2.6	1.1	0.003	2.58-2.603	
HIV (+)						
Female	229	1.9	0.7	0.05	1.85-1.95	0.9
Male	248	1.8	0.7	0.05	1.75-1.5	
2007*						
HIV (-)*						
Female	68 782	2.7	1.0	0.003	2.697-2.703	0.6
Male	72760	2.6	1.0	0.003	2.597-2.603	
HIV (+)						
Female	216	1.8	0.6	0.04	1.76-1.84	0.6
Male	242	1.8	0.7	0.04	1.76-1.84	
HIV (-)						
Female	47 894	2.6	1.0	0.004	2.59-2.604	0.9
Male	50 618	2.6	1.1	0.004	2.59-2.604	
HIV (+)						
Female	194	1.8	0.7	0.05	1.75-1.85	0.9
Male	221	1.8	0.7	0.04	1.76-1.84	

*Unknown 2007-42
*Unknown 2006-171
*Unknown 2005-294

Table C.8 Average cost per prescription per patient according to age group for total cost (R)

Average cost per prescription per patient						
	N	Mean	Standard deviation	Standard error	95% CI Mean	*p* > F
Total cost						
2005*						
HIV (-)						
>0 ≤ 1 years	9431	125.1	101.5	1.0	124.1-126.1	0.9
>1 ≤ 5 years	69 345	124.7	90.7	0.3	124.4-125.0	
>5 ≤ 12 years	118 145	131.4	102.7	0.3	131.1-131.7	
HIV (+)						
>0 ≤ 1 years	8	61.1	41.4	14.6	46.5-75.7	0.9
>1 ≤ 5 years	151	68.7	59.8	4.7	64.0-73.4	
>5 ≤ 12 years	229	78.3	77.7	5.1	73.2-83.4	
2006*						
HIV (-)						
>0 ≤ 1 years	8 897	133.0	157.1	1.7	131.3-134.7	0.6
>1 ≤ 5 years	67 693	121.9	100.0	0.4	121.5-122.3	
>5 ≤ 12 years	116 260	129.8	108.4	0.3	129.5-130.1	
HIV (+)						
>0 ≤ 1 years	13	52.8	40.0	11.1	51.7-53.9	0.6
>1 ≤ 5 years	181	64.4	53.5	4.0	60.4-68.4	
>5 ≤ 12 years	283	76.6	67.7	4.0	72.6-80.6	
2007*						
HIV (-)						
>0 ≤ 1 years	2 042	153.9	284.4	6.3	147.6-160.2	0.5
>1 ≤ 5 years	48 317	125.2	141.4	0.6	124.6-125.8	
>5 ≤ 12 years	91 225	131.3	112.2	0.4	130.9-131.7	
HIV (+)						
>0 ≤ 1 years	4	46.6	26.5	13.25	33.4-85.4	0.5
>1 ≤ 5 years	159	72.1	59.8	4.7	67.4-76.8	
>5 ≤ 12 years	295	67.7	70.6	4.1	63.6-70.8	
2008						
HIV (-)						
>0 ≤ 1 years	18	46.7	58.5	13.7	33.0-60.5	0.9
>1 ≤ 5 years	28 910	128.7	109.7	0.6	128.1-129.3	
>5 ≤ 12 years	69 584	136.1	122.1	0.5	135.6-136.6	
HIV (+)						
>0 ≤ 1 years	-	-	-	-	-	0.9
>1 ≤ 5 years	121	63.1	55.5	5.0	58.1-68.1	
>5 ≤ 12 years	294	72.2	87.2	5.0	67.1-77.2-	

*Unknown 2007-42
*Unknown 2006-171
*Unknown 2005-294

Table C.9 Average cost per prescription per patient according to age group for scheme amount (R)

Average cost per prescription per patient						
	N	Mean	Standard deviation	Standard error	95% CI Mean	Pr > F
Scheme amount						
2005*						
HIV (-)						
>0 ≤ 1 years	9 431	110.9	94.4	1.0	109.9-111.9	1.0
>1 ≤ 5 years	69 345	114.6	87.0	0.3	114.3-114.9	
>5 ≤ 12 years	118 145	120.4	97.4	0.3	120.1-120.7	
HIV (+)						
>0 ≤ 1 years	8	59.1	40.9	14.5	44.6-73.6	1.0
>1 ≤ 5 years	151	65.8	58.3	4.7	61.1-70.5	
>5 ≤ 12 years	229	72.9	76.1	5.0	67.9-77.7	
2006*						
HIV (-)						
>0 ≤ 1 years	8 897	109.1	142.4	1.5	107.5-110.6	0.9
>1 ≤ 5 years	67 693	107.8	91.3	0.4	107.4-108.2	
>5 ≤ 12 years	116 260	115.5	100.9	0.3	115.2-115.8	
HIV (+)						
>0 ≤ 1 years	13	48.3	38.3	10.6	37.7-58.9	0.9
>1 ≤ 5 years	181	58.2	49.0	3.6	54.6-61.8	
>5 ≤ 12 years	283	69.1	61.9	3.7	65.4-72.8	
2007*						
HIV (-)						
>0 ≤ 1 years	2 042	112.9	184.0	4.0	108.9-116.9	0.5
>1 ≤ 5 years	48 317	102.8	106.3	0.5	102.3-103.3	
>5 ≤ 12 years	91 225	111.0	100.3	0.3	110.7-111.3	
HIV (+)						
>0 ≤ 1 years	4	39.6	31.5	15.8	23.8-47.3	0.5
>1 ≤ 5 years	159	63.6	55.2	4.4	32.2-68.0	
>5 ≤ 12 years	295	60.3	65.4	3.8	66.2-64.1	
2008						
HIV (-)						
>0 ≤ 1 years	18	18.5	28.9	6.8	11.7-25.3	1.0
>1 ≤ 5 years	28 910	103.2	95.9	0.6	102.8-103.8	
>5 ≤ 12 years	69 584	111.9	106.4	0.4	111.5-112.3	
HIV (+)						
>0 ≤ 1 years	-	-	-	-	-	1.0
>1 ≤ 5 years	121	55.0	47.5	6.8	48.2-61.8	
>5 ≤ 12 years	294	63.3	78.8	0.6	62.7-63.9	

