

A RETROSPECTIVE ANALYSIS OF THE USAGE PATTERNS OF ANTIRETROVIRAL DRUGS: A PHARMACOECONOMIC APPROACH

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Knowing is not enough; we must apply.

Willing is not enough; we must do.

- Johann Wolfgang von Goethe -

In loving memory of Johan Kruger

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ABSTRACT

TITLE: A retrospective analysis of the usage patterns of antiretroviral drugs: a pharmacoeconomic approach.

KEYWORDS: HIV/AIDS, antiretroviral drugs (ARVs), pharmacoeconomics, drug utilisation review, prevalence and medicine treatment cost.

More people living with HIV/AIDS reside in South Africa than any other country in the world, and the nation faces colossal challenges in broadening its response to the now-mature and widespread HIV epidemic (WHO, 2005:1). According to South Africa's Medical Research Council, HIV/AIDS has now become the single largest cause of death in South Africa (Dorrington *et al.*, 2001:6) and has triggered a prominent transferral in the pattern of mortality from the elderly to the young, particularly among young women (Dorrington, 2001:4).

The routine treatment of HIV/AIDS with antiretroviral drugs has transformed HIV-infection from an unvaryingly rapidly terminal illness to a somewhat expensive treatable, chronic disease. Triple therapy or highly active antiretroviral therapy (three-drug combinations of ARVs or HAART) in particular have had paramount impacts on HIV-related morbidity and mortality in settings where these drugs are generally accessible. Objectives of ARV treatment are "maximum, durable suppression of viral load, restoration and/or preservation of immune function, improvement of quality of life and reduction of HIV related morbidity and mortality" (Martinson *et al.*, 2003:236; Martinez *et al.*, 2007:251; Hellinger, 2006:1; Kumarasamy, 2004:3).

The Joint United Nations Programme on HIV/AIDS (UNAIDS) estimated that a total of 111 827 South Africans were accessing free antiretroviral treatment in the 200 public health sector facilities across 53 districts and a further 60 000 via the private sector by late December 2005 (UNAIDS, 2005:1).

The objective of this study was to review, analyse and interpret the usage and prescribing patterns of antiretroviral drugs in a section of the South African private health care sector for the period 1 January 2005 to 31 December 2006 by utilising a medicine claims database of a pharmacy benefit management company, and to investigate the costs associated with these drugs by performing a quantitative, retrospective drug utilisation review.

It was found that the prevalence as well as the total medicine cost of ARV medicine items had increased during the study period but the average number of ARV medicine items per prescription as well as both the average cost per ARV medicine item and the average cost per ARV prescription decreased during the study period.

Original innovator ARV medicine items and original ARV medicine items with no generic were found to be relatively expensive in comparison with ARV medicine items in general. Conversely, generic ARV medicine items were ascertained to be relatively inexpensive with reference to ARV medicine items in general.

It was perceived that the average cost of ARV medicine items and prescriptions for both genders decreased from 2005 to 2006, while there was an increase in the prevalence of medicine items and prescriptions claimed for both female and male patients. The prevalence and cost of all types of ARV medicine items were found to be higher for female patients in general.

It was also established that the prevalence of patients receiving antiretroviral treatment in the private health care sector peaks at the age of >30 to ≤44 years, in comparison with the lower age of >25 to ≤39 years in the public health care sector. ARV medicine items claimed for patients in the age group >35 to ≤39 years represented the highest percentage of the total medicine cost incurred during both study years for all ARV medicine types.

The majority of ARV medicine items were prescribed by general medical practitioners, and most ARV medicine items were dispensed by community or private institutional pharmacies.

It was determined that combinations of 2NRTI + NNRTI were prescribed with the highest frequency, which is compliant with traditional HAART or 'triple therapy' regimens.

Lastly, it was found that none of the top 20 prescriptions for one, two and six ARV medicine items were compliant with the National Antiretroviral Treatment (ART) Guidelines. The majority of the top 20 prescriptions for three ARV medicine items (92.67 per cent during 2005 and 89.94 per cent during 2006) were compliant with the National ART Guidelines. Finally, less than half of the top 20 prescriptions for four ARV medicine items (49.60 per cent during 2005 and 36.11 per cent during 2006) were compliant with the National ART Guidelines. Only 5.56 per cent and 3.92 per cent of the top 16 prescriptions for five ARV medicine items were compliant with the National ART Guidelines during the two study years respectively.

OPSOMMING

TITEL: 'n Retrospektiewe ontleding van die gebruikspatrone van antiretrovirale middels: 'n farmako-ekonomiese benadering.

SLEUTELWOORDE: MIV/VIGS, antiretrovirale middels (ARV), farmako-ekonomie, medisyneverbruik evaluering, voorkoms, medisynekoste van behandeling.

In Suid-Afrika is daar meer MIV/VIGS lyers as in enige ander land ter wêreld. Reaksies op hierdie gevorderde en omvangryke probleem van die MIV/VIGS epidemie moet steeds verbeter en dit stel besondere groot uitdagings aan die land en sy mense (WHO, 2005:1). Volgens die Suid-Afrikaanse Mediese Navorsingsraad, het MIV/VIGS nou die grootste enkele oorsaak van dood in Suid-Afrika geword (Dorrington *et al.*, 2001:6) en het ook 'n prominente uitwerking op die dodetalpatrone van oud en jonk uitgeoefen, veral met betrekking tot die sterftesyfers van jong vroulikes (Dorrington, 2001:4).

Roetinebehandeling vir MIV/VIGS met antiretrovirale middels het MIV infeksie omgeswaai sodat dit van 'n onvermydelik dodelike siekte na 'n chroniese siekte verander het wat teen redelike hoë onkoste behandel kan word. Driedelige terapie of hoogs aktiewe antiretrovirale terapie (drie-middel kombinasies of HAART) het in die besonder 'n uiters belangrike invloed op MIV verwante morbiditeit en mortaliteit uitgeoefen, veral in omgewings waar groter toeganklikheid tot sulke geneesmiddels bestaan.

Doelwitte van antiretrovirale behandeling het te make met die maksimum standhoudende onderdrukking van virale lading, herstel en/of behoud van immuunfunksies, verbetering van lewenskwaliteit en bekamping van morbiditeit en mortaliteit wat met MIV verband hou (Martinson *et al.*, 2003:236; Hellinger, 2006:1; Kumarasamy, 2004:3).

Volgens 'n skatting (getalle soos vir laat Desember 2005) van die 'Joint United Nations Programme on HIV/AIDS (UNAIDS)' [*Gesamentlike Verenigde Volke Program vir MIV/VIGS*] het 'n totaal van 111 827 Suid-Afrikaners in die 200 publieke gesondheidsorgeenhede van 53 streke gratis antiretrovirale behandeling ontvang en 'n verdere 60 000 deur middel van die privaat sektor (UNAIDS, 2005:1).

Die doelstelling met hierdie studie was om op analitiese en interpreterende wyse ondersoek in te stel na antiretrovirale middels met betrekking tot die gebruikspatrone, voorskryfpatrone en onkoste daarvan. Die fokus was op 'n geselekteerde deel van die privaat gesondheidsorgsektor in Suid-Afrika vir die tydperk 1 Januarie 2005 tot 31 Desember 2006. Die medisyne eise databasis van 'n firma vir die apteekvoordelebestuursmaatskappy is

gebruik om data te verkry. Om die gepaardgaande medisynekostes van die middels na te gaan, is 'n kwantitatiewe, retrospektiewe medisyneverbruiksevaluering uitgevoer.

Bevindings dui daarop dat beide die voorkoms en die medisynekostes van antiretrovirale middels tydens die studietydperk gestyg het, maar dat die gemiddelde hoeveelheid antiretrovirale middels per voorskrif sowel as beide die gemiddelde koste per antiretrovirale middel en antiretrovirale voorskrif afgeneem het gedurende die studieperiode.

Oorspronklike innoveerder antiretrovirale medisyne items en ook dié hiervan sonder 'n generiese ekwivalent, het as relatief duur medisyne items uitgewys, veral in vergelyking met antiretrovirale middels in die algemeen. Daarteenoor is bevestig dat generiese antiretrovirale middels, in vergelyking met antiretrovirale middels in die algemeen, as relatief goedkoop medisyne items vertoon.

Vir beide die manlike en vroulike geslagte het die gemiddelde koste van antiretrovirale middels, sowel as die voorskrifte, volgens waarneming tussen 2005 en 2006 afgeneem. Hierteenoor is 'n toename in die voorkoms en die eise wat vir voorskrifte ingedien is gedurende dieselfde tydperk vir albei geslagte waargeneem. Die voorkoms en koste van al die soorte/klasse antiretrovirale middels het geblyk oor die algemeen hoër te wees vir vroulike pasiënte.

Die ouderdomsgroep met die meeste pasiënte wat antiretrovirale behandeling ontvang het, soos in die privaat gesondheidsorg sektor aangetref, was >30 tot ≤44 jaar. In vergelyking hiermee is die hoogste punt vir genoemde pasiënte in die publieke gesondheidsorg sektor vasgestel op die jonger ouderdomsgroep >25 tot ≤39 jaar. Eise wat vir antiretrovirale medisyne items ingedien is, het binne die ouderdomsgroep >35 tot <39 jaar die hoogste persentasie van die totale antiretrovirale onkoste vir die twee studiejaar getoon.

Die meerderheid van die voorskrifte vir antiretrovirale medisyne items is deur algemene praktisyns gedoen en die meerderheid antiretrovirale voorskrifte is by gemeenskapsapteke of privaat institusionele apteke afgehaal.

Kombinasies wat die meeste hoeveelheid kere voorgeskryf is, was 2NRTI + NNRTI. Dit is in lyn met die tradisionele HAART of 'driedelige terapie' middels.

Daar is bevind dat nie een van die hoogste 20 voorskrifte vir een of twee of ses antiretrovirale medisyne items met die Nasionale antiretrovirale behandelingsriglyne ooreenstem nie. Die meerderheid van die hoogste 20 voorskrifte vir drie antiretrovirale medisyne items (92.67 persent vir 2005 en 89.94 persent vir 2006) het met genoemde riglyne ooreengestem. Minder as die helfte van die hoogste 20 voorskrifte vir vier

antiretrovirale medisyne items (49.60 persent vir 2005 en 36.11 persent vir 2006) het met die Nasionale antiretrovirale behandelingsriglyne ooreengestem. Slegs 5.56 persent (2005) en 3.92 persent (2006) van die 16 hoogste voorskrifte vir vyf antiretrovirale medisyne items het aan die bepalings van die Nasionale antiretrovirale behandelingsriglyne voldoen.

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CHAPTER 1: INTRODUCTION

1.1 Introduction

The focus of the dissertation is the prescribing patterns of antiretroviral drugs in a section of the private health care sector in South Africa. In this chapter the problem statement, research objectives, and research methodology will be discussed. The chapter will conclude with the division of chapters.

1.2 Problem statement

The Mayo Clinic (2008:1) defines AIDS as “*a chronic, life-threatening condition caused by the human immunodeficiency virus (HIV)*”. HIV disturbs the capability of the human body to successfully combat and prevent infection by disease-causing micro-organisms as it interferes with the functioning of the immune system. This increases susceptibility to a variety of tumours and opportunistic infections that the body would normally withstand, for instance pneumonia and meningitis (Mayo Clinic, 2008:1).

According to the United Nations Aids Reference Group's annual report of 2007, the number of individuals living with HIV worldwide by the end of 2007 was estimated to be 33.2 million (in the range of 30.6–36.1 million) (UNAIDS, 2007:8). In excess of 6 800 persons are newly infected with HIV daily, and over 5 700 people die from AIDS-related causes every day, generally as a consequence of insufficient access to services for HIV treatment and prevention (UNAIDS, 2007:8). South Africa is home to the largest population of individuals living with HIV/AIDS in the world (Ijumba *et al.*, 2004:320), and women aged 15-49 are affected the worst (Statistics South Africa, 2006:3).

Antiretroviral treatment inhibits HIV-1 replication, which alters the natural history of the infection considerably (Wood *et al.*, 2000:2095), and the correct utilisation of antiretroviral therapies has remarkably reduced HIV-associated mortality over the last several years (Saag, 2003:359). The distribution of protease inhibitors in 1996, the subsequent use of non-nucleoside reverse transcriptase inhibitors in 1998, and more recently the introduction of protease inhibitors boosted with ritonavir have produced valuable treatment possibilities for management of HIV infection (Sabbatani, 2003:476). HIV therapy is constantly evolving and the pharmaceutical industry is progressively developing new antiretroviral drugs (Wilson *et al.*, 2004:341), but a cure has not been developed yet (Avert, 2008a:1).

The Declaration of Commitment by the United Nations released by the Office of the United Nations High Commissioner for Human Rights in 2001 (OHCHR, 2001:1) accentuated the fact that all people infected with HIV have the right to treatment. The Declaration also

observed that the cardinal elements of any effective response to HIV include treatment, care and support (Handford *et al.*, 2007:2).

Affordability has been one of the limitations concerning comprehensive use of ARVs in developing settings (Martinson *et al.*, 2003:247-248). However, a study by Scholtz (2005:168) showed that the cost of antiretroviral drug therapy in the South African private health care sector decreased from 2002 to 2004. Due to this significant reduction in the prices of patented ARVs in recent years, accessibility has been made possible to people who formerly could not afford them, regardless of private-sector medical scheme cover (McLeod *et al.*, 2003:92).

Less than 15 per cent of the 47 million citizens of South Africa have medical scheme membership (Anon, 2007:1). As a result the public health care sector is heavily burdened by HIV epidemic, but the private sector is also under a great deal of pressure. Research has indicated that approximately 6 per cent of medical scheme beneficiaries are living with HIV (McLeod *et al.*, 2003:86).

Since the implementation of amendments to the regulations under the Medical Schemes Act (No. 131 of 1998) on 1 January 2005, all medical schemes must provide prescribed minimum benefits to HIV-positive beneficiaries. All beneficiaries now have access to highly active antiretroviral therapy (no less than to the extent provided for the public sector) and all the fundamental monitoring tests (South Africa, 2004a:3-4).

It is clear that further research should be conducted regarding prescribing patterns and utilisation of antiretroviral drugs in the private health care sector of South Africa.

1.3 Research questions

The subsequent research questions can be formulated on account of the preceding discussion:

- How do South African medical aids manage beneficiaries living with HIV/AIDS and what are the associated costs?
- How can HIV/AIDS be conceptualised?
- How can antiretroviral drugs be conceptualised?
- Are generic antiretroviral drugs being utilised to minimise costs?

- How do prescribing patterns of antiretroviral agents in the private health care sector reflect in medicine claim databases so that insight may be gained in prescribing practices?
- What are the prescribing patterns of antiretroviral drugs and what are the costs associated with these drugs in the South African private health care sector?
- Does appropriate prescription of combination antiretroviral therapy occur and what are the costs associated with these combinations?

1.4 Research objectives

The research encompasses a general as well as various specific research objectives.

1.4.1 General objective

The objective of this study was to review the usage and prescribing patterns of antiretroviral drugs in a section of the South African private health care sector for the period 2005 to 2006 by utilising a medicine claims database, and to investigate the costs associated with these drugs.

1.4.2 Specific objective

The research project was composed of two phases, a literature review and an empirical investigation. The research objectives of the two respective phases were as follows:

1.4.2.1 Phase 1: Literature review

The specific research objectives of the literature review were:

- To conceptualise the HIV/AIDS pandemic from available literature.
- To describe HIV/AIDS treatment protocols and the antiretroviral drugs involved therein.
- To conceptualise from the literature some pharmacoeconomic principles involved in the South African health care system.
- To study the health care system of South Africa and ascertain through the literature how South African medical aid funds approach and manage antiretroviral therapy.

1.4.2.2 Phase 2: Empirical investigation

The specific research objectives of the empirical investigation included:

- To determine the usage patterns and cost of drugs in general according to all medicine items and prescriptions in the total medicine claims database for the study period 2005 to 2006.
- To analyse utilisation patterns and cost of antiretroviral agents and antiretroviral prescriptions in the medicine claims database according to gender, age group, prescriber and provider for the two study years.
- To investigate generic substitution of innovator antiretroviral drugs within the two study years.
- To identify combination therapy of antiretroviral drugs and determine the costs associated with these combinations for 2005 and 2006.

1.5 Research method

The research consisted of two phases corresponding to the specific objectives, namely a literature review and an empirical investigation.

1.5.1 Phase 1: Literature review

The following steps were followed in the literature study as contained in Chapter 2:

- **Step 1: The HIV/AIDS pandemic.** This step of the literature study focuses on the extent of the HIV/AIDS epidemic, the social impact of the epidemic, the transmission of HIV, certain clinical aspects of HIV/AIDS and the stages of HIV disease.
- **Step 2: Antiretroviral drugs.** This step constitutes the classification and mechanism of action of antiretroviral drugs, treatment protocols for HIV/AIDS, indications for antiretroviral therapy, and drug-drug interactions between antiretroviral agents.
- **Step 3: Health care concepts.** This step explores the South African health care system, pharmacoeconomic principles and health care concepts, drug utilisation review, and health insurance in South Africa pertaining to HIV/AIDS.

1.5.2 Phase 2: Empirical investigation

The empirical investigation involved several steps which are discussed in-depth in Chapter 3. A retrospective drug utilisation was performed on the antiretroviral medicine items claimed via a pharmacy benefit company for the periods 1 January 2005 to 31 December 2005 and 1 January 2006 to 31 December 2006.

The study population was selected in accordance with prescriptions analysed on the medicine claims database, and the study focused on the claims data of patients who were prescribed one or more antiretroviral agents during the study period. In order to achieve the objectives of the empirical investigation the innovator and generic forms, prevalence, cost, prescriber and provider of antiretroviral medicine items, as well as patient gender and age were applied as measuring instruments for data analysis.

The data analysis was conducted through the Statistical Analysis System®, SAS 9.1® (SAS Institute Inc., 2003).

The results obtained from the empirical investigation are reported and discussed in Chapter 4. The conclusion, recommendations and limitations derived from the results of the study are discussed in Chapter 5.

1.6 Division of chapters

The division of chapters is as follows:

Chapter 1: Introduction

Chapter 2: HIV/AIDS and antiretroviral treatment protocols in South Africa today

Chapter 3: Empirical investigation

Chapter 4: Results and discussion

Chapter 5: Conclusion and recommendations

1.7 Chapter summary

In this chapter, the problem statement, research questions, research objectives, empirical research method, and division of chapters were explored. HIV/AIDS, antiretroviral drug treatment, and South African health care concepts are discussed in Chapter 2.

CHAPTER 2: HIV/AIDS AND ANTIRETROVIRAL TREATMENT PROTOCOLS IN SOUTH AFRICA

2.1 Introduction

This chapter focuses on HIV/AIDS disease in a South African context. The magnitude of the epidemic and the resulting impact on different levels of society are reviewed. Different means of transmission of the infection and progression of the disease are examined, and treatment options with antiretroviral drugs are explored. Pharmacoeconomic principles and health care concepts in the South African health care system, especially health insurance, are investigated as pertaining to HIV/AIDS.

2.2 The extent of the HIV/AIDS epidemic in South Africa

South Africa is staggering under the increasingly heavy yoke of HIV-related mortality and disease. The Medical Research Council (Dorrington *et al.*, 2001:21) has forecast that the cumulative number of HIV/AIDS deaths will surpass 6 million by 2010. The estimated prediction for 2005 was that HIV/AIDS would be the cause of almost 60.00 per cent of all deaths in South Africa (Martinson *et al.*, 2003:236).

The World Health Organization (WHO) states that more people living with HIV/AIDS reside in South Africa than any other country in the world, and the nation faces colossal challenges in broadening its response to the now-mature and widespread HIV epidemic. In all age groups, with the exception of pregnant women over 40 years of age, there has been a continuous increase in prevalence rates, and there has been no indication of a decline in the epidemic. Over the past six years there has been an estimated increase of more than 40.00 per cent in adult deaths in South Africa (WHO, 2005:1). According to South Africa's Medical Research Council, HIV/AIDS has now become the single largest cause of death in South Africa (Dorrington *et al.*, 2001:6) and has triggered a prominent transferral in the pattern of mortality from the elderly to the young, particularly among young women (Dorrington *et al.*, 2001:4).

2.2.1 Spread of the epidemic

In 1981 the first cases of acquired immunodeficiency syndrome (AIDS) were reported (CDC, 2006:841). Since then, infection with human immunodeficiency virus (HIV) has expanded to pandemic proportions, giving rise to approximately 65 million infections and 25 million deaths. According to the Centers for Disease Control and Prevention (CDC), for the period of 2005 alone, an estimated 2.8 million individuals died from AIDS, 4.1 million new HIV infections occurred, and 38.6 million people were living with HIV (CDC, 2006:841).

It is currently estimated that South Africa has the largest number of people living with HIV/AIDS worldwide (Ijumba *et al.*, 2004:320). Although estimates differ, it is generally acknowledged that between 4 and 6 million people are infected and that HIV/AIDS is the foremost cause of death in the country (Ijumba *et al.*, 2004:320).

According to Rehle and co-workers new infections with HIV in South Africa occur at a rate of about 1 500 additional infections each day, accounting for about 571 000 newly-infected people in 2005 according to the Human Sciences Research Council (Rehle *et al.*, 2007:198).

The HIV prevalence rate peaks among women aged 15-49 years. The total prevalence rate of women in this age group is 20.00 per cent. The projected HIV prevalence rate swelled from less than 9.00 per cent in 2005 to 11.00 per cent in 2006 (Statistics South Africa, 2006:3).

The following Table 2.1 illustrates cases of AIDS reported annually in South Africa throughout the eighties at the onset of the epidemic. This demonstrates the enormous escalation of the epidemic when compared to current actuarial projections of the epidemic as exemplified in Table 2.2. The number of patients known to have died is indicated in brackets. Monthly releases show a discrepancy owing to the fact that the disease is not officially notifiable and death figures are in all probability inaccurate.

Table 2.1 AIDS cases reported in South Africa 1982-1991 (Lachman, 1991:65)

Year	Total seen	South African	Non-South African
1982	2 (2)	1 (1)	1 (1)
1983	4 (3)	4 (3)	-
1984	8 (8)	8 (8)	-
1985	8 (8)	7 (7)	1 (1)
1986	24 (23)	14 (13)	10 (10)
1987	39 (32)	30 (26)	9 (6)
1988	88 (54)	82 (50)	6 (4)
1989	173 (88)	170 (87)	3 (1)
1990	297 (66)	290 (61)	7 (5)
1991	79 (8)	74 (8)	5 (?)
Total	722 (292)	680 (264)	42 (28)

The progression of the South African epidemic in the 21st century is further illustrated in Table 2.2 from the Actuarial Society of South Africa (ASSA), which indicates an estimated

rise in the total number of people infected with HIV of about 2 341 270 from 2000 to 2008, and an increase of 1 051 616 in AIDS sick. Accumulated AIDS deaths, for the same period of time, is estimated to have risen by 3 418 874 (ASSA, 2000).

Table 2.2 Actuarial projection of the epidemic: National summary statistics (ASSA, 2000)

	2000	2007	2008
Numbers (total and infected)			
Total population	45 078 805	47 683 822	47 645 665
Total HIV infections	5 263 841	7 695 201	7 605 111
Total births	1 142 387	1 061 205	1 045 853
Births infected perinatally	58 048	71 815	70 748
Babies newly infected by mother's milk	16 259	21 651	21 385
AIDS sick			
Total AIDS sick (in the middle of year)	236 228	1 182 710	1 287 844
Deaths			
Non-AIDS deaths	387 667	406 824	406 961
AIDS deaths	139 009	664 966	721 915
Accumulated AIDS deaths (to middle of the year)	298 645	3 019 659	3 717 519
Prevalence rates			
Antenatal clinics	25.20%	31.70%	31.70%
Women aged 15 - 49	21.50%	29.70%	29.50%
Adult women (ages 20 - 65)	19.60%	26.80%	26.50%
Adult men (ages 20 - 65)	20.50%	27.60%	27.20%
Adults (ages 20 - 65)	20.10%	27.20%	26.80%
Total population	11.70%	16.10%	16.00%
Incidence rates			
Total new infections	892 241	663 514	644 682
Mortality statistics			
Life expectancy at birth	56	43	42
Maternal orphan statistics			
Total orphans (in middle of the year)	493 860	1 339 615	1 506 386
Total AIDS orphans (in middle of the year)	124 989	1 039 210	1 218 488

2.2.2 Impact of HIV on society

Unfortunate circumstances including hardship, maltreatment, violent behaviour, bigotry and lack of knowledge help HIV to prosper in communities. Susceptibility to HIV infection and its subsequent influence may be enhanced by unfavourable communal and economic conditions in a society as stated by Lyons (1998:1). In the same manner, HIV/AIDS also instigates and intensifies situations that make it possible for the epidemic to surge. To the same extent that the virus weakens the human body's innate immune defences, it is additionally able to drain family units and the populace of vital resources and social structures essential for productive prevention and care-giving and therapy for HIV/AIDS patients (Lyons, 1998:1).

HIV has a great impact on society, and vice versa. Why do social factors affect HIV/AIDS epidemics? The first explanation is that HIV is transmitted through fundamentally social phenomena, such as sexual and drug injection networks (Friedman *et al.*, 2006:959).

Social standards regarding suitable choice, numbers and timing of sexual partners, and on the subject of acceptable behaviour with those partners, shape essential network variables such as concomitant sexual and drug injection relationships; partner turnover rates; mixing patterns; the size, integration and microstructures of community network components; and the degree of semi-anonymous risk points such as group sex parties, bath-houses, and "shooting galleries" where intravenous drug users convene (Friedman *et al.*, 2006:959).

Sexual and drug-taking behaviours are influenced by social norms, conventions, educational structures and law enforcement practices. Social networks, norms and social support have an effect on how people access, interpret and apply HIV-prevention information and education, the degree to which individuals utilise sexually transmitted disease treatments and HIV therapies, HIV counselling and testing, and affect adherence to therapies. Economic and political conditions and dynamics shape what services are accessible and how problematic, expensive, or stigmatising it is to use them (Friedman *et al.*, 2006:959).

Ultimately, events - like large-scale epidemics - that disturb local or national social networks, communities, services, or social norms, bring about large-scale migration, or instigate large-scale amalgamation across new sexual or injecting networks, create the potential for risk behaviours or adherence failures that would have formerly been prevented – and these, in turn, might produce epidemic outbreaks (Friedman *et al.*, 2006:959).

Severely afflicted regions will likely be harshly affected by the HIV/AIDS epidemic at multiple levels across the board. Impending outcomes of this pandemic include extensive transformation of demographic patterns, economic decline, volatile social situation, and

impediment of democracy and authority. Productive adults that are socially and economically valuable are targeted in particular, leading to orphaned children and afflicting sectors of society, government, health care and economy (Manning, 2002:6).

The majority of respondents who participated in a study by Manning (2002:12) stated that “*silence, denial, and stigma around HIV/AIDS*” were the causes of social dilemmas in the district.

The end results of stigma, segregation and prejudice against people living with HIV/AIDS obligate infected individuals to fail to disclose their affliction and to persist with unsafe behaviour that is potentially hazardous to themselves and others (South Africa, 2007a:33). An additional outcome of discrimination against persons infected with HIV/AIDS is denial. Silence and denial regarding HIV and AIDS are equally significant since they inhibit persons from truthfully evaluating their personal risk of infection in addition to gaining access to the extensive variety of existing services concerning HIV/AIDS (South Africa, 2007a:33).

2.2.3 Impact of HIV on population growth

After reviewing projections on population growth, the Bureau for Economic Research (2001:1) concluded that the South African population could grow by merely 1.5 million people between 2000 and 2015 – or 10 million people fewer in contrast to a no-AIDS projection.

Accordingly, Table 2.3, by Statistics South Africa (2006:6), demonstrates that there has been a progressive waning in the implied growth rate for the South African population between 2001 and 2006. The inclusive rate of growth for 2005–2006 is projected at 1.06 per cent with a lower rate for females than males.

Table 2.3 Estimated annual population growth rates (%), 2001 to 2006 (Statistics South Africa, 2006:6)

Estimated annual growth rate (%) for time period:					
	2001-2002	2002-2003	2003-2004	2004-2005	2005-2006
Male	1.27	1.24	1.21	1.20	1.09
Female	1.23	1.20	1.16	1.14	1.02
Total	1.25	1.22	1.19	1.17	1.06

2.2.4 Economic impact of HIV

Those regions with a higher prevalence or incidence of HIV infection, like sub-Saharan Africa, is likely to bear the greatest brunt of the economic burden of HIV. Over and above the

direct costs of treatment and care, the encumbrance related to lost economic productivity as a result of premature morbidity and mortality from HIV is a further critical loss to any society (Beck *et al.*, 2001:14).

Worryingly, only 2.00 per cent of those who need treatment on the African continent are receiving it (Ijumba *et al.*, 2004:332). Several years after UNGASS, antiretroviral therapy (ART) coverage for people in low and middle income countries continues to be exceptionally low, with barely about 400 000 (7.00 per cent) patients accessing ARVs in 2003 out of an estimated 6 million who require treatment.

Ijumba and co-workers (2004:327) specified that reasons indicated as responsible for poor access to ARVs in the developing world and predominantly in sub-Saharan Africa include the following:

- Financial limitations
- Inadequate management systems
- Ineffective health systems
- Clinical guidelines that are overly complex or inadequate
- Weak laboratory standards
- Defective coordination among players and stakeholders
- Stigma and prejudice against people living with HIV/AIDS

2.2.4.1 The influence of poverty and low socio-economic conditions on the spread of HIV.

AIDS and other sexually transmitted diseases are frequently more widespread in countries with lower socio-economic status.

A few explanations citing why low socio-economic conditions advance the spread of sexually transmitted infections are described by Evian (2003:21) as follows:

- The perceived “inferior status” of women leads to sexual exploitation and deterioration of relations between men and women. In several communities, women have almost no control over their sexual lives, and consequentially little means to avert sexually transmitted infections. The situation is often exacerbated by poverty, and this further enhances the spread of sexually transmitted infections.

- Migrant work and family disruption is a result of high unemployment levels. People are forced to abandon their homes and hence their loved ones, friends, familiar surroundings and local community life. In consequence, migrants often find themselves in lonely, harsh, hostile or estranging surroundings. The ensuing natural need for sex and intimacy results in risky multiple-partner sexual relationships.
- Women often have to turn to prostitution to earn sorely needed money for food and basic needs, and to help raise their children. Young girls may also have transactional sex with older men as a means to earn an income.
- Health care services are often not easily accessible to people in poor living conditions. Therefore, persons with sexually transmitted infections are often not treated and the infections spread more easily.
- Deficient education and low literacy levels contribute to lack of awareness of how to avoid diseases like AIDS. This undermines educational efforts.
- People often abuse alcohol, or turn to drugs as a means of escapism from the reality of everyday hardships. This promotes loss of inhibition and increases the likelihood of sex with multiple partners.
- Family and community life are additionally strained by criminal and violent events that are abundant in urban or poverty-stricken areas.
- Many of the issues depicted above also bring about the collapse of the conventional traditions, customs, values and cultural practices in a society. The norms of accepted sexual conduct and constraints in a community are usually governed by these practices. When these norms are done away with, it often initiates multiple sexual partnerships and indiscriminate sexual behaviour (Evian, 2003:21).

Economic disempowerment can be triggered by poverty and redundancy. Gender vulnerability stems from this economic incapacity and this manipulates choice of sexual conduct and introduction to broader sexual networks. Greater exposure to risk factors such as multiple sexual partners or prostitution, intensify susceptibility to HIV for persons who undertake job hunting, mobile types of employment or migrant labour (South Africa, 2007a:34).

According to the Reports on Mobile Populations and HIV/AIDS by the International Organization for Migration in conjunction with the United Nations Aids Reference Group (IOM-UNAIDS, 2003:8) "mobile types of employment" may refer to informal merchants, sex

workers, domestic workers, border-traversing labourers, agricultural farm workers, migrant employees (e.g. miners, builders, and militia), long-distance transport drivers, travelling vendors and business travellers, as well as refugees and internally displaced persons.

The prevalence and distribution of the outbreak is essentially influenced by many compelling social, political, structural and economic aspects (Shisana *et al.*, 2005:xix).

Poverty acts within a socio-epidemiological framework via multiple means as a risk factor for potential HIV infection. It operates by means of various interconnected issues, such as disproportionate income distribution and gender-based economic disparities, or poor governance which leads to deficient public health structure (Piot *et al.*, 2007:1571-1572).

Elevated vulnerability to HIV transmission has been linked to poverty-related influences. These stressors are the result of the destitute state of affairs in townships, including inadequate and crowded accommodation, as well as unsatisfactory services relating to health and sanitation, transport and food. The situation is further worsened by economic and social issues including unemployment, ineffective education, violence and crime (Kalichman *et al.*, 2006:1641-1642).

2.2.4.2 Impact of HIV on women

The San Francisco Aids Foundation postulates that presently, virtually half of the 40 million people living with HIV worldwide are represented by women (SFAF, 2006a:1). Women are affected by AIDS most harshly in areas where heterosexual sex is the prevailing mode of transmission. All the same, women (and men) are additionally at risk of acquiring HIV due to unprotected sex, prostitution, and injecting drugs with contaminated needles (SFAF, 2006a:1).

There is a high prevalence of teenage pregnancy in South Africa, yet not enough attention has been called to teenage girls as a target group. The reality that women and girls are more heavily affected by the epidemic than men and boys remains a fundamental concern to the South African National response regarding HIV/AIDS (South Africa, 2007a:35).

The progression and distribution of HIV in women can be affected by an array of gender inequalities. Societal inequalities that women have to cope with can thwart their access to accurate information, quality health care, and suitable emotional assistance pertaining to aspects such as (SFAF, 2006a:1):

- Child care or guardianship
- Food or accommodation

- Reproductive and gynaecological information and services
- Poverty and hardship
- Obtaining providers and organisations that are perceptive of women's needs
- Legal concerns, for instance employment, housing, divorce, and child custody
- Social and emotional matters, including domestic violence, forced sex, and isolation
- Pregnancy and motherhood or single parenting

Unfortunately, South Africa is one of the highest ranking countries pertaining to violence against women worldwide, with more than 53 000 cases of rape reported to law enforcement authorities in 2000, accounting for 123 rapes reported per 100 000 population (South Africa, 2007a:31).

Incidences of sexual assault correlate with a way of life accommodating of violence. It involves destructive mind-sets (for example, premeditated transmission of HIV) and is also associated with the inability to make beneficial choices or to act fittingly in response to HIV prevention campaigns. The occurrence of sexual assault has also been associated with the threat of HIV infection (South Africa, 2007a:31).

An environment is produced for men to have several simultaneous sexual mates and their disinclination to make use of condoms is promoted by inequality over dominance and command in relationships (South Africa, 2007a:32).

Women evidently bear the brunt of the HIV/AIDS epidemic, which should draw attention to the issue of gender vulnerability that necessitates serious contemplation as one of the elements that should be focused on to expand women empowerment and security. Women also routinely shoulder the burden of nursing sick relatives and taking the lead in HIV/AIDS projects in their communities. Taking the high prevalence and incidence of HIV amongst women into consideration, it is crucial that their deep-seated participation in, and derivation of benefits from HIV/AIDS initiatives grow to be a main concern (South Africa, 2007a:35).

2.2.4.3 Impact of HIV on children

A considerable number of South African children are living with HIV and AIDS. A survey conducted by the HSRC (Human Sciences Research Council) in 2005 estimated that there were approximately 129 621 children aged between two and four years and 214 102 children in the age group five to nine years living with HIV or AIDS (Shisana *et al.*, 2005:142). HIV/AIDS was considered to be responsible for inflating the mortality of children under five years of age in South Africa by 42.00 per cent in 2004. (South Africa, 2007a:37).

The HIV/AIDS epidemic that is currently ravaging South Africa, will affect all children in one way or the other, and will continue to do so for the foreseeable future. Yet a number of children will be more negatively afflicted than others – predominantly those children who are born HIV-positive or are infected soon after birth (Gow *et al.*, 2002:4).

Adequate AIDS treatment and care is commonly not accessible to children in view of the fact that existing services are predominantly adult-oriented. There are still significant hurdles concerning the proficiency of personnel in the health care sector and their ability to supervise and care for children with AIDS, in addition to the need for development of suitable pediatric ART formulations (South Africa, 2007a:37).

If access to antiretroviral drugs is lacking, these children will suffer, living only short lives and typically dying in pain. If the children of HIV-positive parents are in good health, they will be adversely affected throughout their parents' illnesses and as a rule be confronted with harsh outcomes once one or both of their parents die (Gow *et al.*, 2002:4).

Minors (e.g. children younger than 18 years of age) encompass 40.00 per cent of the South African populace. It was approximated in 2004 that about 2.2 million children were orphans (implying that 13.00 per cent of all children under 18 had suffered the loss of either parent). Virtually half of these orphans' parents passed away as a consequence of AIDS (South Africa, 2007a:36; UNAIDS, UNICEF & USAID 2004:7-12, 26).

The children in those families that take in orphans will be adversely affected since fewer resources are on hand for their care and development, since these households often function in very resource constrained circumstances to begin with. Even children coming from unscathed households will be involved as their playmates leave school, through disintegration of their households following death, or suffer the loss of their friends as abandoned children are forced to provide for themselves and relocate away from their homes and villages seeking resources to survive (Gow *et al.*, 2002:4).

Children are subjected to physical, emotional and developmental impediments as a consequence of the epidemic (Gow *et al.*, 2002:4). Children in severely disadvantaged households are usually affected to the worst degree, and some may be subjected to deficiency pertaining to somatic, material and psychosocial matters. Their health is also under threat due to poverty, parental negligence and absence of nurturing surroundings. These children are frequently removed from guardians and siblings and passed on to reside with other relatives or different caretakers or other social groups (South Africa, 2007a:36).

Child sexual molestation is also a risk factor for HIV infection in vulnerable children (Kistner *et al.*, 2004:25). Despite the fact that there is little data on the magnitude of child sexual abuse in South Africa, it may be rather widespread and therefore it is a threat that necessitates enquiry (South Africa, 2007a:37).