*Unknown 2007-42
*Unknown 2006-171
*Unknown 2005-294

Table C.10 Average cost per prescription per patient according to age group for patient contribution (R)

Average cost per medicine item per patient						
	N	Mean	Standard deviation	Standard error	95% CI Mean	*p* > F
Scheme amount						
2005*						
HIV (-)						
>0 ≤ 1 years	9 431	52.5	53.8	0.6	51.8-53.2	0.7
>1 ≤ 5 years	69 345	48.3	39.4	0.2	48.1-48.5	
>5 ≤ 12 years	118 145	53.0	51.4	0.1	52.9-53.1	
HIV (+)						
>0 ≤ 1 years	8	23.1	10.7	3.8	19.3-26.9	0.7
>1 ≤ 5 years	151	31.3	18.4	1.5	29.8-33.8	
>5 ≤ 12 years	229	37.2	32.4	2.1	35.1-39.3	
2006*						
HIV (-)						
>0 ≤ 1 years	8 897	52.1	102.4	1.1	51.0-53.3	0.8
>1 ≤ 5 years	67 693	45.3	42.6	0.2	45.1-45.5	
>5 ≤ 12 years	116 260	50.4	53.3	0.2	50.2-50.6	
HIV (+)						
>0 ≤ 1 years	13	28.2	22.1	6.1	22.1-34.3	0.8
>1 ≤ 5 years	181	29.8	18.6	1.4	28.4-31.2	
>5 ≤ 12 years	283	35.5	34.3	2.0	33.5-37.5	
2007*						
HIV (-)						
>0 ≤ 1 years	2 042	52.0	118.1	2.6	49.4-54.6	0.6
>1 ≤ 5 years	48 317	40.8	64.7	0.3	40.5-51.1	
>5 ≤ 12 years	91 225	46.8	49.3	0.2	46.6-50.0	
HIV (+)						
>0 ≤ 1 years	4	28.0	21.3	10.7	27.3-37.7	0.6
>1 ≤ 5 years	159	31.4	23.1	1.8	29.6-33.2	
>5 ≤ 12 years	295	31.9	29.7	1.7		
2008						
HIV (-)						
>0 ≤ 1 years	18	10.0	15.6	3.7	6.3-13.7	0.7
>1 ≤ 5 years	28 910	41.1	41.0	0.2	40.9-41.3	
>5 ≤ 12 years	69 584	48.0	53.5	0.2	47.8-48.2	
HIV (+)						
>0 ≤ 1 years	-	-	-	-	-	0.7
>1 ≤ 5 years	121	28.0	17.1	1.6	26.4-29.6	
>5 ≤ 12 years	294	33.1	35.2	2.1	31.0-35.2	

*Unknown 2007-42
*Unknown 2006-171
*Unknown 2005-294

Table C.11 Average cost per medicine item per patient according scheme amount (R)

Average cost per prescription per patient						
	N	Mean	Standard deviation	Standard error	95% CI Mean	*P* > F
Patient contribution						
2005*						
HIV (-)						
>0 ≤ 1 years	9 431	52.0	210.4	2.2	49.8-54.2	0.2
>1 ≤ 5 years	69 345	57.7	159.5	0.6	57.0-58.3	
>5 ≤ 12 years	118 145	48.2	154.7	0.4	47.8-48.6	
HIV (+)						
>0 ≤ 1 years	8	21.7	38.6	13.6	8.1-35.3	0.2
>1 ≤ 5 years	151	40.5	88.5	7.2	33.2-47.9	
>5 ≤ 12 years	229	58.9	115.1	7.6	51.3-66.5	
2006*						
HIV (-)*						
>0 ≤ 1 years	13	4.5	6.1	1.7	2.8-6.2	0.4
>1 ≤ 5 years	181	6.2	22.0	1.6	4.6-7.8	
>5 ≤ 12 years	283	7.5	16.0	0.9	6.6-8.4	
HIV (+)						
>0 ≤ 1 years	8 897	24.0	63.1	0.7	23.3-24.7	0.4
>1 ≤ 5 years	67 693	14.1	33.7	0.1	14.0-14.2	
>5 ≤ 12 years	116 260	14.2	34.0	0.1	14.1-14.3	
2007*						
HIV (-)						
>0 ≤ 1 years	2 042	41.0	150.4	3.3	37.7-44.3	0.7
>1 ≤ 5 years	48 317	22.3	73.3	0.3	22.0-22.6	
>5 ≤ 12 years	91 225	20.3	38.6	0.1	20.2-20.4	
HIV (+)						
>0 ≤ 1 years	4	7.0	7.2	3.6	3.4-10.6	0.7
>1 ≤ 5 years	159	8.5	14.7	1.2	7.4-8.6	
>5 ≤ 12 years	295	7.4	15.0	0.9	6.6-8.3	
2008						
HIV (-)						
>0 ≤ 1 years	18	28.2	56.7	13.4	14.9-41.6	0.7
>1 ≤ 5 years	28 910	25.5	45.8	0.3	25.2-25.8	
>5 ≤ 12 years	69 584	24.2	43.0	0.2	24.0-24.4	
HIV (+)						
>0 ≤ 1 years	-	-		-	-	0.7
>1 ≤ 5 years	121	8.1	13.0	1.2	7.0-9.3	
>5 ≤ 12 years	294	8.9	15.6	0.9	8.0-9.8	