2.2.4.4 Impact of HIV on the South African National health care system

The South African Department of Health has set an objective for reduction of HIV infection by 50.00 per cent by 2011 (South Africa, 2007a:10). This programme aims to furnish 80.00 per cent of sufferers and their families with care in a country with the second highest incidence of HIV in the world (South Africa, 2007a:12).

The hospital sector is undoubtedly the most involved department of the public health sector in the fight against HIV. HIV-related admissions comprised 24.00 per cent of all public hospital admissions and 12.50 per cent of the total public health budget in the year 2000. The cost of both private and public health care sectors' inpatient and ambulatory health care is expected to escalate swiftly (Badri *et al.*, 2006:48).

Health analysts are hopeful that South Africa is undergoing a basic revision in its official attitude to a disease that by now infects 5.5 million of the nation's 47 million people and takes the lives of an estimated 1 000 South Africans on a daily basis (News24, 2007:1).

By late December 2005, the Joint United Nations Programme on HIV/AIDS (UNAIDS) estimated that a total of 111 827 South Africans were accessing free antiretroviral treatment in the 200 public health sector facilities across 53 districts and a further 60 000 via the private sector. Some 2 369 facilities were also providing voluntary counselling and testing in 2004 (UNAIDS, 2005:1).

The intermingling of weak infrastructure and human capacity limitations are key challenges in intensifying HIV and AIDS programmes. Already overstretched health services being additionally burdened by the AIDS pandemic, have further compounded the capacity predicament (UNAIDS, 2005:1).

In addition, numerous health care professionals are inadequately prepared for providing AIDS care. Comparatively few have been educated regarding the clinical management of the disease, or pertaining to counselling and testing. Professional nurses are responsible for supervision of primary health care facilities, yet the majority are not trained in clinical use of antiretrovirals. Ensuring balance between interventions to provide access to antiretroviral therapy and broader social and economic interventions to assuage poverty and malnutrition, will be one of the key challenges confronting South Africa (Ntuli *et al.*, 2004:4).

HIV/AIDS has an impact on the dynamics of provision as well as requirement (e.g. supply and demand) of health care structures. There are dual consequences of HIV on human resources and supply in health systems. HIV/AIDS brings about epidemiological, demand and mortality profiles that quickly shift and vary in patients, which in turn has a negative impact on morale and stress levels in health care workers. Secondly, HIV infection in the actual caregivers is also a challenge (South Africa, 2007a:44).

Extensive use of antiretroviral regimens in more developed countries has significantly diminished AIDS-related morbidity and mortality, and perinatal transmission has been nearly eradicated by the application of antiretroviral prophylaxis among HIV-1-positive pregnant women (Wood *et al.*, 2000:2095).

There has been a considerable decrease in the price of antiretroviral drugs over the past couple of years, largely due to the generic forms of some of these drugs being made available. A number of multinational drug companies that manufacture originator products have also reduced prices and are allegedly selling these antiretroviral drugs at 'no-profit' or 'at a financial loss' in developing countries (Pinheiro *et al.*, 2006:1746).

Valuation of HIV-related health care costs is evolving, basically reflecting the achievements in development of successful prevention and treatment approaches; expanded screening programmes; longer life expectancies of AIDS patients, accessibility of HAART; emergence of viral resistance to HAART, and the shifting demographics of patients newly diagnosed with HIV infection. Infected persons are increasingly those without health insurance (Roberts *et al.*, 2006:877).

Equally as important as even-handedness in the allotment of resources is the need to guarantee that the funds allocated to health are adequate to provide satisfactory levels of health care. The South African Department of Health aims to be treating just over 1 million patients with ART by March 2009 (Cleary *et al.*, 2005:59).

In countries in sub-Saharan Africa, expenditure for therapy and care are lower in absolute terms relative to industrialised countries. However, when expressed as a percentage of resources spent on health care delivery these costs are to be expected to represent a greater liability for developing countries (Beck *et al.*, 2001:14).

A comprehensive plan of action has been developed by the National Department of Health to address the South African HIV/AIDS epidemic (South Africa, 2006:5).

- The comprehensive programmes include the following:
 - Ensuring that the largest fraction of South Africans who are not infected with HIV at present remain uninfected. Educational efforts comprising of messages of prevention and on the subject of lifestyle and behaviour changes are consequently the vitally important bases in managing both the spread of HIV and the impact of AIDS.
 - Healthier nutrition and lifestyle choices to ensure and augment the health benefits of good nutrition and wholesome living for persons who are infected as well as those who are not infected.
 - Intensifying the utilisation of prophylaxis and treatment of opportunistic infections.
 - Suitable treatment of AIDS-related conditions to successfully manage those HIV-infected individuals who have acquired opportunistic infections.
 - Supplying antiretroviral therapy for patients exhibiting low CD4 counts to improve functional health status and to prolong life.
 - Integration of traditional and complementary medicine into the comprehensive care, management and treatment programme.
 - Making a comprehensive continuum of care, support and treatment available.
 - Ensuring the fulfilment of the standard of non discrimination in the provision of services overall and specifically in the provision of HIV and AIDS services.
- Fortification of the National Health System overall to facilitate the effective distribution of comprehensive HIV and AIDS care and treatment and other similarly imperative health care priorities and programmes. These encompass the improvement in laboratory services, information systems, human resources and capacity development, drug procurements and distribution (South Africa, 2006:5).

Two of these aforementioned factors concentrate on prevention, and six topics relate to HIV and “medicine” treatments. This may perhaps have a fairly important influence on antiretroviral treatment resources – the accessibility and distribution accompanied by the required health worker counselling skills.

The programme is anchored in the principle of universal access to care, corresponding to the stipulation of the Constitution of the Republic of South Africa (South Africa, 2006:6) – widespread access to basic and unbiased primary health care services, management and treatment for all, despite race, colour, gender and economic status. This agenda endeavours to deal with the challenge of making service provision available impartially in both rural and urban settings without compromising the quality of care. The goal of the Comprehensive Plan is to attain a balance between areas that can straightforwardly put the programme into operation and those that need supplementary resources and investments to improve their general health capacity (South Africa, 2006:6).

It is important to set targets, both internationally and locally. For instance, the World Health Organization set its aim on treating 3 million people in the developing world by the end of 2005. Even though these objectives were not achieved by then, it created the drive to upgrade treatment access in various regions worldwide – including South Africa and countries that did not have internal capability to start ART up till then (Hassan, 2006:32).

Highly Active Antiretroviral Therapy is not yet readily accessible. In 2004, in the order of 5 million South Africans were infected with HIV, and in excess of 500 000 people could derive benefit from HAART, yet only about 20 000 were receiving treatment. The bulk of individuals who had access to the drugs received it through private sector medical schemes or workplace programmes (Ntuli *et al.*, 2004:4).

The Ministry of Health has reported that a total of 44 600 people were receiving antiretroviral therapy throughout all nine provinces via the public sector as at March 2005. WHO/UNAIDS approximations indicate that nearly 60 000 additional people were receiving treatment through private-sector suppliers in March 2005 (WHO, 2005:1).

By January 2006, an estimated total of 200 000 – 220 000 South Africans were receiving ARV treatment in both the public and private sectors (Hassan, 2006:33). Approximately 110 000 – 120 000 of these people were apparently accessing ARVs in the public sector, with a further 90 000 – 100 000 accessing it by means of the private and not-for-profit sectors (Hassan, 2006:33).

2.3 What is HIV?

HIV belongs to the genus *Lentivirus* of the family *Retroviridae* and has been classified into two types according to the Oxford Southern Africa Handbook of HIV Medicine (Wilson *et al.*, 2004:15):

- HIV Type 1 (HIV-1), the source of the global pandemic
- HIV Type 2 (HIV-2), less virulent than HIV-1, and mainly limited to West Africa, with some degree of distribution to other countries.

2.4 Transmission of HIV

Epidemiological studies have verified that HIV is a retrovirus that is transmitted among humans by means of three primary methods: sexual contact, parenteral transmission via infected blood or blood products and vertical transmission from mother to child. These exposure categories are the source of practically all cases of HIV transmission (Postma *et al.*, 2004; Greenblatt and Hessol, 2000:3).

2.4.1 Methods of transmission

HIV is generally spread in three ways. The major modes of transmission, in order of importance according to Barnett and Whiteside (2002:38) are the following:

2.4.1.1 Unsafe sexual intercourse

The American National Institute of Allergy and Infectious Diseases state that the overwhelming majority of HIV infections worldwide are the consequence of sexual transmission with an infected partner (NIAID, 2007:1), as semen and possibly cervical secretions are markedly infectious (Adler, 2001:2).

Anal sex has the highest element of risk for transmitting HIV of all sexual practices. During anal intercourse the lining of the anal-rectal area is damaged fairly easily, which permits the virus to enter the body without difficulty (Avert, 2008b:1). In addition, vaginal sex remains an effective form of transmission (Evian, 2003:14).

A slight possibility that HIV can be transmitted through oral sex does exist, and a person is particularly at risk if he/she has oral abrasions or gum disease (Barnett & Whiteside, 2002:38).

Sexual transmission of HIV can occur indiscriminately through male-to-female, female-to-male, male-to-male, and female-to-female sexual contact from an infected partner to an uninfected partner (Greenblatt & Hessol, 2000:3).

Transmission of HIV is facilitated by the presence of other sexually transmitted diseases (UNAIDS, 2008:4) and these other infections can markedly increase the risk of transmission of HIV through sexual intercourse (Beck *et al.*, 2001:15). Apparently other genital ulcers or lesions, which may be attributable to syphilis, chancroid, gonorrhoea, herpes virus and other sexually transmitted infections (STIs) aid the HIV virus in entering the body (Evian, 2003:13).

2.4.1.2 Mother to child during pregnancy, childbirth and via breastfeeding

HIV-infected pregnant women can transmit the virus to their infants *in utero* during pregnancy (UNAIDS, 2008:1, 3) and additionally at birth (NIAID, 2007:2). According to the South African Department of Health (South Africa, 2000:1), in excess of 90.00 per cent of pediatric HIV infection is transmitted from mothers to their children. The majority of HIV-positive babies are infected on the point of birth or via breastfeeding (South Africa, 2000:1) as the virus can also be transmitted through breast milk (UNAIDS, 2008:1,3).

The probability of an infant acquiring HIV from an infected mother is to the extent of 25.00 per cent to 35.00 per cent (South Africa, 2000:1). Thus there is approximately a 1 in 3 chance an infant will be born with HIV infection to a mother that is HIV positive (Evian, 2003:16).

Apparently a woman is more likely to transmit the virus to her foetus during pregnancy when she presents with the following (Evian, 2003:16):

- Recent infection (she has become infected just prior to or during the pregnancy)
- She has a high viral load
- She has symptomatic HIV disease
- She has a low CD4 count

2.4.1.3 HIV-infected blood

HIV transmission via infected blood has been classified by Barnett and Whiteside (2002:38) (in order of importance) in the following way:

- Use of infected blood or blood products, including transfusions of infected blood or blood clotting factors (CDC, 1999:1). Other methods of transmission include the receipt of infected donated organs and even semen (Adler, 2001:2).
- Intravenous drug use with infected blood-contaminated needles, through sharing of needles and syringes for intravenous drug use (NIAID, 2007:1) or via infected

needles and syringes (e.g. accidental needle pricks), razor blades and other sharp utensils (Evian, 2003:15).

- Other modes of transmission with reference to blood, such as bleeding wounds (Barnett & Whiteside, 2002:38). In rare cases it is possible for HIV to enter the body through an open skin wound or sore (Evian, 2003:15).

Most infectious phases

Evian (2003:17) noted that the most infectious phases during which an HIV-infected person is almost certain to pass on the HIV virus would include the following:

- The first 4 to 8 weeks after becoming infected with the HIV virus
- During periods of high HIV viral load
- Throughout the later phase of infection, when symptoms of HIV infection/AIDS appear

2.4.2 No transmission of HIV

An advantage for humankind lies therein that HIV is a rather fragile virus and it is hard to transmit (Barnett & Whiteside, 2002:38). HIV is not well equipped for survival in the outside environment, meaning that the likelihood of environmental transmission is highly improbable (CDC, 1999:1).

Its solitary means of transmission is through contaminated body fluids, unlike a variety of other diseases. The virus has to enter the body in adequate quantities and then pass through an entry point in the skin and/or mucous membranes into the bloodstream to successfully infect a person (CDC, 1999:1). HIV has been shown to be present in semen, cervical secretions, lymphocytes, cell free plasma, cerebrospinal fluid, tears, saliva, urine, and breast milk. These fluids, however, do not all necessarily transmit infection because the concentrations of virus in them vary to a great extent (Adler, 2001:2). The virus is unable to penetrate normal, healthy and undamaged skin, and will also not easily enter through the mouth or eye (Evian, 2003:18).

HIV is a comparatively large virus and thus has a short half-life *in vitro*. It can solely subsist in primates and cannot be transmitted via casual or surface contact or via insect bites (Greenblatt & Hessel, 2000:3).

According to Evian (2003:18) transmission of HIV does not normally occur by the following means:

- Airborne routes, for example coughing, sneezing, laughing, talking and kissing (Avert, 2008b:1)
- Casual or simple skin contact, such as hand shaking, hugging and touching, etc. (Avert, 2008a:1)
- Surface contact (Greenblatt & Hessol, 2000:3), including shared food, water, or on plates, cups, spoons, baths, pools and showers, or contact with towels, bed linen, clothes, etc. (Evian, 2003:18)
- Insect bites, i.e. mosquito bites, are not recognised as a method of transmission of HIV from one person to another since HIV cannot reproduce in insects (UNAIDS, 2008:4)

Evian (2003:18) confirms that HIV does not appear to be transmitted via casual contact. There is no definite indication that HIV is spread through typical, everyday, casual contact between individuals.

2.4.3 Factors facilitating transmission

The mode of transmission and the particular circumstances both influence the rate of transmission from the infected host to the uninfected recipient (Greenblatt & Hessol, 2000:3).

The relationship between the mode of transmission and the number of infections incurred per exposure are illustrated in Table 2.5.

Table 2.4 Probability of HIV-1 infection per exposure (Barnett and Whiteside, 2002:38)

Mode of transmission	Infections per 1 000 exposures
Female-to-male, unprotected vaginal sex	0.33 - 1
Male-to-female, unprotected vaginal sex	1 - 2
Male-to-male, unprotected anal sex	5 - 30
Needle stick (injection needles)	3
Mother-to-child transmission	130 - 480
Exposure to contaminated blood products	900 - 1 000

According to Greenblatt and Hessel (2000:4), several factors can have an effect on transmission of HIV infection, including features of the HIV-infected host, the recipient, and the degree of infectivity and quantity of the virus. This is demonstrated in Table 2.4:

Table 2.5 Biologic and host-related factors affecting sexual transmission of HIV (Greenblatt & Hessel, 2000:5)

Biologic factors	Host-related Infectivity Factors		
	HIV concentration in genital secretions	Infectiousness (Transmission)	Susceptibility (Acquisition)
Mutation of chemokine-receptor gene	?	?	---
Late stage of HIV infection	++	+++	Not applicable
Primary HIV infection	++	++	Not applicable
Antiretroviral therapy	-	--	-?
Local infection	++	+	++
Presence of cervical ectopy?	++	+	++
Presence of foreskin?	?	++	++
Method of contraception			
Barrier	Not applicable	---	---
Hormonal contraceptives	++	+?	+-
Spermicidal agents	?	-?	+-
Intrauterine devices	?	?	++
Menstruation	?	++	+
Factors that lower cervicovaginal pH?	-?	-?	-?
Immune activation	+	+	+
Genital tract trauma?	+	++	++
Pregnancy	++	+	+

2.4.4 Patterns of HIV spread

Already a decade ago, Webb (1997:11) described the three global epidemiological patterns of HIV spread by pointing out the following:

- Pattern I spread occurs mainly by means of homosexual activity and intravenous drug use. The majority of those infected by pattern I spread are male, with a male-to-female infection ratio of about 10-15:1. Regions with Pattern I spread are the United States, Western Europe and Australia.

- Pattern II spread takes place primarily by means of heterosexual intercourse with the male-to-female ratio at roughly 1:1. Pattern II spread is also accountable for the increasing incidence of paediatric AIDS due to vertical transmission from mother to child (Webb, 1997:11). Districts affected by Pattern II include sub-Saharan Africa, and increasingly, Latin America, together with parts of South America and India. It is assumed that Pattern II eventually takes over from Pattern I as the principal manner of transmission in terms of the number of cases, if behavioural adjustment is negligible and HIV starts to spread through the heterosexual population. In certain countries, including Britain, the reproductive rate has thus far been low enough to postpone the extensive spread of the virus from high risk groups to the general 'background' population (Webb, 1997:11).
- The spread of the virus in Pattern III regions is minor in comparison with Pattern I and Pattern II areas. Infected needles are often to blame (as in a children's hospital in Romania) or the virus is mostly contained within a small prostitute population (Webb, 1997:11). There is evidently the potential for a Pattern III area to progress speedily into a Pattern II area; countries of South East Asia (e.g. Thailand), with their active sex tourism industry are most susceptible. Eastern Europe is also a very vulnerable area, owing to the taboo nature of sexual intercourse in some societies. For instance, in Russia, homosexual activity was prohibited by law until recently, and this could surely have hampered the efficiency of education programmes (Webb, 1997:11).

The spread of HIV in all regions is for the largest part pre-dominant in urban areas, with an estimated urban-rural ratio of 3.6:1 in sub-Saharan Africa (Webb, 1997:12). The reason for this geographical differentiation is inherent in the concentration of high risk behaviour in urban regions, related to prostitution and poly-amorous behaviour, in addition to the fact that cities and large towns are frequently the first entry point of the virus into a country, setting in motion a 'cascade' distribution down the urban hierarchy (Webb, 1997:12).

2.5 The stages of HIV disease

HIV infection can be regarded as a chronic disease that results in a continuous weakening of the immune system which may cause secondary neoplasms or opportunistic infections and, ultimately, death (Tramarin *et al.*, 2004:44).

WHO clinical staging of HIV/AIDS for adults and adolescents with confirmed HIV infection (2006)

Despite the fact that there are hypothetical stages into which HIV disease progression is categorised, these stages lack readily recognisable margins that make them discrete or conspicuously divergent from each other in a real-life practice situation. Patients infected with HIV do not automatically undergo well-defined progression of HIV infection from Stage I to Stage IV. The CD4 cell count relative to the viral load will determine the advancement of opportunistic infections and symptoms associated with HIV (Van Dyk, 2008:51).

- **Clinical stage I**

Infected individuals present no symptoms during the asymptomatic latent (or “silent”) first clinical stage of HIV infection. Patients usually have a CD4 cell count in the region of 500 to 800 cells/mm³, compared to the typical CD4 cell count of nearly 600 to 1 500 cells/mm³ in healthy, HIV-negative persons (Van Dyk, 2008:53).

Characteristics of the first clinical stage include (WHO, 2006:1):

- Asymptomatic
- Persistent generalised lymphadenopathy

- **Clinical stage II**

The first minor indications of HIV disease typically become apparent during the second stage of infection. Throughout the minor symptomatic stage, patients usually display a CD4 cell count of approximately 350 to 500 cells/mm³ (Van Dyk, 2008:54).

During this stage individuals with HIV antibodies start displaying one or more of the following symptoms (WHO, 2006:1):

- Unexplained moderate weight loss (<10% of presumed or measured body weight)
- Recurrent respiratory tract infections (sinusitis, tonsillitis, otitis media and pharyngitis)
- Herpes zoster
- Angular cheilitis
- Recurrent oral ulceration
- Papular pruritic eruptions
- Seborrhoeic dermatitis

- Fungal nail infections

- **Clinical stage III**

The unrelenting weakening and deterioration of the immune system trigger the manifestation of major symptoms and opportunistic infections. The CD4 cell count now drastically decreases while the viral load increases significantly. The major symptomatic stage generally correlates with a CD4 cell count in the order of 200 to 350 cell/mm³ (Van Dyk, 2008:54-55).

According to the World Health Organization (WHO, 2006:1) this stage is characterised by factors such as the following:

- Unexplained severe weight loss (>10% of presumed or measured body weight)
- Unexplained chronic diarrhoea for longer than one month
- Unexplained persistent fever (above 37.5°C intermittent or constant, for longer than one month)
- Persistent oral candidiasis
- Oral hairy leukoplakia
- Pulmonary tuberculosis (TB)
- Severe bacterial infections (such as pneumonia, empyema, pyomyositis, bone or joint infection, meningitis or bacteraemia)
- Acute necrotising ulcerative stomatitis, gingivitis or periodontitis
- Unexplained anaemia (<8g/dl), neutropenia (<0.5x10⁹ per litre) and/or chronic thrombocytopaenia (<50x10⁹ per litre)

- **Clinical stage IV (AIDS)**

Patients are described as having developed AIDS solely when they undergo the final phase of HIV infection. The major symptomatic stage commonly progresses into AIDS within only about 18 months in patients who are not treated with antiretrovirals. Extremely elevated viral loads and serious immune deficiencies in addition to CD4 cell counts lower than 200 cells/mm³ are typical of patients with AIDS (Van Dyk, 2008:55).

Symptoms of AIDS include the following (WHO, 2006:1):

- HIV wasting syndrome*
- Pneumocystis pneumonia
- Recurrent severe bacterial pneumonia
- Chronic herpes simplex infection (orolabial, genital or anorectal of more than one month's duration or visceral at any site)
- Oesophageal candidiasis (or candidiasis of trachea, bronchi or lungs)
- Extrapulmonary tuberculosis
- Kaposi's sarcoma
- Cytomegalovirus infection (retinitis or infection of other organs)
- Central nervous system toxoplasmosis
- HIV encephalopathy**
- Extrapulmonary cryptococcosis including meningitis
- Disseminated non-tuberculous mycobacterial infection
- Progressive multifocal leukoencephalopathy
- Chronic cryptosporidiosis
- Chronic isosporiasis
- Disseminated mycosis (extrapulmonary histoplasmosis or coccidiomycosis)
- Recurrent septicaemia (including non-typhoidal *Salmonella*)
- Lymphoma (cerebral or B-cell non-Hodgkin)
- Invasive cervical carcinoma
- Atypical disseminated leishmaniasis
- Symptomatic HIV-associated nephropathy or symptomatic HIV-associated cardiomyopathy

**HIV wasting syndrome: weight loss of >10% of body weight, plus either unexplained chronic diarrhoea (>1 month) or chronic weakness and unexplained prolonged fever (>1 month).*

***HIV encephalopathy: clinical findings of disabling cognitive functioning and/or motor dysfunction interfering with activities of daily living, progressing over weeks to months, in the*

absence of a concurrent illness or condition other than HIV infection which could explain the findings. (Regensberg and Whitelaw, 2007:7).

2.5.1 Primary infection

Primary HIV infection is defined by the San Francisco Aids Foundation (SFAF, 2006b:1) as the initial phase of HIV disease. This stage characteristically lasts only about a fortnight, frequently causing flu-like symptoms while the virus first establishes itself in the body (Avert, 2007:1). The term acute HIV infection can also be used to define the phase between initial infection with HIV and production of antibodies by the immune system in response to infection against the virus (usually after 6 to 12 weeks) which can be detected by an HIV test (SFAF, 2006b:1).

During this period, large amounts of HIV are present in the peripheral blood and this triggers production of HIV antibodies and cytotoxic lymphocytes in a response known as seroconversion. On performing an HIV antibody test prior to complete seroconversion it may give a false negative result since sufficient antibodies have not yet been produced by the body (Avert, 2007:1).

Nearly 70.00 per cent of people recently infected by HIV will suffer from some symptoms that mimic influenza throughout this stage, including fevers, chills, night sweats, and rashes which ordinarily persist only for a number of days, after which the infected person feels and looks in full health again (SFAF, 2006b:1). The remaining 30.00 per cent of people either are not subjected to symptoms of acute infection or their symptoms are so insignificant that they may not be aware of them (SFAF, 2006b:1).

Within three to five days during acute HIV infection, the virus progresses to the lymph nodes. Subsequently HIV actively replicates and rapidly unleashes new virus particles into circulation for about two months. A very high viral load (VL) is often detectable in HIV-infected people during this stage. Given that antibody production takes around one to three months, people with acute HIV infection typically will not test positive for HIV antibodies (SFAF, 2006b:1).

Conventionally a window period occurs between infection and production of antibodies and this lasts about three months for most of the population. In extremely rare cases, a person may take six months to produce antibodies. An HIV antibody test must be done three months or longer after to exposure to the virus to obtain a definite result of HIV status. An additional test should be done six months after the exposure had occurred to ensure accurate results (SFAF, 2006b:1).

2.5.2 Asymptomatic stage

HIV infection brings about a characteristic steady deterioration of the immune system along with a prolonged interlude of clinical dormancy where the virus is undetectable (Regensberg and Whitelaw, 2007:9). The duration of this window-period differs among patients, but usually lasts eight years (Regensberg and Whitelaw, 2007:9). Patients who do not receive antiretroviral treatment ultimately contract one or more AIDS-defining diseases or general cachexia that frequently ends in fatality, but individual patients' immunity wanes at unpredictable rates. A minute fraction of patients have very low viral loads and do not go through disease progression, whereas patients presenting high viral loads undergo more speedy disease progression. The instant the patient's CD4 count slumps below 50, median survival is 12 months unless antiretroviral treatment is given (Regensberg & Whitelaw, 2007:9).

Becoming HIV antibody positive

A large number of people are often unaware that they have been infected with HIV. Some may experienced short-lived seroconversion illness soon after infection had occurred. The condition may present as a sore throat and a fever or a rash, or, rarely, more severe illness (Aidsmap, 2004:1).

2.5.3 Seroconversion illness

The stage during which an HIV-positive person's immune system counters the infection by generating antibodies against the virus is referred to as seroconversion. The majority of people develop antibodies in the course of three months following infection. Certain patients can take up to six months to produce antibodies (SFAF, 2006b:1).

Prior to the emergence of antibodies to HIV in the blood, several people may develop characteristic symptoms of seroconversion illness after exposure to HIV. Antibodies typically become detectable simultaneously with this illness.

The symptoms (Aidsmap, 2004:1; Van Dyk, 2008:52) include the following:

- Prolonged mild fever (4 – 14 days)
- Aching muscles and joints
- Swollen lymph nodes
- Red blotchy rash over the trunk
- Sore throat (pharyngitis)

- Ulceration in the mouth or genitals
- Diarrhoea and gastrointestinal symptoms
- Severe headaches
- Aversion to the light
- Exhaustion or tiredness

Much more uncommon symptoms are paralysis, meningitis and opportunistic infections due to severe immune suppression (Aidsmap, 2004:1). Some patients suffer an illness sufficiently serious to necessitate hospitalisation. The longer the duration and the higher the severity of the illness, the more likely an untreated patient would be to develop AIDS within five years (Aidsmap, 2004:1).

2.5.4 Immunopathogenesis of acute infection

The acute symptomatic illness is presumably triggered by the significant escalation in plasma viremia that ensues during the acute infection, and it is linked to stimulation of both inherent and adaptive immune responses in reply to the virus. Not much information is currently available on the subject of innate immunity (e.g. natural killer cells) in the course of acute infection. However, significant new insights into HIV pathogenesis and prospects for immune-based therapies for HIV infection have come to light following studies of adaptive immunity in persons with acute HIV infection (Robbins & Walker, 2003:314-315).

2.5.5 Symptomatic stage

Evian (2003:9) postulates that signs and symptoms are usually attributable to, *inter alia*, the following:

- New infections, particularly opportunistic infections
- Reactivation of old, inactive or dormant infections, such as tuberculosis, herpes or unusual cancers
- The HIV virus itself and its impact on various organs and tissues in the body

The stage of viral infection caused by HIV (human immunodeficiency virus) where symptoms have presented but where no signs of development of AIDS have yet set in (which entails life-threatening infections), is referred to as early symptomatic HIV infection. It is distinguished by signs and symptoms representative of HIV infection but not full-blown AIDS. During asymptomatic HIV infection these symptoms are ordinarily absent (Ghandi, 2006:1).

Table 2.6 Symptoms associated with acute HIV infection (Robbins & Walker, 2003:316)

Symptom	Incidence (%)
Fever	96
Lymphadenopathy	74
Pharyngitis	70
Rash ^a	70
Myalgias or arthralgias	54
Diarrhoea	32
Headache	32
Nausea and vomiting	27
Hepatosplenomegaly	14
Weight loss	13
Thrush	12
Neurologic disorders ^b	12

^aIncluding erythematous macupapular, vesicopapular, vasculitis, and oral/genital ulcers.

^bIncluding meningoencephalitis, aseptic meningitis, peripheral neuropathy, facial palsy, Guillian-Barré syndrome, brachial neuritis, cognitive impairment, and psychosis.

The conversion from HIV infection to HIV disease is signified by the onset of symptoms. The patient does not show signs of AIDS symptoms like opportunistic infections or particular cancers or a CD4 count below 200 at this stage of HIV infection (Ghandi, 2006:1).

According to Ghandi (2006:1) symptoms would include the following:

- Mouth disorders
- Oral hairy leukoplakia of tongue, due to a viral infection
- Oral thrush
- Gingivitis
- Prolonged diarrhoea
- Skin disorders
- Seborrheic dermatitis
- Molluscum contagiosum
- Chronic dermatophyte infection
- Swollen lymph glands

- Excessive sweating or night sweats
- Bacterial pneumonia
- Prolonged fever
- Prolonged fatigue
- Malaise
- Weight loss
- Joint pain
- Peripheral neuropathy
- Pap smear indicating cervical dysplasia
- Recurrent herpes zoster infection that occurs over a very small patch of skin
- ITP (idiopathic thrombocytopenic purpura) which causes the number of platelets in the bloodstream to be very low

Symptomatic HIV infection

Ultimately HIV causes severe damage to the immune system. There are three key explanations regarding this: Years of HIV activity damages and causes deterioration of the lymph nodes and tissues; HIV mutates into more pathogenic and diverse strains, causing increased annihilation of T helper cells; the body cannot successfully keep pace with supplanting the destroyed T helper cells (Avert, 2007:1).

Symptoms develop in conjunction with the collapse of the immune system. Many of the symptoms seem mild at the outset, but worsen as the immune system deteriorates (Avert, 2007:1).

The cause of symptomatic HIV infection is essentially the manifestation of opportunistic infections and cancers, that can occur virtually throughout all the body systems, that the immune system would usually ward off. Symptomatic HIV infection is commonly distinguished by multi-system disease. The specific infection or cancer is typically treated accordingly, but the underlying cause remains the action of HIV as it destroys the immune system. The symptoms of immune suppression will continue to intensify except if HIV itself can be slowed down (Avert, 2007:1).

2.5.6 Advanced HIV (AIDS)

The Centers for Disease Control (CDC, 1993:1) defines AIDS as a combination of signs and symptoms and afflictions that stem from a compromised immune system. For an AIDS diagnosis to be confirmed, the definitive or presumptive diagnosis of one or more 'indicator diseases' must be made and laboratory evidence of HIV infection may possibly be mandatory, subject to certain criteria. Physicians in the United States make use of the following outline to arrive at an AIDS diagnosis:

- A diagnosis of AIDS can be made if laboratory evidence of HIV infection has been established and a definitive diagnosis of any of the indicator diseases has been made – regardless of the presence of other causes of immunodeficiency (CDC, 1993:1). The indicator diseases include
 - adolescents and adults with CD4 and lymphocyte counts lower than 200 cells/mm³;
 - candidiasis of the oesophagus, trachea, bronchi or lungs;
 - coccidiomycosis, disseminated (extrapulmonary);
 - cryptococcosis (extrapulmonary);
 - cryptosporidiosis with diarrhoea persisting more than 1 month;
 - cytomegalovirus disease of an organ other than the liver, spleen or lymph nodes in a patient older than 1 month;
 - herpes simplex virus infection causing a mucocutaneous ulcer (e.g. in eyes, nose, mouth, and genitor-anal areas) that persists for more than 1 month; or bronchitis, pneumonitis or oesophagitis caused by herpes simplex virus in a patient older than 1 month;
 - histoplasmosis, disseminated (extrapulmonary);
 - HIV encephalopathy; also called subacute encephalopathy due to HIV; also referred to as HIV dementia or AIDS dementia complex (ADC), which is clinically defined as disabling cognitive functioning or causing motor dysfunction interfering with the patient's occupation or activities of daily living, or loss of behavioural developmental milestones in the absence of a concurrent illness or condition;
 - HIV wasting syndrome, defined as involuntary weight loss of greater than 10% of body weight plus chronic diarrhoea or chronic weakness and fever in the absence of a concurrent illness or condition; also referred to as 'Slims disease';

- isosporiasis with diarrhoea persisting for longer than 1 month;
 - Kaposi's sarcoma;
 - lymphoma (primary) of the brain;
 - lymphoid interstitial pneumonitis (LIP) and/or pulmonary lymphoid hyperplasia affecting a child under 13 years of age;
 - mycobacterial disease including pulmonary infection, disseminated and extrapulmonary *Mycobacterium tuberculosis* disease;
 - *Mycobacterium avium*, disseminated;
 - Non-Hodgkin's lymphoma;
 - *Pneumocystis carinii* pneumonia;
 - progressive multifocal leukoencephalopathy;
 - salmonella septicaemia, recurrent;
 - toxoplasmosis of the brain;
 - strongyloidosis extraintestinal;
 - any combination of at least two of the following bacterial infections within a 2-year period affecting a patient less than 13 years of age: septicaemia, pneumonia, meningitis, bone or joint infection, or abscess of an internal organ or body cavity caused by haemophilus, streptococcus or other fever-inducing bacteria;
 - recurrent pneumonia;
 - invasive cervical cancer.
- A diagnosis of AIDS can be made if laboratory evidence of HIV is positive and any of the following indicator diseases are diagnosed presumptively (CDC, 1993:1). (A presumptive diagnosis is generally made in situations in which the patient's condition does not permit the performance of definitive testing.) Presumptively diagnosed indicator diseases include the following:
 - Candidiasis of the oesophagus
 - Cytomegalovirus retinitis with loss of vision
 - Kaposi's sarcoma

- Lymphoid interstitial pneumonitis and/or pulmonary lymphoid hyperplasia affecting a patient younger than 13 years of age
- Mycobacterial disease, disseminated
- *Pneumocystis carinii* pneumonia
- Toxoplasmosis of the brain in a patient older than one month
- A diagnosis of AIDS can be made if laboratory evidence of HIV infection is lacking or inconclusive but a definitive diagnosis of any of the following indicator diseases is made, provided other known causes of immunodeficiency are ruled out (CDC, 1993:1):
 - Candidiasis of the oesophagus, trachea, bronchi, or lungs
 - Cryptococcosis, extrapulmonary
 - Cryptosporidiosis with diarrhoea persisting longer than 1 month
 - Cytomegalovirus disease of an organ other than the liver, spleen, or lymph nodes in a patient older than 1 month
 - Herpes simplex virus infection causing a mucocutaneous ulcer that persists longer than 1 month; or bronchitis, pneumonitis or oesophagitis affecting a patient older than 1 month
 - Kaposi's sarcoma affecting a patient below 60 years of age
 - Lymphoma of the brain (primary) affecting a patient younger than 60 years of age
 - Lymphoid interstitial pneumonitis and/or pulmonary lymphoid hyperplasia affecting a patient younger than 13 years of age
 - Mycobacterium avium complex or Mycobacterium kansasii disease, disseminated
 - Pneumocystis carinii pneumonia
 - Progressive multifocal leukoencephalopathy
 - Toxoplasmosis of the brain in a patient older than 1 month
- A diagnosis of AIDS can also be made when laboratory evidence of HIV infection is negative. If all other causes of immunodeficiency are excluded and the patient has had either a definitive diagnosis of *Pneumocystis carinii* pneumonia or a definitive diagnosis of any of the indicator diseases of AIDS and a CD4 cell count less than 400 cells/mm³ (Evian, 2003:118).

2.6 Antiretroviral drugs

The routine treatment of HIV/AIDS with antiretroviral drugs has transformed HIV infection from an unvaryingly rapidly terminal illness to a somewhat expensive treatable, chronic disease. Triple therapy or highly active antiretroviral therapy (three-drug combinations of ARVs or HAART) in particular have had paramount impacts on HIV related morbidity and mortality in settings where these drugs are generally accessible. Objectives of ARV treatment are "*maximum, durable suppression of viral load, restoration and/or preservation of immune function, improvement of quality of life and reduction of HIV related [cit] morbidity and mortality*" (Martinson *et al.*, 2003:236; Martinez *et al.*, 2007:251; Hellinger, 2006:1; Kumarasamy, 2004:3).

Due to the proper application of antiretroviral therapies, HIV-associated mortality has been remarkably reduced over the last several years (Saag, 2003:359). However, the long-term benefits of chronic therapy are restricted due to recently documented toxicities of antiretroviral treatment. In addition, the constancy of the antiretroviral effect is fairly unpredictable. The ability to maintain inhibition of viral replication is influenced by numerous aspects, including pharmacokinetic properties of the regimen, tissue penetration, cellular penetration, appropriate intracellular processing, antiretroviral drug history, tolerability of the regimen, adherence, potency of the regimen, and the development of resistance (Saag, 2003:359). In order to attain the most enduring antiretroviral effect, a tactical approach that diminishes the possibility of failure of a given regimen and maximises the number of possible future alternatives must be developed by clinicians. This is best accomplished by establishing a comprehensive understanding of the biology of HIV disease and the principles of antiretroviral therapy (Saag, 2003:359).

Martinson *et al.* (2003:247-248) concluded that ARVs are a considerable component of total expenditure of any HAART programme. During the past 4 years, prices of patented ARVs have been significantly reduced in South Africa, making accessibility possible to people who formerly could not afford them, regardless of private-sector medical scheme cover (McLeod *et al.*, 2003:92). Affordability has been one of the restrictions concerning pervasive use of ARVs in developing settings (Martinson *et al.*, 2003:247-248). Costly ARVs are unaffordable in most high HIV-prevalence settings where supplying ARVs at current prices may lead to health budgets being diverted from more cost-effective interventions (Martinson *et al.*, 2003:247-248).