*Unknown 2007-42
*Unknown 2006-171
*Unknown 2005-294

Table C.12 Average cost per medicine item per patient per year according total cost

Average cost per medicine item per patient per year (R)						
	N	Mean	Standard deviation	Standard error	95% CI Mean	*p* > F
Total cost						
2005*						
HIV (-)						
>0 ≤ 1 years	9431	59.6	59.1	0.6	59.0-60.2	0.6
>1 ≤ 5 years	69 345	52.6	40.9	0.2	52.4-52.8	
>5 ≤ 12 years	118 145	57.8	54.4	0.2	57.6-60.0	
HIV (+)						
>0 ≤ 1 years	8	23.8	10.5	3.7	20.1-26.5	0.6
>1 ≤ 5 years	151	32.7	18.8	1.5	31.2-34.2	
>5 ≤ 12 years	229	39.8	32.4	2.1	37.7-41.9	
2006*						
HIV (-)						
>0 ≤ 1 years	8 897	63.6	108.1	1.1	62.5-64.7	0.6
>1 ≤ 5 years	67 693	51.2	45.8	0.2	51.0-51.4	
>5 ≤ 12 years	116 260	56.7	57.9	0.2	56.5-56.9	
HIV (+)						
>0 ≤ 1 years	13	30.4	22.5	6.2	24.2-36.6	0.6
>1 ≤ 5 years	181	32.8	20.7	1.5	31.2-34.3	
>5 ≤ 12 years	283	39.2	38.4	2.3	36.9-41.5	
2007*						
HIV (-)						
>0 ≤ 1 years	2 042	72.7	190.3	4.2	68.5-76.9	0.6
>1 ≤ 5 years	48 317	50.2	83.5	0.4	49.8-50.6	
>5 ≤ 12 years	91 225	55.8	56.0	0.2	55.6-60.0	
HIV (+)						
>0 ≤ 1 years	4	32.1	18.8	9.4	22.7-41.5	0.6
>1 ≤ 5 years	159	35.6	24.6	2.0	33.6-37.6	
>5 ≤ 12 years	295	35.7	31.5	1.8	33.9-37.5	
2008						
HIV (-)						
>0 ≤ 1 years	18	24.0	28.5	6.7	17.3-30.7	0.8
>1 ≤ 5 years	28 910	51.8	47.1	0.3	51.5-52.1	
>5 ≤ 12 years	69 584	59.0	62.2	0.2	58.8-59.2	
HIV (+)						
>0 ≤ 1 years	-	-	-	-	-	0.8
>1 ≤ 5 years	121	31.8	19.4	1.8	31.0-33.6	
>5 ≤ 12 years	294	37.4	38.1	2.2	35.2-39.6	

*Unknown 2007-42
*Unknown 2006-171
*Unknown 2005-294

Table C.13 Average cost per medicine item per patient per year according patient contribution (R)