2.6.1 Classification of ARVs

The circulation of protease inhibitors in 1996, followed by the application of non-nucleoside reverse transcriptase inhibitors in 1998, and in recent times the utilisation of protease inhibitors boosted with ritonavir have created valuable therapeutic possibilities for physicians to strategically manage HIV infection (Sabbatani, 2003:476).

2.6.1.1 Nucleoside and nucleotide reverse transcriptase inhibitors

Presently obtainable nucleoside and nucleotide reverse transcriptase inhibitors NRTIs are abacavir, didanosine, lamivudine, stavudine, zidovudine, and zalcitabine (Gibbon, 2005:307; Van Dyk, 2008:98). The nucleotide RTI tenofovir (registration expected shortly) has a similar mechanism of action (Gibbon, 2005:307).

2.6.1.2 Non-nucleoside reverse transcriptase inhibitors

Non-nucleoside reverse transcriptase inhibitors (NNRTIs) that are currently available are nevirapine and efavirenz (Gibbon, 2005:312; Van Dyk, 2008:98). Delavirdine is not accessible in South Africa at present.

2.6.1.3 Protease inhibitors

Protease inhibitors (PIs) currently on the market include amprenavir, atazanavir, indinavir, lopinavir, nelfinavir, ritonavir and saquinavir (Gibbon, 2005:313; Van Dyk, 2008:98). Darunavir, fosamprenavir and tipranavir are not yet marketed in South Africa

2.6.1.4 Fusion inhibitors

Enfurvitide has not yet been made available in South Africa (Van Dyk, 2008:98).

2.6.1.5 Integrase inhibitors

Antiretroviral agents within this class of drugs have not yet been approved for commercial use. Several are undergoing clinical investigation (SAHIVCS, 2008:19).

2.6.1.6 Other

HIV therapy is constantly evolving and the pharmaceutical industry is progressively developing new antiretroviral drugs. According to the Oxford Southern Africa Handbook of HIV medicine (Wilson *et al.*, 2004:341), interest is centred on drugs with

- once daily dosage;
- fewer side-effects; and
- application in salvage therapy.

2.6.2 Mechanism of action of ARVs

Antiretroviral treatment curbs HIV-1 replication, which alters the natural history of the infection considerably (Wood *et al.*, 2000:2095).

The mechanism of action of most antiretroviral drugs that are available at present involves inhibition of the reverse transcriptase and protease enzymes of the human immunodeficiency virus (HIV). Antiretrovirals may assist in preventing infection (subsequent to exposure or to avert mother-to-child transmission) or to deal with established HIV infection (Gibbon, 2005:304).

Some nucleoside analogues, such as nucleoside reverse transcriptase inhibitors (NRTIs), behave like false substrates for reverse transcriptase and result in termination of the DNA chain (Gibbon, 2005:307).

Non-nucleoside reverse transcriptase inhibitors (NNRTIs) potently suppress HIV replication via direct inhibition of reverse transcriptase activity. NNRTIs should be used in combination at all times, typically with two NRTIs to prevent rapid development of high-level resistance. Cross-resistance takes place within this class of ARV (Gibbon, 2005:311-312).

The HIV protease enzyme is inhibited when protease inhibitors are utilised (Van Dyk, 2008:98). Immature, non-infectious HIV viral particles are formed because cleavage of viral polyproteins is prevented when this enzyme is inhibited (Gibbon, 2005:313) and thus formation of new viruses is inhibited (Van Dyk, 2008:96).

Fusion inhibitors prevent HIV attachment to CD4 cells and thus may prevent HIV from entering CD4 cells. Fusion inhibitors could play a future role in salvage therapy (Spencer, 2005:14).

HIV replication is hindered by integrase inhibitors as they affect the integrase enzyme of the virus and thereby inhibit the HIV from integrating into the DNA in the core of the CD4 host cell which is needed for viral reproduction (Van Dyk, 2008:97).

2.6.3 ARVs registered in South Africa

Table 2.7 supplies a list of antiretroviral medications that have been registered in South Africa as of 2004.

Table 2.7 Antiretroviral medications registered in South Africa (Wilson *et al.*, 2004: 333-334); (Van Dyk, 2008: 98); (SAHIVCS, 2008:20)

Generic name Trade name®	Recommended dosage	Usual no. of tablets per day	Other restrictions
Nucleoside reverse transcriptase inhibitors (NRTIs)			
Zidovudine (AZT) <i>Retrovir</i> ®	300mg 12 hourly	6	None.
Lamivudine (3TC) <i>3TC</i> ®	150mg 12 hourly or 300mg daily	2	None.
Didanosine (ddI) <i>Videx</i> ®	>60kg: 400mg daily or <60kg: 250mg daily	2-4	Take on an empty stomach, 1 hour before or 2 hours after food. Dissolve the tablets in water.
Stavudine (d4T) <i>Zerit</i> ®	30mg 12 hourly	2	Higher doses (40mg) >60kg no longer recommended due to toxicity.
Zalcitabine (ddC) <i>Hivid</i> ®	0.75mg 8 hourly	6	None.
Abacavir (ABC) <i>Ziagen</i> ®	300mg 12 hourly or 600mg daily	2	Alcohol increases ABC levels.
AZT + 3TC* <i>Combivir</i> ®	300mg/150mg 12 hourly	2	None
Tenofovir (TDF) <i>Viread</i> ®	300mg daily	1	Take with a fatty meal, or up to 2 hours after light meals.
Emtricitabine/Tenofovir (FTC/TDF) <i>Truvada</i> ®	200mg/300mg daily	1	None.
Non-nucleoside reverse transcriptase inhibitors (NNRTIs)			
Nevirapine (NVP) <i>Viramune</i> ®	200mg daily for 14 days then 200mg 12 hourly	2	None.
Efavirenz (EFV) <i>Stocrin</i> ®	600mg daily	3	Take at night to decrease CNS side-effects. Avoid taking with high-fat meals. Avoid during pregnancy.

Table 2.7 (continued) Antiretroviral medications registered in South Africa (Wilson *et al.*, 2004:333-334); (Van Dyk, 2008: 98); (SAHIVCS, 2008:20)

Protease inhibitors (PIs)			
Nelfinavir (NFV) <i>Viracept</i> ®	1250mg 12 hourly or 750mg 8 hourly	10	Take with a meal to increase absorption.
Indinavir (IDV) <i>Crixivan</i> ®	800mg 8 hourly or 800mg with 100-200mg ritonavir 12 hourly	6-8	Take while fasting, or with a low-fat meal (not necessary when taken with ritonavir). Drink 1.5 litres of water a day.
Saquinavir (SQV) <i>Fortovase</i> ® (soft gel)	1200mg 8 hourly or 400mg 12 hourly with ritonavir 400mg 12 hourly	12	Take with a meal to increase absorption (not necessary when taken with ritonavir).
Saquinavir (SQV) <i>Invirase</i> ® (hard gel)	1000mg with ritonavir 100mg 12 hourly or 1600mg with ritonavir 100mg daily (only if PI naïve)	10	Take with a fatty meal, or up to 2 hours after light meals.
Ritonavir (RTV) <i>Norvir</i> ®	600mg 12 hourly	12	Food improves tolerability.
Lopinavir/Ritonavir <i>Kaletra</i> ®	400/100mg 12 hourly (combination capsule)	6	Take with a meal to increase absorption.
Atazanavir <i>Reyataz</i> ®	400mg daily (only if PI naïve) or 300mg with ritonavir 100mg daily	1-2	Take with a meal. Take 2 hours before or 1 hour after didanosine if co-administered.
Amprenavir <i>Preclir</i> ®	>50kg: 1200mg 12 hourly and <50kg: 20mg/kg 12 hourly or 15mg/kg 8 hourly	24	Avoid taking with high-fat meals. Avoid during pregnancy. Avoid alcohol.
Fosamprenavir <i>Telzir</i> ®	1400mg 12 hourly; or 1400mg with ritonavir 200mg daily	2	None.

**Note: The combination of AZT, 3TC, and ABC (Trizivir®) has been made available in South Africa. Several other combination products are also available.*

2.7 Treatment protocols

Currently two antiretroviral regimens are suggested for use in the South African public sector: stavudine + lamivudine + efavirenz and stavudine + lamivudine + nevirapine. The second-line regimen is zidovudine + didanosine + lopinavir + ritonavir (South Africa, 2004b:4; WHO, 2005:1).

Participants at a workshop held in Nairobi by Médecins sans Frontières (MSF) in 2003, postulated that a supreme first-line ARV regimen should meet requirements such as the following (Ijumba *et al.*, 2004:322):

- Efficient and positively endured with negligible side effects
- Potent, even in patients with advanced disease, and robust (with an auspicious resistance profile)
- Exempt from problematic interactions or contra-indications
- Suitable for use in TB co-infected patients and in pregnant or lactating women
- Available in a fixed-dose combination, with once or twice daily dosing
- Founded on formulations that are stable in tropical environments
- Free from requirements for intensive laboratory monitoring
- Affordable

2.7.1 Antiretroviral therapy in adults

The National Antiretroviral Treatment guidelines (South Africa, 2004b:2) state that the principal target of adult antiretroviral therapy is to reduce morbidity and mortality associated with HIV.

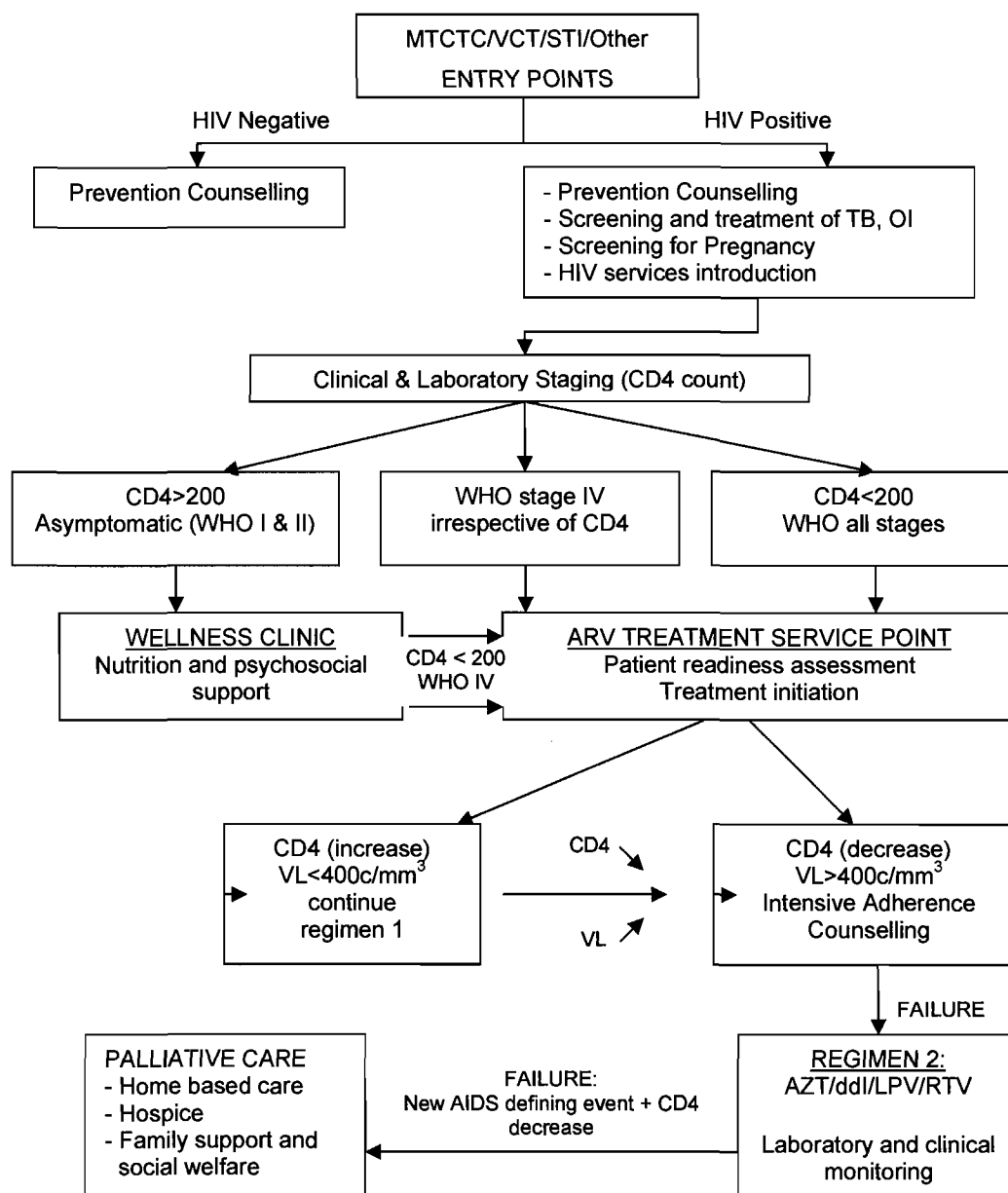
- The patient ought to suffer fewer illnesses that correlate with HIV
- The CD4 count of the patient should increase and be maintained above the baseline tally
- The patient's viral load should be converted to untraceable concentrations (<400 copies/ml) and stay undetectable throughout ART

The secondary aim (South Africa, 2004b:2) is to lessen the incidence of HIV via the following:

- The derived increase in voluntary testing and counselling with more individuals aware of their status and implementing safer sex

- The decrease of transmission in couples with conflicting HIV status
- Reducing the possibility of mother-to-child HIV transmission

Figure 2.1 Adult HIV management (South Africa, 2004b:1)



MTCT = Mother to child transmission
 STI = Sexually transmitted infection
 VCT = Voluntary counselling and testing
 TB = Tuberculosis
 OI = Opportunistic infection
 VL = Viral load

According to the Guidelines for the use of antiretroviral agents in HIV-1-infected adults and adolescents (OARAC, 2006:1), continual advancement in antiretroviral therapy for treatment of HIV-1 has come to pass since the establishment of combination therapy in 1996. In recent times, innovative drugs demonstrating extra dosing convenience and advanced safety profiles have been approved (OARAC, 2006:1). Accordingly, the use of various drugs that were formerly popular have declined as their limitations became more evident. Additionally, resistance testing is utilised more regularly in clinical practice, and interactions between antiretroviral agents and other drugs have become increasingly intricate (OARAC, 2006:1).

Management and monitoring of the toxicities of antiretroviral drugs is a skill that requires boundless experience and commitment. It is necessary to suitably educate physicians prior to expansion of antiretroviral programmes. Physicians ought to adhere faithfully to standard treatment guidelines to steer clear of antiretroviral failure and resistance which is potentially an imminent public-health challenge in the presence of rising use of generic antiretroviral drugs (Kumarasamy, 2004:3).

No international agreement exists concerning any one specific or standard drug regimen (Sendi *et al.*, 2001:709). In spite of this, triple combination therapy consisting of two nucleoside reverse transcriptase inhibitors and a protease inhibitor or a non-nucleoside reverse transcriptase inhibitor is the recommended standard of care in treatment-naïve patients (Sendi *et al.*, 2001:709).

According to Evian (2003:84) the course of antiretroviral drug therapy is influenced by, and hinges on numerous aspects such as the following:

- Affordability
- Clinical history, e.g. if there is a compelling history of hepatitis, peripheral neuropathy, pancreatitis, bone marrow suppression, renal calculi (stones) or psychiatric disturbance, it is prudent to avoid the ARV drugs which may cause these side effects
- Disease progression, i.e. in a more advanced phase of the disease there is greater need for more potent drug regimens
- Contemplating longer-term future drug options lest the initial regimen eventually fail, e.g. use of PI-sparing regimens, thus avoiding some of their side-effects (they can furthermore be used as a second-line option)
- Drug dosage convenience i.e. once or twice daily dosage intervals are more convenient than thrice daily

- Previous history of ART, or which drugs have been used in the past

ARV therapy is fundamental regarding the management of HIV/AIDS (McLeod *et al.*, 2003:92), and Evian (2003:84) aptly remarked that the “*first shot at ART should be your best shot*”.

Table 2.8 South African National Department of Health regimens for antiretroviral therapy (South Africa, 2004b:4)

Regimen	Drugs	Indications (WHO stage 4 disease or CD4 count <200cells/mm ³)	Changes required when used in combination with rifampicin-based TB treatment
Regimen 1a	Stavudine + lamivudine + efavirenz	Men and women who are not of childbearing potential or are using injectable contraception	No change required
Regimen 1b	Stavudine + lamivudine + nevirapine	Women who are unable to guarantee reliable contraception while on antiretroviral therapy	Do not initiate nevirapine in patients on TB treatment. Patients on Regimen 1b who commence TB treatment may be switched to efavirenz, or continued on nevirapine with monthly ALT monitoring
Regimen 2	Zidovudine + didanosine + lopinavir-ritonavir	Second-line therapy for patients who fail Regimen 1 virologically despite good adherence to treatment	Additional ritonavir must be added to the regimen, to make a total dose of lopinavir 400mg 12 hourly + ritonavir 400mg 12 hourly. Monthly ALT monitoring advised

2.7.2 Monotherapy

Antiretroviral treatment originated in the form of a one-drug regimen, labelled 'monotherapy' (McLeod *et al.*, 2003:92). However, when antiretrovirals are incorrectly prescribed, taken erratically or at subtherapeutic doses (including monotherapy or dual therapy), resistant viral genes are preferentially selected, potentially resulting in treatment failure (Martinson *et al.*, 2003:249).

HIV mutates swiftly and there is a high viral turnover, thus improper drug prescribing may instigate rapid development of drug resistance (Gibbon, 2005:304). It has been established that monotherapy and dual therapy furthers development of resistance to ARV medication, resulting in diminished efficacy of triple therapy (McLeod *et al.*, 2003:92-93).

2.7.3 Combination therapy

The objective of managing established HIV infection with antiretroviral therapy (ART) is to accomplish durable suppression of replication (eventually an undetectable viral load). This is usually achieved by means of a combination of three or more antiretrovirals. Combination ART that successfully undertakes virological suppression is also described as highly active antiretroviral therapy (HAART) (Gibbon, 2005:304). The triple regimen is highly effective and can reduce the viral load to undetectable levels, while dual therapy leads to sub-optimal therapy (McLeod *et al.*, 2003:92-93).

2.7.3.1 Highly active antiretroviral therapy

Ground-breaking randomised studies concerning chronic HIV infection have confirmed the superior value of triple drug combination antiretroviral therapy, versus mono or dual therapy, in stimulating sustained viral load suppression to less than 50 copies HIV RNA/ml. Highly active antiretroviral therapy (HAART) also facilitates immune reconstitution and cutbacks in morbidity and mortality while diminishing the occurrence of drug resistance (Fidler *et al.*, 2006:247-248).

Dual NRTI accompanied by either a non-nucleoside reverse transcriptase inhibitor or a protease inhibitor represents traditional HAART or 'triple therapy' (Gibbon, 2005:307).

2.7.3.2 Mega highly active antiretroviral therapy

The phrase "mega-HAART" refers to the approach of combining between six to nine drugs, which inevitably include several "recycled" agents (Gallant, 1999:1). In theory, this tactic seems sensible: although virus resistance to various (one, two and three) drug combinations is likely to be present in patients with wide-ranging drug experience, it is improbable that any single virion would be resistant to all of the drugs in such a multifaceted multidrug regimen.

Unsurprisingly, patients are forced to discontinue all or part of these intricate regimens due to high toxicity causing intolerability. An approach like this may have a purpose in the treatment of extremely motivated and adherent patients. Nonetheless, the cost, toxicity, and comparatively meagre efficacy of mega-HAART make it doubtful that this method will be the solution to the predicament of multidrug resistance for the greater part of patients (Gallant, 1999:1).

2.8 Indications for ARV therapy

The accessibility of antiretroviral therapy has drastically decreased the morbidity and mortality caused by HIV infection (Robertson *et al.*, 2005:1). Additionally, enhanced treatment of opportunistic infections and comorbidities frequently found in patients with HIV is further extending the lives of patients (Robertson *et al.*, 2005:1).

Antiretroviral therapy consisting of three drugs delivers effective suppression of plasma HIV RNA levels to undetectable quantities in numerous patients. This brings about immunologic recovery, fewer HIV-related complications, and prolonged survival. At this point in time approximately twenty separate antiretroviral drugs, four fixed dose two-drug combinations, and two fixed dose three-drug combinations are obtainable, generating 364 three-drug combinations with potential for treatment (Bartlett *et al.*, 2006:2051). The ultimate drug combinations will increase antiretroviral effectiveness, immunologic reconstitution, and quality of life while at the same time reducing medication-related toxicities and the likelihood of drug resistance. Existing guidelines employ the evidence base available at present to make particular suggestions concerning treatment, but every single one of the three-drug combinations can obviously not be compared directly in clinical trials (Bartlett *et al.*, 2006:2051).

2.8.1 When to start treatment for HIV

The intention of ART is to accomplish HIV viral suppression and minimise the level of HIV ribonucleic acid to levels as low as achievable, for the longest possible time. This will consequently lead to a reduced amount of immune damage and will diminish any persistent deterioration in the patient's health status. ART is thus valuable in postponing the onset of AIDS. ART is required to uphold very low viral levels and preferably an undetectable HIV viral load (Evian, 2003:79).

Absolute and durable inhibition of HIV replication continues to be the principal target of antiretroviral therapy. It is apparent that this objective is straightforwardly realisable in compliant patients for whom suitable treatment is selected. This goal may also be attainable using carefully selected second and even third regimens. However, patients who have

experienced multiple antiretroviral failures have commonly exhausted all existing options. For these patients the ambition of undetectable virus load may not be viable, and frequent or early switches do not yield any significant benefit. Continually adding single new drugs as they are made available only serves to deplete agents that might be better applied in subsequent combination regimens (Gallant, 1999:1).

2.8.1.1 Role of ART in asymptomatic patients who are not severely immune-deficient

HIV activity and replication are obstructed and suppressed by ART, averting additional immune damage and resulting in a recuperation of the immune capacity. Upholding sufficient or enhanced immune-function will consequently inhibit disease progression, and enhance ongoing wellness and health (Evian, 2003:79).

2.8.1.2 Role of ART in symptomatic patients with immune-deficiency

ART may prevent further deterioration and damage to the immune status and will make important and significant cost savings possible.

According to Evian (2003:79-80) ART may help to

- encourage some recuperation of immune status;
- enhance immune function and capability;
- hamper disease progression;
- ease the frequency and severity of severe opportunistic infections;
- improve general health, weight gain and increase appetite; and
- avoid the need for hospital admissions and other expensive health care.

Table 2.9 2005 SA HIV Clinicians Society guidelines for commencing antiretroviral therapy (Gibbon, 2005:306)

Stage of disease	Recommendation
Asymptomatic OR WHO stage 1 or 2	
CD4 count < 200 cells/mm ³	Treatment recommended
CD4 count 200-350 cells/mm ³	Consider treatment
CD4 count > 350 cells/mm ³	Defer treatment
Severely symptomatic patient	
WHO stage 3 or 4 disease (excluding tuberculosis – see below)	Treatment recommended
Patient with tuberculosis	
CD4 count <200 cells/mm ³	Delay treatment until after 2-month intensive phase of TB therapy, unless the patient has other serious HIV-related illness or a CD4 count <50 cells/mm ³ , when ART should be introduced earlier
CD4 count >200cells/mm ³	Defer treatment until after 6 months of TB therapy completed. If asymptomatic TB, consider CD4 criteria above.

The Office of Aids Research Advisory Council (OARAC, 2006:1) assert that the main objectives of antiretroviral therapy are

- lowering HIV-related morbidity and mortality;
- improved quality of life;
- restoration and maintenance of immunologic function; and
- resilient suppression of viral load to the greatest extent.

Chronic administration of HIV therapy can be regarded as having a dual purpose: avoidance of clinical progression and prevention of occurrence of resistance (Saag, 2003:365).

2.9 ARV-ARV interactions

Advances in HIV therapy has initiated a substantial increase in the quantity of HIV drugs available to caregivers, which equip them to manage HIV/AIDS. Antiretroviral medications, and also several of the drugs applied in the management of opportunistic infections and primary care (for example, macrolide antibiotics, azole antifungals, cholesterol-lowering medications), are especially inclined to drug interactions. The tempo at which the latest data on drug metabolism and transport are being presented causes difficulties with the interpretation of clinically significant interactions (Robertson *et al.*, 2005:1).

There is a high potential for drug interaction with antiretroviral agents, and in spite of the risks being clearly recognised, the risk factors for, and frequency of clinically significant drug interactions (CSDIs) with antiretroviral agents is still poorly exemplified (Miller *et al.*, 2007:1379). Drug interactions concerning the NNRTIs and PIs are generally triggered by the considerable effects on major hepatic metabolic pathways such as cytochrome P450 (CYP) 3A4. Several other identified and unidentified mechanisms are also to blame for drug interactions with many classes of antiretroviral drugs (Miller *et al.*, 2007:1379). Therefore, significant variations can develop in serum concentrations which lead to clinically significant adverse outcomes, for instance drug toxicity and treatment failure. The development of novel antiretroviral agents along with studies on existing products constantly expands the quantity of recognised drug interactions with these agents (Miller *et al.*, 2007:1379).

Antiretroviral therapy is ongoing, long-term treatment that necessitates a large quantity of medication to be taken by the patient, and all drugs are potentially linked to adverse effects that can differ from patient to patient (Sabbatani, 2003:474).

Over and above the required expertise pertaining to the clinical efficacy, adverse effect profile, and possibility of manifestation of resistance, the physician responsible for an HIV-infected patient ought to be knowledgeable on the subject of basic pharmacokinetics as well (Safrin, 2004:814). These patients are typically using numerous drugs simultaneously, consisting of an assortment of antiretroviral agents, prophylaxis or treatment for opportunistic infections, and opioid analgesics or methadone for maintenance therapy (Safrin, 2004:814).

A high prevalence of drug interactions, including clinically significant interactions, was observed amid an antiretroviral therapy-receiving study population investigated by Miller *et al.* (2007:1382). Though the potential for antiretroviral drug interactions has been proficiently documented, the results of their study emphasise the incidence and most frequent categories of clinically significant drug interactions noticed in the bona fide drug regimens prescribed to the study patients. In addition, particular patient and drug properties most closely linked with

clinically significant drug interactions were characterised. Identification of these characteristics ought to encourage improved consciousness of drug interactions among prescribers.

According to the Office Of Aids Research Advisory Council (OARAC, 2006:1) toxicities of antiretroviral drugs may overlap. Some examples are given in Table 2.10.

Table 2.10 HIV-related drugs with overlapping toxicities

Bone Marrow Suppression	Peripheral Neuropathy	Pancreatitis	Nephro-toxicity	Hepato-toxicity	Rash	Diarrhoea	Ocular Effects
Zidovudine	Didanosine	Didanosine	Adefovir	Delavirdine	Abacavir	Darunavir	Didanosine
	Stavudine	Lamivudine (children)	Indinavir	Efavirenz	Amprenavir	Lopinavir/Ritonavir	
	Zalcitabine	Ritonavir	Tenofovir	Nevirapine	Atazanavir	Nelfinavir	
		Stavudine		NRTIs	Darunavir	Ritonavir	
		Zalcitabine		PI (esp. Tipranavir)	Delavirdine	Tipranavir	
					Efavirenz		
					Nevirapine		
					Tipranavir		

It is imperative to possess comprehensive knowledge of those drug interactions with a predictable or high probability for clinical adverse effects to facilitate educated selections regarding drug groupings that must be avoided, combinations that are safe, and ones that are prudent only when coupled with vigilant observation and/or dosage adjustments. In a study performed by Miller *et al.* (2007:1383), it was shown that one of the most frequently recognised non-clinically significant drug interactions (non-CSDIs) arise between lamivudine and trimethoprim-sulfamethoxazole. Even though this interaction is cited in the majority of drug-references and appears on the package insert for lamivudine, no clinical adverse effects have been reported, and these drugs are still frequently prescribed in combination to HIV-infected patients without necessitating dosage adjustment or specialised supervision (Miller *et al.*, 2007:1383).

2.10 The South African health care system

Allotment of human resources and monetary funding is flagrantly disproportionate between the private and public health sectors. Similar disparity exists in the public sector between the primarily rural underprivileged provinces and urbanised provinces. The private sector serves only between 17.00-18.00 per cent of the population, yet it drains in excess of 60.00 per cent of the health care budget and monopolise more than 70.00 per cent of the health care specialists. There is also inequality between expenditure on different levels of care. Only 15.00 per cent of health care spending is allocated to primary health care and assessments demonstrate that it is doubtful that this will increase in the medium term. South Africa's health services are being overwhelmed by the burden of the HIV/AIDS epidemic (Ntuli *et al.*, 2004:3; Martinson *et al.*, 2003:238).

In May 2002 the Report of the Social Security Committee of Enquiry by the Taylor Committee was released (South Africa, 2002:1-4), defining the expectations for the South African health care system in the future. Additionally, a more comprehensive treatise on health care was published by the Department of Health in 2002. Above-mentioned reports advocated that South Africa should head towards a Social Health Insurance system that would incorporate the public sector and private medical schemes in a collective contributory structure (IAAHS, 2007:1).

2.10.1 Public health care system

Highly Active Antiretroviral Treatment (HAART) has been made available for several years now, mainly to the private sector's medically insured community and to a number of persons through non-profit enterprises (Stewart and Loveday, 2006:225).

2.10.2 Private health care system

In the private sector, patients have the option to either pay for their ARVs out-of-pocket or obtain medication by means of their health insurance or via an employer sponsored programme (Martinson *et al.*, 2003:238).

2.10.3 Health care expenditure

The International Actuarial Association Health Section (IAAHS) claims that budgeted health care allocations have been under mounting pressure attributable to the escalating prevalence of HIV/AIDS in the populace of South Africa. This impact differs from province to province (IAAHS, 2007:1).

The expense of combination HIV-antiretroviral treatment has recently decreased to a great extent (Kumarasamy, 2004:3). Decreasing prices of medication are permitting physicians in

the developing world to make triple antiretroviral regimens available to increasingly more patients, who have urgent need of the life-saving drugs (Kumarasamy, 2004:3).

However, as a consequence of patents granting exclusive rights to proprietary companies, the generic companies are not authorised to manufacture newer antiretrovirals, which may be a significant encumbrance to patients needing medication in developing countries (Kumarasamy, 2004:3).

In areas with restricted resources, numerous patients are forced to buy antiretrovirals from a pharmacy because treatment is unattainable in government programmes. These patients may well discontinue taking their drugs as soon as they can no longer meet the expenses incurred. This state of affairs could bring about the development of multidrug-resistant strains of HIV (Kumarasamy, 2004:3).

Additionally, patients who require antiretrovirals in developing countries are often inflicted with various opportunistic and coexistent infections (Kumarasamy, 2004:3).

Establishing the direct expenses (namely the health resources consumed) of bestowing medical care on HIV/AIDS patients is essential for both interim and long-term management and for proper resource distribution. The evolving character of the HIV-epidemic, in addition to the introduction of HAART (and continuous alterations in management protocols when making use of this treatment), demands uninterrupted observation of resources expended if reliable estimates are to be drawn on to sustain both optimal care and prevention programming (Krentz *et al.*, 2003:106).

HAART is the most valuable treatment intervention for adults, but as a rule it is the most expensive, with the price tag of adult HAART surpassing the other interventions to a great extent. It is projected to escalate until 2015 when it will crest at R18.2 billion (Geffen *et al.*, 2003:16). At that stage 2.3 million adults will collect HAART in the public sector (approximately 220 000 adults will receive HAART through medical schemes). The cost of HAART will decline again after 2015 as the total number of HIV-positive people decrease (from an estimated 6 million in 2015 to about 5 million in 2025) (Geffen *et al.*, 2003:16).

At present 8.80 per cent of South Africa's gross domestic product is spent on health care. This is relatively high compared to international standards. Nonetheless, the extent to which health care services are accessible to diverse segments of the South African population demonstrates obvious inequities (IAAHS, 2007:1). Government is the principal provider of health care funding. Money from tax revenue is allotted to health care and this approach essentially finances the provision of public sector health care services at provincial level.

Government additionally grant a tax benefit to individuals who procure private health cover through medical schemes (IAAHS, 2007:1). Household spending is considered to be the second largest source of health finance. This financing transpires through contributions to medical schemes, direct out-of-pocket payments and to a degree to other categories of private insurance. Even family units who have private cover are compelled to make out-of-pocket payments for services that are not completely covered (IAAHS, 2007:1). Employers subsidise health care for their workforce either straightforwardly through health services offered at the workplace or ultimately via contributions to medical schemes on behalf of their employees (IAAHS, 2007:1).

The IAAHS (2007:1) estimated the distribution of per capita health care expenditure for the 2003 period as follows in Table 2.11:

Table 2.11 Health expenditure in South Africa 2003/4

	Public sector	Private sector
Total expenditure (Rbn)	37	43
% of expenditure	46%	54%
Population covered (thousands)	38 541	6 962
% of population	85%	15%
Expenditure per person pa (2003 Rand values)	R960	R6 176

Data on the expense of therapy and care for HIV infection facilitate the evaluation of the fiscal impact of the epidemic on health care structures; the appraisal of the affordability of the latest and existing interventions; a foundation for health care resource strategies; and recognition of resource needs for HIV service provision (Beck *et al.*, 2001:14).

2.11 Pharmacoeconomic principles

2.11.1 Pharmacoeconomics

Pharmacoeconomics can be classified as a division of health economics with a specific concentration on the resulting costs and benefits of medical treatment (Walley & Haycox, 1997:343). Pharmacoeconomic analysis calculates the general worth of medicine in disease prevention and treatment therapy (Kelly, 2007: 276).

Pharmacoeconomics can illustrate and explore the costs of drug treatment with regard to health care structures along with the public (Carriere & Huang, 2001:19).

2.11.2 Classification of cost

Pharmacoeconomics entails various perspectives, and several different types of costs exist. Cost can be defined as the overall worth of the total resources that are expended whilst producing commodities or services. Accordingly in a pharmacoeconomic sense, cost can be viewed as the expenses encountered in the imparting of health care goods and provisions. Examples of costs may include fixed cost, variable cost, direct medical cost, direct nonmedical cost, indirect cost, average cost, marginal cost, and opportunity cost (Wilson, 1999:1).

2.11.2.1 Fixed cost

A distinction is made between fixed and variable costs in pharmacoeconomics. Cost that does not fluctuate with variations in the quantity or degree of output yielded in the short-term (usually within a one-year period) is described as fixed cost. Fixed costs typically change with time, and examples may include rent, equipment lease payments, and some wages and salaries (Wilson, 1999:66).

2.11.2.2 Variable cost

Variable costs are described in pharmacoeconomics as those costs that fluctuate with variations in production volume. Drugs, devices, supplies, and procedures supplied via a fee-for-service reimbursement system are all examples of variable costs (Wilson, 1999:66).

2.11.2.3 Direct medical cost

Direct medical costs include both fixed and variable costs directly connected to a treatment intervention or illness (Wolters Kluwer Health, 2005:1). Direct medical costs take account of the costs of services and commodities utilised in patient care and treatment, and may incorporate expenses for hospitalisation, consultations with physicians and other health authorities and trips to the emergency room, dental appointments, health care house calls, prescribed medication, as well as medical paraphernalia and provisions. When this concept is applied to pharmaceutical products and services, it also includes the attainment, storage, management, and monitoring costs of medication. In the usual course of events, costs that can be compensated for money-wise are considered to be direct costs (Wilson, 1999:66).

2.11.2.4 Direct nonmedical cost

Direct nonmedical cost incorporates the cost related to provision of all nonmedical aid, meals, accommodation, and transportation owing to the medical condition or health care intervention (such as transportation of a patient to a hospital) (Wolters Kluwer Health, 2005:1; Wilson, 1999:66).

2.11.2.5 Indirect cost

The costs incurred when productivity diminishes or ceases as a consequence of morbidity or untimely mortality, attributable to illness or the management thereof, including unofficial caregiving costs, are referred to as indirect costs or productivity costs (Wilson, 1999:66). Indirect medical cost is thus the cost of medical management (measured in life-years) profited by means of a prior intervention (Wolters Kluwer Health, 2005:1).

Morbidity costs take account of commodities and benefits that the patient was not able to yield on account of ill health. Mortality costs consist of goods or services the individual would have been able to generate had the patient not fallen ill and passed away prematurely (Wilson, 1999:66). Indirect non-medical cost is cost related to decreased output attributable to morbidity, disability or mortality (Wolters Kluwer Health, 2005:1). Another facet of indirect cost is linked to shortfall of employee productivity when they leave work in order to provide care for the patient, typically a relative. It is the cost of not being able to partake in a different endeavour as a result of lost time. Universally, indirect costs may not be compensated for money-wise (Wilson, 1999:66).

2.11.2.6 Intangible cost

Intangible cost can be defined as the cost of pain and distress that results from an illness or the treatment thereof (Wolters Kluwer Health, 2005:1).

2.11.2.7 Average cost

Average costs are calculated as the sum of health care intervention costs (for example management programmes), divided by the aggregate magnitude of the intervention (i.e., number of treatment units supplied) (Wolters Kluwer Health, 2005:1).

2.11.2.8 Marginal cost

Marginal cost is the variation in total cost of generating one unit of production extra, or one unit less (Wilson, 1999:66). It is thus the added cost of one additional product or service component (Wolters Kluwer Health, 2005:1). Total cost may rise as a consequence of manufacturing one extra unit of outcome (Wilson, 1999:66). Marginal costs may also be seen as the average variable cost (Wilson, 1999:66).

2.11.2.9 Opportunity cost

The earnings that a resource could produce in its alternative use which yields maximum value, is referred to as opportunity cost; it is the value of the option that must be bypassed in favour of manufacturing a different item (Wilson, 1999:66).