Average cost per medicine item per patient						
	N	Mean	Standard deviation	Standard error	95% CI Mean	*p* > F
Patient contribution						
2005						
HIV (-)*						
>0 ≤ 1 years	9431	7.0	26.0	0.3	6.7-7.3	0.7
>1 ≤ 5 years	69 345	4.3	11.8	0.04	4.26-4.34	
>5 ≤ 12 years	118 145	4.9	14.3	0.04	4.86-4.94	
HIV (+)						
>0 ≤ 1 years	8	0.6	1.3	0.5	0.1-1.1	0.7
>1 ≤ 5 years	151	1.4	3.0	0.2	1.2-1.6	
>5 ≤ 12 years	229	2.6	5.4	0.4	2.2-3.0	
2006*						
HIV (-)						
>0 ≤ 1 years	8 897	11.5	32.0	0.3	11.2-11.8	0.4
>1 ≤ 5 years	67 693	5.9	14.9	0.1	5.8-6.0	
>5 ≤ 12 years	116 260	6.3	17.7	0.1	6.2-6.4	
HIV (+)						
>0 ≤ 1 years	13	2.2	2.7	0.7	1.5-2.9	0.4
>1 ≤ 5 years	181	3.0	10.1	0.8	2.2-3.8	
>5 ≤ 12 years	283	3.7	7.8	0.5	3.2-4.2	
2007*						
HIV (-)						
>0 ≤ 1 years	2 042	20.7	100.0	2.2	18.5-22.9	0.8
>1 ≤ 5 years	48 317	9.4	38.4	0.2	9.2-9.6	
>5 ≤ 12 years	91 225	9.0	19.8	0.1	8.9-9.1	
HIV (+)						
>0 ≤ 1 years	4	4.1	3.0	1.5	2.6-5.6	0.8
>1 ≤ 5 years	159	4.1	6.1	0.5	3.6-4.6	
>5 ≤ 12 years	295	3.8	6.3	0.4	3.4-4.2	
2008						
HIV (-)						
>0 ≤ 1 years	18	13.9	26.9	6.3	7.6-20.2	1.0
>1 ≤ 5 years	28 910	10.7	19.9	0.1	10.6-10.8	
>5 ≤ 12 years	69 684	11.0	22.5	0.1	10.9-11.1	
HIV (+)						
>0 ≤ 1 years	-	-	-	-	-	1.0
>1 ≤ 5 years	121	3.8	5.0	0.5	3.3-4.2	
>5 ≤ 12 years	294	4.3	6.4	0.4	3.9-4.7	

*Unknown 2007-42
*Unknown 2006-171
*Unknown 2005-294

Table C.14 Average cost per medicine item per prescription according age groups for total costs (R)

Average number of medicine items per prescription						
	N	Mean	Standard deviation	Standard error	95% CI Mean	*p* > F
Total cost						
2005						
HIV (-)						
>0 ≤ 1 years	9 431	2.3	1.0	0.01	2.29-2.31	0.1
>1 ≤ 5 years	69 345	2.6	1.0	0.004	2.596-2.604	
>5 ≤ 12 years	118 145	2.6	1.1	0.003	2.597-2.603	
HIV (+)						
>0 ≤ 1 years	8	2.3	1.1	0.4	1.9-2.7	0.1
>1 ≤ 5 years	151	1.9	0.8	0.07	1.83-1.93	
>5 ≤ 12 years	229	1.9	0.7	0.05	1.85-1.95	
2006						
HIV (-)*						
>0 ≤ 1 years	8 897	2.3	1.0	0.01	2.29-2.31	0.9
>1 ≤ 5 years	67 693	2.6	1.0	0.004	2.596-2.604	
>5 ≤ 12 years	116 260	2.6	1.1	0.003	2.597-2.603	
HIV (+)						
>0 ≤ 1 years	13	1.7	0.5	0.1	1.6-1.8	0.9
>1 ≤ 5 years	181	1.9	0.6	0.04	1.86-1.94	
>5 ≤ 12 years	283	1.9	0.8	0.05	1.85-1.95	
2007						
HIV (-)						
>0 ≤ 1 years	2 042	2.4	0.9	0.02	2.38-2.42	0.9
>1 ≤ 5 years	48 317	2.7	1.0	0.005	2.695-2.705	
>5 ≤ 12 years	91 225	2.6	1.1	0.004	2.596-2.604	
HIV (+)						
>0 ≤ 1 years	4	1.6	0.4	0.2	1.4-1.8	0.9
>1 ≤ 5 years	159	1.9	0.7	0.1	1.8-2.0	
>5 ≤ 12 years	295	1.8	0.6	0.03	1.77-1.83	
2008						
HIV (-)						
>0 ≤ 1 years	18	2.1	0.8	0.2	1.9-2.3	0.8
>1 ≤ 5 years	28 910	2.7	1.0	0.01	2.69-2.71	
>5 ≤ 12 years	69 584	2.6	1.1	0.004	2.596-2.604	
HIV (+)						
>0 ≤ 1 years	-	-	-	-	-	0.8
>1 ≤ 5 years	121	1.9	0.7	0.1	1.8-2.0	
>5 ≤ 12 years	294	1.8	0.7	0.04	1.76-1.84	