2.11.3 Discounting

Discounting is a method applied in economic studies to convey those costs and benefits that will arise in the future at current rates. Two principles form the basis of this procedure: persons would rather be given benefits in the present day than in the future; and assets invested in carefully selected programmes at this time may well earn revenue in due course (Wilson, 1999:66).

Discounting is employed in pharmacoeconomics to justify the time preference related to money in its approach. People usually desire to receive money sooner, rather than later owing to the profits that can be made in the meantime. Individuals also favour having to spend money at a later time instead of in the present day (Wilson, 1999:66).

2.11.4 Types of pharmacoeconomic analyses

Drug treatments and therapies may be compared with each other by applying different types of pharmacoeconomic analyses, including cost-minimisation analysis (CMA), cost-effectiveness analysis (CEA), cost-benefit analysis (CBA), and cost-utility analysis (CUA) (Li, 2003:193).

2.11.4.1 Cost-minimization analysis

Cost minimisation analysis (CMA) is the most straightforward and basic of all pharmacoeconomic evaluation methods (Wilson, 1999:66; McCloskey, 2001:69). It is a form of cost comparison study utilised to compare two or more treatments deemed to be of equivalent efficacy in relation to clinical and quality-of-life outcomes, with monetary cost being the only distinguishing feature, and ordinarily, the least costly of the alternatives is selected (Kelly, 2007:277; Wilson, 1999:66; McCloskey, 2001:69). Thus, when more than one intervention deliver equal results, a CMA is the proper means for calculating the cost associated with each outcome (Wilson, 1999:66).

Since the outcomes of two distinct drugs are hardly ever identical, this kind of analysis is appropriate and most practical for assessing different dosage forms of the same drug, or for reviewing generically equivalent drugs with outcomes that have been verified to be identical (Wilson, 1999:66). When using this approach it is crucial that the assessors provide proof that the outcomes of the interventions are indeed identical in all regards (McCloskey, 2001:69). Meticulous and comprehensive examination of both clinical and fiscal outcomes of the two interventions must be performed before the application of a CMA, to avoid making an erroneous cost comparison of two dissimilar things (Wilson, 1999:66). For example, even if two drugs are equally effective in the treatment of a disease, they may vary extensively in the

occurrence of a critical side-effect (McCloskey, 2001:69). The detection of any disparity in results eradicates CMA as a methodologic alternative (Wilson, 1999:66).

2.11.4.2 Cost-effectiveness analysis

Interventions (for instance medicines or treatment programmes) that share a mutual health outcome (for example reduction of cholesterol; years of life saved) are compared using cost-effectiveness analysis (CEA) (Kelly, 2007:277; Wolters Kluwer Health, 2005:1). The total resources applied, as well as the health outcomes resulting from the interventions are studied, and the interventions are also evaluated regarding the net financial costs including a quantification of efficacy (e.g., effects on quality of life; clinical outcomes) brought about by the intervention (Kelly, 2007:277; Wolters Kluwer Health, 2005:1; Wilson, 1999:66).

In CEA, the outcomes of the interventions are not calculated in financial terms, but instead in natural or physical units (such as life-years saved or complication precluded). CEA does not suppose equivalent outcomes, yet the interventions compared should have analogous objectives (McCloskey, 2001:69).

2.11.4.3 Cost-benefit analysis

Cost-benefit analysis (CBA) is a method used to calculate all costs and benefits resulting from interventions in monetary units to establish the variance in cost and effect (Kelly, 2007:277). Thus CBA specifies and compares the net expenditure of a health care intervention with the net benefits that occur as a result of employing said intervention (Wilson, 1999:66). All effects brought about by the utilisation of the intervention (costs and benefits) are quantified in financial terms (Wilson, 1999:66; McCloskey, 2001:69).

Subsequently, a cost-benefit ratio is calculated to establish which intervention offers the maximum benefit proportionate to cost (McCloskey, 2001:69), as the outcomes of the interventions being compared in a CBA are not regarded as identical (McCloskey, 2001:69).

A CBA is ordinarily performed when decisions have to be made regarding the most suitable option to choose under circumstances where resources are restricted (McCloskey, 2001:69). A typical complication with this method is calculating the monetary value of clinical outcomes (McCloskey, 2001:69). Consequently, CBA is more valuable in performing an economic assessment of health care services instead of treatments per se (McCloskey, 2001:69).

2.11.4.4 Cost-utility analysis

Cost-utility analysis (CUA) is a type of CEA wherein values are allocated to assorted health outcomes, indicating how individuals perceive the comparative significance of the various

types of health outcomes (Wilson, 1999:66). Expenses and effects due to an intervention are assessed regarding the patient's quality of life (QOL), including the capacity to manage the expenses, or predilection for a specific kind of treatment over other alternatives (Kelly, 2007:277). Thus the outcomes allow for patient health preferences or values (McCloskey, 2001:69-70). The outcomes are conveyed in units like quality-adjusted life-years (QALYs) (Wilson, 1999:66), that take into account that patients do not perceive each year of life gained from an intervention to be of equal worth (McCloskey, 2001:69-70). CUA is the proper technique to apply when the focus of the health care intervention is quality of life (Wilson, 1999:66).

2.11.5 Quality of life

Quality of life (QOL) may be defined as the combination of different aspects that the patient considers to be crucial, and that promotes a full life (Wolters Kluwer Health, 2005:1). Thus it is the fusion of the social, economic, physical, and emotional realms. Additionally, it includes some fundamental issues that have an effect on quality of life for example everyday life conditions (Soni & Cella, 2002:S560).

2.11.5.1 Quality-adjusted life-years

The results of a CUA are most frequently conveyed by means of a unit dubbed quality-adjusted life-years (QALYs). This health utility measure merges both quality and quantity of life, and is established by certain assessment methods whereby the values may be acquired either from patients suffering from the specific disease or from the general public. One year at absolute health is equal to 1.0 QALY. One year at 40.00 per cent of absolute health as valued by patients, is equal to 0.4 QALY. Results expressed in this manner allow for health care interventions with very diverse outcomes to be compared – such as saving lives opposed to reducing disability (Wilson, 1999:66).

2.12 Drug utilisation review (DUR)

The World Health Organization defined drug utilisation research (DUR) 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).

Drug utilisation may be regarded as a strategy that evaluates, examines and clarifies rates or costs and reviews the suitability of drug usage to determine improper use, avert adverse drug interactions and boost proper use (Wolters Kluwer Health, 2005:1).

2.12.1 Purpose of DUR

The American Pharmaceutical Association (2000:538) states that the objectives of DUR include improving the appropriateness of medicinal treatment by concentrating on whether a drug is utilised efficiently (for instance, correct dosage, treatment interval, etc.). DUR is also applied in quality assessment and assurance in pharmacy. It is usually a sanctioned, controlled, and uninterrupted programme that assesses, evaluates, and interprets drug usage patterns against standards indicating how the drug ought to be used (Kelly, 2007:271).

2.12.2 Types of drug utilisation studies

According to the American National Health Policy Forum (2001:3) prospective, concurrent, and retrospective drug utilisation reviews are employed to guarantee safety, enhance quality of treatment, and encourage adherence to the formulary.

2.12.2.1 Prospective DUR

Prospective DUR entails the evaluation of the prescription prior to the dispensing process, e.g. throughout the prescription assessment. Pharmacists are able to recognise and resolve problems such as therapeutic duplication, contraindications, interactions, erroneous dosage or therapy duration, drug allergies, and clinical abuse via prospective DUR (Chui & Rupp, 2000:27).

2.12.2.2 Concurrent DUR

During concurrent DUR, prescriptions are reviewed while patients are receiving treatment. The appropriateness of the patient's current drug use is reviewed and verified against predetermined criteria. If problems are identified, corrective action (e.g. personal response from a pharmacist to the prescriber) may be taken to benefit the patient (Peterson, 2004:198).

2.12.2.3 Retrospective DUR

Retrospective DUR is carried out by examining patient files and records to evaluate patient therapy and interventions subsequent to the patient's release from a treatment centre or after the therapy has been initiated, following a certain period of time during which the patient has been undergoing treatment or taking a drug (Kelly, 2007:272; The U.S. Pharmacopoeia Drug Utilization Review Advisory Panel, 2000:1). Retrospective studies may entail review of drug use in specific patients or investigation of prescribing and dispensing patterns or trends (The U.S. Pharmacopoeia Drug Utilization Review Advisory Panel, 2000:1). Additionally, DUR criteria may be implemented retrospectively to pharmacy claims data to single out prescribers or providers who are in need of tutoring regarding proper drug use in the hopes

of positively influencing prescribing and dispensing in the future (The U.S. Pharmacopoeia Drug Utilization Review Advisory Panel, 2000:1).

The benefits of retrospective review include that it costs less than other DUR methods, and is not as time consuming (Kelly, 2007:272).

2.13 Health care concepts

2.13.1 Managed care

Managed care can be described as a controlled method of health care provision intended to manage expenditure and quality, via fixed drug formularies, preadmission monitoring, case management, etc. (Wolters Kluwer Health, 2005:1).

2.13.2 Disease management programmes

The goals of disease management programmes include enhancing the level of care and treatment effects while striving to diminish squandering of resources (Maue & Segal, 2001:144).

Disease management includes three vital aspects (Maue & Segal, 2001:146):

- An incorporated administrative system that is equipped to manage health care interventions in due course across several disciplines.
- A continuous system for quality enhancement that makes use of process information, results, and the latest scientific literature to direct transformation.
- An all-inclusive database comprising of information on the subject of the economic configuration of a disease and patient subdivision, and which keeps a record of treatment flow and pinpoints vital junctures or interventions. Furthermore, this database must incorporate up to date guidelines, pathways, and algorithms to augment care for the particular group of patients.

2.14 Health insurance

The majority of economic models regard health insurance as a barricade against financial risk from ill health. But the advantages from health insurance are not restricted to the evasion of monetary risk; further benefits are founded on insurance's capacity to grant access to medical care that would otherwise be unaffordable (Bhattacharya *et al.*, 2003:1105).

2.14.1 Medical schemes

According to the website www.medicalscheme.co.za (Anon, 2007:1) there are nearly 160 South African medical schemes consisting of roughly 7 million beneficiaries. The overall annual contributions to medical schemes total close to R35-billion as maintained by the Council for Medical Schemes. Considering that South Africa has a population greater than 47 million people, fewer than 15.00 per cent of the general public have medical scheme membership (Anon, 2007:1). All medical schemes are not open to the public. In actual fact, of the 160 medical schemes, no more than 40 are described as being open to the public. As the smaller schemes are absorbed by larger companies, this number might dwindle further over time (Anon, 2007:1).

Medical schemes are the foremost means for providing risk-pooling for health care in the private sector. Medical schemes are communal funds that allot benefits on a basis that settles medical expense (insurance), ordinarily administrated by third party supervisor and managed care organisations. The National Health Accounts for 1998 illustrated that direct expenditure on medical schemes equalled 73.00 per cent of total private health expenditure, but this escalated to 89.10 per cent when out-of-pocket expenses by members were taken into account (IAAHS, 2007:1).

Health insurance plans offer non-indemnity benefits for particular health events. This entails that the insurer supplies a preordained sum of money on the occurrence of the event, instead of compensating the actual cost of health care (IAAHS, 2007:1).

2.14.2 Types of medical schemes

Medical schemes can be classified in several categories in accordance with certain characteristics: registered or exempted; open or restricted; and medical benefit or medical aid.

2.14.2.1 Registered and exempted schemes

Registered schemes enlist with the Office of the Registrar and are required to act fully in accordance with the requirements of the Medical Schemes Act 131 of 1998. These schemes have to submit mandatory annual returns (Rama & McLeod, 2001:4).

In terms of the Medical Schemes Act of 1967, various schemes were relieved from acquiescence with selected provisions of the Act, given that they are governed by other legislation managed by other Government departments (Annual Report of the Registrar, 1989). Nearly all Exempted schemes are low cost schemes and their benefit structures frequently differ considerably from Registered schemes. Exempted schemes are schemes

conventionally founded for industrial companies and government departments (Rama & McLeod, 2001:4).

2.14.2.2 Medical aid and medical benefit schemes

Two kinds of registered schemes existed prior to 1993: Medical Aid schemes and Medical Benefit schemes. Medical Benefit schemes diverged from Medical Aid schemes in that they provided services to their members through their own amenities and practiced managed health care. Medical Benefit schemes therefore managed to limit expenses more competently than Medical Aid schemes. Nonetheless, the Medical Schemes Amendment Act of 1993 asserted that the division between a Medical Aid scheme and a Medical Benefit scheme was not required anymore and hence the distinction would no longer be made (Rama & McLeod, 2001:4).

2.14.2.3 Open and restricted schemes

Registered schemes can be categorised as open or restricted. Restricted schemes confine membership, typically established on employment, membership of a union or professional association. Membership in open schemes is open to the public. At present, open schemes may not deny membership to any person. The administration and risk pools of these two types of schemes commonly show a discrepancy (Rama and McLeod, 2001:5).

2.14.3 Medical scheme legislation regarding prescribed minimum benefits and ART: a short overview

The Medical Scheme Act, No 131 of 1998 instructs that a registered medical aid scheme may not wrongly exhibit prejudice directly or indirectly against its members on account of the condition of their health. The Act stipulates that schemes cannot reject membership founded on a medical condition, including HIV. The Act additionally requires that all schemes shall put forward a minimum level of benefits to its members. The medical schemes are obligated to compensate completely devoid of co-payments or use of deductibles for the diagnosis, treatment and care costs of the prescribed minimum benefits conditions. The prescribed minimum benefits are to be reassessed at least every two years and the evaluation will concentrate in particular on the development of protocols for medical management of HIV and AIDS (South Africa, 2006:18).

Martinson and colleagues (2003:238-239) affirm that the Medical Schemes Act makes arrangements for the medical and surgical treatment of opportunistic infections along with localised malignancies as part of the Prescribed Minimum Benefits. The Amendment to the General Regulations made in terms of the Medical Schemes Act No. 131 of 1998 (South

Africa, 2004a:3-4) has included the following as minimum benefits in the management of HIV infection:

- HIV voluntary counselling and testing
- Co-trimoxazole as precautionary therapy
- Screening and preventive therapy for TB
- Diagnosis and treatment of sexually transmitted infections
- Pain management in palliative care
- Treatment of opportunistic infections
- Prevention of mother-to-child transmission of HIV
- Post-exposure prophylaxis following occupational exposure or sexual assault
- Medical management and drug treatment, including the provision of antiretroviral therapy, and continual observation for medicine effectiveness and safety, in so far as provided for in the national guidelines applicable in the public sector

As of 1 January 2005, access to highly active antiretroviral therapy (HAART) has been incorporated as part of the prescribed minimum benefits (South Africa, 2004a:4).

The Medical Schemes Act, No. 131 of 1998, relaunched prescribed minimum benefits as a policy instrument for delineating minimum acceptable levels of medical scheme cover (McLeod *et al.*, 2003:78). Incorporated in the purpose of the Act of The National Health Bill of November 2001, was the founding of a national health system which encompasses public, private and non-governmental providers of health services; and makes the finest possible health services available to the population of South Africa that available resources can provide (McLeod *et al.*, 2003:78). The Committee of Inquiry into a Comprehensive System of Social Security for South Africa (South Africa, 2002), suggested the development of an operative policy process on defining and executing basic essential services throughout the public and private sectors in March 2002 (McLeod *et al.*, 2003:79). The report asserts that the public and private health care sectors should offer a minimum core collection of services that are regulated within medical schemes as prescribed minimum benefits. Within the public sector these are regarded as minimum norms and standards (McLeod *et al.*, 2003:79). The revised Medical Schemes Act (Act 131 of 1998), standardises medical scheme coverage for certain selected health conditions in terms of PMBs, operational from 1 January 2005 (South Africa, 2004a:4). According to McLeod *et al.* (2003:79) the intention of stipulating a collection of PMBs is stated in the 1999 regulations. The following aspects are included:

- To preclude episodes where persons suffer the loss of their medical scheme cover in the event of serious illness and the ensuing risk of unfunded utilisation of public hospitals
- To promote enhanced competence in the distribution of Private and Public health care resources

Medical schemes are not allowed to enforce financial restrictions on members for the cost of diagnosis or therapy of, or care for, the circumstances covered by PMBs. However, they may employ managed-care procedures such as pre-authorisation, the development of formularies and the employment of restricted networks of providers to facilitate regulation of care (McLeod *et al.*, 2003:79). As from 1 January 2004, PMBs have been appreciably broadened to encompass the costs of diagnosis, treatment with chronic medicine and medical management with reference to a list of distinctive conditions, also known as the 'chronic disease list' (CDL) illnesses. HIV/AIDS has recently been included in this list (Profmed, 2008:1). The PMBs for HIV/AIDS that came into force on 1 January 2000 consisted solely of the treatment and management of opportunistic infections and localised malignancies. The 2002 regulations, effective from 1 January 2003, expanded the PMBs to embrace a supplementary package of benefits regarding HIV/AIDS-related conditions. Cover must be supplied for voluntary counselling and testing; treatment for tuberculosis, sexually transmitted infections and opportunistic infections, in addition to pain management in palliative care. Importantly, the PMBs were extended to cover the prevention of mother-to-child transmission (MCTC) of HIV and post-exposure prophylaxis subsequent to sexual assault (McLeod *et al.*, 2003:80-81). The Medical Schemes Act of 1998 mandates community rating, consequently schemes are barred from using age or health status as rating factors. The Act also demands guaranteed acceptance, under which schemes are disallowed from underwriting members on admission to the scheme, thus preventing discrimination on account of any medical condition, including HIV status (McLeod *et al.*, 2003:81).

2.14.4 HIV/AIDS coverage of medical schemes

Monotherapy, dual-therapy and triple-therapy are covered by health insurance schemes. However, either dual or triple-therapy is accessible to the majority of beneficiaries. The use of ARVs is supplemented by other services such as counselling, treatment of side-effects, drug monitoring, diagnostic measures and support groups (Martinson *et al.*, 2003:239-240).

2.14.4.1 Coverage and benefits

Due to the privileged nature of the group of medical scheme beneficiaries, the HIV prevalence in medical schemes is lower than in the conventional population but HIV is

nonetheless a critical risk factor. Accordingly, treatment for HIV is included in the prescribed minimum benefits for medical schemes (IAAHS, 2007:1).

A scheme may present certain options that offer PMBs only and others that offer all-inclusive HIV/AIDS benefits (McLeod *et al.*, 2003:81). Seventy-seven medical schemes were analysed in a study by McLeod and colleagues (McLeod *et al.*, 2003:83). These schemes were grouped into four categories in accordance with the HIV/AIDS benefits provided and the manner in which these were managed:

- Schemes that simply provide PMBs with no additional HIV benefits
- Schemes that offer auxiliary HIV benefits but are not managed by any disease management programme
- Schemes that provide additional benefits and are managed by Aid-for-AIDS, a programme regarded as the industry benchmark
- Schemes that make additional HIV benefits available and are managed by another disease management programme, including their own internal programme

Table 2.12 Categories of HIV/AIDS benefits and benefit management* taken from McLeod *et al.* (2003:84)

Categorisation	Percentage of schemes	Percentage of beneficiaries
No additional benefit	9.10%	2.50%
No disease management	13.00%	7.70%
Aid-for-AIDS programme	41.60%	36.20%
Other disease management	36.30%	53.60%

**Number of participating Medical Schemes: N = 77*

It was observed that only seven (or 9.10 per cent) of the 77 schemes participating in the study, were offering no benefits other than PMBs. Approximately 2.50 per cent of beneficiaries belonged to these schemes (McLeod *et al.*, 2003:84).

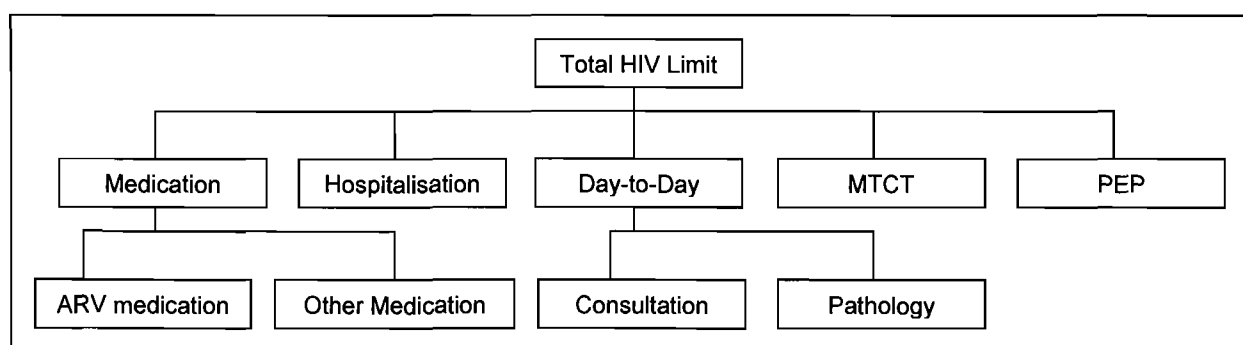
In 2002, access to ARV therapy was provided by 73.00 per cent of options - this translates to access for 92.00 per cent of beneficiaries (McLeod *et al.*, 2003:93).

Table 2.13 Access to ARV therapy for medical scheme beneficiaries from McLeod *et al.* (2003:93)

Therapy	Percentage of options	Percentage of beneficiaries
No ARV therapy	27%	8%
Monotherapy	20%	21%
Dual therapy	58%	73%
Triple therapy	71%	90%

Diagnostics, drug monitoring, treatment of any potential side-effects and counselling for people on drug treatment are some of the medical scheme costs involved in providing ARV therapy, excluding the drugs themselves (McLeod *et al.*, 2003:94).

Figure 2.2 Categorisation of costs and financial limits for HIV/AIDS benefits (McLeod *et al.*, 2003:95)



MTCT = Mother-to-child transmission

PEP = Post-exposure prophylaxis

2.14.4.2 HIV disease management programmes

Schemes have welcomed the application of specialised disease management programmes for HIV/AIDS; 78.00 per cent of schemes employ this alternative, covering 86.00 per cent of options and 90.00 per cent of beneficiaries in the survey conducted by McLeod and co-workers (2003:84). Disease management programmes were established with the purpose of providing a comprehensive management approach for beneficiaries of contracted medical schemes. In order to receive more generous benefits, members are usually obliged to register with the programmes. In the instance of HIV/AIDS, procedures have been designed within these programmes to guarantee client confidentiality (McLeod *et al.*, 2003:84).

Disease management registration makes better data collection possible on those patients and their drug-utilisation behaviour, thus maximising cost-effectiveness. It may also serve as an opportunity for intervention on the part of the schemes. Disease management programmes furnish clinicians with up to date data on best practice for the treatment of each disease, within the constraints implemented by the scheme (McLeod *et al.*, 2003:84).

Disease management programmes (DMPs) prospectively cover 89.00 per cent of all health insurance beneficiaries (Martinson *et al.*, 2003:239). Although beneficiaries of medical schemes have access to the DMPs, only a small number are registered into the programme. Only 18 000 medical scheme members are enlisted with a DMP, signifying less than 1.00 per cent of all beneficiaries. This is a trivial number in proportion to the magnitude of the epidemic in South Africa given that an estimated 5.00 per cent of all medical scheme members are HIV-positive (Martinson *et al.*, 2003:239).

Workplace programmes (for instance Anglo-American, Daimler-Chrysler), commonly augmented with donor funds, have led the way to ART provision in South Africa. By the end of 2004 it was calculated that approximately 45 000 patients were receiving treatment by means of assorted private sector outlets (e.g. medical schemes; employer assisted programmes). According to Stewart and Loveday (2006:236) ART is at present a prescribed minimum benefit through all medical aid schemes.

The Aid-for-AIDS programme (AfA) provides inclusive HIV and AIDS management outcomes for medium to large businesses as well as medical aid schemes. The Sunday Times of January 15, 2006 related that in excess of 53 medical schemes and numerous companies are patrons of AfA. It was reported in January 2006 that there were 25 000 private medical aid members who were signed on as members of the AfA programmes and that over 70.00 per cent of these patients were receiving antiretroviral drugs at that time (Department of Health, 2006).

According to McLeod and co-workers (2003:84) the Aid-for-AIDS programme is used to demonstrate the characteristic scope of HIV/AIDS disease management. The aspirations of the programme include the following (McLeod *et al.*, 2003:84):

- To provide managed access to ARV therapy
- To facilitate access to benefits for the treatment of post-exposure prophylaxis (in the event of occupational injury or sexual assault)
- To provide therapy for the prevention of MTCT

- To offer expert counselling to the primary-care physician chosen by the member
- To provide a comprehensive education and awareness programme to members and employee groups
- To help with medication-related dilemmas and lifestyle issues by means of nurse counsellors

Disease management programmes are likely to increase cost-effectiveness regarding the treatment of HIV/AIDS (McLeod *et al.*, 2003:85).

When South Africa's HIV prevalence rates are taken into account, one of the most significant findings of the research done by McLeod and co-workers was the extremely low participation rate of beneficiaries in the HIV/AIDS disease management programmes (McLeod *et al.*, 2003:85). Apart from Aid-for-AIDS, a mere 0.16 per cent of beneficiaries that have access to disease management programmes are enrolled with these programmes. Aid-for-AIDS manages 79.00 per cent of the 17 745 beneficiaries stated to be registered on disease management programmes. Overall, including Aid-for-AIDS, only 0.42 per cent of beneficiaries with access to programmes are registered on those programmes. Evidence from major industry participants indicates that altogether 22 500 beneficiaries are enlisted on programmes, which amounts to 0.30 per cent of all beneficiaries in medical schemes. This is regarded as the most reliable existing estimate for the medical schemes industry in total (McLeod *et al.*, 2003:86).

The fraction of beneficiaries of medical schemes who may be HIV positive is estimated to be roughly 6.00 per cent in 2002. Accordingly the discovery that only 0.30 per cent of the total beneficiaries in the industry are registered on HIV/AIDS disease management programmes, brings a significant problem to light (McLeod *et al.*, 2003:86).

2.15 Chapter summary

In this chapter the extent of the HIV-epidemic in South Africa, the impact of HIV on South African society, possible methods of HIV transmission, and the stages of HIV/AIDS disease were discussed. This chapter explored the realm of antiretroviral therapy – classification of ARVs, treatment protocols, indications to start treatment, and interactions between antiretroviral drugs. The South African health care system was reviewed vis-à-vis principles of pharmacoeconomics, drug utilisation review, and health care concepts including health insurance by medical schemes.

CHAPTER 3: EMPIRICAL INVESTIGATION

3.1 Introduction

The contents of this chapter encompass the research objectives, empirical research methodology, data source and database utilised in this dissertation.

3.2 General research objectives

The general research objective of this study was to review the usage and prescribing patterns of antiretroviral drugs in a section of the South African private health care sector for the period 2005 to 2006 by utilising a medicine claims database of a pharmacy benefit management company, and to investigate the costs associated with these drugs.

3.3 Specific research objectives

The research project is composed of two phases, a literature review and an empirical investigation. The research objectives of the two respective phases were as follows:

3.3.1.1 Phase 1: Literature review

The specific research objectives of the literature review were:

- To conceptualise the HIV/AIDS pandemic from available literature.
- To describe HIV/AIDS treatment protocols and the antiretroviral drugs involved therein.
- To conceptualise from the literature some pharmacoeconomic principles involved in the South African health care system.
- To study the health care system of South Africa and ascertain through the literature how South African medical aid funds approach and manage antiretroviral therapy.

3.3.1.2 Phase 2: Empirical investigation

The specific research objectives of the empirical investigation included:

- To determine the usage patterns and cost of drugs in general according to all medicine items and prescriptions in the total medicine claims database for the study period 2005 to 2006.
- To investigate generic substitution of innovator antiretroviral drugs within the two study years.

- To analyse utilisation patterns and cost of antiretroviral agents and antiretroviral prescriptions in the medicine claims database according to gender, age group, prescriber and provider for the two study years.
- To identify combination therapy of antiretroviral drugs and determine the costs associated with these combinations for 2005 and 2006.

3.4 Research design

Quantitative, retrospective drug utilisation review (The U.S. Pharmacopeia Drug Utilization Review Advisory Panel, 2000:1) was applied to data from a medicine claims database of a pharmacy benefit management company in order to review, analyse and interpret prescribing patterns and associated costs of antiretroviral drugs. Claims data of patients who were prescribed one or more antiretroviral agents during the study period were used to determine the patterns of drug utilisation, after the medicine items had been dispensed and paid for by the pharmacy benefit management company.

3.5 Data source used for the empirical investigation

The data used in this study were acquired from the central database of the pharmacy benefit management company, which applies managed care concepts to claims data to ensure that the therapeutic outcomes of treatment are satisfactory to the provider, payer, and patient.

The data for the two year study period from 1 January 2005 to 31 December 2005, and 1 January 2006 to 31 December 2006 were extracted from the database.

3.6 Measuring instruments/criteria for the data analysis

In order to achieve the objectives set for this study, the following were selected as measuring instruments or criteria for data analysis:

3.6.1 Medicine items

The Medicines and Related Substances Control Act 101 of 1965 defines medicine items 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”* (South Africa, 1965:3). Medicine items claimed via the pharmacy benefit management company were used as a research instrument in this study to portray prescribing patterns by making use of the total number of medicine items prescribed, in addition to the average number of medicine items per prescription for both the total database and antiretroviral medicine items.

3.6.2 Prevalence

Waning and Montagne (2001:21) define prevalence as the likelihood that a condition is present in a particular population or the odds of the occurrence of a condition.

In this study, the prevalence of the following medicine items was analysed in the following manner:

- The prevalence of all medicine items of the total database claimed during the two year study period.
- The prevalence of antiretroviral medicine items claimed during the study period.
- The prevalence of innovator and generic antiretroviral medicine items claimed during the study period.
- The prevalence of individual antiretroviral medicine items by trade name and active ingredient.
- The prevalence of antiretroviral medicine items by prescriber, provider, patient age and gender.
- The prevalence of combination therapy of antiretroviral medicine items claimed during the study period.

3.6.3 Costs

According to Wilson (1999:1) cost can be defined as the overall worth of the total resources that are expended (input) whilst producing commodities or services (output).

The total medicine cost, the average cost per prescription, the average cost per medicine item, and the cost-prevalence index were calculated as follows:

- The total cost of all medicine items claimed during the two year study period were compared.
- The total cost of all antiretroviral medicine items claimed during the study period were compared.
- The total costs of all antiretroviral medicine items claimed during the study period were compared regarding prescriber, provider, patient age and gender.

- The cost differences between innovator and generic antiretroviral medicine items claimed during the study period were analysed.
- The cost of combination therapy of antiretroviral medicine items claimed during the study period was calculated.

3.7 Data analysis

3.7.1 Data application and data analysis

The selected criteria firstly were applied to the database by means of viewing the criteria retrospectively. Any deviations from the criteria were marked either for further review or as potential targets for intervention. The Statistical Analysis System®, SAS 9.1® (SAS Institute Inc., 2003) was then applied to analyse the data.

3.7.2 Statistical analysis

For the purpose of the empirical investigation, various statistical methods and calculations were applied to analyse the data according to the measuring instruments/criteria as follows:

3.7.2.1 Arithmetic mean (Average)

The mean (or arithmetic average) of a set of numerical observations is the sum of observations divided by the number of observations (Devore & Peck, 1993:69):

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

Where:

$\bar{x}$ = mean

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

n = number of observations

3.7.2.2 Standard deviation

Marczyk and co-workers (2005: 92) define standard deviation as a measure of variability indicating the average amount that scores vary from the mean. Standard deviation is calculated as follows (Lind & Mason, 1997: 91-92):

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

Where:

s = standard deviation

x = any value in the data set

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

n = number of observations

3.7.2.3 Cost-prevalence index

The following equation is used by Serfontein (1989:180) to calculate the cost-prevalence index:

$$\text{Cost - prevalence index} = \frac{\text{Cost}(\%)}{\text{Prevalence}(\%)}$$

In this study the cost-prevalence index is used as an indicator of the relative expensiveness of antiretroviral medicine items.

For the purpose of this study the cost-prevalence index may be interpreted as follows:

- If cost-prevalence index < 1 the medicine item is considered relatively inexpensive.
- If cost-prevalence index = 1 there is equilibrium between the cost and prevalence of the medicine item.
- If cost-prevalence index > 1 the medicine item is considered relatively expensive.

3.7.2.4 Effect sizes (d-values)

Effect size is the magnitude of the differences between group means or other test statistics (Marczyk *et al.*, 2005: 92). Steyn (1999:3) calculates effect size as follows:

$$d = \frac{\overline{x_a} - \overline{x_b}}{s_{max}}$$

Where:

d = effect size.

$\overline{x_a}$ = average medicine treatment cost of a .

$\overline{x_b}$ = average medicine treatment cost of b .

s_{max} = maximum standard deviation between a and b .

A value of $d \geq 0.8$ indicated a practically significant difference, while $d \leq 0.8$ suggested no practically significant difference between the two values compared with each other.

3.8 Reliability and validity of the research instruments

The data for analysis were directly obtained from the central database of Interpharm Data Systems®, and thus no direct manipulation of the data by the researcher was possible. Data for the analysis were obtained for a two-year period (1 January 2005 to 31 December 2005 and 1 January 2006 to 31 December 2006), thus limiting external validity, meaning that the results can be generalised to the specific database and study population only.

The research was conducted from the perspective that all data obtained from the database were correct and accurate (this is a limitation of the study and listed as such in Chapter 5).

The PBM's administrator granted permission to conduct the study and approval was also garnered from the NWU Ethical Committee. The ethical permission was granted by the NWU for the study "A Retrospective Analysis of the Usage Patterns of Antiretroviral Drugs: A Pharmacoeconomic Approach" and the ethical committee awarded the study with the following number of permission: NWU-0046-08-S5.

3.9 Results and discussion

The results and discussion of the empirical investigation are presented in Chapter 4.

3.10 Conclusions and recommendations

The conclusions and recommendations derived from the results of the literature review and the empirical investigation are discussed in Chapter 5.

3.11 Chapter summary

In this chapter the objectives of the empirical study, design and methodology of the research project, data source, measuring instruments/criteria for the data analysis, and statistical analysis of the data were discussed, as well as the reliability and validity of the research instruments.

CHAPTER 4: RESULTS AND DISCUSSION

4.1 Introduction

In this chapter, the results of the empirical investigation of the prescribing patterns and cost of antiretroviral medicine items for the study periods 1 January 2005 to 31 December 2005 and 1 January 2006 to 31 December 2006 are summarised and discussed.

For the purpose of this study, the total database was analysed and compared with the antiretroviral medicine items (selected from pharmacological group 18.12 according to the MIMS® classification, antiviral medicine items). Thus the focus of this study was specifically on the ARV medicine items.

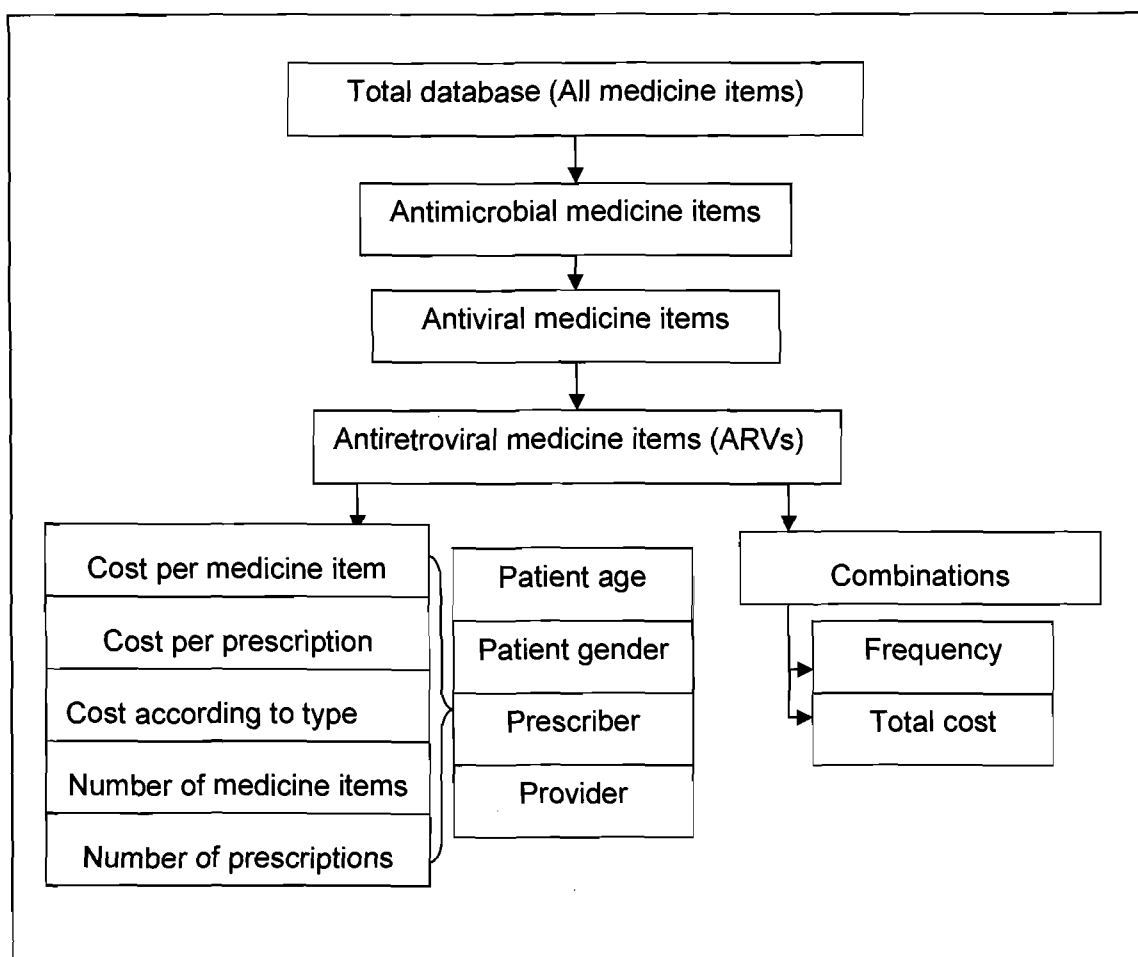


Figure 4.1: Schematic classification system of the data as extracted from the database

4.2 Terms and definitions

For the purpose of this study, the following terms and definitions were used:

4.2.1.1 Generic medicine items

Generic medicine items contain equal quantities of identical active pharmaceutical ingredients in the same dosage form in comparison with the original medicine item (Adcock Ingram, 2008:1; MCC, 2003:2). The World Health Organization and Health Action International (WHO & HAI, 2008:232) define generic medicine items as *“a pharmaceutical product usually intended to be interchangeable with the originator brand product, manufactured without a licence from the originator manufacturer and marketed after the expiry of patent or other exclusivity rights”*.