*Unknown 2007-42
*Unknown 2006-171
*Unknown 2005-294

APPENDIX D

Table D.1 Total medication with Sulphonamides and combinations for 2005

Frequency Column (%)	HIV (-)	HIV (+)	Total
Central nervous system	67 302 3.52	127 1.48	67 429 3.51
Respiratory system	507 570 26.54	1 552 18.15	509 122 26.50
Ear, nose and throat	117 386 6.14	321 3.75	117 707 6.13
Gastro-intestinal tract	79 665 4.17	243 2.84	79 908 4.16
Antihelmintics	22 377 1.17	56 0.65	22 433 1.17
Dermatologicals	111 253 5.82	484 5.66	111 737 5.82
Ophtalmics	41 692 2.18	129 1.51	41 821 2.18
Urinary system	2 968 0.16	6 0.07	2 974 0.15
Genital system	1 254 0.07	1 0.01	1 255 0.07
Antimicrobials	406 396 21.25	3 955 46.24	410 351 21.36
Endocrine system	75 166 3.93	155 1.81	75 321 3.92
Anaesthetics.	2 274 0.12	6 0.07	2 280 0.12
Vitamines, tonics, minerals and electrolytes	17 035 0.89	199 2.33	17 234 0.90
Special foods	18 0.00	0 0.00	18 0.00
Cytostatics	192 0.01	0 0.00	192 0.01
Immunological	29 0.00	0 0.00	29 0.00
Biologicals	13 837 0.72	12 0.14	13 849 0.72
Others	127 0.01	0 0.00	127 0.01
Analgesics	256 625 13.42	808 9.45	257 433 13.40
Medical gases	12 0.00	0 0.00	12 0.00
Musculo-skeletal agents	22 340 1.17	42 0.49	22 382 1.17
Non-classified medicinal items	77 368 4.05	206 2.41	77 574 4.04
Autonomic	2 078 0.11	0 0.00	2 078 0.11
Autacoids	81 522 4.26	223 2.61	81 745 4.26
Cardio-vascular agents	1 992 0.10	3 0.04	1 995 0.10
Blood and haemopoeitic	3 944 0.21	25 0.29	3 969 0.21
Total	1 912 422 99.55	8 553 0.45	1 920 975 100.00
Statistic	**Value**		
p-value	<.0001		
Phi Coefficient	0.04		

Table D.2 Total medication with Sulphonamides and combinations for 2006

Frequency Colum (%)	HIV (-)	HIV (+)	Total
Central nervous system	71 947 3.61	176 1.52	72 123 3.59
Respiratory system	535303 26.83	2035 17.58	537338 26.78
Ear, nose and throat	122486 6.14	444 3.84	122930 6.13
Gastro-intestinal tract	81 476 4.08	280 2.42	81 756 4.07
Antihelmintics	21 343 1.07	78 0.67	21 421 1.07
Dermatologicals	119 271 5.98	588 5.08	119 859 5.97
Ophtalmics	41 847 2.10	181 1.56	42 028 2.09
Urinary system	2 796 0.14	11 0.10	2 807 0.14
Genital system	1 176 0.06	1 0.01	1 177 0.06
Antimicrobials	410 544 20.58	5 425 46.88	415 969 20.73
Endocrine system	81 100 4.06	231 2.00	81 331 4.05
Anaesthetics	2 413 0.12	13 0.11	2 426 0.12
Vitamines, tonics, minerals and electrolytes	18 868 0.95	398 3.44	19 266 0.96
Amino-acids	1 0.00	0 0.00	1 0.00
Special foods	39 0.00	0 0.00	39 0.00
Cytostatics	261 0.01	0 0.00	261 0.01
Immunological	35 0.00	0 0.00	35 0.00
Biologicals	18 573 0.93	16 0.14	18 589 0.93
Others	90 0.00	0 0.00	90 0.00
Analgesics	276 520 13.86	1 090 9.42	277 610 13.83
Medical gases	86 0.00	0 0.00	86 0.00
Musculo-skeletal agents	22 054 1.11	40 0.35	22 094 1.10
Non-classified medicinal items	72 953 3.66	236 2.04	73 189 3.65
Autonomic	2 271 0.11	3 0.03	2 274 0.11
Autacoids	86 224 4.32	294 2.54	86 518 4.31
Cardio-vascular agents	1 900 0.10	5 0.04	1 905 0.09
Blood and haemopoeitic	3 713 0.19	28 0.24	3 741 0.19
Total	1 995 290 99.42	11 573 0.58	2 006 863 100.00

Statistic	Value
***p*-value**	<.0001
Phi Coefficient	0.05

Table D.3 Total medication with Sulphonamides and combinations for 2007

Frequency Column (%)	HIV (-)	HIV (+)	Total
Central nervous system.	62 283 3.79	163 1.42	62 446 3.77
Respiratory system	439 323 26.73	2 038 17.79	441 361 26.67
Ear, nose and throat	102 971 6.27	411 3.59	10 3382 6.25
Gastro-intestinal tract	65 305 3.97	296 2.58	65 601 3.96
Antihelmintics	18 155 1.10	86 0.75	18 241 1.10
Dermatologicals	100 391 6.11	524 4.57	100 915 6.10
Ophtalmics	33 446 2.04	164 1.43	336 10 2.03
Urinary system	2 315 0.14	8 0.07	2323 0.14
Genital system	931 0.06	4 0.03	935 0.06
Antimicrobials	328 277 19.98	5 467 47.72	333 744 20.17
Endocrine system	70 415 4.29	237 2.07	70 652 4.27
Anaesthetics.	2 053 0.12	4 0.03	2 057 0.12
Vitamines, tonics, minerals and electrolytes	14 972 0.91	333 2.91	15 305 0.92
Special foods	14 0.00	2 0.02	16 0.00
Cytostatics	358 0.02	0 0.00	358 0.02
Immunological	37 0.00	0 0.00	37 0.00
Chelating agents, ion exchange preperations	1 0.00	0 0.00	1 0.00
Biologicals	16 917 1.03	18 0.16	16 935 1.02
Poison antidotes	1 0.00	0 0.00	1 0.00
Others	76 0.00	0 0.00	76 0.00
Analgesics	225 991 13.75	1 041 9.09	227 032 13.72
Medical gases	64 0.00	0 0.00	64 0.00
Musculo-skeletal agents	19 301 1.17	51 0.45	19 352 1.17
Non-classified medicinal items	65 787 4.00	310 2.71	66 097 3.99
Autonomic.	2 093 0.13	0 0.00	2093 0.13
Autacoids.	67 832 4.13	274 2.39	68 106 4.12
Cardio-vascular agents.	1 035 0.06	2 0.02	1037 0.06
Blood and haemopoeitic	2 934 0.18	24 0.21	2 958 0.18
Alcoholism	1 0.00	0 0.00	1 0.00
Total	1 643 279 99.31	11 457 0.69	1 654 736 100.00
Statistic	**Value**		
***p*-value**			<.0001
Phi Coefficient			0.06

Table D.4 Total medication with Sulphonamides and combinations for 2008

Frequency Colum (%)	HIV (-)	HIV (+)	Total
Central nervous system	46 805 4.38	138 1.40	46 943 4.35
Respiratory system	282 186 26.38	1 688 17.17	283 874 26.29
Ear, nose and throat	67 869 6.34	371 3.77	68 240 6.32
Gastro-intestinal tract	40 712 3.81	216 2.20	40 928 3.79
Antihelmintics	12118 1.13	61 0.62	12 179 1.13
Dermatologicals	70 508 6.59	527 5.36	71 035 6.58
Ophtalmics	20 740 1.94	176 1.79	20 916 1.94
Urinary system	1 525 0.14	21 0.21	1 546 0.14
Genital system	723 0.07	2 0.02	725 0.07
Antimicrobials	210 535 19.68	4 757 48.38	215 292 19.94
Endocrine system	4 7193 4.41	170 1.73	47 363 4.39
Anaesthetics	1 505 0.14	12 0.12	1 517 0.14
Vitamines, tonics, minerals and electrolytes	7 940 0.74	223 2.27	8 163 0.76
Amino-acids	1 0.00	0 0.00	1 0.00
Special foods	6 0.00	0 0.00	6 0.00
Cytostatics	244 0.02	3 0.03	247 0.02
Immunological	68 0.01	0 0.00	68 0.01
Chelating agents, ion exchange preperations	11 0.00	0 0.00	11 0.00
Biologicals	6 694 0.63	15 0.15	6 709 0.62
Others	55 0.01	0 0.00	55 0.01
Analgesics	140 963 13.18	828 8.42	141 791 13.13
Medical gases	58 0.01	1 0.01	59 0.01
Musculo-skeletal agents.	14 082 1.32	52 0.53	14 134 1.31
Non-classified medicinal items	45 888 4.29	286 2.91	46174 4.28
Autonomic.	1 270 0.12	0 0.00	1270 0.12
Autacoids	47 239 4.42	259 2.63	47 498 4.40
Cardio-vascular agents.	907 0.08	11 0.11	918 0.09
Blood and haemopoeitic	1911 0.18	16 0.16	1 927 0.18
Total	1 069 756 99.09	9 833 0.91	1 079 589 100.00
Statistic	**Value**		
***p*-value**			<.0001
Phi Coefficient			0.07

Table D.5 Total medication without Sulphonamides and combinations for 2005

Frequency Colum (%)	HIV (-)	HIV (+)	Total
Central nervous system.	67 302 3.55	127 2.16	67 429 3.55
Respiratory system	507 570 26.80	1 552 26.42	509 122 26.80
Ear, nose and throat	117 386 6.20	321 5.46	117 707 6.20
Gastro-intestinal tract	79 665 4.21	243 4.14	79 908 4.21
Antihelmintics	22 377 1.18	56 0.95	22433 1.18
Dermatologicals	111 253 5.87	484 8.24	111 737 5.88
Ophtalmics	41 692 2.20	129 2.20	41 821 2.20
Urinary system	2 968 0.16	6 0.10	2 974 0.16
Genital system	1 254 0.07	1 0.02	1 255 0.07
Antimicrobials	387 952 20.48	1 276 21.72	389 228 20.49
Endocrine system	75 166 3.97	155 2.64	75 321 3.96
Anaesthetics	2 274 0.12	6 0.10	2 280 0.12
Vitamines, tonics, minerals and electrolytes	17 035 0.90	199 3.39	17 234 0.91
Special foods	18 0.00	0 0.00	18 0.00
Cytostatics	192 0.01	0 0.00	192 0.01
Immunological	29 0.00	0 0.00	29 0.00
Biologicals	13 837 0.73	12 0.20	13 849 0.73
Others	127 0.01	0 0.00	127 0.01
Analgesics	256 625 13.55	808 13.76	257 433 13.55
Medical gases	12 0.00	0 0.00	12 0.00
Musculo-skeletal agents.	22 340 1.18	42 0.72	22 382 1.18
Non-classified medicinal items	77 368 4.08	206 3.51	77 574 4.08
Autonomic	2 078 0.11	0 0.00	2 078 0.11
Autacoids.	81 522 4.30	223 3.80	81 745 4.30
Cardio-vascular agents	1 992 0.11	3 0.05	1 995 0.11
Blood and haemopoeitic	3 944 0.21	25 0.43	3 969 0.21
Total	1 893 978 99.69	5 874 0.31	1 899 852 100.00