4.2.1.2 Innovator medicine items

The “originator pharmaceutical product” or “originator brand” is normally the product that has been initially certified globally for retail (typically as a product patented on its chemical formulation or manufacturing process) by reason of the certification of its efficiency, safety and quality, and is usually sold under a brand name (WHO & HAI, 2008:232; Kermani & Bonacossa, 2008:1).

4.2.1.3 Number of medicine items

The number of medicine items refers to the total number of medicine items claimed through the database during a specific time period (refer to section 3.6.1 for a definition of medicine items).

4.2.1.4 Number of prescriptions

The number of prescriptions refers to the total number of prescriptions claimed through the database during a specified time period.

4.2.1.5 Prescriber

According to the Medicines and Related Substances Control Act 101 of 1965 'authorised prescriber' means *“a medical practitioner, dentist, veterinarian, practitioner, nurse or other person registered under the Health Professions Act, 1974”* (South Africa, 1997:12).

4.2.1.6 Provider

For the purpose of this study, a provider is defined as the entity that dispensed the prescribed medication to the patient.

4.2.2 Comments of interest with the interpretation of the results

The values of the data that were used have been “rounded off” to two decimals and may not add up to 100 per cent.

The effect sizes (d-values) were calculated (refer to section 3.7.2.4) and described in the text, but not indicated in any tables. Only $d \geq 0.8$ (practically significant difference) was used as this value indicated that the effect is large and of practical importance (refer to section 3.7.2.4).

Percentage increases or decreases in the total number of ARV medicine items or prescriptions between the two study years were calculated by subtracting the percentage values the respective ARV medicine items represented of the total number of medicine items claimed through the database.

4.3 General prescribing patterns

Table 4.1 gives the prescribing patterns of the total database and ARV medicine items for the two study years, 1 January 2005 to 31 December 2005 and 1 January 2006 to 31 December 2006.

4.3.1 General prescribing patterns for the years 2005 and 2006

Table 4.1 General prescribing patterns for the years 2005 and 2006

Description	2005		2006	
	Total database	Antiretroviral medicine items	Total database	Antiretroviral medicine items
Total number of patients	1 218 358	7 664	1 259 099	10 162
Total number of prescriptions	8 506 355	49 995	9 029 912	81 096
Total number of medicine items	19 860 679	128 403	21 473 074	204 823
Average number of medicine items per prescription	2.33 ± 1.56	2.57 ± 0.74	2.37 ± 1.58	2.53 ± 0.66
Average cost per medicine item (R)	95.33 ± 192.21	203.00 ± 122.47	95.33 ± 227.99	191.56 ± 113.72
Average cost per prescription (R)	222.16 ± 463.13	521.36 ± 177.21	226.28 ± 557.49	483.82 ± 159.10
Total cost (R)	1 893 376 921.00	26 065 335.07	2 046 944 383.00	39 235 744.15

The total number of **patients of the total database** increased with 3.34 per cent ($n = 40\,741$), and the total number of **patients receiving antiretroviral therapy** increased with 0.18 per cent ($n = 2\,498$) from 2005 to 2006. Table 4.1 shows that **patients receiving ARVs** represented 0.63 per cent ($n = 7\,664$), and 0.81 per cent ($n = 10\,162$) of the total number of **patients from the total database** during 2005 ($n = 1\,218\,358$) and 2006 ($n = 1\,259\,099$) respectively.

Table 4.1 indicates that the total number of **prescriptions claimed through the total database** increased with 6.15 per cent ($n = 523\,557$), and the total number of **ARV prescriptions** increased with 0.31 per cent ($n = 31\,101$) from 2005 to 2006. The number of **ARV prescriptions** represented 0.59 per cent ($n = 49\,995$), and 0.90 per cent ($n = 81\,096$) respectively of the total number of **prescriptions claimed through the database** during 2005 ($n = 8\,506\,355$) and 2006 ($n = 9\,029\,912$).

The total number of **medicine items claimed through the total database** increased with 8.12 per cent ($n = 1\,612\,395$), and the total number of **ARV medicine items** increased with 0.3 per cent ($n = 76\,420$) from 2005 to 2006. The total number of **ARV medicine items** represented 0.65 per cent ($n = 128\,403$), and 0.95 per cent ($n = 204\,823$) of the total number of **medicine items claimed through the total database** during 2005 ($n = 19\,860\,679$) and 2006 ($n = 21\,473\,074$), as can be seen in table 4.1.

No practically significant differences in the **average cost per medicine item** or **average cost per prescription** were found between the **total database** and **ARV** medicine items and prescriptions for the two study years ($d < 0.8$).

According to table 4.1, the **total cost of all medicine items claimed through the total database** increased with 8.11 per cent ($n = R153\,567\,462.00$), and the **total cost of ARV medicine items** increased with 0.54 per cent ($n = R13\,170\,409.08$) from 2005 to 2006. The **total cost of ARV medicine items** represented 1.38 per cent ($n = R26\,065\,335.07$) and 1.92 per cent ($n = R39\,235\,744.15$) of the **total cost of all medicine items claimed through the total database** claimed during 2005 ($n = R1\,893\,376\,921.00$) and 2006 ($n = R2\,046\,944\,383.00$).

Prescriptions claimed through the total database showed an average of 2.33 ± 1.56 **medicine items per prescription** during 2005, and 2.37 ± 1.58 medicine items per prescription during 2006. The number of **ARV medicine items per prescription** was 2.57 ± 0.74 during 2005, and it was 2.53 ± 0.66 during 2006, indicating no practically significant difference in the average number of medicine items per prescription for the two study years ($d < 0.8$).

The **cost-prevalence index (CPI)** of **ARV medicine items** in comparison with medicine items from the total database was 2.12 during 2005 and it was 2.02 during 2006, indicating that ARV medicine items are relatively expensive.

Table 4.2 shows that there is no practically significant difference in the **average number of prescriptions per patient per year** between patients of the total database and patients receiving ARVs ($d < 0.8$).

On average, patients received 6.52 ± 4.54 ARV prescriptions per year during 2005, and 7.98 ± 4.64 ARV prescriptions per year during 2006 (*refer to table 4.2*).

Table 4.2 Average number of prescriptions per patient per year

Description	2005		2006	
	Total database	ARV	Total database	ARV
Average number of prescriptions per patient per year	6.98 ± 7.83	6.52 ± 4.54	7.17 ± 8.05	7.98 ± 4.64
Total number of patients	1 218 358	7 664	1 259 099	10 162
Total number of prescriptions	8 506 355	49 995	9 029 912	81 096

Of the total number of patients in the total database, 25.33 per cent received one prescription per year during 2005, and 26.64 per cent received one prescription per year during 2006. Patients receiving one ARV prescription per year constituted 17.00 per cent and 11.89 per cent of patients receiving ARVs during 2005 and 2006 respectively (*refer to table 4.3*).

The **average number of prescriptions per patient per year** can be analysed in terms of the top three percentages per study year. This demonstrates the following:

During the first study year 25.33 per cent of patients from the total database received one prescription per patient per year; and 13.40 per cent of patients from the total database received two prescriptions per patients per year; and 9.27 per cent of patients from the total database received three prescriptions per patient per year during 2005 (*refer to table 4.3*).

During the second study year 26.64 per cent of patients from the total database received one prescription per patient per year; and 12.45 per cent per cent of patients from the total database received two prescriptions per patients per year; and 8.68 per cent per cent of patients from the total database received three prescriptions per patient per year during 2006 (*refer to table 4.3*).

Patients receiving ARVs showed a different trend, where 17.00 per cent of patients received one ARV prescription per year; and 9.80 per cent received two ARV prescriptions per patient per year, but 9.53 per cent of patients received 13 ARV prescriptions per patient per year during 2005 (*refer to table 4.3*).

A similar pattern can be seen in the second study year, where 12.08 per cent of patients received 13 ARV prescriptions per patient per year, and 11.89 per cent of patients received one ARV prescription per patient per year; and 9.41 per cent of patients received 12 ARV prescriptions per patient per year (*refer to table 4.3*)

Table 4.3 Number of prescriptions per patient per year according to frequency

Number of prescriptions per patient per year	2005				2006			
	Total database		ARV		Total database		ARV	
	N	%	N	%	N	%	N	%
1	308 605	25.33	1303	17.00	335 401	26.64	1208	11.89
2	163 272	13.40	751	9.80	156 797	12.45	705	6.94
3	112 898	9.27	637	8.31	109 286	8.68	604	5.94
4	85 025	6.98	626	8.17	82 468	6.55	514	5.06
5	66 566	5.46	458	5.98	65 142	5.17	517	5.09
6	53 919	4.43	542	7.07	53 258	4.23	690	6.79
7	44 045	3.62	297	3.88	43 858	3.48	458	4.51
8	37 002	3.04	303	3.95	37 488	2.98	417	4.10
9	31 404	2.58	303	3.95	33 022	2.62	474	4.66
10	27 747	2.28	356	4.65	29 545	2.35	576	5.67
11	26 215	2.15	435	5.68	28 000	2.22	664	6.53
12	26 991	2.22	532	6.94	28 595	2.27	956	9.41
13	26 586	2.18	730	9.53	28 608	2.27	1228	12.08
14	24 970	2.05	236	3.08	27 058	2.15	859	8.45
15	22 562	1.85	89	1.16	24 113	1.92	190	1.87
16	19 841	1.63	31	0.40	21 236	1.69	68	0.67
17	17 369	1.43	18	0.23	18 787	1.49	21	0.21
18	15 159	1.24	7	0.09	16 743	1.33	4	0.04
19	13 222	1.09	3	0.04	14 560	1.16		
20	11 665	0.96	1	0.01	12 783	1.02	6	0.06
21	10 108	0.83	1	0.01	11 065	0.88	2	0.02
22	8 908	0.73	2	0.03	9 798	0.78	1	0.01
23	7 834	0.64	1	0.01	8 464	0.67		
24	6 899	0.57	1	0.01	7 328	0.58		
25	6 015	0.49			6 662	0.53		
26	5 188	0.43			5 715	0.45		
27	4 603	0.38			4 987	0.40		
28	3 968	0.33	1	0.01	4 517	0.36		
29	3 511	0.29			4 034	0.32		
30	3 088	0.25			3 450	0.27		
31	2 741	0.22			3 036	0.24		
32	2 394	0.20			2 771	0.22		
33	2 021	0.17			2 404	0.19		
34	1 896	0.16			2 013	0.16		
35	1 591	0.13			1 762	0.14		
36	1 330	0.11			1 631	0.13		
37	1 289	0.11			1 449	0.12		
38	1 079	0.09			1 247	0.10		
39	9 28	0.08			1 113	0.09		
40	856	0.07			932	0.07		
41	836	0.07			905	0.07		
42	685	0.06			777	0.06		
43	568	0.05			687	0.05		
44	538	0.04			625	0.05		
45	861	0.07			1 005	0.08		
46	411	0.03			459	0.04		
47	337	0.03			397	0.03		
48	315	0.03			360	0.03		
49	270	0.02			297	0.02		
50	229	0.02			262	0.02		
51	213	0.02			241	0.02		
52	207	0.02			207	0.02		
53	171	0.01			179	0.01		
54	1 407	0.12			1 572	0.12		

4.3.2 Prescribing patterns according to type of medicine for 2005 and 2006

Table 4.4 Prescribing patterns according to type of medicine for the years 2005 and 2006

Description	2005		2006	
	Total database	Antiretroviral medicine items	Total database	Antiretroviral medicine items
Total number of original innovator medicine items	2 728 603	14 401	3 281 896	9 378
Total number of original medicine items with no generic	8 501 370	39 810	8 133 997	69 778
Total number of generic medicine items prescribed	8 492 741	74 192	10 024 315	125 667
Average cost of original innovator medicine items (R)	100.22 ± 139.34	284.88 ± 164.13	102.98 ± 164.66	293.06 ± 162.21
Average cost of original medicine items with no generic (R)	140.14 ± 267.20	252.69 ± 84.53	145.55 ± 339.64	229.38 ± 83.80
Average cost of generic medicine items (R)	49.05 ± 66.41	160.44 ± 111.62	52.07 ± 70.13	162.98 ± 113.30
Total cost of original innovator medicine items (R)	273 454 160.00	4 102 616.95	337 960 440.00	2 748 323.41
Total cost of original medicine items with no generic (R)	1 191 350 141.00	10 059 667.23	1 183 914 105.00	16 005 971.22
Total cost of generic medicine items (R)	416 570 452.00	11 903 050.89	521 923 204.00	20 481 449.52

The total number of **original innovator medicine items** increased with 20.28 per cent ($n = 553\,293$), and the total number of items that **original innovator ARV medicine items** represented of all medicine items decreased with 0.24 per cent ($n = 5\,023$) from 2005 to 2006. The total number of **original innovator ARV medicine items** represented 0.53 per cent ($n = 14\,401$) and 0.29 per cent ($n = 9\,378$) of the total number of **original medicine**

items claimed during 2005 ($n = 2\,728\,603$) and 2006 ($n = 3\,281\,896$) respectively (*refer to table 4.4*).

The total number of **original medicine items with no generic** alternative decreased with 4.32 per cent ($n = 367\,373$), and the total number that **original ARV medicine items with no generic** alternative represented of all medicine items increased with 0.39 per cent ($n = 29\,968$) from 2005 to 2006. The total number of **original ARV medicine items with no generic** alternative represented 0.47 per cent ($n = 39\,810$) and 0.86 per cent ($n = 69\,778$) of the total number of **original medicine items with no generic** alternative claimed during 2005 ($n = 8\,501\,370$) and 2006 ($n = 8\,133\,997$) respectively (*refer to table 4.4*).

As seen in table 4.4, the total number of **generic medicine items** increased with 18.03 per cent ($n = 1\,531\,574$), and the total number of items that **generic ARV medicine items** represented of all medicine items increased with 0.38 per cent ($n = 51\,475$) from 2005 to 2006. The total number of **generic ARV medicine items** represented 0.87 per cent ($n = 74\,192$) and 1.25 per cent ($n = 125\,667$) of the total number of **generic medicine items** claimed during 2005 ($n = 8\,492\,741$) and 2006 ($n = 10\,024\,315$).

A practically significant difference was found between the average cost per **original innovator medicine item** claimed through the total database and **original innovator ARV medicine items**, as well as between the average cost per **generic medicine item** claimed through the total database and **generic ARV medicine item** during 2005 and 2006 ($d > 0.8$) (*refer to table 4.4*).

A practically significant difference between the average cost per **original ARV medicine item with no generic** and **generic ARV medicine items** was found for medicine items claimed during 2005 ($d > 0.8$) and a practically significant difference between the average cost per **original innovator ARV medicine item** and **generic ARV medicine items** was found for medicine items claimed during 2006 ($d > 0.8$) (*refer to table 4.4*).

Table 4.4 demonstrates that the total cost of **original innovator medicine items** claimed through the total database increased with 23.59 per cent ($n = R64\,506\,280.00$), and the total cost that **original innovator ARV medicine items** represented of the total database decreased with 0.69 per cent ($n = R1\,354\,293.54$) from 2005 to 2006. The total cost of **original innovator ARV medicine items** represented 1.50 per cent ($n = R4\,102\,616.95$) and 0.81 per cent ($n = R2\,748\,323.41$) of the total cost of **original innovator medicine items** claimed during 2005 ($n = R273\,454\,160.00$) and 2006 ($n = R337\,960\,440.00$).

The total cost of **original medicine items with no generic** claimed through the total database decreased with 0.62 per cent ($n = R7\,436\,036.00$), and the total cost that **original ARV medicine items with no generic** represented of all medicine items increased with 0.51 per cent ($n = R5\,946\,303.99$) from 2005 to 2006. The total cost of **original ARV medicine items with no generic** represented 0.84 per cent ($n = R10\,059\,667.23$) and 1.35 per cent ($n = R16\,005\,971.22$) of the total cost of **original medicine items with no generic** claimed during 2005 ($n = R1\,191\,350\,141.00$) and 2006 ($n = R1\,183\,914\,105.00$) (*Refer to table 4.4*).

The total cost of **generic medicine items** claimed through the total database increased with 25.29 per cent ($n = R105\,352\,752.00$), and the total cost that **generic ARV medicine items** represented of all medicine items increased with 1.06 per cent ($n = R8\,578\,398.63$) from 2005 to 2006. The total cost of **generic ARV medicine items** represented 2.86 per cent ($n = R11\,903\,050.89$) and 3.92 per cent ($n = R20\,481\,449.52$) of the total cost of **generic medicine items** claimed during 2005 ($n = R416\,570\,452.00$) and during 2006 ($n = R521\,923\,204.00$) through the total database (*refer to table 4.4*).

Table 4.5 Cost prevalence index of ARVs according to type of medicine

Description	Cost-prevalence index (CPI)	
	2005	2006
Original innovator ARV medicine items vs. total number of ARV medicine items	1.40	1.53
Original ARV medicine items with no generic vs. total number of ARV medicine items	1.24	1.20
Generic ARV medicine items vs. total number of ARV medicine items	0.79	0.85

Table 4.5 indicates that both **original innovator ARV medicine items** and **original ARV medicine items with no generic** have CPI values >1 , meaning that they are relatively expensive types of ARV medicine items. **Generic ARV medicine items** have a CPI <1 , indicating that they are relatively inexpensive ARV medicine items, implying that generic substitution would benefit cost-savings.

4.4 Prescribing patterns according to patient gender

Table 4.6 Prescribing patterns according to patient gender for the years 2005 and 2006

Description	2005		2006	
	Total database	Antiretroviral Medicine items	Total database	Antiretroviral Medicine items
Total number of medicine items prescribed for female patients	11 974 255	72 711	12 924 812	116 495
Total number of medicine items prescribed for male patients	7 870 112	55 692	8 537 499	88 328
Average cost per medicine item for female patients (R)	94.26 ± 185.03	201.91 ± 120.08	93.86 ± 219.20	193.67 ± 111.76
Average cost per medicine item for male patients (R)	96.98 ± 202.27	204.41 ± 125.51	97.54 ± 240.49	188.77 ± 116.20
Total number of prescriptions for female patients	5 101 405	28 266	5 409 498	46 378
Total number of prescriptions for male patients	3 397 763	21 729	3 615 544	34 718
Average cost of per prescription for female patients (R)	220.77 ± 455.62	519.39 ± 176.63	223.77 ± 532.49	486.48 ± 156.59
Average cost per prescription for male patients (R)	224.27 ± 473.73	523.92 ± 177.93	229.97 ± 592.88	480.27 ± 162.05
Total cost of medicine items for female patients (R)	1 128 652 112.00	14 681 179.71	1 213 068 356.00	22 561 804.79
Total cost of medicine items for male patients (R)	763 226 111.00	11 384 155.36	832 725 542.00	16 673 939.36

The **average number of prescriptions per patient per year** claimed through the total database amounted to 7.55 ± 8.27 prescriptions per year for female patients, and 6.28 ± 7.18 prescriptions per year for male patients during 2005. During 2006, female patients received 7.74 ± 8.51 **prescriptions per patient per year** and male patients received 6.46 ± 7.38 prescriptions per patient per year. Female patients receiving antiretroviral therapy received an average of 6.43 ± 4.50 ARV prescriptions per year, and male patients received 6.65 ± 4.59 **ARV prescriptions per patient per year** during 2005. During 2006, female patients

received 7.96 ± 4.67 ARV prescriptions per patient per year and male patients received 8.01 ± 4.59 ARV prescriptions per patient per year ($d < 0.8$).

There was an average of 2.57 ± 0.74 ARV **medicine items per prescription** during 2005 for female patients, and 2.56 ± 0.73 ARV medicine items per prescription for male patients during 2005. Female patients received an average of 2.51 ± 0.66 **ARV medicine items per prescription** during 2006, and male patients received 2.54 ± 0.65 ARV medicine items per prescription during 2006 ($d < 0.8$).

The **total number of medicine items** claimed for **female** patients claimed through the total database increased with 7.94 per cent ($n = 950\,557$), and the total number of medicine items that **ARV medicine items** claimed for **female** patients increased with 0.29 per cent ($n = 43\,784$) from 2005 to 2006. The **total number of ARV medicine items** claimed for **female** patients represented 0.61 per cent ($n = 72\,711$) and 0.90 per cent ($n = 116\,495$) of the **total number of medicine items** claimed for **female** patients during 2005 ($n = 11\,974\,255$) and 2006 ($n = 12\,924\,812$) (*refer to table 4.6*).

The **total number of medicine items** claimed for **male** patients through the total database increased with 8.48 per cent ($n = 667\,387$), and the total number of items that **ARV medicine items** claimed for **male** patients represented increased with 0.32 per cent ($n = 32\,636$) from 2005 to 2006, as illustrated in table 4.6. The **total number of ARV medicine items** claimed for **male** patients represented 0.71 per cent ($n = 55\,692$) and 1.03 per cent ($n = 88\,328$) of the **total number of medicine items** claimed for **male** patients through the total database during 2005 ($n = 7\,870\,112$) and 2006 ($n = 8\,537\,499$).

No practically significant difference was found between the **average cost per medicine item** for the total database and the **average cost per ARV medicine item** claimed for **female** and **male** patients during both study years ($d < 0.8$) (*refer to table 4.6*).

As illustrated in table 4.6, the **total number of prescriptions** claimed for **female** patients through the total database increased with 6.04 per cent ($n = 308\,093$), and the percentage that **ARV prescriptions** claimed for **female** patients represented of all medicine items increased with 0.31 per cent ($n = 18\,112$) from 2005 to 2006. The total number of ARV prescriptions claimed for **female** patients represented 0.55 per cent ($n = 28\,266$) and 0.86 per cent ($n = 46\,378$) of the total number of prescriptions claimed for **female** through the total database during 2005 ($n = 5\,101\,405$) and 2006 ($n = 5\,409\,498$).

The **total number of prescriptions** for **male** patients claimed through the total database increased with 6.41 per cent ($n = 217\,781$), and the percentage that **ARV prescriptions**

claimed for **male** patients represented of all medicine items increased with 0.32 per cent ($n = 12\,989$) from 2005 to 2006. The **total number of ARV prescriptions** claimed for **male** patients represented 0.64 per cent ($n = 21\,729$) and 0.96 per cent ($n = 34\,718$) of the **total number of prescriptions** claimed for **male** patients through the total database during 2005 ($n = 3\,397\,763$) and 2006 ($n = 3\,615\,544$) (*refer to table 4.6*).

No practically significant difference was found between the **average cost per prescription** for the total database and **average cost per ARV prescription** claimed for **female** and **male** patients during 2005 and 2006 ($d < 0.8$) (*refer to table 4.6*).

The **total cost of all medicine items** claimed for **female** patients through the total database increased with 7.48 per cent ($n = R84\,416\,244$), and the percentage that **ARV medicine items** claimed for **female** patients represented of all medicine cost increased with 0.56 per cent ($n = R7\,880\,625.08$) from 2005 to 2006. The **total cost of ARV medicine items** claimed for **female** patients represented 1.30 per cent ($n = R14\,681\,179.71$) and 1.86 per cent ($n = R22\,561\,804.79$) of the **total cost of all medicine items** for **female** patients claimed for the total database during 2005 ($n = R1\,128\,652\,112.00$) and 2006 ($n = R1\,213\,068\,356.00$) (*Refer to table 4.6*).

The **total cost of all medicine items** claimed for **male** patients through the total database increased with 9.11 per cent ($n = R69\,499\,431$), and the percentage that **ARV medicine items** claimed for **male** patients represented of all medicine cost increased with 0.51 per cent ($n = R5\,289\,784$) from 2005 to 2006. The **total cost of ARV medicine items** claimed for **male** patients represented 1.49 per cent ($n = R11\,384\,155.36$) and 2.00 per cent ($n = R16\,673\,939.36$) of the **total cost of all medicine items** for **male** patients claimed through the total database during 2005 ($n = R763\,226\,111.00$) and 2006 ($n = R832\,725\,542.00$) (*Refer to table 4.6*).

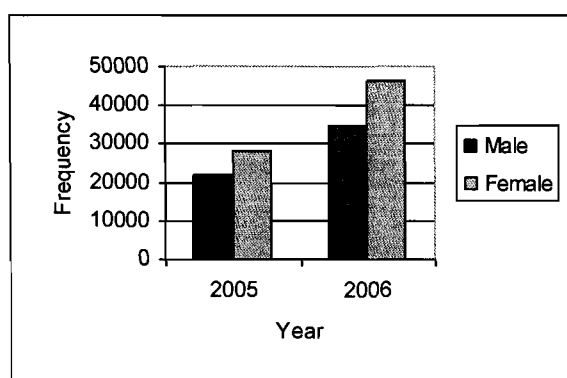


Figure 4.2: Number of ARV prescriptions according to patient gender for 2005 and 2006

Table 4.7 CPI of ARVs in relation to total database according to patient gender

CPI	2005		2006	
	Female	Male	Female	Male
ARV medicine items	2.13	2.10	2.07	1.94

Table 4.7 indicates that ARV medicine items are relatively expensive for patients of both genders.

4.5 Prescribing patterns according to patient age

Table 4.8 Prescribing patterns according to patient age group for the years 2005 and 2006 for patients in the age group 0 to ≤4 years

Description	Age group 0 to ≤4 years			
	2005		2006	
	Total database	Antiretroviral medicine items	Total database	Antiretroviral medicine items
Total number of medicine items	796 959	3 046	840 790	4 188
Average cost of medicine items (R)	53.39 ± 69.91	241.82 ± 187.60	53.04 ± 98.14	170.03 ± 141.58
Total cost of medicine items (R)	42 551 896.62	736 572.51	44 598 649.37	712 104.74
Total number of prescriptions	319 820	1 050	331 600	1 453
Average cost per prescription (R)	133.05 ± 146.64	701.50 ± 341.48	134.49 ± 189.28	490.09 ± 251.86

An average of 2.49 ± 1.36 **medicine items per prescription** was observed during 2005, and 2.54 ± 1.38 medicine items per prescription were claimed on average during 2006 for patients in the age group 0 to ≤4 years. In the age group 0 to ≤4 years there was an average of 2.90 ± 0.53 **ARV medicine items per prescription** during 2005 and 2.88 ± 0.59 ARV medicine items per prescription during 2006 ($d < 0.8$).

In the age group 0 to ≤4 years, patients received an average of 4.36 ± 4.20 and 4.60 ± 4.36 **prescriptions per patient per year** during 2005 and 2006 respectively. Patients in the age group 0 to ≤4 years received an average of 6.65 ± 4.54 **ARV prescriptions per patient per year** during 2005, and an average of 7.53 ± 4.70 ARV prescriptions per patient per year during 2006 ($d < 0.8$).

The **total number of patients** in the age group 0 to ≤ 4 years decreased with 1.54 per cent ($n = 1\,132$) and the **total number of HIV patients** increased with 0.05 per cent ($n = 35$) from 2005 to 2006. The **total number of HIV patients** represented 0.22 per cent ($n = 158$) and 0.27 per cent ($n = 193$) of the **total number of patients** during 2005 ($n = 73\,288$) and 2006 ($n = 72\,156$) in the age group 0 to ≤ 4 years.

The **total number of medicine items** claimed for patients in the age group 0 to ≤ 4 years increased with 5.50 per cent ($n = 43\,831$), and the percentage that **ARV medicine items** represented of the total number of items increased with 0.12 per cent ($n = 1\,142$) from 2005 to 2006. The **total number of ARV medicine items** represented 0.38 per cent ($n = 3\,046$) and 0.50 per cent ($n = 4\,188$) of the **total number of medicine items** claimed during 2005 ($n = 796\,959$) and 2006 ($n = 840\,790$) for patients in this age group (*refer to table 4.8*).

A practically significant difference between the **average cost per medicine item** for the total database and the **average cost per ARV medicine item** was found for both study years ($d > 0.8$) for the age group 0 to ≤ 4 years (*refer to table 4.8*).

The **total cost of all medicine items** claimed for patients in the age group 0 to ≤ 4 years increased by 4.81 per cent ($n = R2\,046\,752.75$), and the percentage that the **total cost of ARV medicine items** represented of the total medicine cost decreased with 0.13 per cent ($n = R24\,467.77$) from 2005 to 2006 for patients in this age group. The **total cost of ARV medicine items** represented 1.73 per cent ($n = R736\,572.51$) and 1.60 per cent ($n = R712\,104.74$) of the **total cost of all medicine items** claimed during 2005 ($n = R42\,551\,896.62$) and 2006 ($n = R44\,598\,649.37$) respectively (*refer to table 4.8*).

Table 4.8 illustrates that the **total number of prescriptions** claimed through the total database increased with 3.68 per cent ($n = 11\,780$), and the percentage that **ARV prescriptions** represented of all prescriptions increased with 0.11 per cent ($n = 403$) from 2005 to 2006. The **total number of ARV prescriptions** represented 0.33 per cent ($n = 1\,050$) and 0.44 per cent ($n = 1\,453$) of the **total number of prescriptions** claimed through the total database during 2005 ($n = 319\,820$) and 2006 ($n = 331\,600$) for the age group 0 to ≤ 4 years (*refer to table 4.8*).

A practically significant difference was found between the **average cost per prescription** for the total database and the **average cost per ARV prescription** for the age group 0 to ≤ 4 years for 2005 and 2006 ($d > 0.8$) (*refer to table 4.8*).

Table 4.9 Prescribing patterns according to patient age group for the years 2005 and 2006 for patients in the age group >5 to ≤9 years

Description	Age group >5 to ≤9 years			
	2005		2006	
	Total database	Antiretroviral medicine items	Total database	Antiretroviral medicine items
Total number of medicine items	803 960	4 704	827 497	6 916
Average cost of medicine items (R)	25.18 ± 75.21	197.11 ± 179.79	57.94 ± 81.95	162.93 ± 148.39
Total cost of medicine items (R)	46 777 303.98	927 228.38	47 942 246.95	1 126 799.34
Total number of prescriptions	323 089	1 476	329 115	2 179
Average cost per prescription (R)	144.78 ± 151.42	628.20 ± 374.60	145.57 ± 176.79	517.12 ± 283.55

An average of 2.49 ± 1.34 **medicine items per prescription** was observed during 2005, and 2.51 ± 1.37 medicine items per prescription were claimed on average during 2006 for patients in the age group >5 to ≤9 years. In the age group >5 to ≤9 years there was an average of 3.19 ± 0.98 **ARV medicine items per prescription** during 2005 and 3.17 ± 0.80 ARV medicine items per prescription during 2006 ($d < 0.8$).

In the age group >5 to ≤9 years, patients received an average of 3.54 ± 3.42 and 3.67 ± 3.52 **prescriptions per patient per year** during 2005 and 2006 respectively. Patients in the age group >5 to ≤9 years received an average of 7.17 ± 4.47 **ARV prescriptions per patient per year** during 2005, and an average of 8.25 ± 4.82 ARV prescriptions per patient per year during 2006 (signifying a practically significant difference between the average number of prescriptions and the average number of ARV prescriptions per patient per year for patients in the age group >5 to ≤9 years).

The **total number of patients** in the age group >5 to ≤9 years decreased with 1.95 per cent ($n = 1\,781$) and the **total number of HIV patients** increased with 0.06 per cent ($n = 58$) from 2005 to 2006. The **total number of HIV patients** represented 0.23 per cent ($n = 206$) and 0.29 per cent ($n = 264$) of the **total number of patients** in the total database during 2005 ($n = 91\,377$) and 2006 ($n = 89\,596$) for the age group >5 to ≤9 years.

The **total number of medicine items** claimed for patients in the age group >5 to ≤9 years increased with 2.93 per cent (n = 23 537), and the percentage that **ARV medicine items** represented of the total number of medicine items increased with 0.25 per cent (n = 2 212) from 2005 to 2006. The **total number of ARV medicine items** represented 0.59 per cent (n = 4 704) and 0.84 per cent (n = 6 916) of the **total number of medicine items** claimed during 2005 (n = 803 960) and 2006 (n = 827 497) (*refer to table 4.9*).

A practically significant difference between the **average cost per medicine item** for the total database and the **average cost per ARV medicine item** was found for 2005 (d>0.8) for the age group >5 to ≤9 years (*refer to table 4.9*).

As indicated by table 4.9, the **total cost of all medicine items** increased by 2.49 per cent (n = R1 164 942.97), and the percentage that the **total cost of all ARV medicine items** represented of the total medicine cost decreased with 0.37 per cent (n = R199 570.96) from 2005 to 2006 for the age group >5 to ≤9 years. The **total cost per ARV medicine item** represented 1.98 per cent (n = R927 228.38) and 2.35 per cent (n = R1 126 799.34) of the **total cost per medicine item** claimed during 2005 (n = R46 777 303.98) and 2006 (n = R47 942 246.95) respectively.

The **total number of prescriptions** claimed for patients in the age group >5 to ≤9 years increased with 1.87 per cent (n = 6 026), and the percentage that **ARV prescriptions** represented of all prescriptions increased with 0.20 per cent (n = 703) from 2005 to 2006. The **total number of ARV prescriptions** represented 0.46 per cent (n = 1 476) and 0.66 per cent (n = 2 179) of the **total number of prescriptions** claimed during 2005 (n = 323 089) and 2006 (n = 329 115) for patients in the age group >5 to ≤9 years (*refer to table 4.9*).

A practically significant difference was found between the **average cost per prescription** for the total database and the **average cost per ARV prescription** for the age group >5 to ≤9 years for both study years (d>0.8) (*refer to table 4.9*).

Table 4.10 Prescribing patterns according to patient age group for the years 2005 and 2006 for patients in the age group >10 to ≤14 years

Description	Age group >10 to ≤14 years			
	2005		2006	
	Total database	Antiretroviral medicine items	Total database	Antiretroviral medicine items
Total number of medicine items	646 761	1 815	694 636	3 718
Average cost of medicine items (R)	64.72 ± 95.43	162.32 ± 137.51	65.14 ± 100.91	151.04 ± 123.24
Total cost of medicine items (R)	41 856 654.86	294 608.82	45 245 324.99	561 559.59
Total number of prescriptions	270 699	587	285 999	1 182
Average cost per prescription (R)	154.62 ± 188.82	501.89 ± 241.70	158.18 ± 186.01	475.09 ± 216.34

An average of 2.39 ± 1.32 **medicine items per prescription** was observed during 2005, and 2.43 ± 1.35 medicine items per prescription were claimed on average during 2006 for patients in the age group >10 to ≤14 years. In the age group >10 to ≤14 years there was an average of 3.09 ± 0.91 **ARV medicine items per prescription** during 2005 and 3.15 ± 0.84 ARV medicine items per prescription during 2006 ($d < 0.8$).

In the age group >10 to ≤14 years, patients received an average of 3.07 ± 3.04 and 3.25 ± 3.24 **prescriptions per patient per year** during 2005 and 2006 respectively. Patients in the age group >10 to ≤14 years received an average of 6.83 ± 4.76 **ARV prescriptions per patient per year** during 2005, and an average of 8.04 ± 4.60 ARV prescriptions per patient per year during 2006 (indicating a practically significant difference between the **average number of prescriptions** and the **average number of ARV prescriptions** per patient per year claimed during 2006 for patients in the age group >10 to ≤14 years).

The **total number of patients** in the age group >10 to ≤14 years decreased with 0.18 per cent ($n = 161$) and the **total number of HIV patients** increased with 0.33 per cent ($n = 61$) from 2005 to 2006. The **total number of HIV patients** represented 0.10 per cent ($n = 86$) and 0.43 per cent ($n = 147$) of the **total number of patients** in the total database during 2005 ($n = 88\,082$) and 2006 ($n = 87\,921$) for the age group >10 to ≤14.

The **total number of medicine items** claimed for patients in the age group >10 to ≤14 years increased with 7.4 per cent ($n = 47\,875$), and the percentage that **ARV medicine items** represented of the **total number of medicine items** increased with 0.26 per cent ($n = 1\,903$) from 2005 to 2006. The **total number of ARV medicine items** represented 0.28 per cent ($n = 1\,815$) and 0.54 per cent ($n = 3\,718$) of the **total number of medicine items** claimed during 2005 ($n = 646\,761$) and 2006 ($n = 694\,636$) (*refer to table 4.10*).

No practically significant difference was found between the **average cost per medicine item** for the total database and the **average cost per ARV medicine item** for both study years ($d < 0.8$) for the age group >10 to ≤14 years (*refer to table 4.10*).

As indicated by table 4.10, the **total cost of all medicine items** claimed through the total database increased by 8.10 per cent ($n = R3\,388\,670.13$), and the percentage that the **total cost of all ARV medicine items** represented of the total medicine cost increased with 0.54 per cent ($n = R266\,950.77$) from 2005 to 2006 for the age group >10 to ≤14 years. The **total cost of ARV medicine items** represented 0.70 per cent ($n = R294\,608.82$) and 1.24 per cent ($n = R561\,559.59$) of the **total cost of all medicine items** claimed during 2005 ($n = R41\,856\,654.86$) and 2006 ($n = R45\,245\,324.99$) respectively.

Table 4.10 illustrates that the **total number of prescriptions** claimed increased with 5.65 per cent ($n = 15\,300$), and percentage that **ARV prescriptions** represented of the **total number of prescriptions** increased with 0.19 per cent ($n = 595$) from 2005 to 2006. The **total number of ARV prescriptions** represented 0.22 per cent ($n = 587$) and 0.41 per cent ($n = 1\,182$) of the **total number of prescriptions** claimed during 2005 ($n = 270\,699$) and 2006 ($n = 285\,999$) for the age group >10 to ≤14 years (*refer to table 4.10*).

A practically significant difference was found between the **average cost per prescription** for the total database and the **average cost per ARV prescription** for the age group >10 to ≤14 years for 2005 and 2006 ($d > 0.8$) (*refer to table 4.10*).

Table 4.11 Prescribing patterns according to patient age group for the years 2005 and 2006 for patients in the age group >15 to ≤19 years

Description	Age group >15 to ≤19 years			
	2005		2006	
	Total database	Antiretroviral medicine items	Total database	Antiretroviral medicine items
Total number of medicine items	743 812	484	804 581	815
Average cost of medicine items (R)	74.77 ± 126.78	188.83 ± 112.78	73.22 ± 141.58	199.36 ± 134.77
Total cost of medicine items (R)	55 613 737.66	91 393.19	58 913 507.68	162 477.76
Total number of prescriptions	329 376	180	347 360	302
Average cost per prescription (R)	168.80 ± 247.49	507.74 ± 195.22	169.60 ± 296.63	538.01 ± 234.50

An average of 2.26 ± 1.31 **medicine items per prescription** was observed during 2005, and 2.32 ± 1.35 medicine items per prescription were claimed on average during 2006 for patients in the age group >15 to ≤19 years. In the age group >15 to ≤19 years there was an average of 2.69 ± 0.88 **ARV medicine items per prescription** during 2005 and 2.70 ± 0.77 ARV medicine items per prescription during 2006 ($d < 0.8$).

In the age group >15 to ≤19 years, patients received an average of 3.50 ± 3.63 and 3.64 ± 3.75 **prescriptions per patient per year** during 2005 and 2006 respectively. Patients in the age group >15 to ≤19 years received an average of 3.83 ± 4.25 **ARV prescriptions per patient per year** during 2005, and an average of 4.14 ± 3.86 ARV prescriptions per patient per year during 2006 ($d < 0.8$).

The **total number of patients** in the age group >15 to ≤19 years increased with 1.19 per cent ($n = 1\,124$) and the **total number of HIV patients** in this age group increased with 0.03 per cent ($n = 26$) from 2005 to 2006. The **total number of HIV patients** represented 0.05 per cent ($n = 47$) and 0.08 per cent ($n = 73$) of the **total number of patients** of the total database during 2005 ($n = 94\,237$) and 2006 ($n = 95\,361$) for the age group >15 to ≤19 years.

The **total number of medicine items** claimed for patients in the age group >15 to ≤19 years increased with 8.17 per cent ($n = 60\,769$), and the percentage that **ARV medicine items**

represented of the **total number of medicine items** increased with 0.03 per cent ($n = 331$) from 2005 to 2006. The **total number of ARV medicine items** represented 0.07 per cent ($n = 484$) and 0.10 per cent ($n = 815$) of the **total number of medicine items** claimed during 2005 ($n = 743\,812$) and 2006 ($n = 804\,581$) for patients in the age group >15 to ≤ 19 years (*refer to table 4.11*).

A practically significant difference exists between the **average cost per medicine item** for the total database and the **average cost per ARV medicine item** for both 2005 and 2006 ($d>0.8$) for the age group >15 to ≤ 19 years (*refer to table 4.11*).

The **total cost of all medicine items** increased by 5.93 per cent ($n = R3\,299\,770.02$), and the percentage that the **total cost of all ARV medicine items** represented of the total medicine cost increased with 0.12 per cent ($n = R71\,084.57$) from 2005 to 2006 for the age group >15 to ≤ 19 years. **ARV medicine items** represented 0.16 per cent ($n = R91\,393.19$) and 0.28 per cent ($n = R162\,477.75$) of the **total medicine cost** during 2005 ($n = R55\,613\,737.66$) and 2006 ($n = R58\,913\,507.68$) respectively (*refer to table 4.11*).

The **total number of prescriptions** claimed increased with 5.46 per cent ($n = 17\,984$), and the percentage that **ARV prescriptions** represented of all prescriptions increased with 0.04 per cent ($n = 122$) from 2005 to 2006. The **total number of ARV prescriptions** represented 0.05 per cent ($n = 180$) and 0.09 per cent ($n = 302$) of the **total number of prescriptions** claimed during 2005 ($n = 329\,376$) and 2006 ($n = 347\,360$) for the age group >15 to ≤ 19 years (*refer to table 4.11*).

A practically significant difference was found between the **average cost per prescription** for the total database and the **average cost per ARV prescription** for the age group >15 to ≤ 19 years for 2005 and 2006 ($d>0.8$) (*refer to table 4.11*).

Table 4.12 Prescribing patterns according to patient age group for the years 2005 and 2006 for patients in the age group >20 to ≤24 years

Description	Age group >20 to ≤24 years			
	2005		2006	
	Total database	Antiretroviral medicine items	Total database	Antiretroviral medicine items
Total number of medicine items	650 718	1 830	722 495	2 687
Average cost of medicine items (R)	81.01 ± 145.56	208.10 ± 115.54	78.49 ± 154.39	196.99 ± 111.19
Total cost of medicine items (R)	52 714 461.95	380 831.32	56 711 201.08	529 303.82
Total number of prescriptions	304 290	733	330 384	1 052
Average cost per prescription (R)	173.22 ± 290.78	519.55 ± 182.30	171.63 ± 292.73	503.14 ± 202.78

An average of 2.14 ± 1.29 **medicine items per prescription** was observed during 2005, and 2.19 ± 1.32 **medicine items per prescription** were claimed on average during 2006 for patients in the age group >20 to ≤24 years. In the age group >20 to ≤24 years there was an average of 2.50 ± 0.80 ARV medicine items per prescription during 2005 and 2.55 ± 0.76 ARV medicine items per prescription during 2006 ($d < 0.8$).

In the age group >20 to ≤24 years, patients received an average of 3.87 ± 4.23 and 4.03 ± 4.38 **prescriptions per patient per year** during 2005 and 2006 respectively. Patients in the age group >20 to ≤24 years received an average of 3.96 ± 3.59 **ARV prescriptions per patient per year** during 2005, and an average of 4.33 ± 3.91 ARV prescriptions per patient per year during 2006 ($d < 0.8$).

The **total number of patients** in the age group >20 to ≤24 years increased with 4.34 per cent ($n = 3\,412$) and the **total number of HIV patients** increased with 0.06 per cent ($n = 58$) from 2005 to 2006. The **total number of HIV patients** represented 0.24 per cent ($n = 185$) and 0.30 per cent ($n = 243$) of the **total number of patients** in the age group >20 to ≤24 years during 2005 ($n = 78\,637$) and 2006 ($n = 82\,049$) for the age group >20 to ≤24 years.

The **total number of medicine items** claimed for patients in the age group >20 to ≤24 years increased with 11.03 per cent ($n = 71\,777$), and the percentage that **ARV medicine items**

represented of the **total number of medicine items** increased with 0.09 per cent ($n = 857$) from 2005 to 2006. The **total number of ARV medicine items** represented 0.28 per cent ($n = 1\,830$) and 0.37 per cent ($n = 2\,687$) of the **total number of medicine items** claimed during 2005 ($n = 650\,718$) and 2006 ($n = 722\,495$) (*refer to table 4.12*).

A practically significant difference between the **average cost per medicine item** for the total database and the **average cost per ARV medicine item** was found during 2005 ($d > 0.8$) for the age group >20 to ≤ 24 years (*refer to table 4.12*).

As indicated by table 4.12, the **total cost of all medicine items** increased by 7.58 per cent ($n = R3\,996\,739.13$), and the percentage that the **total cost of all ARV medicine items** represented of the **total medicine cost** increased with 0.21 per cent ($n = R148\,472.50$) from 2005 to 2006 for the age group >20 to ≤ 24 years. **ARV medicine items** represented 0.72 per cent ($n = R380\,831.32$) and 0.93 per cent ($n = R529\,303.82$) of the **total cost of all medicine items** claimed during 2005 ($n = R52\,714\,461.95$) and 2006 ($n = R56\,711\,201.08$) respectively.

Table 4.12 illustrates that the **total number of prescriptions** claimed through the total database increased with 8.58 per cent ($n = 26\,094$), and the percentage that **ARV prescriptions** represented of all prescriptions increased with 0.08 per cent ($n = 319$) from 2005 to 2006. The **total number of ARV prescriptions** represented 0.24 per cent ($n = 733$) and 0.32 per cent ($n = 1\,052$) of the **total number of prescriptions** claimed during 2005 ($n = 304\,290$) and 2006 ($n = 330\,384$) for the age group >20 to ≤ 24 years (*refer to table 4.12*).

A practically significant difference was found between the **average cost per prescription** for the total database and the **average cost per ARV prescription** for the age group >20 to ≤ 24 years for both study years ($d > 0.8$) (*refer to table 4.12*).

Table 4.13 Prescribing patterns according to patient age group for the years 2005 and 2006 for patients in the age group >25 to ≤29 years

Description	Age group >25 to ≤29 years			
	2005		2006	
	Total database	Antiretroviral medicine items	Total database	Antiretroviral medicine items
Total number of medicine items	566 310	6 320	626 459	9 198
Average cost of medicine items (R)	79.05 ± 168.67	211.94 ± 113.31	76.40 ± 178.78	195.37 ± 108.44
Total cost of medicine items (R)	44 764 945.55	1 339 449.90	47 862 123.50	1 797 002.38
Total number of prescriptions	266 357	2 528	290 186	3 667
Average cost per prescription (R)	167.99 ± 345.07	529.85 ± 158.71	164.84 ± 334.87	490.05 ± 161.62

An average of 2.13 ± 1.27 **medicine items per prescription** was observed during 2005, and 2.16 ± 1.31 medicine items per prescription were claimed on average during 2006 for patients in the age group >25 to ≤29 years. In the age group >25 to ≤29 years there was an average of 2.50 ± 0.72 **ARV medicine items per prescription** during 2005 and 2.51 ± 0.68 ARV medicine items per prescription during 2006 ($d < 0.8$).

In the age group >25 to ≤29 years, patients received an average of 4.46 ± 5.10 and 4.47 ± 5.18 **prescriptions per patient per year** during 2005 and 2006 respectively. Patients in the age group >25 to ≤29 years received an average of 4.73 ± 3.89 **ARV prescriptions per patient per year** during 2005, and an average of 5.59 ± 4.31 ARV prescriptions per patient per year during 2006 ($d < 0.8$).

The **total number of patients** in the age group >25 to ≤29 years increased with 8.80 per cent ($n = 5\,250$) and the **total number of HIV patients** increased with 0.11 per cent ($n = 121$) from 2005 to 2006. The **total number of HIV patients** represented 0.90 per cent ($n = 535$) and 1.01 per cent ($n = 656$) of the **total number of patients** in the total database during 2005 ($n = 59\,686$) and 2006 ($n = 64\,936$) in the age group >25 to ≤29 years.

The **total number of medicine items** claimed for patients in the age group >25 to ≤29 years increased with 10.62 per cent ($n = 60\,149$), and the percentage that **ARV medicine**

items represented of the **total number of medicine items** increased with 0.35 per cent ($n = 2\,878$) from 2005 to 2006. The **total number of ARV medicine items** represented 1.12 per cent ($n = 6\,320$) and 1.47 per cent ($n = 9\,198$) of the **total number of medicine items** claimed for patients in the age group >25 to ≤ 29 years during 2005 ($n = 566\,310$) and 2006 ($n = 626\,459$) (*refer to table 4.13*).

No practically significant difference between the **average cost per medicine item** for the total database and the **average cost per ARV medicine item** was found for 2005 or 2006 ($d > 0.8$) for the age group >25 to ≤ 29 years (*refer to table 4.13*).

As indicated in table 4.13, the **total cost of all medicine items** increased by 1.02 per cent ($n = R457\,552.48$), and the percentage that the **total cost of all ARV medicine items** represented of the **total medicine cost** increased with 0.76 per cent ($n = R457\,552.48$) from 2005 to 2006 for patients in the age group >25 to ≤ 29 years. **ARV medicine items** represented 2.99 per cent ($n = R1\,339\,449.90$) and 3.75 per cent ($n = R1\,797\,002.38$) of the **total cost of all medicine items** claimed during 2005 ($n = R44\,764\,945.55$) and 2006 ($n = R47\,862\,123.50$) respectively.

Table 4.13 illustrates that the **total number of prescriptions** claimed for patients in the age group >25 to ≤ 29 years increased with 8.95 per cent ($n = 23\,829$), and the percentage that **ARV prescriptions** for patients in this age group represented of the all prescriptions increased with 0.31 per cent ($n = 1\,139$) from 2005 to 2006. The **total number of ARV prescriptions** represented 0.95 per cent ($n = 2\,528$) and 1.26 per cent ($n = 3\,667$) of the **total number of prescriptions** claimed during 2005 ($n = 266\,357$) and 2006 ($n = 290\,186$) for patients in the age group >25 to ≤ 29 years (*refer to table 4.13*).

A practically significant difference was found between the **average cost per prescription** for the total database and the **average cost per ARV prescription** for the age group >25 to ≤ 29 years for both study years ($d > 0.8$) (*refer to table 4.13*).

Table 4.14 Prescribing patterns according to patient age group for the years 2005 and 2006 for patients in the age group >30 to ≤34 years

Age group >30 to ≤34 years				
Description	2005		2006	
	Total database	Antiretroviral medicine items	Total database	Antiretroviral medicine items
Total number of medicine items	1 059 611	19 604	1 075 965	28 181
Average cost of medicine items (R)	77.19 ± 158.40	203.66 ± 118.40	75.63 ± 174.81	199.34 ± 113.03
Total cost of medicine items (R)	81 795 137.18	3 992 572.23	81 377 245.37	5 617 677.54
Total number of prescriptions	479 327	7 688	482 075	11 402
Average cost per prescription (R)	170.55 ± 334.31	519.33 ± 163.04	168.72 ± 355.49	492.69 ± 154.63

An average of 2.21 ± 1.33 **medicine items per prescription** was observed during 2005, and 2.23 ± 1.34 medicine items per prescription were claimed on average through the total database during 2006 for the age group >30 to ≤34 years. In the age group >30 to ≤34 years there was an average of 2.55 ± 0.73 **ARV medicine items per prescription** during 2005 and 2.47 ± 0.63 ARV medicine items per prescription during 2006 ($d < 0.8$).

In the age group >30 to ≤34 years, patients received an average of 5.25 ± 5.86 and 5.23 ± 6.00 **prescriptions per patient per year** during 2005 and 2006 respectively. Patients in the age group >30 to ≤34 years received an average of 5.52 ± 4.22 **ARV prescriptions per patient per year** during 2005, and an average of 6.78 ± 4.45 ARV prescriptions per patient per year during 2006 ($d < 0.8$).

The **total number of patients** in the age group >30 to ≤34 years increased with 0.91 per cent ($n = 828$) and the **total number of HIV patients** in this age group increased with 0.30 per cent ($n = 288$) from 2005 to 2006. The **total number of HIV patients** represented 1.53 per cent ($n = 1\,394$) and 1.83 per cent ($n = 1\,682$) of the **total number of patients** in the age group >30 to ≤34 years during 2005 ($n = 91\,325$) and 2006 ($n = 92\,153$).

The **total number of medicine items** claimed through the total database in the age group >30 to ≤34 years increased with 1.54 per cent ($n = 16\,354$), and the percentage that **ARV medicine items** represented of the total number of medicine items increased with 0.77 per

cent ($n = 8\,577$) from 2005 to 2006. The **total number of ARV medicine items** represented 1.85 per cent ($n = 19\,604$) and 2.62 per cent ($n = 28\,181$) of the **total number of medicine items** claimed during 2005 ($n = 1\,059\,611$) and 2006 ($n = 1\,075\,965$) (*refer to table 4.14*).

No practically significant difference was found between the **average cost per medicine item** for the total database and the **average cost per ARV medicine item** for both study years ($d > 0.8$) for the age group >30 to ≤ 34 years (*refer to table 4.14*).

The **total cost of all medicine items** claimed through the total database decreased by 0.51 per cent ($n = R417\,891.81$), and the percentage that the **total cost of all ARV medicine items** represented of the total medicine cost increased with 2.02 per cent ($n = R1\,625\,105.31$) from 2005 to 2006 for patients in the age group >30 to ≤ 34 years. **ARV medicine items** represented 4.88 per cent ($n = R3\,992\,572.23$) and 6.90 per cent ($n = R5\,617\,677.54$) of the **total cost of all medicine items** claimed during 2005 ($n = R81\,795\,137.18$) and 2006 ($n = R81\,377\,245.37$) respectively (*refer to table 4.14*).

Table 4.14 illustrates that the **total number of prescriptions** claimed through the total database increased with 0.57 per cent ($n = 2\,748$), and the percentage that **ARV prescriptions** represented of all prescriptions increased with 0.77 per cent ($n = 3\,714$) from 2005 to 2006. The **total number of ARV prescriptions** represented 1.60 per cent ($n = 7\,688$) and 2.37 per cent ($n = 11\,402$) of the **total number of prescriptions** claimed during 2005 ($n = 479\,327$) and 2006 ($n = 482\,075$) for the age group >30 to ≤ 34 years (*refer to table 4.14*).

A practically significant difference was found between the **average cost per prescription** for the total database and the **average cost per ARV prescription** for the age group >30 to ≤ 34 years for 2005 and 2006 ($d > 0.8$) (*refer to table 4.14*).

Table 4.15 Prescribing patterns according to patient age group for the years 2005 and 2006 for patients in the age group >35 to ≤39 years

Description	Age group >35 to ≤39 years			
	2005		2006	
	Total database	Antiretroviral medicine items	Total database	Antiretroviral medicine items
Total number of medicine items	1 555 148	30 783	1 646 157	46 636
Average cost of medicine items (R)	79.49 ± 166.60	204.39 ± 113.94	79.56 ± 191.62	195.56 ± 110.88
Total cost of medicine items (R)	123 617 356.00	6 291 763.90	130 972 648.00	9 120 066.79
Total number of prescriptions	689 038	12 193	718 322	18 812
Average cost per prescription (R)	179.31 ± 369.01	516.01 ± 149.36	182.16 ± 413.70	484.80 ± 146.95

An average of 2.26 ± 1.36 **medicine items per prescription** was observed during 2005, and 2.29 ± 1.38 medicine items per prescription were claimed on average during 2006 for patients in the age group >35 to ≤39 years. In the age group >35 to ≤39 years there was an average of 2.52 ± 0.74 **ARV medicine items per prescription** during 2005 and 2.48 ± 0.64 ARV medicine items per prescription during 2006 ($d < 0.8$).

In the age group >35 to ≤39 years, patients received an average of 5.96 ± 6.51 and 6.08 ± 6.77 **prescriptions per patient per year** during 2005 and 2006 respectively. Patients in the age group >35 to ≤39 years received an average of 6.31 ± 4.35 **ARV prescriptions per patient per year** during 2005, and an average of 7.55 ± 4.55 ARV prescriptions per patient per year during 2006 ($d < 0.8$).

The **total number of patients** in the age group >35 to ≤39 years increased with 2.29 per cent ($n = 2\,648$) and the **total number of HIV patients** in this age group increased with 0.44 per cent ($n = 561$) from 2005 to 2006. The **total number of HIV patients** represented 1.67 per cent ($n = 1\,931$) and 2.11 per cent ($n = 2\,492$) of the **total number of patients** in the age group >35 to ≤39 years during 2005 ($n = 115\,556$) and 2006 ($n = 118\,204$).

The **total number of medicine items** claimed for patients in the age group >35 to ≤39 years increased with 5.85 per cent ($n = 91\,009$), and the percentage that **ARV medicine items** represented of the total number of medicine items increased with 0.85 per cent ($n = 15\,853$)

from 2005 to 2006. The **total number of ARV medicine items** represented 1.98 per cent ($n = 30\,783$) and 2.83 per cent ($n = 46\,636$) of the **total number of medicine items** claimed during 2005 ($n = 1\,555\,148$) and 2006 ($n = 1\,646\,157$) (*refer to table 4.15*).

No practically significant difference between the **average cost per medicine item** for the total database and the **average cost per ARV medicine item** was found for both study years ($d > 0.8$) for the age group >35 to ≤ 39 years (*refer to table 4.15*).

The **total cost of all medicine items** increased by 5.95 per cent ($n = R7\,355\,292$), and the percentage that the **total cost of all ARV medicine items** represented of the **total medicine cost** increased with 1.87 per cent ($n = R2\,828\,302.89$) from 2005 to 2006 for patients in the age group >35 to ≤ 39 years. **ARV medicine items** represented 5.09 per cent ($n = R6\,291\,763.90$) and 6.96 per cent ($n = R9\,120\,066.79$) of the **total cost of all medicine items** claimed during 2005 ($n = R123\,617\,356.00$) and 2006 ($n = R130\,972\,648.00$) respectively (*refer to table 4.15*).

The **total number of prescriptions** claimed through the total database increased with 4.25 per cent ($n = 29\,284$), and the percentage that **ARV prescriptions** represented of all prescriptions increased with 0.85 per cent ($n = 6\,619$) from 2005 to 2006. The **total number of ARV prescriptions** represented 1.77 per cent ($n = 12\,193$) and 2.62 per cent ($n = 18\,812$) of the **total number of prescriptions** claimed during 2005 ($n = 689\,038$) and 2006 ($n = 718\,322$) for patients in the age group >35 to ≤ 39 years (*refer to table 4.15*).

A practically significant difference exists between the **average cost per prescription** for the total database and the **average cost per ARV prescription** claimed for patients in the age group >35 to ≤ 39 years for 2005 ($d > 0.8$) (*refer to table 4.15*).

Table 4.16 Prescribing patterns according to patient age group for the years 2005 and 2006 for patients the age group >40 to ≤44 years

Description	Age group >40 to ≤44 years			
	2005		2006	
	Total database	Antiretroviral medicine items	Total database	Antiretroviral medicine items
Total number of medicine items	1 746 033	26 806	1 913 773	44 120
Average cost of medicine items (R)	82.74 ± 175.04	200.17 ± 118.91	81.84 ± 195.23	191.59 ± 109.43
Total cost of medicine items (R)	144 459 473.00	5 365 880.01	156 626 469.00	8 452 791.46
Total number of prescriptions	768 640	10 415	825 432	17 609
Average cost per prescription (R)	187.73 ± 411.08	515.21 ± 162.18	189.58 ± 442.15	480.05 ± 143.96

An average of 2.27 ± 1.39 **medicine items per prescription** was observed during 2005, and 2.32 ± 1.42 medicine items per prescription were claimed on average during 2006 for patients in the age group >40 to ≤44 years. In the age group >40 to ≤44 years there was an average of 2.57 ± 0.69 **ARV medicine items per prescription** during 2005 and 2.51 ± 0.61 ARV medicine items per prescription during 2006 ($d < 0.8$).

In the age group >40 to ≤44 years, patients received an average of 6.49 ± 6.97 and 6.69 ± 7.25 **prescriptions per patient per year** during 2005 and 2006 respectively. Patients in the age group >40 to ≤44 years received an average of 6.23 ± 4.29 **ARV prescriptions per patient per year** during 2005, and an average of 7.55 ± 4.48 ARV prescriptions per patient per year during 2006 ($d < 0.8$).

The **total number of patients** in the age group >40 to ≤44 years increased with 4.21 per cent ($n = 4\,987$) and the **total number of HIV patients** increased with 0.48 per cent ($n = 660$) from 2005 to 2006. The **total number of HIV patients** represented 1.41 per cent ($n = 1\,672$) and 1.89 per cent ($n = 2\,332$) of the **total number of patients** in the age group >40 to ≤44 years during 2005 ($n = 118\,386$) and 2006 ($n = 123\,373$).

The **total number of medicine items** claimed for patients in the age group >40 to ≤44 years increased with 9.61 per cent ($n = 167\,740$), and the percentage that **ARV medicine items** represented of the **total number of medicine items** increased with 0.77 per cent

(n = 17 314) from 2005 to 2006. The **total number of ARV medicine items** represented 1.54 per cent (n = 26 806) and 2.31 per cent (n = 44 120) of the **total number of medicine items** claimed during 2005 (n = 1 746 033) and 2006 (n = 1 913 773) (*refer to table 4.16*).

No practically significant difference was found between the **average cost per medicine item** or the **average cost per prescription** between the total database and ARV medicine items and prescriptions for both study years ($d < 0.8$) for the age group >40 to ≤44 years (*refer to table 4.16*).

The **total cost of all medicine items** increased by 8.42 per cent (n = R12 166 996), and the percentage that the **total cost of all ARV medicine items** represented of the **total medicine cost** increased with 1.69 per cent (n = R3 086 911.45) from 2005 to 2006 for patients in the age group >40 to ≤44 years. **ARV medicine items** represented 3.71 per cent (n = R5 365 880.01) and 5.40 per cent (n = R8 452 791.46) of the **total cost of all medicine items** claimed during 2005 (n = R144 459 473.00) and 2006 (n = R156 626 469.00) respectively (*refer to table 4.16*).

Table 4.16 illustrates that the **total number of prescriptions** claimed for patients in the age group >40 to ≤44 years increased with 7.39 per cent (n = 56 792), and the percentage that **ARV prescriptions** represented of the **total number of prescriptions** with 0.78 per cent (n = 7 194) from 2005 to 2006. The **total number of ARV prescriptions** represented 1.35 per cent (n = 10 415) and 2.13 per cent (n = 17 609) of the **total number of prescriptions** claimed during 2005 (n = 768 640) and 2006 (n = 825 432) for patients in the age group >40 to ≤44 years (*refer to table 4.16*).

Table 4.17 Prescribing patterns according to patient age group for the years 2005 and 2006 for patients in the age group >45 to ≤49 years

Age group >45 to ≤49 years				
Description	2005		2006	
	Total database	Antiretroviral medicine items	Total database	Antiretroviral medicine items
Total number of medicine items	1 819 683	17 830	2 025 420	30 386
Average cost of medicine items (R)	89.99 ± 183.88	197.14 ± 113.57	89.08 ± 213.99	189.44 ± 110.56
Total cost of medicine items (R)	163 759 287.00	3 514 939.23	180 427 821.00	5 756 279.29
Total number of prescriptions	803 404	7 051	875 554	12 140
Average cost per prescription (R)	203.59 ± 417.13	498.50 ± 134.14	205.84 ± 538.31	474.16 ± 142.09

An average of 2.26 ± 1.44 **medicine items per prescription** was observed during 2005, and 2.31 ± 1.46 medicine items per prescription were claimed on average during 2006 for patients in the age group >45 to ≤49 years. In the age group >45 to ≤49 years there was an average of 2.53 ± 0.71 **ARV medicine items per prescription** during 2005 and 2.50 ± 0.61 ARV medicine items per prescription during 2006 ($d < 0.8$).

In the age group >45 to ≤49 years, patients received an average of 7.14 ± 7.52 and 7.31 ± 7.74 **prescriptions per patient per year** during 2005 and 2006 respectively. Patients in the age group >45 to ≤49 years received an average of 6.56 ± 4.42 **ARV prescriptions per patient per year** during 2005, and an average of 7.55 ± 4.44 ARV prescriptions per patient per year during 2006 ($d < 0.8$).

The **total number of patients** in the age group >45 to ≤49 years increased with 6.54 per cent ($n = 7\,354$) and the **total number of HIV patients** increased with 0.38 per cent ($n = 533$) from 2005 to 2006. The **total number of HIV patients** represented 0.96 per cent ($n = 1\,075$) and 1.34 per cent ($n = 1\,608$) of the **total number of patients** in the age group >45 to ≤49 years during 2005 ($n = 112\,488$) and 2006 ($n = 119\,842$).

The **total number of medicine items** claimed for patients in the age group >45 to ≤49 years increased with 11.31 per cent ($n = 205\,737$), and the percentage that **ARV medicine items** represented of the total number of medicine items claimed for patients in this age group

increased with 0.52 per cent ($n = 12\,556$) from 2005 to 2006. The **total number of ARV medicine items** represented 0.98 per cent ($n = 17\,830$) and 1.50 per cent ($n = 30\,386$) of the **total number of medicine items** claimed during 2005 ($n = 1\,819\,683$) and 2006 ($n = 2\,025\,420$) for patients in the age group >45 to ≤ 49 years (*refer to table 4.17*).

No practically significant difference between the **average cost per medicine item** for the total database and the **average cost per ARV medicine item** was found for 2005 or 2006 ($d < 0.8$) for the age group >45 to ≤ 49 years (*refer to table 4.17*).

The **total cost of all medicine items** increased by 10.18 per cent ($n = R16\,668\,534$), and the percentage that the **total cost of all ARV medicine items** represented of the total medicine cost increased with 1.04 per cent ($n = R2\,241\,340.06$) from 2005 to 2006 for patients in the age group >45 to ≤ 49 years. **ARV medicine items** represented 2.15 per cent ($n = R3\,514\,939.23$) and 3.19 per cent ($n = R5\,756\,279.29$) of the **total cost of all medicine items** claimed during 2005 ($n = R163\,759\,287.00$) and 2006 ($n = R180\,427\,821.00$) respectively (*refer to table 4.17*).

Table 4.17 illustrates that the **total number of prescriptions** claimed for patients in the age group >45 to ≤ 49 years increased with 0.09 per cent ($n = 72\,150$), and the percentage that **ARV prescriptions** represented of **all prescriptions** increased with 0.51 per cent ($n = 5\,089$) from 2005 to 2006. The **total number of ARV prescriptions** represented 0.88 per cent ($n = 7\,051$) and 1.39 per cent ($n = 12\,140$) of the **total number of prescriptions** claimed during 2005 ($n = 803\,404$) and 2006 ($n = 875\,554$) for patients in the age group >45 to ≤ 49 years (*refer to table 4.17*).

No practically significant difference was found between the **average cost per prescription** for the total database and the **average cost per ARV prescription** for the age group >45 to ≤ 49 years for 2005 and 2006 ($d > 0.8$) (*refer to table 4.17*).

Table 4.18 Prescribing patterns according to patient age group for the years 2005 and 2006 for patients in the age group >50 to ≤54 years

Description	Age group >50 to ≤54 years			
	2005		2006	
	Total database	Antiretroviral medicine items	Total database	Antiretroviral medicine items
Total number of medicine items	1 761 635	8 455	1 983 367	15 834
Average cost of medicine items (R)	99.88 ± 197.41	204.84 ± 117.96	99.98 ± 247.78	191.21 ± 109.27
Total cost of medicine items (R)	175 943 940.00	1 731 920.74	198 302 317.00	3 027 694.90
Total number of prescriptions	777 423	3 386	852 545	6 349
Average cost per prescription (R)	225.93 ± 461.47	511.49 ± 156.21	232.17 ± 657.55	476.88 ± 154.18

An average of 2.26 ± 1.50 **medicine items per prescription** was observed during 2005, and 2.32 ± 1.54 **medicine items per prescription** were claimed on average during 2006 for patients in the age group >50 to ≤54 years. In the age group >50 to ≤54 years there was an average of 2.50 ± 0.68 **ARV medicine items per prescription** during 2005 and 2.49 ± 0.63 ARV medicine items per prescription during 2006 ($d < 0.8$).

In the age group >50 to ≤54 years, patients received an average of 8.03 ± 8.20 and 8.15 ± 8.38 **prescriptions per patient per year** during 2005 and 2006 respectively. Patients in the age group >50 to ≤54 years received an average of 6.04 ± 4.37 **ARV prescriptions per patient per year** during 2005, and an average of 7.36 ± 4.39 ARV prescriptions per patient per year during 2006 ($d < 0.8$).

The **total number of patients** in the age group >50 to ≤54 years increased with 8.04 per cent ($n = 7\,778$) and the **total number of HIV patients** increased with 0.25 per cent ($n = 302$) from 2005 to 2006. The **total number of HIV patients** represented 0.58 per cent ($n = 561$) and 0.83 per cent ($n = 863$) of the **total number of patients** in the age group >50 to ≤54 years during 2005 ($n = 96\,794$) and 2006 ($n = 104\,572$).

The **total number of medicine items** claimed for patients in the age group >50 to ≤54 years increased with 12.59 per cent ($n = 221\,732$), and the percentage that **ARV medicine items** represented of the total number of medicine items increased with 0.32 per cent ($n = 7\,379$).

from 2005 to 2006. The **total number of ARV medicine items** represented 0.48 per cent ($n = 8\,455$) and 0.80 per cent ($n = 15\,834$) of the **total number of medicine items** claimed during 2005 ($n = 1\,761\,635$) and 2006 ($n = 1\,983\,367$) (*refer to table 4.18*).

No practically significant difference was found between the **average cost per medicine item** or **average cost per prescription** for the total database and ARV medicine items and prescriptions for 2005 and 2006 ($d < 0.8$) for the age group >50 to ≤ 54 years (*refer to table 4.18*).

The **total cost of all medicine items** increased by 12.71 per cent ($n = R22\,358\,377$), and the percentage that the **total cost of all ARV medicine items** represented of the **total medicine cost** increased with 0.55 per cent ($n = R1\,295\,774.16$) from 2005 to 2006 for the age group >50 to ≤ 54 years. **ARV medicine items** represented 0.98 per cent ($n = R1\,731\,920.74$) and 1.53 per cent ($n = R3\,027\,694.90$) of the **total cost of all medicine items** claimed during 2005 ($n = R175\,943\,940.00$) and 2006 ($n = R198\,302\,317.00$) respectively (*refer to table 4.18*).

The **total number of prescriptions** claimed for patients in the age group >50 to ≤ 54 years increased with 9.66 per cent ($n = 75\,122$), and the percentage that **ARV prescriptions** represented of the **total number of prescriptions** increased with 0.30 per cent ($n = 2\,963$) from 2005 to 2006. The **total number of ARV prescriptions** represented 0.44 per cent ($n = 3\,386$) and 0.74 per cent ($n = 6\,349$) of the **total number of prescriptions** claimed during 2005 ($n = 777\,423$) and 2006 ($n = 852\,545$) for patients in the age group >50 to ≤ 54 years (*refer to table 4.18*).

Table 4.19 Prescribing patterns according to patient age group for the years 2005 and 2006 for patients in the age group >55 to ≤59 years

Age group >55 to ≤59 years				
Description	2005		2006	
	Total database	Antiretroviral medicine items	Total database	Antiretroviral medicine items
Total number of medicine items	1 676 076	3 890	1 830 501	7 697
Average cost of medicine items (R)	112.47 ± 235.96	207.56 ± 125.13	111.49 ± 271.23	189.23 ± 109.90
Total cost of medicine items (R)	188 503 459.00	807 422.72	204 088 046.00	1 456 539.65
Total number of prescriptions	730 251	1 558	776 909	3 082
Average cost per prescription (R)	257.57 ± 564.22	518.24 ± 185.23	262.10 ± 651.28	472.60 ± 137.52

An average of 2.29 ± 1.59 **medicine items per prescription** was observed during 2005, and 2.35 ± 1.63 medicine items per prescription were claimed on average during 2006 for patients in the age group >55 to ≤59 years. In the age group >55 to ≤59 years there was an average of 2.50 ± 0.74 **ARV medicine items per prescription** during 2005 and 2.50 ± 0.61 ARV medicine items per prescription during 2006 ($d < 0.8$).

In the age group >55 to ≤59 years, patients received an average of 8.93 ± 8.74 and 8.94 ± 8.88 **prescriptions per patient per year** during 2005 and 2006 respectively. Patients in the age group >55 to ≤59 years received an average of 5.58 ± 4.32 **ARV prescriptions per patient per year** during 2005, and an average of 7.13 ± 4.29 ARV prescriptions per patient per year during 2006 ($d < 0.8$).

The **total number of patients** in the age group >55 to ≤59 years increased with 6.25 per cent ($n = 5\,112$) and the **total number of HIV patients** increased with 0.16 per cent ($n = 153$) from 2005 to 2006. The **total number of HIV patients** represented 0.34 per cent ($n = 279$) and 0.50 per cent ($n = 432$) of the **total number of patients** in the age group >55 to ≤59 years during 2005 ($n = 81\,815$) and 2006 ($n = 86\,927$).

The **total number of medicine items** claimed for patients in the age group >55 to ≤59 years increased with 9.21 per cent ($n = 154\,425$), and the percentage that **ARV medicine items** represented of the **total number of medicine items** increased with 0.19 per cent ($n = 3\,807$)

from 2005 to 2006. The **total number of ARV medicine items** represented 0.23 per cent ($n = 3\,890$) and 0.42 per cent ($n = 7\,697$) of the **total number of medicine items** for the total database claimed during 2005 ($n = 1\,676\,076$) and 2006 ($n = 1\,830\,501$) for patients in the age group >55 to ≤ 59 years (*refer to table 4.19*).

No practically significant difference was found between the **average cost per medicine item** or the **average cost per prescription** for the total database and ARV medicine items for both study years ($d < 0.8$) for the age group >55 to ≤ 59 years (*refer to table 4.19*).

As indicated by table 4.19, the **total cost of all medicine items** increased by 8.27 per cent ($n = R15\,584\,587.00$), and the percentage that the **total cost of all ARV medicine items** represented of the **total medicine cost** increased with 0.28 per cent ($n = R649\,116.92$) from 2005 to 2006 for patients in the age group >55 to ≤ 59 years. **ARV medicine items** represented 0.43 per cent ($n = R807\,422.72$) and 0.71 per cent ($n = R1\,456\,539.65$) of the **total cost of all medicine items** claimed during 2005 ($n = R188\,503\,459.00$) and 2006 ($n = R204\,088\,046.00$) respectively.

The **total number of prescriptions** claimed for patients in the age group >55 to ≤ 59 years increased with 6.39 per cent ($n = 46\,658$), and the percentage that **ARV prescriptions** represented of **all prescriptions** increased with 0.19 per cent ($n = 1\,524$) from 2005 to 2006. The **total number of ARV prescriptions** represented 0.21 per cent ($n = 1\,558$) and 0.40 per cent ($n = 3\,082$) of the **total number of prescriptions** claimed during 2005 ($n = 730\,251$) and 2006 ($n = 776\,909$) for patients in the age group >55 to ≤ 59 years (*refer to table 4.19*).