Statistic	Value
***p*-value**	<.0001
Phi Coefficient	0.02

Table D.6 Total medication without Sulphonamides and combinations for 2006

Frequency Colum (%)	HIV (-)	HIV (+)	Total
Central nervous system.	71 947 3.64	176 2.25	72 123 3.63
Respiratory system	535 303 27.06	2 035 25.97	537 338 27.06
Ear, nose and throat	122 486 6.19	444 5.67	122 930 6.19
Gastro-intestinal tract	81 476 4.12	280 3.57	81 756 4.12
Antihelmintics	21 343 1.08	78 1.00	21 421 1.08
Dermatologicals	119 271 6.03	588 7.50	119 859 6.04
Ophtalmics	41 847 2.12	181 2.31	42 028 2.12
Urinary system	2 796 0.14	11 0.14	2807 0.14
Genital system	1 176 0.06	1 0.01	1177 0.06
Antimicrobials	393 277 19.88	1 689 21.55	394 966 19.89
Endocrine system	81 100 4.10	231 2.95	81 331 4.10
Anaesthetics.	2413 0.12	13 0.17	2426 0.12
Vitamines, tonics, minerals and electrolytes	18 868 0.95	398 5.08	19 266 0.97
Amino-acids	1 0.00	0 0.00	1 0.00
Special foods	39 0.00	0 0.00	39 0.00
Cytostatics	261 0.01	0 0.00	261 0.01
Immunological	35 0.00	0 0.00	35 0.00
Biologicals	18 573 0.94	16 0.20	18 589 0.94
Others	90 0.00	0 0.00	90 0.00
Analgesics	276 520 13.98	1 090 13.91	277 610 13.98
Medical gases	86 0.00	0 0.00	86 0.00
Musculo-skeletal agents.	22 054 1.11	40 0.51	22 094 1.11
Non-classified medicinal items	72 953 3.69	236 3.01	73 189 3.69
Autonomic	2271 0.11	3 0.04	2 274 0.11
Autacoids	86 224 4.36	294 3.75	86 518 4.36
Cardio-vascular agents.	1 900 0.10	5 0.06	1905 0.10
Blood and haemopoeitic	3 713 0.19	28 0.36	3 741 0.19
Total	1 978 023 99.61	7 837 0.39	1 985 860 100.00
Statistic	**Value**		
***p*-value**			<.0001
***Phi* Coefficient**			0.03

Table D.7 Total medication without Sulphonamides and combinations for 2007

Frequency Colum (%)	HIV (-)	HIV (+)	Total
Central nervous system	62 283 3.82	163 2.17	62 446 3.81
Respiratory system	439 323 26.94	2 038 27.18	441 361 26.94
Ear, nose and throat	102 971 6.31	411 5.48	103 382 6.31
Gastro-intestinal tract	65 305 4.00	296 3.95	65 601 4.00
Antihelmintics	18 155 1.11	86 1.15	18 241 1.11
Dermatologicals	100 391 6.16	524 6.99	100 915 6.16
Ophtalmics	33 446 2.05	164 2.19	33 610 2.05
Urinary system	2 315 0.14	8 0.11	2323 0.14
Genital system	931 0.06	4 0.05	935 0.06
Antimicrobials	315 761 19.36	1 507 20.10	317 268 19.37
Endocrine system	70 415 4.32	237 3.16	70 652 4.31
Anaesthetics	2 053 0.13	4 0.05	2057 0.13
Vitamines, tonics, minerals and electrolytes	14 972 0.92	333 4.44	15 305 0.93
Special foods	14 0.00	2 0.03	16 0.00
Cytostatics	358 0.02	0 0.00	358 0.02
Immunological	37 0.00	0 0.00	37 0.00
Chelating agents, ion exchange preperations	1 0.00	0 0.00	1 0.00
Biologicals	16 917 1.04	18 0.24	16 935 1.03
Poison antidotes	1 0.00	0 0.00	1 0.00
Others	76 0.00	0 0.00	76 0.00
Analgesics	225 991 13.86	1 041 13.89	227 032 13.86
Medical gases	64 0.00	0 0.00	64 0.00
Musculo-skeletal agents.	19301 1.18	51 0.68	19 352 1.18
Non-classified medicinal items	65 787 4.03	310 4.13	66 097 4.03
Autonomic	2 093 0.13	0 0.00	2093 0.13
Autacoids	67 832 4.16	274 3.65	68 106 4.16
Cardio-vascular agents	1 035 0.06	2 0.03	1 037 0.06
Blood and haemopoeitic	2 934 0.18	24 0.32	2 958 0.18
Alcoholism	1 0.00	0 0.00	1 0.00
Total	1 630 763 99.54	7 497 0.46	1 638 260 100.00