Table 4.20 Prescribing patterns according to patient age group for the years 2005 and 2006 for patients in the age group >60 to ≤64 years

Description	Age group >60 to ≤64 years			
	2005		2006	
	Total database	Antiretroviral medicine items	Total database	Antiretroviral medicine items
Total number of medicine items	1 487 045	1 821	1 634 110	2 976
Average cost of medicine items (R)	120.14 ± 251.62	204.45 ± 138.45	121.83 ± 307.35	210.04 ± 119.38
Total cost of medicine items (R)	178 660 508.00	372 298.50	199 087 822.00	625 075.48
Total number of prescriptions	628 967	718	678 756	1 246
Average cost per prescription (R)	283.35 ± 702.44	518.52 ± 204.79	292.37 ± 778.67	501.67 ± 189.02

An average of 2.36 ± 1.71 **medicine items per prescription** was observed during 2005, and 2.40 ± 1.72 medicine items per prescription were claimed on average during 2006 for the age group >60 to ≤64 years. In the age group >60 to ≤64 years there was an average of 2.54 ± 0.74 **ARV medicine items per prescription** during 2005 and 2.39 ± 0.71 ARV medicine items per prescription during 2006 ($d < 0.8$).

In the age group >60 to ≤64 years, patients received an average of 9.75 ± 9.14 and 9.76 ± 9.38 **prescriptions per patient per year** during 2005 and 2006 respectively. Patients in the age group >60 to ≤64 years received an average of 6.47 ± 4.45 **ARV prescriptions per patient per year** during 2005, and an average of 7.42 ± 4.67 ARV prescriptions per patient per year during 2006 ($d < 0.8$).

The **total number of patients** in the age group >60 to ≤64 years increased with 7.73 per cent ($n = 4\,989$) and the **total number of HIV patients** in this age group increased with 0.11 per cent ($n = 57$) from 2005 to 2006. The **total number of HIV patients** represented 0.17 per cent ($n = 111$) and 0.28 per cent ($n = 168$) of the **total number of patients** in the age group >60 to ≤64 years during 2005 ($n = 64\,521$) and 2006 ($n = 69\,510$).

The **total number of medicine items** claimed for patients in the age group >60 to ≤64 years increased with 9.89 per cent ($n = 147\,065$), and the percentage that **ARV medicine items** represented of the **total number of medicine items** increased with 0.06 per cent ($n = 1\,155$).

from 2005 to 2006. The **total number of ARV medicine items** represented 0.12 per cent ($n = 1\,821$) and 0.18 per cent ($n = 2\,976$) of the **total number of medicine items** claimed during 2005 ($n = 1\,487\,045$) and 2006 ($n = 1\,634\,110$) for patients in this age group (*refer to table 4.20*).

No practically significant difference was found between the **average cost per medicine item** or the **average cost per prescription** for the total database and ARV medicine items and prescriptions for both study years ($d < 0.8$) for the age group >60 to ≤ 64 years (*refer to table 4.20*).

The **total cost of all medicine items** increased by 11.43 per cent ($n = R20\,427\,314$), and the percentage that the **total cost of all ARV medicine items** represented of the **total medicine cost** increased with 0.10 per cent ($n = R252\,776.98$) from 2005 to 2006 for patients in the age group >60 to ≤ 64 years. **ARV medicine items** represented 0.21 per cent ($n = R372\,298.50$) and 0.31 per cent ($n = R625\,075.48$) of the **total cost of all medicine items** claimed during 2005 ($n = R178\,660\,508.00$) and 2006 ($n = R199\,087\,822.00$) respectively (*refer to table 4.20*).

The **total number of prescriptions** claimed for patients in the age group >60 to ≤ 64 years increased with 7.92 per cent ($n = 49\,789$), and the percentage that **ARV prescriptions** represented of the **total number of prescriptions** increased with 0.07 per cent ($n = 528$) from 2005 to 2006. The **total number of ARV prescriptions** represented 0.11 per cent ($n = 718$) and 0.18 per cent ($n = 1\,246$) of the **total number of prescriptions** claimed during 2005 ($n = 628\,967$) and 2006 ($n = 678\,756$) for patients in this age group (*refer to table 4.20*).

Table 4.21 Prescribing patterns according to patient age group for the years 2005 and 2006 for patients in the age group >65 to ≤69 years

Age group >65 to ≤69 years				
Description	2005		2006	
	Total database	Antiretroviral medicine items	Total database	Antiretroviral medicine items
Total number of medicine items	1 299 322	568	1 382 156	887
Average cost of medicine items (R)	122.42 ± 231.84	208.37 ± 109.59	124.86 ± 297.63	184.98 ± 134.56
Total cost of medicine items (R)	159 057 951.00	118 354.49	172 575 792.00	164 074.24
Total number of prescriptions	532 019	245	557 900	372
Average cost per prescription (R)	298.04 ± 583.51	483.08 ± 138.86	308.41 ± 799.30	441.06 ± 214.19

An average of 2.43 ± 1.84 **medicine items per prescription** was observed during 2005, and 2.47 ± 1.85 **medicine items per prescription** were claimed on average during 2006 for patients in the age group >65 to ≤69 years. In the age group >65 to ≤69 years there was an average of 2.32 ± 0.80 **ARV medicine items per prescription** during 2005 and 2.38 ± 0.81 **ARV medicine items per prescription** during 2006 ($d < 0.8$).

In the age group >65 to ≤69 years, patients received an average of 10.67 ± 9.60 and 10.62 ± 9.78 **prescriptions per patient per year** during 2005 and 2006 respectively. Patients in the age group >65 to ≤69 years received an average of 5.00 ± 4.40 **ARV prescriptions per patient per year** during 2005, and an average of 6.64 ± 4.86 **ARV prescriptions per patient per year** during 2006 ($d < 0.8$).

The **total number of patients** in the age group >65 to ≤69 years increased with 5.42 per cent ($n = 2\,700$) and the **total number of HIV patients** increased with 0.01 per cent ($n = 7$) from 2005 to 2006. The **total number of HIV patients** represented 0.10 per cent ($n = 49$) and 0.11 per cent ($n = 56$) of the **total number of patients** during 2005 ($n = 49\,842$) and 2006 ($n = 52\,542$) in the age group >65 to ≤69 years.

The **total number of medicine items** claimed for patients in the age group >65 to ≤69 years increased with 6.38 per cent ($n = 82\,834$), and the percentage that **ARV medicine items** represented of the **total number of medicine items** claimed for patients in this age group

increased with 0.02 per cent ($n = 319$) from 2005 to 2006. The **total number of ARV medicine items** represented 0.04 per cent ($n = 568$) and 0.06 per cent ($n = 887$) of the **total number of medicine items** claimed during 2005 ($n = 1\,299\,322$) and 2006 ($n = 1\,382\,156$) claimed for patients in the age group >65 to ≤ 69 years (*refer to table 4.21*).

No practically significant difference was found between the **average cost per medicine item** or the **average cost per prescription** for the total database and ARV medicine items and prescriptions for 2005 or 2006 ($d < 0.8$) for the age group >65 to ≤ 69 years (*refer to table 4.21*).

The **total cost of all medicine items** increased by 8.50 per cent ($n = R13\,517\,841$), and the percentage that the **total cost of all ARV medicine items** represented of the total medicine cost increased with 0.03 per cent ($n = R45\,719.75$) from 2005 to 2006 for patients in the age group >65 to ≤ 69 years. **ARV medicine items** represented 0.07 per cent ($n = R118\,354.49$) and 0.10 per cent ($n = R164\,074.24$) of the **total cost of all medicine items** claimed for patients in the age group >65 to ≤ 69 years during 2005 ($n = R159\,057\,951.00$) and 2006 ($n = R172\,575\,792.00$) respectively (*refer to table 4.21*).

The **total number of prescriptions** claimed for patients in the age group >65 to ≤ 69 years increased with 4.86 per cent ($n = 25\,881$), and the percentage that **ARV prescriptions** represented of **all prescriptions** increased with 0.02 per cent ($n = 127$) from 2005 to 2006. The **total number of ARV prescriptions** represented 0.05 per cent ($n = 245$) and 0.07 per cent ($n = 372$) of the **total number of prescriptions** claimed during 2005 ($n = 532\,019$) and 2006 ($n = 557\,900$) for patients in the age group >65 to ≤ 69 years (*refer to table 4.21*).

Table 4.22 Prescribing patterns according to patient age group for the years 2005 and 2006 for patients in the age group >70 to ≤74 years

Age group >70 to ≤74 years				
Description	2005		2006	
	Total database	Antiretroviral medicine items	Total database	Antiretroviral medicine items
Total number of medicine items	1 124 216	254	1 194 984	401
Average cost of medicine items (R)	124.30 ± 249.53	226.02 ± 126.00	126.40 ± 298.88	241.35 ± 120.28
Total cost of medicine items (R)	139 737 132.00	57 409.85	151 051 621.00	96 782.58
Total number of prescriptions	445 017	105	465 240	177
Average cost per prescription (R)	312.95 ± 641.39	546.76 ± 161.18	323.63 ± 726.09	546.79 ± 153.22

An average of 2.52 ± 1.94 **medicine items per prescription** was observed during 2005, and 2.56 ± 1.95 medicine items per prescription were claimed on average during 2006 for the age group >70 to ≤74 years. In the age group >70 to ≤74 years there was an average of 2.42 ± 0.68 **ARV medicine items per prescription** during 2005 and 2.27 ± 0.64 ARV medicine items per prescription during 2006 ($d < 0.8$).

In the age group >70 to ≤74 years, patients received an average of 11.51 ± 9.99 and 11.56 ± 10.26 **prescriptions per patient per year** during 2005 and 2006 respectively. Patients in the age group >70 to ≤74 years received an average of 4.57 ± 4.80 **ARV prescriptions per patient per year** during 2005, and an average of 8.05 ± 5.23 ARV prescriptions per patient per year during 2006 ($d < 0.8$).

The **total number of patients** in the age group >70 to ≤74 years increased with 4.11 per cent ($n = 1\,590$) and the **total number of HIV patients** in this age group decreased with 0.01 per cent ($n = 1$) from 2005 to 2006. The **total number of HIV patients** represented 0.06 per cent ($n = 23$) and 0.05 per cent ($n = 22$) of the **total number of patients** during 2005 ($n = 38\,656$) and 2006 ($n = 40\,246$) in the age group >70 to ≤74 years.

The **total number of medicine items** claimed for patients in the age group >70 to ≤74 years increased with 6.29 per cent ($n = 70\,768$), and the percentage that **ARV medicine items** represented of the **total number of medicine items** increased with 0.01 per cent ($n = 147$)

from 2005 to 2006 for patients in this age group. The **total number of ARV medicine items** represented 0.02 per cent ($n = 254$) and 0.03 per cent ($n = 401$) of the **total number of medicine items** claimed during 2005 ($n = 1\,124\,216$) and 2006 ($n = 1\,194\,984$) for patients in the age group >70 to ≤ 74 years (*refer to table 4.22*).

No practically significant difference was found between the **average cost per medicine item** or the **average cost per prescription** for the total database and ARV medicine items and prescriptions for both study years ($d < 0.8$) for the age group >70 to ≤ 74 years (*refer to table 4.22*).

The **total cost of all medicine items** increased by 8.10 per cent ($n = R11\,314\,489$), and the percentage that the **total cost of all ARV medicine items** represented of the **total medicine cost** increased with 0.02 per cent ($n = R39\,372.73$) from 2005 to 2006 for patients in the age group >70 to ≤ 74 years. **ARV medicine items** represented 0.04 per cent ($n = R57\,409.85$) and 0.06 per cent ($n = R96\,782.58$) of the **total cost of all medicine items** claimed during 2005 ($n = R139\,737\,132.00$) and 2006 ($n = R151\,051\,621.00$) for patients in this age group (*refer to table 4.22*).

The **total number of prescriptions** claimed for patients in the age group >70 to ≤ 74 years increased with 4.54 per cent ($n = 20\,223$), and the percentage that **ARV prescriptions** for patients in this age group represented of the **total number of prescriptions** increased with 0.02 per cent ($n = 72$) from 2005 to 2006. The **total number of ARV prescriptions** represented 0.02 per cent ($n = 105$) and 0.04 per cent ($n = 177$) of the **total number of prescriptions** claimed during 2005 ($n = 445\,017$) and 2006 ($n = 465\,240$) for patients in the age group >70 to ≤ 74 years (*refer to table 4.22*).

Table 4.23 Prescribing patterns according to patient age group for the years 2005 and 2006 for patients in the age group >75 to ≤79 years

Description	Age group >75 to ≤79 years			
	2005		2006	
	Total database	Antiretroviral medicine items	Total database	Antiretroviral medicine items
Total number of medicine items	975 749	158	1 030 310	138
Average cost of medicine items (R)	123.43 ± 226.86	219.59 ± 125.20	124.34 ± 280.09	157.69 ± 101.65
Total cost of medicine items (R)	120 441 444.00	34 694.49	128 113 588.00	21 761.89
Total number of prescriptions	382 766	67	396 525	50
Average cost per prescription (R)	313.24 ± 573.85	517.83 ± 225.32	321.79 ± 765.04	435.24 ± 136.67

An average of 2.54 ± 1.98 **medicine items per prescription** was observed during 2005, and 2.59 ± 1.99 medicine items per prescription were claimed on average during 2006 for the age group >75 to ≤79 years. In the age group >75 to ≤79 years there was an average of 2.36 ± 0.87 **ARV medicine items per prescription** during 2005 and 2.76 ± 0.69 ARV medicine items per prescription during 2006 ($d < 0.8$).

In the age group >75 to ≤79 years, patients received an average of 12.32 ± 10.51 and 12.37 ± 10.70 **prescriptions per patient per year** during 2005 and 2006 respectively. Patients in the age group >75 to ≤79 years received an average of 4.79 ± 6.00 **ARV prescriptions per patient per year** during 2005, and an average of 5.00 ± 4.67 ARV prescriptions per patient per year during 2006 ($d < 0.8$).

The **total number of patients** in the age group >75 to ≤79 years increased with 3.21 per cent ($n = 996$) and the **total number of HIV patients** in this age group displayed a 0.02 per cent decrease ($n = 4$) from 2005 to 2006. The **total number of HIV patients** represented 0.05 per cent ($n = 14$) and 0.03 per cent ($n = 10$) of the **total number of patients** during 2005 ($n = 31\,057$) and 2006 ($n = 32\,053$) in the age group >75 to ≤79 years.

The **total number of medicine items** claimed for patients in the age group >75 to ≤79 years increased with 5.59 per cent ($n = 54\,561$), and the percentage that **ARV medicine items** represented of the **total number of medicine items** decreased with 0.01 per cent ($n = 20$)

from 2005 to 2006. The **total number of ARV medicine items** represented 0.02 per cent ($n = 158$) and 0.01 per cent ($n = 138$) of the **total number of medicine items** claimed during 2005 ($n = 975\,749$) and 2006 ($n = 1\,030\,310$) for patients in this age group (*refer to table 4.23*).

No practically significant difference was found between the **average cost per medicine item** or the **average cost per prescription** for the total database and ARV medicine items and prescriptions for both study years ($d < 0.8$) for the age group >75 to ≤ 79 years (*refer to table 4.23*).

The **total cost of all medicine items** increased by 6.37 per cent ($n = R7\,672\,144.00$), and the percentage that the **total cost of all ARV medicine items** represented of the **total medicine cost** decreased with 0.01 per cent ($n = R12\,932.60$) from 2005 to 2006 for patients in the age group >75 to ≤ 79 years. **ARV medicine items** represented 0.03 per cent ($n = R34\,694.49$) and 0.02 per cent ($n = R21\,761.89$) of the **total cost of all medicine items** claimed during 2005 ($n = R120\,441\,444.00$) and 2006 ($n = R128\,113\,588.00$) for patients in the age group >75 to ≤ 79 years (*refer to table 4.23*).

The **total number of prescriptions** claimed for patients in the age group >75 to ≤ 79 years increased with 3.59 per cent ($n = 13\,759$), and the percentage that **ARV prescriptions** represented of the **total number of prescriptions** for patients in this age group decreased with 0.01 per cent ($n = 17$) from 2005 to 2006. The **total number of ARV prescriptions** represented 0.02 per cent ($n = 67$) and 0.01 per cent ($n = 50$) of the **total number of prescriptions** claimed during 2005 ($n = 382\,766$) and 2006 ($n = 396\,525$) for patients in the age group >75 to ≤ 79 years (*refer to table 4.23*).

Table 4.24 Prescribing patterns according to patient age group for the years 2005 and 2006 for patients in the age group >80 to ≤84 years

Description	Age group >80 to ≤84 years			
	2005		2006	
	Total database	Antiretroviral medicine items	Total database	Antiretroviral medicine items
Total number of medicine items	676 557	13	716 717	33
Average cost of medicine items (R)	119.71 ± 196.21	313.21 ± 232.63	118.66 ± 215.85	171.82 ± 107.89
Total cost of medicine items (R)	80 992 810.05	4 071.77	85 048 165.07	5 670.16
Total number of prescriptions	266 381	6	278 102	16
Average cost per prescription (R)	302.62 ± 460.43	678.63 ± 373.58	304.30 ± 492.10	354.39 ± 214.83

An average of 2.53 ± 1.97 **medicine items per prescription** was observed during 2005, and 2.56 ± 1.99 medicine items per prescription were claimed on average during 2006 for patients in the age group >80 to ≤84 years. In the age group >80 to ≤84 years there was an average of 2.17 ± 0.75 **ARV medicine items per prescription** during 2005 and 2.06 ± 0.85 ARV medicine items per prescription during 2006 ($d < 0.8$).

In the age group >80 to ≤84 years, patients received an average of 12.91 ± 10.82 and 13.20 ± 11.15 **prescriptions per patient per year** during 2005 and 2006 respectively. Patients in the age group >80 to ≤84 years received an average of 1.50 ± 1.00 **ARV prescriptions per patient per year** during 2005, and an average of 3.20 ± 2.17 ARV prescriptions per patient per year during 2006 (demonstrating a practically significant difference in the **average number of prescriptions** and **average number of ARV prescriptions** received per year by patients in the age group >80 to ≤84 years).

The **total number of patients** in the age group >80 to ≤84 years increased with 2.11 per cent ($n = 436$) and the **total number of HIV patients** in this age group increased with 0.005 per cent ($n = 1$) from 2005 to 2006. The **total number of HIV patients** represented 0.019 per cent ($n = 4$) and 0.024 per cent ($n = 5$) of the **total number of patients** in the age group >80 to ≤84 years during 2005 ($n = 20\,626$) and 2006 ($n = 21\,062$).

The **total number of medicine items** claimed for patients in the age group >80 to ≤84 years increased with 5.94 per cent (n = 40 160), and the percentage that **ARV medicine items** represented of the **total number of medicine items** increased with 0.003 per cent (n = 20) from 2005 to 2006 for patients in this age group. The **total number of ARV medicine items** represented 0.002 per cent (n = 13) and 0.005 per cent (n = 33) of the **total number of medicine items** claimed during 2005 (n = 676 557) and 2006 (n = 716 717) for patients in the age group >80 to ≤84 years (*refer to table 4.24*).

A practically significant difference between the **average cost per medicine item** as well as the **average cost per prescription** for the total database and ARV medicine items and prescriptions was found during 2005 ($d > 0.8$) for the age group >80 to ≤84 years (*refer to table 4.24*).

The **total cost of all medicine items** increased by 5.01 per cent (n = R4 055 355.02), and the percentage that the **total cost of all ARV medicine items** represented of the **total medicine cost** increased with 0.06 per cent (n = R1 598.39) from 2005 to 2006 for patients in the age group >80 to ≤84 years. **ARV medicine items** represented 0.01 per cent (n = R4 071.77) and 0.07 per cent (n = R5 670.16) of the **total cost of all medicine items** claimed during 2005 (n = R80 992 810.05) and 2006 (n = R85 048 165.07) for patients in this age group (*refer to table 4.24*).

The **total number of prescriptions** claimed for patients in the age group >80 to ≤84 years increased with 4.40 per cent (n = 11 721), and the percentage that **ARV prescriptions** represented of **all prescriptions** increased with 0.004 per cent (n = 10) from 2005 to 2006. The **total number of ARV prescriptions** represented 0.002 per cent (n = 6) and 0.006 per cent (n = 16) of the **total number of prescriptions** claimed during 2005 (n = 266 381) and 2006 (n = 278 102) for patients in the age group >80 to ≤84 years (*refer to table 4.24*).

Table 4.25 Prescribing patterns according to patient age group for the years 2005 and 2006 for patients in the age group >85 years

Description	Age group >85 years			
	2005		2006	
	Total database	Antiretroviral medicine items	Total database	Antiretroviral medicine items
Total number of medicine items	471 063	22	523 117	12
Average cost of medicine items (R)	110.66 ± 154.16	178.32 ± 112.07	110.87 ± 185.57	173.55 ± 114.18
Total cost of medicine items (R)	52 128 171.44	3 923.02	57 998 308.29	2 082.54
Total number of prescriptions	191 694	9	210 560	6
Average cost per prescription (R)	270.79 ± 345.30	435.89 ± 122.85	273.98 ± 433.23	347.09 ± 199.75

An average of 2.45 ± 1.92 **medicine items per prescription** was observed during 2005, and 2.47 ± 1.91 medicine items per prescription were claimed on average during 2006 for patients in the age group >85 years. In the age group >85 years there was an average of 2.44 ± 0.88 **ARV medicine items per prescription** during 2005 and 2.00 ± 0.63 ARV medicine items per prescription during 2006 ($d < 0.8$).

In the age group >85 years, patients received an average of 13.78 ± 11.26 and 14.27 ± 11.60 **prescriptions per patient per year** during 2005 and 2006 respectively. Patients in the age group >85 years received an average of 2.25 ± 0.96 **ARV prescriptions per patient per year** during 2005, and an average of 1.00 ± 0.00 ARV prescriptions per patient per year during 2006 (indicative of a practically significant difference in the **average number of prescriptions** and **average number of ARV prescriptions** received per year by patients in the age group >85 years).

The **total number of patients** in the age group >85 years increased with 6.12 per cent ($n = 851$) and the **total number of HIV patients** in this age group increased with 0.01 per cent ($n = 2$) from 2005 to 2006. The **total number of HIV patients** represented 0.03 per cent ($n = 4$) and 0.04 per cent ($n = 6$) of the **total number of patients** during 2005 ($n = 13\,909$) and 2006 ($n = 14\,760$) in the age group >85 years.

The **total number of medicine items** claimed for patients in the age group >85 years increased with 11.05 per cent ($n = 52\,054$), and the percentage that **ARV medicine items** represented of the total number of medicine items decreased with 0.003 per cent ($n = 10$) from 2005 to 2006. The **total number of ARV medicine items** represented 0.005 per cent ($n = 22$) and 0.002 per cent ($n = 12$) of the **total number of medicine items** claimed during 2005 ($n = 471\,063$) and 2006 ($n = 523\,117$) for patients in the age group >85 years (*refer to table 4.25*).

No practically significant difference was found between the **average cost per medicine item** as well as the **average cost per prescription** for the total database and ARV medicine items and prescriptions for 2005 or 2006 ($d < 0.8$) for the age group >85 years (*refer to table 4.25*).

The **total cost of all medicine items** increased by 11.26 per cent ($n = R5\,870\,136.85$), and the percentage that the **total cost of all ARV medicine items** represented of the **total medicine cost** decreased with 0.004 per cent ($n = R1\,840.48$) from 2005 to 2006 for patients in the age group >85 years. **ARV medicine items** represented 0.008 per cent ($n = R3\,923.02$) and 0.004 per cent ($n = R2\,082.54$) of the **total cost of all medicine items** claimed during 2005 ($n = R52\,128\,171.44$) and 2006 ($n = R57\,998\,308.29$) for patients in this age group (*refer to table 4.25*).

The **total number of prescriptions** claimed for patients in the age group >85 years increased with 9.84 per cent ($n = 18\,866$), and the percentage that **ARV prescriptions** for patients in this age group represented of the **total number of prescriptions** decreased with 0.002 per cent ($n = 3$) from 2005 to 2006. The **total number of ARV prescriptions** represented 0.005 per cent ($n = 9$) and 0.003 per cent ($n = 6$) of the **total number of prescriptions** claimed during 2005 ($n = 191\,694$) and 2006 ($n = 210\,560$) for patients in the age group >85 years (*refer to table 4.25*).

4.5.1 Cost prevalence index of ARV medicine items according to patient age group

Antiretroviral medicine items are relatively expensive in comparison with medicine items claimed through the total database (*refer to table 4.26*). Age group 0 to ≤ 4 years represented the age group with the **highest CPI for medicine items** throughout the two study years, indicating that antiretroviral treatment is relatively expensive for patients in this age group in comparison with other age groups receiving antiretroviral treatment.

The **lowest CPI** as calculated for **medicine items** was observed in age group >75 to ≤ 79 years during 2005 and age group >80 to ≤ 84 years during 2006, indicating that **ARV**

medicine items in this group were relatively inexpensive in comparison to the cost of ARV medicine items in the other age groups ($d < 0.8$) (refer to table 4.26).

Table 4.26 Cost-prevalence index of ARVs in relation to total database according to patient age

Patient age group	ARV medicine items	
	2005	2006
0 to ≤4	4.55	3.20
>5 to ≤9	3.36	2.80
>10 to ≤14	2.50	2.30
>15 to ≤19	2.29	2.80
>20 to ≤24	2.57	2.51
>25 to ≤29	2.67	2.55
>30 to ≤34	2.64	2.63
>35 to ≤39	2.57	2.46
>40 to ≤44	2.41	2.34
>45 to ≤49	2.19	2.13
>50 to ≤54	2.04	1.91
>55 to ≤59	1.87	1.69
>60 to ≤64	1.75	1.72
>65 to ≤69	1.75	1.67
>70 to ≤74	2.00	2.00
>75 to ≤79	1.50	2.00
>80 to ≤84	2.50	1.40
>85	1.60	2.00

According to table 4.27 (*inserted two pages to follow*) an estimated 16.85 per cent of the total South African population were receiving antiretroviral treatment during 2004. Of these patients, 3.20 per cent were in the age group >25 to ≤29 years, 3.20 per cent were in the age group >30 to ≤34 years, and 2.90 per cent were in the age group >35 to ≤39 years (Lubbe *et al.*, 2007).

A study done by Lubbe and co-workers (2007) on another medicine claims database for the year 2006 demonstrated that 7.40 per cent of patients receiving ARVs were in the age group >40 to ≤44 years, 6.60 per cent were in the age group >45 to ≤49 years, and 5.90 per cent were in the age group >35 to ≤39 years. Thus the prevalence of patients receiving antiretroviral treatment in the private health care sector was shown to crest at a higher age than suggested by the national assessments based on the 2001 Census data and the estimations of the South African Medical Research Council (Lubbe *et al.*, 2007) (refer to table 4.27).

Correspondingly, of the patients receiving ARVs in the medicine claims database of this study during 2005, 1.67 per cent were in the age group >35 to ≤ 39 years, 1.53 per cent were in the age group >30 to ≤ 34 years, and 1.41 per cent were in the age group >40 to ≤ 44 years. During 2006, 2.11 per cent of the patients receiving ARVs in the medicine claims database of this study were in age group >35 to ≤ 39 years, 1.89 per cent were in age group >40 to ≤ 44 years, and 1.83 per cent were in age group >30 to ≤ 34 years (*refer to table 4.27*).

This affirms that the prevalence of patients receiving ARVs in the private health care sector peaks at a higher age (>30 to ≤ 44 years) than patients in the public health sector (>25 to ≤ 39 years).

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Table 4.27 Comparison of prevalence of patients receiving ARVs according to patient age groups for 2004 to 2006

2004				2006 (PBM1*)			2005 (PBM2*)			2006 (PBM2*)		
South African population				Study population on database			Study population on database			Study population on database		
Age group (years)	Total population	Estimated number of HIV patients on ARV treatment		Total number of patients	Total number of HIV patients on ARV treatment	Percentage of HIV patients on ARV treatment %	Total number of patients	Total number of HIV patients on ARV treatment	Percentage of HIV patients on ARV treatment %	Total number of patients	Total number of HIV patients on ARV treatment	Percentage of HIV patients on ARV treatment %
		n	%									
0 to ≤4	4 449 766	19 383	0.40	20 913	87	0.40	73 288	158	0.22	72 156	193	0.27
>5 to ≤9	4 853 543	7 047	0.10	22 195	214	1.00	91 377	206	0.23	89 596	264	0.29
>10 to ≤14	5 061 893	0	0.00	16 986	125	0.70	88 082	86	0.10	87 921	147	0.17
>15 to ≤19	4 981 711	24 740	0.50	15 326	50	0.30	94 237	47	0.05	95 361	73	0.08
>20 to ≤24	4 294 513	89 742	0.20	11 646	38	0.30	78 637	185	0.24	82 049	243	0.30
>25 to ≤29	3 934 908	126 703	3.20	20 808	257	1.20	59 686	535	0.90	64 936	656	1.01
>30 to ≤34	3 340 931	107 568	3.20	27 994	945	3.40	91 325	1 394	1.53	92 153	1 682	1.83
>35 to ≤39	3 071 770	88 210	2.90	30 645	1 793	5.90	115 556	1 931	1.67	118 204	2 492	2.11
>40 to ≤44	2 619 463	61 308	2.30	30 503	2 242	7.40	118 386	1 672	1.41	123 373	2 332	1.89
>45 to ≤49	2 087 358	35 250	1.90	26 687	1 770	6.60	112 488	1 075	0.96	119 842	1 608	1.34
>50 to ≤54	1 637 986	18 236	1.10	19 273	887	4.60	96 794	561	0.58	104 572	863	0.83
>55 to ≤59	1 205 246	8 206	0.70	12 892	448	3.50	81 815	279	0.34	86 927	432	0.50
>60 to ≤64	1 065 289	3 272	0.30	7 681	114	1.50	64 521	111	0.17	69 510	168	0.24
>65 to ≤69	787 886	369	0.05	4 656	19	0.40	49 842	49	0.10	52 542	56	0.11
>70 to ≤74	631 460	0	0.00	2 657	3	0.10	38 656	23	0.06	40 246	22	0.05
>75 to ≤79	367 532	0	0.00	1 620	0	0.00	31 057	14	0.05	32 053	10	0.03
>80 to ≤84	270 923	0	0.00	639	3	0.50	20 626	4	0.02	21 062	5	0.02
>85	157 295	0	0.00	2 171	3	0.10	13 909	4	0.03	14 760	6	0.04

Adapted from Lubbe et al. (2007)

* Data retrieved from two different pharmacy benefit management companies' databases

4.6 Prescribing patterns according to type of prescriber

A prescriber can be defined as “a medical practitioner, dentist, veterinarian, practitioner, nurse or other person registered under the Health Professions Act, 1974” (South Africa, 1997:12) (refer to section 4.1.1.5).

Table 4.28 Prescribing patterns according to prescriber for the years 2005 and 2006 for general medical practitioners

Description	Prescriber: General medical practitioner			
	2005		2006	
	Total database	Antiretroviral medicine items	Total database	Antiretroviral medicine items
Total number of medicine items	14 538 227	118 792	15 521 292	188 693
Average cost per medicine item (R)	85.02 ± 109.11	200.16 ± 120.66	83.29 ± 110.56	189.08 ± 111.66
Total cost of medicine items (R)	1 236 028 622.00	23 777 690.34	1 292 764 898.00	35 678 933.84
Total number of prescriptions	6 031 354	45 947	6 313 792	74 336
Average cost per prescription (R)	204.93 ± 248.39	517.50 ± 167.76	204.75 ± 253.50	479.97 ± 151.75

The **total number of medicine items** prescribed by general medical practitioners increased with 6.76 per cent ($n = 983\,065$) throughout the two study years. The percentage that **ARV medicine items** prescribed by general medical practitioners represented of the **total number of medicine items** increased with 0.40 per cent ($n = 69\,901$) from 2005 to 2006. The **total number of ARV medicine items** represented 0.82 per cent ($n = 118\,792$) and 1.22 per cent ($n = 188\,693$) of the **total number of medicine items** claimed during 2005 ($n = 14\,538\,227$) and 2006 ($n = 15\,521\,292$) (refer to table 4.28).

Averages of 2.41 ± 1.54 and 2.46 ± 1.56 **medicine items per prescription** were prescribed by general medical practitioners during 2005 and 2006 respectively. The **average number of ARV medicine items per prescription** prescribed by general medical practitioners amounted to 2.59 ± 0.71 ARV medicine items during 2005 and 2.54 ± 0.64 ARV medicine items during 2006 ($d < 0.8$).

A practically significant difference was found between the **average cost per medicine item** as well as the **average cost per prescription** for the total database and ARV medicine items and prescriptions prescribed by general medical practitioners for 2005 or 2006 ($d > 0.8$) (refer to table 4.28).

The **total cost of all medicine items** increased by 4.59 per cent ($n = R56\,736\,279.00$), and the percentage that the **total cost of ARV medicine items** prescribed by general medical practitioners represented of the **total medicine cost** increased with 0.84 per cent ($n = R11\,901\,243.50$) from 2005 to 2006. **ARV medicine items** represented 1.92 per cent ($n = R23\,777\,690.34$) and 2.76 per cent ($n = R35\,678\,933.84$) of the **total cost of all medicine items** claimed during 2005 ($n = R1\,236\,028\,622.00$) and 2006 ($n = R1\,292\,764\,898.00$) respectively (refer to table 4.28).

The **total number of prescriptions** prescribed by general medical practitioners increased with 4.68 per cent ($n = 282\,438$), and the percentage that **ARV prescriptions** represented of **all prescriptions** increased with 0.42 per cent ($n = 28\,389$) from 2005 to 2006. The **total number of ARV prescriptions** represented 0.76 per cent ($n = 45\,947$) and 1.18 per cent ($n = 74\,336$) of the **total number of prescriptions** claimed during 2005 ($n = 6\,031\,354$) and 2006 ($n = 6\,313\,792$) (refer to table 4.28).

Table 4.29 Prescribing patterns according to prescriber for the years 2005 and 2006 for other practitioners

Description	Prescriber: Other practitioners (e.g. specialists)			
	2005		2006	
	Total database	Antiretroviral medicine items	Total database	Antiretroviral medicine items
Total number of medicine items	3 576 876	9 562	3 889 002	16 107
Average cost per medicine item (R)	161.16 ± 387.26	238.06 ± 138.36	169.64 ± 479.17	220.43 ± 132.16
Total cost of medicine items (R)	576 460 723.00	2 276 340.15	659 728 894.00	3 550 510.69
Total number of prescriptions	1 634 788	4 032	1 734 895	6 758
Average cost per prescription (R)	352.62 ± 921.62	564.57 ± 255.71	380.27 ± 1155.73	525.38 ± 219.27

The **total number of medicine items** prescribed by other practitioners increased with 8.73 per cent ($n = 312\,126$), and the percentage that **ARV medicine items** represented of **all medicine items** decreased with 0.14 per cent ($n = 6\,545$) from 2005 to 2006. The **total number of ARV medicine items** represented 0.27 per cent ($n = 9\,562$) and 0.41 per cent ($n = 16\,107$) of the **total number of medicine items** claimed during 2005 ($n = 3\,576\,876$) and 2006 ($n = 3\,889\,002$) (*refer to table 4.29*).

Averages of 2.19 ± 1.67 and 2.24 ± 1.71 **medicine items per prescription** were prescribed by other practitioners during 2005 and 2006 respectively. The **average number of ARV medicine items per prescription** prescribed by other practitioners amounted to 2.37 ± 0.98 ARV medicine items during 2005 and 2.38 ± 0.82 ARV medicine items during 2006 ($d < 0.8$).

No practically significant difference was found between the **average cost per medicine item** as well as the **average cost per prescription** for the total database and ARV medicine items and prescriptions prescribed by other practitioners for 2005 or 2006 ($d < 0.8$) (*refer to table 4.29*).

The **total cost of all medicine items** increased by 14.44 per cent ($n = R83\,268\,171.00$), and the percentage that the **total cost of all ARV medicine items** prescribed by other practitioners represented of the **total medicine cost** increased with 0.15 per cent ($n = R1\,274\,170.54$) from 2005 to 2006. **ARV medicine items** represented 0.39 per cent ($n = R2\,276\,340.15$) and 0.54 per cent ($n = R3\,550\,510.69$) of the **total cost of all medicine items** claimed during 2005 ($n = R576\,460\,723.00$) and 2006 ($n = R659\,728\,894.00$) respectively (*refer to table 4.29*).

The **total number of prescriptions** prescribed by other practitioners increased with 6.12 per cent ($n = 100\,107$), and the percentage that **ARV prescriptions** represented of **all prescriptions** increased with 0.14 per cent ($n = 6\,758$) from 2005 to 2006. The **total number of ARV prescriptions** represented 0.25 per cent ($n = 4\,032$) and 0.39 per cent ($n = 6\,758$) of the **total number of prescriptions** claimed during 2005 ($n = 1\,634\,788$) and 2006 ($n = 1\,734\,895$) (*refer to table 4.29*).

Table 4.30 Prescribing patterns according to prescriber for the years 2005 and 2006 for pharmacies

Description	Prescriber: Pharmacies			
	2005		2006	
	Total database	Antiretroviral medicine items	Total database	Antiretroviral medicine items
Total number of medicine items	1 704 808	49	2 020 781	23
Average cost per medicine item (R)	46.19 ± 40.98	230.71 ± 121.36	45.58 ± 44.71	273.90 ± 104.00
Total cost of medicine items (R)	78 739 814.70	11 304.58	92 097 572.15	6 299.62
Total number of prescriptions	1 031 344	24	1 202 756	13
Average cost per prescription (R)	76.34 ± 66.26	471.02 ± 271.26	76.57 ± 72.21	484.59 ± 233.89

The **total number of medicine items** prescribed by pharmacies increased with 18.53 per cent ($n = 315\,973$), and the percentage that **ARV medicine items** prescribed by pharmacies represented of the **total number of medicine items** decreased with 0.002 per cent ($n = 26$) from 2005 to 2006. The **total number of ARV medicine items** represented 0.003 per cent ($n = 49$) and 0.001 per cent ($n = 23$) of the **total number of medicine items** claimed during 2005 ($n = 1\,704\,808$) and 2006 ($n = 2\,020\,781$) (*refer to table 4.30*).