Table D.7 Total medication without Sulphonamides and combinations for 2007

Statistic	Value
***p*-value**	<.0001
***Phi* Coefficient**	0.03

Table D.8 Total medication without Sulphonamides and combinations for 2008

Frequency Colum (%)	HIV (-)	HIV (+)	Total
Central nervous system	46 805 4.41	138 2.21	46943 4.40
Respiratory system	282 186 26.58	1 688 26.98	283 874 26.58
Ear, nose and throat	67 869 6.39	371 5.93	68 240 6.39
Gastro-intestinal tract	40 712 3.83	216 3.45	40 928 3.83
Antihelmintics	12 118 1.14	61 0.98	12 179 1.14
Dermatologicals	70 508 6.64	527 8.42	71 035 6.65
Ophtalmics	20 740 1.95	176 2.81	20 916 1.96
Urinary system	1 525 0.14	21 0.34	1 546 0.14
Genital system	723 0.07	2 0.03	725 0.07
Antimicrobials	202 536 19.08	1180 18.86	203 716 19.07
Endocrine system	47 193 4.44	170 2.72	47 363 4.43
Anaesthetics	1 505 0.14	12 0.19	1 517 0.14
Vitamines, tonics, minerals and electrolytes	7 940 0.75	223 3.56	8 163 0.76
Amino-acids	1 0.00	0 0.00	1 0.00
Special foods	6 0.00	0 0.00	6 0.00
Cytostatics	244 0.02	3 0.05	247 0.02
Immunological	68 0.01	0 0.00	68 0.01
Chelating agents, ion exchange preperations	11 0.00	0 0.00	11 0.00
Biologicals	6 694 0.63	15 0.24	6 709 0.63
Others	55 0.01	0 0.00	55 0.01
Analgesics	140 963 13.28	828 13.24	141 791 13.28
Medical gases	58 0.01	1 0.02	59 0.01
Musculo-skeletal agents	14 082 1.33	52 0.83	14 134 1.32
Non-classified medicinal items	45 888 4.32	286 4.57	46 174 4.32
Autonomic	1 270 0.12	0 0.00	1 270 0.12
Autacoids	47 239 4.45	259 4.14	47 498 4.45
Cardio-vascular agents	907 0.09	11 0.18	918 0.09
Blood and haemopoeitic	1 911 0.18	16 0.26	1 927 0.18
Total	1 061 757 99.41	6 256 0.59	1 068 013 100.00

Table D.8 Total medication without Sulphonamides and combinations for 2008

Statistic	Value
***p*-value**	<.0001
Phi Coefficient	0.03

APPENDIX E

Abstract submitted to and accepted by ISPOR 14th Annual European Congres

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15 August 2011

Pharmacy Practice
North-West University
School of Pharmacy Faculty of Health Sciences
Potchefstroom, 2531 South Africa

Acceptance Code: PIH52

Thank you for submitting your abstract entitled:

MEDICINE PRESCRIBING PATTERNS IN HIV/AIDS AND NON-HIV/AIDS CHILDREN: A COMPARITIVE STUDY IN THE PRIVATE HEALTH CARE SECTOR OF SOUTH AFRICA

for presentation at the **ISPOR 14th Annual European Congress** to be held 5-8 November 2011 at the Hotel Auditorium Madrid in Madrid, Spain. Congratulations, your abstract has been **accepted** as a **POSTER PRESENTATION** during the following session:

Poster Session II: Monday, 7 November 2011
Poster Display Hours: 8:00-19:30
Poster Author Discussion Hour: 17:30-18:30

One author is required to be with the poster for questions and answers during the Poster Author Discussion Hour noted above. You are also requested to have at least 200 copies of your presentation at your poster for attendees. **Each poster board has a usable area of approximately 2 meters high by 1 meter wide.**

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MEDICINE PRESCRIBING PATTERNS IN HIV/AIDS AND NON-HIV/AIDS CHILDREN: A COMPARITIVE STUDY IN THE PRIVATE HEALTH CARE SECTOR OF SOUTH AFRICA

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OBJECTIVES: To compare medicine prescribing patterns of HIV/AIDS and non-HIV/AIDS children in the private health care sector of South Africa. **METHODS**: A quantitative, retrospective drug utilisation review was performed utilising medicine claims data of a pharmacy benefit management company. Data for a four-year period (Jan 1, 2005 to Dec 31, 2008) were used. The study population consisted of all children ≤ 12 years who received one or more prescriptions during the study period. Data were analysed using the SAS® Programme (9.1). **RESULTS:** The number of HIV/AIDS children increased from 0.2% of all children on the database in 2005 (N = 197 323) to 0.4% in 2008 (N = 98 939). The average number of antiretroviral medicine items (ARVs) per prescription prescribed to HIV/AIDs children did not changed from 2005 to 2008 (3.05 ± 0.65 in 2005 and 3.19 ± 0.58 in 2008). HIV/AIDS children received an average of 7.39 ± 4.69 ARV prescriptions per year during 2005 and this increase to 9.72 ± 4.49 in 2008. HIV/AIDS children received during 2005 an average or 11.51 ± 7.17 prescription for other medication (non-ARVs) per year and it increased to 13.46 ± 7.14 during 2008. This is practically significant more than the average of 3.86 ± 3.71 (d = 0.8) prescriptions per year per non-HIV/AIDS children in 2005 and 4.36 ± 4.05 (d = 1.25) in 2008. Non-ARV medication mostly prescribed to HIV/AIDs children during 2008 included sulphonamides and combinations, antitussives and expectorants, penicillin and combination analgesics. Non-HIV/AIDS children received mostly penicillins, antitussives and expectorants, combination analgesics and analgesics and antipyretics. **CONCLUSION:** HIV/AIDS children received per year more prescriptions for non-ARVs compare to non-HIV/AIDS children. Further research is needed to investigate the future medicine treatment cost of HIV/AIDS children in the South African private health care sector.