Averages of 1.65 ± 0.94 and 1.68 ± 0.98 **medicine items per prescription** were prescribed by pharmacies during 2005 and 2006 respectively. The **average number of ARV medicine items per prescription** prescribed by pharmacies amounted to 2.04 ± 0.75 ARV medicine items during 2005 and 1.77 ± 0.73 ARV medicine items during 2006 ($d < 0.8$).

A practically significant difference was found between the **average cost per medicine item** as well as the **average cost per prescription** for the total database and ARV medicine items and prescriptions prescribed by pharmacies for both study years ($d > 0.8$) (*refer to table 4.30*).

The **total cost of all medicine items** increased by 16.96 per cent ($n = R13\,357\,757.45$), and the percentage that the **total cost of all ARV medicine items** prescribed by pharmacies represented of the **total medicine cost** decreased with 0.007 per cent ($n = R5\,004.96$) from 2005 to 2006. **ARV medicine items** represented 0.014 per cent ($n = R11\,304.58$) and 0.007

per cent ($n = R6\ 299.62$) of the **total cost of all medicine items** claimed during 2005 ($n = R78\ 739\ 814.70$) and 2006 ($n = R92\ 097\ 572.15$) respectively.

The **total number of prescriptions** prescribed by pharmacies increased with 16.62 per cent ($n = 171\ 412$), and the percentage of **ARV prescriptions** prescribed by pharmacies decreased with 0.001 per cent ($n = 11$) from 2005 to 2006. The **total number of ARV prescriptions** represented 0.002 per cent ($n = 24$) and 0.001 per cent ($n = 13$) of the **total number of prescriptions** claimed during 2005 ($n = 1\ 031\ 344$) and 2006 ($n = 1\ 202\ 756$) (refer to table 4.30).

Table 4.31 CPI of ARV medicine items according to prescriber

CPI	2005	2006
Prescriber		
General medical practitioner	2.34	2.26
Other	1.44	1.32
Pharmacy	4.67	7.00

Table 4.31 illustrates that **ARV medicine items** prescribed by **pharmacies** are relatively expensive in comparison with ARV medicine items prescribed by general medical practitioners and other prescribers, as indicated by the high CPI value.

General medical practices prescribed the highest **average number of prescriptions** per patient per year during 2005 and 2006. **General medical practices** also prescribed the highest **total number of prescriptions** to the highest **total number of patients** during 2005 and 2006 (refer to table 4.32).

The highest **average numbers of ARV prescriptions per patient per year** were prescribed by **other prescribers** during both 2005 and 2006. **General medical practices** prescribed the highest **total number of ARV prescriptions** to the highest **total number of HIV patients** during both study years (refer to table 4.32).

Table 4.32 Average number of prescriptions per patient per year according to prescriber

2005								
Description	General medical practice		Other		Pharmacotherapy		Pharmacy	
	Total database	ARV	Total database	ARV	Total database	ARV	Total database	ARV
Average number of prescriptions per patient per year	5.87 ± 6.56	1.15 ± 0.39	4.04 ± 5.24	1.16 ± 0.51	2.06 ± 2.26	-	2.51 ± 2.74	1.00 ± 0.00
Total number of patients	1 026 060	40 115	404 203	3 466	10 493	-	410 270	24
Total number of prescriptions	6 026 767	45 947	1 633 080	4 032	21 641	-	1 031 267	24
2006								
Average number of prescriptions per patient per year	6.09 ± 6.69	1.15 ± 0.38	4.23 ± 5.44	1.15 ± 0.42	2.30 ± 2.54	-	2.54 ± 2.84	1.00 ± 0.00
Total number of patients	1 037 052	64 916	410 011	5 876	8 805	-	472 633	13
Total number of prescriptions	6 311 218	74 337	1 733 469	6 758	20 295	-	1 202 676	13

(Note: Pharmacotherapies only acted as prescribers for medicine items claimed through the total database and no ARV medicine items were prescribed by pharmacotherapies during the study period. Pharmacotherapies did not act as provider for any medicine items during the two study years.)

4.7 Prescribing patterns according to type of provider

A provider can be defined as the entity that dispensed the prescribed medication to the patient (*refer to section 4.1.1.6*).

Table 4.33 Prescribing patterns according to provider for the years 2005 and 2006 for general medical practitioners

Provider: General medical practitioners				
Description	2005		2006	
	Total database	Antiretroviral medicine items	Total database	Antiretroviral medicine items
Total number of medicine items	3 849 539	241	4 148 630	572
Average cost per medicine item (R)	39.34 ± 63.97	201.42 ± 129.77	35.92 ± 57.82	204.83 ± 100.14
Total cost of medicine items (R)	151 430 854.00	48 541.86	149 025 448.00	117161.25
Total number of prescriptions	1 405 928	117	1 465 402	266
Average cost per prescription (R)	107.71 ± 139.40	414.89 ± 209.21	101.70 ± 133.34	440.46±132.49

The **total number of medicine items** provided by general medical practitioners increased with 7.77 per cent ($n = 299\,091$), and the percentage that **ARV medicine items** represented of **all medicine items** increased with 0.008 per cent ($n = 331$) from 2005 to 2006. The **total number of ARV medicine items** represented 0.006 per cent ($n = 241$) and 0.014 per cent ($n = 572$) of the **total number of medicine items** claimed during 2005 ($n = 3\,849\,539$) and 2006 ($n = 4\,148\,630$) (*refer to table 4.33*).

Averages of 2.74 ± 1.50 and 2.83 ± 1.51 **medicine items per prescription** were provided by general medical practitioners during 2005 and 2006 respectively. The **average number of ARV medicine items per prescription** provided by general medical practitioners amounted to 2.06 ± 0.81 ARV medicine items during 2005 and 2.15 ± 0.60 ARV medicine items during 2006 ($d < 0.8$).

A practically significant difference was found between the **average cost per medicine item** as well as the **average cost per prescription** for the total database and ARV medicine items and prescriptions provided by general medical practitioners for 2005 or 2006 ($d > 0.8$) (refer to table 4.33).

The **total cost of all medicine items** decreased by 1.59 per cent ($n = R2\ 405\ 406$), and the percentage that the **total cost of all ARV medicine items** provided by general medical practitioners represented of the **total medicine cost** increased with 0.05 per cent ($n = R68\ 619.39$) from 2005 to 2006. **ARV medicine items** represented 0.03 per cent ($n = R48\ 541.86$) and 0.08 per cent ($n = R117\ 161.25$) of the **total cost of all medicine items** claimed during 2005 ($n = R151\ 430\ 854.00$) and 2006 ($n = R149\ 025\ 448.00$) respectively (refer to table 4.33).

The **total number of prescriptions** provided by general medical practitioners increased with 4.23 per cent ($n = 59\ 474$), and the percentage that **ARV prescriptions** provided by general medical practitioners represented of **all prescriptions** increased with 0.01 per cent ($n = 149$) from 2005 to 2006. The **total number of ARV prescriptions** represented 0.01 per cent ($n = 117$) and 0.02 per cent ($n = 266$) of the **total number of prescriptions** claimed during 2005 ($n = 1\ 405\ 928$) and 2006 ($n = 1\ 465\ 402$) (refer to table 4.33).

Table 4.34 Prescribing patterns according to provider for the years 2005 and 2006 for other practitioners

Description	Provider: Other practitioners			
	2005		2006	
	Total database	Antiretroviral medicine items	Total database	Antiretroviral medicine items
Total number of medicine items prescribed	78 612	10	56 923	-
Average cost per medicine item (R)	188.10 ± 625.09	401.96 ± 22.96	158.15 ± 648.55	-
Total cost of medicine items prescribed (R)	14 786 584.36	4 019.64	9 002 585.31	-
Total number of prescriptions	41 507	6	29 541	-
Average cost per prescription (R)	356.24 ± 1472.91	669.94 ± 221.35	304.75 ± 1350.77	-

No antiretroviral medicine items or prescriptions were provided by other practitioners during 2006 (refer to table 4.34).

The **total number of medicine items** provided by other practitioners decreased with 27.59 per cent ($n = 21\,689$), and the percentage that **ARV medicine items** provided by other practitioners represented of **all medicine items** decreased with 0.01 per cent ($n = 10$) from 2005 to 2006. The **total number of ARV medicine items** represented 0.01 per cent ($n = 10$) and 0.00 per cent ($n = 0$) of the **total number of medicine items** claimed during 2005 ($n = 78\,612$) and 2006 ($n = 56\,923$) (*refer to table 4.34*).

Averages of 1.89 ± 1.61 and 1.93 ± 1.58 **medicine items per prescription** were provided by other practitioners during 2005 and 2006 respectively. The **average number of ARV medicine items** per prescription provided by other practitioners amounted to 1.67 ± 0.52 ARV medicine items during 2005 ($d < 0.8$).

No practically significant difference was found between the **average cost per medicine item** as well as the **average cost per prescription** for the total database and ARV medicine items and prescriptions provided by other practitioners for 2005 ($d < 0.8$) (*refer to table 4.34*).

The **total cost of all medicine items** decreased by 39.12 per cent ($n = R5\,783\,999.05$), and the percentage that the **total cost of all ARV medicine items** provided by other practitioners represented of the **total medicine cost** decreased with 0.03 per cent ($n = R4\,019.64$) from 2005 to 2006. **ARV medicine items** represented 0.03 per cent ($n = R4\,019.64$) and 0.00 per cent ($n = R0.00$) of the **total cost of all medicine items** claimed during 2005 ($n = R14\,786\,584.36$) and 2006 ($n = R9\,002\,585.31$) respectively (*refer to table 4.34*).

The **total number of prescriptions** provided by other practitioners decreased with 28.83 per cent ($n = 11\,966$), and the percentage that **ARV prescriptions** represented of all prescriptions decreased with 0.01 per cent ($n = 6$) from 2005 to 2006. The **total number of ARV prescriptions** represented 0.01 per cent ($n = 6$) and 0.00 per cent ($n = 0$) of the **total number of prescriptions** claimed during 2005 ($n = 41\,507$) and 2006 ($n = 29\,541$) (*refer to table 4.34*).

Table 4.35 Prescribing patterns according to provider for the years 2005 and 2006 for pharmacies

Description	Provider: Pharmacies			
	2005		2006	
	Total database	Antiretroviral medicine items	Total database	Antiretroviral medicine items
Total number of medicine items prescribed	15 926 285	128 152	17 262 616	204 251
Average cost per medicine item (R)	108.40 ± 205.34	202.98 ± 122.45	109.40 ± 247.73	191.52 ± 113.75
Total cost of medicine items prescribed (R)	1 726 420 151.00	26 012 773.57	1 888 460 215.00	39 118 582.90
Total number of prescriptions	7 076 188	49 872	7 548 523	80 829
Average cost per prescription (R)	243.98 ± 488.33	521.59 ± 177.04	250.18 ± 598.47	483.97 ± 132.49

The **total number of medicine items** provided by pharmacies increased with 8.39 per cent ($n = 1\,336\,331$), and the percentage that **ARV medicine items** provided by pharmacies represented of **all medicine items** increased 0.38 with per cent ($n = 76\,099$) from 2005 to 2006. The **total number of ARV medicine items** represented 0.80 per cent ($n = 128\,152$) and 1.18 per cent ($n = 204\,251$) of the **total number of medicine items** claimed during 2005 ($n = 15\,926\,285$) and 2006 ($n = 17\,262\,616$) (*refer to table 4.35*).

Averages of 2.25 ± 1.56 and 2.29 ± 1.58 **medicine items per prescription** were provided by pharmacies during 2005 and 2006 respectively. The **average number of ARV medicine items** per prescription provided by pharmacies amounted to 2.57 ± 0.74 ARV medicine items during 2005 and 2.53 ± 0.66 ARV medicine items during 2006 ($d < 0.8$).

No practically significant difference was found between the **average cost per medicine item** as well as the **average cost per prescription** for the total database and ARV medicine items and prescriptions provided by pharmacies for 2005 or 2006 ($d < 0.8$) (*refer to table 4.35*).

The **total cost of all medicine items** increased by 9.39 per cent ($n = R162\,040\,064.00$), and the percentage that the **total cost of all ARV medicine items** provided by pharmacies represented of the **total medicine cost** increased with 0.56 per cent ($n = R13\,105\,809.33$) from 2005 to 2006. **ARV medicine items** represented 1.51 per cent ($n = R26\,012\,773.57$)

and 2.07 per cent ($n = R39\ 118\ 582.90$) of the **total cost of all medicine items** claimed during 2005 ($n = R1\ 726\ 420\ 151.00$) and 2006 ($n = R1\ 888\ 460\ 215.00$) respectively (*refer to table 4.35*).

The **total number of prescriptions** provided by pharmacies increased with 6.67 per cent ($n = 472\ 335$), and the percentage that **ARV prescriptions** provided by pharmacies represented of **all prescriptions** increased with 0.37 per cent ($n = 30\ 957$) from 2005 to 2006. The **total number of ARV prescriptions** represented 0.70 per cent ($n = 49\ 872$) and 1.07 per cent ($n = 80\ 829$) of the **total number of prescriptions** claimed during 2005 ($n = 7\ 076\ 188$) and 2006 ($n = 7\ 548\ 523$) (*refer to table 4.35*).

Table 4.36 Cost-prevalence index of ARV medicine items according to provider

CPI	2005	2006
Provider		
General medical practitioner	5.33	5.64
Other	2.08	-
Pharmacy	1.89	1.75

ARV medicine items provided by **general medical practitioners** are relatively expensive in comparison with ARV medicine items provided by other providers and pharmacies (*refer to table 4.36*), as indicated by the high CPI value.

Table 4.37 CPI of ARV medicine items according to prescriber and provider in comparison with total number of ARV medicine items for 2005 and 2006

Year	Prescriber		
	General medical practitioner	Other	Pharmacy
2005	0.96	1.17	1.00
2006	0.99	1.15	2.00
Year	Provider		
	General medical practitioner	Other	Pharmacy
2005	1.00	2.00	1.00
2006	1.07	-	1.00

Table 4.37 illustrates that ARVs prescribed by **other prescribers** were relatively expensive during 2005, and ARVs prescribed by **pharmacies** were relatively expensive relative to ARVs prescribed by the different prescribers during 2006.

ARV medicine items provided by **other providers** were relatively expensive during 2005, and ARVs provided by **general medical practitioners** during 2006 were also relatively expensive (*refer to table 4.37*).

Table 4.38 Average number of prescriptions per patient per year according to provider

2005						
Description	General medical practice		Other		Pharmacy	
	Total database	ARV	Total database	ARV	Total database	ARV
Average number of prescriptions per patient per year	3.44 ± 3.85	1.08 ± 0.31	2.08 ± 2.95	1.00 ± 0.00	6.48 ± 7.48	1.15 ± 0.41
Total number of patients	408 230	108	19 889	6	1 091 017	43 440
Total number of prescriptions	1 405 240	117	41 351	6	7 065 758	49 872
2006						
Average number of prescriptions per patient per year	3.46 ± 3.77	1.67 ± 0.50	1.78 ± 2.45	-	6.71 ± 7.77	1.15 ± 0.34
Total number of patients	423 917	228	16 537	-	1 123 267	70 496
Total number of prescriptions	1 465 079	266	29 481	-	7 537 465	80 830

Pharmacies provided the highest **average number of prescriptions** per patient per year during 2005 and 2006. **Pharmacies** also provided the highest **total number of prescriptions** to the highest **total number of patients** during 2005 and 2006 (*refer to table 4.38*).

The highest **average number of ARV prescriptions per patient per year** was provided by **pharmacies** during 2005 and **other providers** during 2006. Additionally, **pharmacies** provided the highest **total number of ARV prescriptions** to the highest **total number of HIV patients** during both study years (*refer to table 4.38*).

4.8 Prescribing patterns according to type of medicine item and patient age group

Table 4.39 Average cost of original ARV medicine items with no generic for 2005 and 2006 according to patient age group

N	Average cost (R)	Standard deviation (R)	Total cost (R)	Age group (years)	N	Average cost (R)	Standard deviation (R)	Total cost (R)
2005					2006			
907	221.17	181.42	200 597.12	0 to ≤4	1 385	128.11	128.82	177 427.56
1 384	157.52	154.52	242 915.66	>5 to ≤9	2 248	140.86	135.82	316 646.20
642	181.36	159.96	116 436.03	>10 to ≤14	1 311	162.81	142.97	213 448.13
164	235.11	83.03	38 558.17	>15 to ≤19	280	253.17	131.81	70 887.77
525	252.99	48.96	132 818.81	>20 to ≤24	869	245.55	72.43	213 379.49
1 742	259.94	57.66	452 814.83	>25 to ≤29	2 480	240.12	63.44	595 498.15
5 523	259.46	79.55	1 433 015.36	>30 to ≤34	8 772	242.09	84.84	2 123 609.50
9 587	255.72	63.85	2 451 560.30	>35 to ≤39	15 767	237.56	75.82	3 745 554.86
8 565	259.72	82.40	2 224 520.93	>40 to ≤44	15 732	233.84	70.73	3 678 763.70
5 629	253.92	51.38	1 429 324.11	>45 to ≤49	10 865	232.89	71.61	2 530 377.16
2 853	255.83	64.32	729 889.59	>50 to ≤54	5 520	231.16	61.78	1 275 991.12
1 352	263.42	95.57	356 147.07	>55 to ≤59	2 808	227.22	61.12	638 037.54
598	275.03	130.72	164 466.19	>60 to ≤64	1 205	248.32	97.03	299 222.69
197	252.83	51.72	49 806.89	>65 to ≤69	317	247.59	136.62	78 484.57
95	239.58	69.10	22 760.27	>70 to ≤74	167	219.91	56.18	36 724.61
33	288.42	80.62	9 517.72	>75 to ≤79	42	222.58	48.88	9 348.52
7	378.89	278.59	2 652.26	>80 to ≤84	8	235.56	78.07	1 884.47
7	266.56	51.99	1 865.92	>85	2	342.59	0.00	685.18

The lowest percentage of medicine items manifested in age groups **>80 to ≤84 years** and **>85 years** which represented 0.018 per cent each (n = 7) during 2005, and age group **>85 years** which represented 0.003 per cent (n = 2) during 2006 of the total number of **original ARV medicine items with no generic**. The highest percentage of original ARV medicine items with no generic manifested in age group **>35 to ≤39 years** for both study years. Age group **>35 to ≤39 years** represented 24.08 per cent (n = 9 587) during 2005, and 22.60 per cent (n = 15 767) during 2006 of the total number of **original ARV medicine items with no generic** claimed for 2005 (n = 39 810) and 2006 (n = 69 778) (refer to table 4.39 and figure 4.3).

Consequently, age group **>35 to ≤39 years** also represented the highest total cost of ARV medicine items at R2 451 560.30 during 2005 and R3 745 554.86 during 2006, or 24.37 per cent and 23.40 per cent respectively of the total cost of **original ARV medicine items with**

no generic during 2005 ($n = R10\ 059\ 667.23$) and 2006 ($n = R16\ 005\ 971.22$) (refer to table 4.39 and figure 4.7).

The highest average cost per **original ARV medicine item with no generic** could be observed for age group **>80 to ≤84 years** at $R378.89 \pm R278.59$ ($n = 7$) during 2005, and age group **>85 years** at $R342.59 \pm R0.00$ ($n = 2$) during 2006. The lowest average cost per **original ARV medicine item with no generic** could be observed for age group **>5 to ≤9 years** at $R157.52 \pm R154.52$ ($n = 1\ 384$) during 2005 ($d < 0.8$), and age group **0 to ≤4 years** at $R128.11 \pm R128.82$ ($n = 1\ 385$) during 2006 ($d > 0.8$) (refer to table 4.39 and figure 4.5).

Table 4.40 Average cost of original innovator ARV medicine items for 2005 and 2006 according to patient age group

N	Average cost (R)	Standard deviation (R)	Total cost (R)	Age group (years)	N	Average cost (R)	Standard deviation (R)	Total cost (R)
2005					2006			
971	366.83	210.91	356 192.59	0 to ≤4	368	356.96	245.00	131 363.00
1 272	345.73	222.87	439 769.09	>5 to ≤9	752	331.76	245.64	249 481.39
315	255.06	145.96	80 343.21	>10 to ≤14	437	264.00	139.96	115 366.35
77	222.46	143.14	17 129.12	>15 to ≤19	48	297.14	138.96	14 262.59
247	294.74	146.27	72 800.26	>20 to ≤24	141	295.57	142.27	41 675.60
709	256.63	148.80	181 948.59	>25 to ≤29	393	253.18	147.23	99 498.86
1 981	269.60	150.99	534 072.06	>30 to ≤34	1 041	305.79	140.03	318 329.74
3 091	264.75	146.05	818 334.04	>35 to ≤39	1 769	290.27	145.10	513 491.46
2 540	270.66	146.12	687 469.85	>40 to ≤44	1 863	269.39	147.43	501 870.71
1 613	276.23	152.42	445 556.25	>45 to ≤49	1 141	276.09	152.72	315 022.18
786	309.85	144.59	243 538.39	>50 to ≤54	749	304.88	140.83	228 352.09
418	290.65	147.92	121 490.34	>55 to ≤59	398	331.05	136.92	131 759.06
226	270.99	155.66	61 244.32	>60 to ≤64	150	303.16	145.43	45 474.52
49	254.30	150.45	12 460.89	>65 to ≤69	56	246.67	156.26	13 796.62
52	331.91	138.19	17 259.12	>70 to ≤74	67	415.53	18.68	27 840.78
43	242.97	151.40	10 447.90	>75 to ≤79	1	204.84	-	204.87
3	310.99	146.51	932.98	>80 to ≤84	-	-	-	-
8	203.49	11.76	1 627.95	>85	4	133.41	67.12	533.62

During 2006, no original innovator ARVs were claimed for patients in age group **>80 to ≤84 years**. The lowest percentage of medicine items could be found in age group **>80 to ≤84 years** which represented 0.02 per cent ($n = 3$) during 2005, and age group **>75 to ≤79 years** which represented 0.01 per cent ($n = 1$) during 2006 of the total number of **original innovator ARV medicine items**. The highest percentage of **original innovator ARV medicine items** came forth in age group **>35 to ≤39 years** which represented 21.46 per cent ($n = 3\ 091$) during 2005, and age group **>40 to ≤44 years** which represented 19.87 per cent ($n = 1\ 863$) during 2006 of the total number of **original innovator ARV medicine items**.

claimed for 2005
(n = 14 401) and 2006 (n = 9 378) respectively (refer to table 4.40 and figure 4.3).

Age group **>35 to ≤39 years** also represented the highest total cost of original innovator ARV medicine items at 19.95 per cent (n = R818 334.04) of the total cost of all original innovator ARV medicine items claimed during 2005 (n = R4 102 616.95). Age group **>35 to ≤39 years** represented the highest total cost at 18.68 per cent (n = R513 491.46) of the total cost of original innovator ARV medicine items claimed during 2006 (n = R2 748 323.41) (refer to table 4.40 and figure 4.7).

The highest average cost per original innovator ARV medicine item could be observed for age group **0 to ≤4 years** at R366.83 ± R210.91 (n = 971) during 2005, and age group **>70 to ≤74 years** at R415.53 ± R18.68 (n = 67) during 2006. The lowest average cost per original innovator ARV medicine item could be observed for age group **>85 years** during both study years, at R203.49 ± R11.76 (n = 8) during 2005 (d<0.8) and R133.41 ± R67.12 (n = 4) during 2006 (d>0.8) (refer to table 4.40 and figure 4.5).

Table 4.41 Average cost of generic ARV medicine items for 2005 and 2006 according to patient age group

N	Average cost (R)	Standard deviation (R)	Total cost (R)	Age group (years)	N	Average cost (R)	Standard deviation (R)	Total cost (R)
2005					2006			
1 168	153.92	90.77	179 782.80	0 to ≤4	2 435	165.63	98.44	403 314.18
2 048	119.41	84.94	244 543.64	>5 to ≤9	3 916	143.17	102.90	560 671.75
858	114.02	85.52	97 829.58	>10 to ≤14	1 970	118.14	82.04	232 745.11
243	146.94	103.61	35 705.90	>15 to ≤19	487	158.78	119.67	77 327.40
1 058	165.61	111.22	175 212.25	>20 to ≤24	1 677	163.54	110.65	274 248.73
3 869	182.14	114.60	704 686.48	>25 to ≤29	6 325	174.23	112.87	1 102 005.37
12 100	167.40	112.45	2 025 484.81	>30 to ≤34	18 368	172.90	113.40	3 175 738.30
18 105	166.91	113.37	3 021 869.56	>35 to ≤39	29 100	167.05	114.00	4 861 020.47
15 701	156.29	111.00	2 453 889.23	>40 to ≤44	26 525	161.06	114.06	4 272 157.05
10 588	154.90	111.03	1 640 058.87	>45 to ≤49	18 380	158.37	114.82	2 910 879.95
4 816	157.49	113.97	758 492.76	>50 to ≤54	9 565	159.26	114.27	1 523 351.69
2 120	155.56	112.01	329 785.31	>55 to ≤59	4 491	152.92	112.71	686 743.05
997	147.03	109.61	146 587.99	>60 to ≤64	1 621	172.97	118.16	280 378.27
322	174.18	116.14	56 086.71	>65 to ≤69	514	139.68	110.77	71 793.05
107	162.53	121.40	17 390.46	>70 to ≤74	167	192.92	128.45	32 217.19
82	179.52	109.96	14 728.87	>75 to ≤79	95	128.51	106.07	12 208.53
3	162.18	145.15	486.53	>80 to ≤84	25	151.43	109.34	3 785.69
7	61.31	32.30	429.15	>85	6	143.96	110.50	863.74

The lowest percentage of **generic ARV medicine items** appeared in age group **>80 to ≤84 years** which represented 0.004 per cent (n = 3) during 2005, and age group **>85 years** which represented 0.005 per cent (n = 6) during 2006 of the total number of **generic ARV medicine items**. The highest percentage of medicine items appeared in age group **>35 to ≤39 years** for both study years, which represented 24.40 per cent (n = 18 105) during 2005, and 23.16 per cent (n = 29 100) during 2006 of the total number of **generic ARV medicine items** claimed for 2005 (n = 74 192) and 2006 (n = 125 667) (refer to table 4.41 and figure 4.3).

Consequently, age group **>35 to ≤39 years** also represented the highest total cost of **generic ARV medicine items** at R3 021 869.56 during 2005 and R4 861 020.47 during 2006, or 25.39 per cent and 23.73 per cent respectively of the total cost of **generic ARV medicine items** during 2005 (n = R11 903 050.89) and 2006 (n = R20 481 449.52) (refer to table 4.41 and figure 4.7).

The highest average cost per **generic ARV medicine item** could be observed for age group **>75 to ≤79 years** at R179.52 ± R109.96 (n = 82) during 2005, and age group **>70 to ≤74 years** at R192.92 ± R128.45 (n = 167) during 2006. The lowest average cost per **generic ARV medicine item** could be observed for age group **>85 years** at R61.31 ± R32.30 (n = 7) during 2005 (d>0.8), and age group **>10 to ≤14 years** at R118.14 ± R82.04 (n = 3) during 2006 (d<0.8) (refer to table 4.41 and figure 4.5).

4.9 Prescribing patterns according to type of medicine item and patient gender

Table 4.42 Average cost of ARV medicine items for 2005 and 2006 according to patient gender

N	Average cost (R)	Standard deviation (R)	Total cost (R)	Patient gender	N	Average cost (R)	Standard deviation (R)	Total cost (R)
2005					2006			
Original ARV medicine items with no generic								
21 316	251.36	78.56	5 357 971.41	Female	37 445	230.86	76.28	8 644 641.07
18 494	254.23	90.90	4 701 695.82	Male	32 333	227.67	91.72	7 361 330.15
Original innovator ARV medicine items								
7 810	283.87	164.07	2 217 038.86	Female	5 225	293.82	166.59	1 535 217.65
6 591	286.08	164.20	1 885 578.09	Male	4 153	292.10	156.54	1 213 105.76
Generic ARV medicine items								
43 585	163.04	110.93	7 106 169.44	Female	73 825	167.72	112.73	12 381 946.07
30 607	156.72	112.50	4 796 881.45	Male	51 842	156.23	113.75	8 099 503.45

The highest **total number** of all types of **ARV medicine items** could be observed for female patients during both study years (*refer to figure 4.4*). Female patients also represented the highest **total cost** of all types of ARV medicine items during 2005 and 2006 (*refer to table 4.42 and figure 4.8*).

Original ARV medicine items with no generic claimed for female patients represented 53.54 per cent (n = 21 316) and 53.66 per cent (n = 37 445) of the total number of original ARV medicine items with no generic claimed during 2005 (n = 39 810) and 2006 (n = 69 778) respectively. **Original innovator ARV medicine items** claimed for female patients represented 54.23 per cent (n = 7 810) and 55.72 per cent (n = 5 225) of the total number of original innovator ARV medicine items claimed during 2005 (n = 14 401) and 2006 (n = 9 378) respectively. **Generic ARV medicine items** claimed for female patients represented 58.75 per cent (n = 43 585) and 58.75 per cent (n = 73 825) of the total number of generic ARV medicine items claimed during 2005 (n = 74 192) and 2006 (n = 125 667) respectively (*refer to table 4.42*).

No practically significant difference in **average cost per ARV medicine** exists between all types of ARV medicine items claimed for female patients and male patients (d <0.8) (*refer to table 4.42*).

The highest average cost per **original ARV medicine items with no generic** could be observed for male patients (R254.23 ± R90.90) during 2005 and female patients (R230.86 ± R76.28) during 2006. The highest average cost per **original innovator ARV medicine item** could be observed for male patients (R286.08 ± R164.20) during 2005 and female patients (R293.82 ± R166.59) during 2006. The highest average cost per **generic ARV medicine item** could be observed for female patients (R163.04 ± R110.93) during 2005 as well as during 2006 (R167.72 ± R112.73) (*refer to table 4.42 and figure 4.6*).

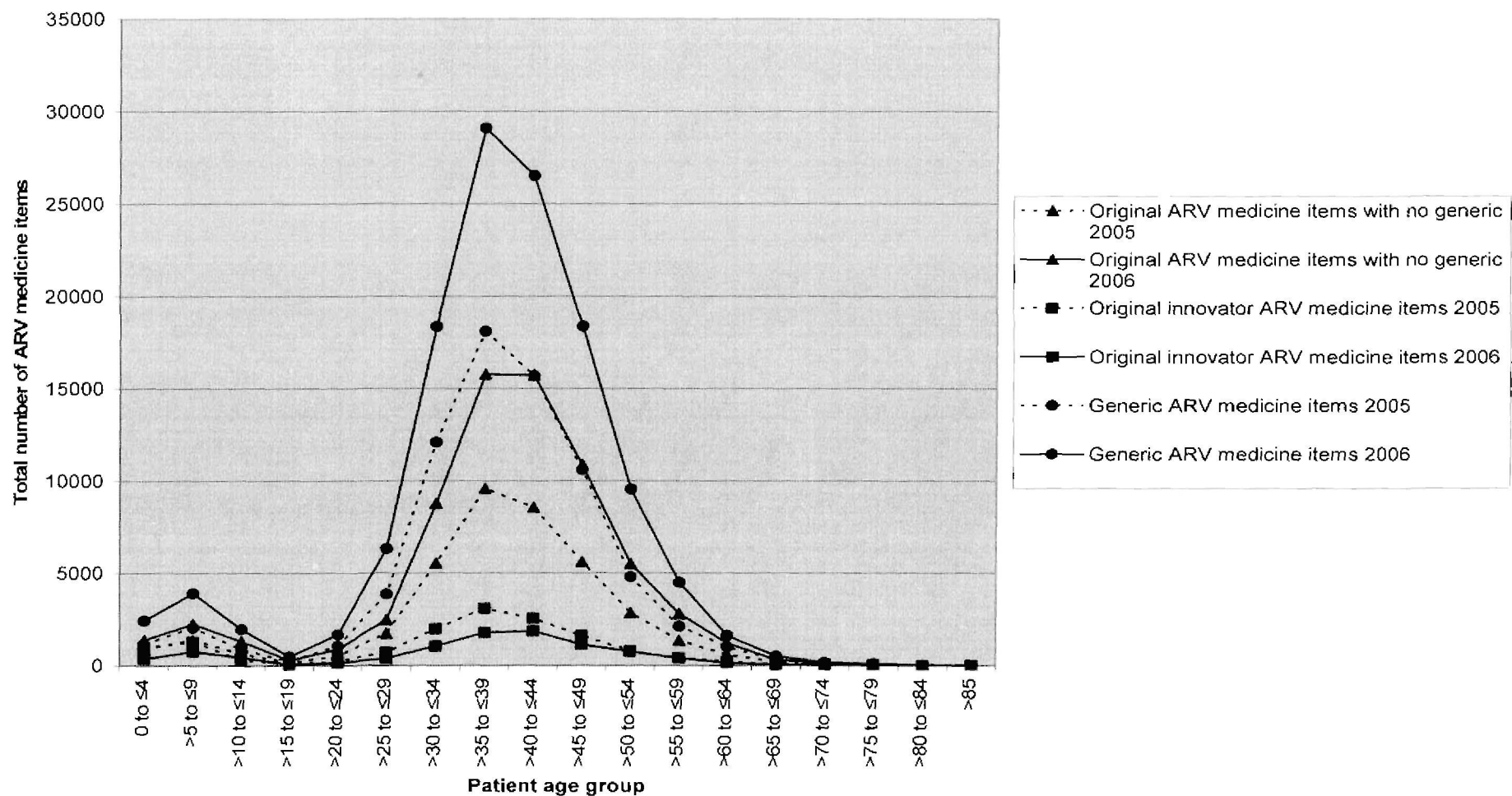


Figure 4.3 Total number of ARV medicine items according to type of medicine and patient age group

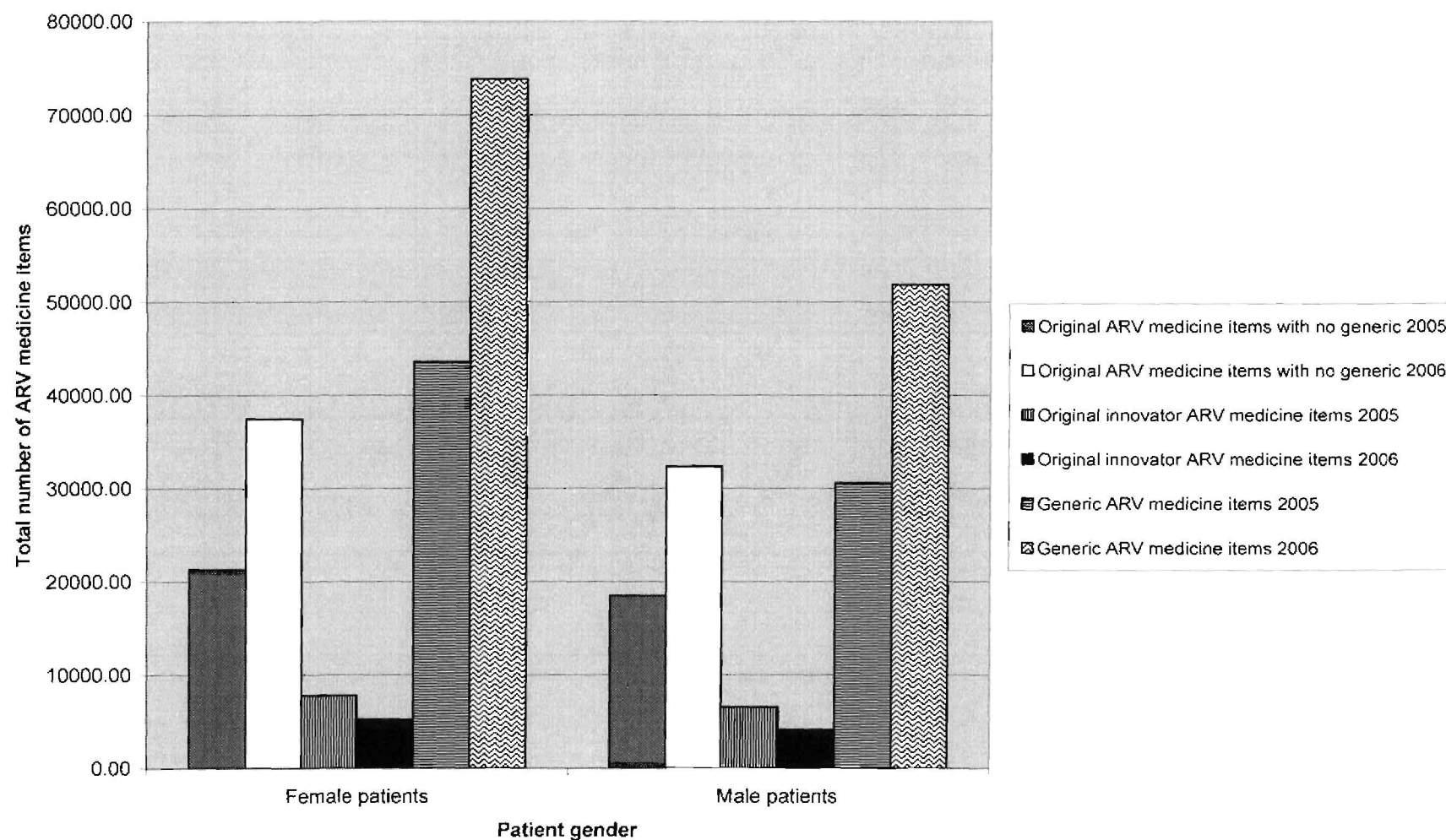


Figure 4.4 Total number of ARV medicine items according to type of medicine and patient gender

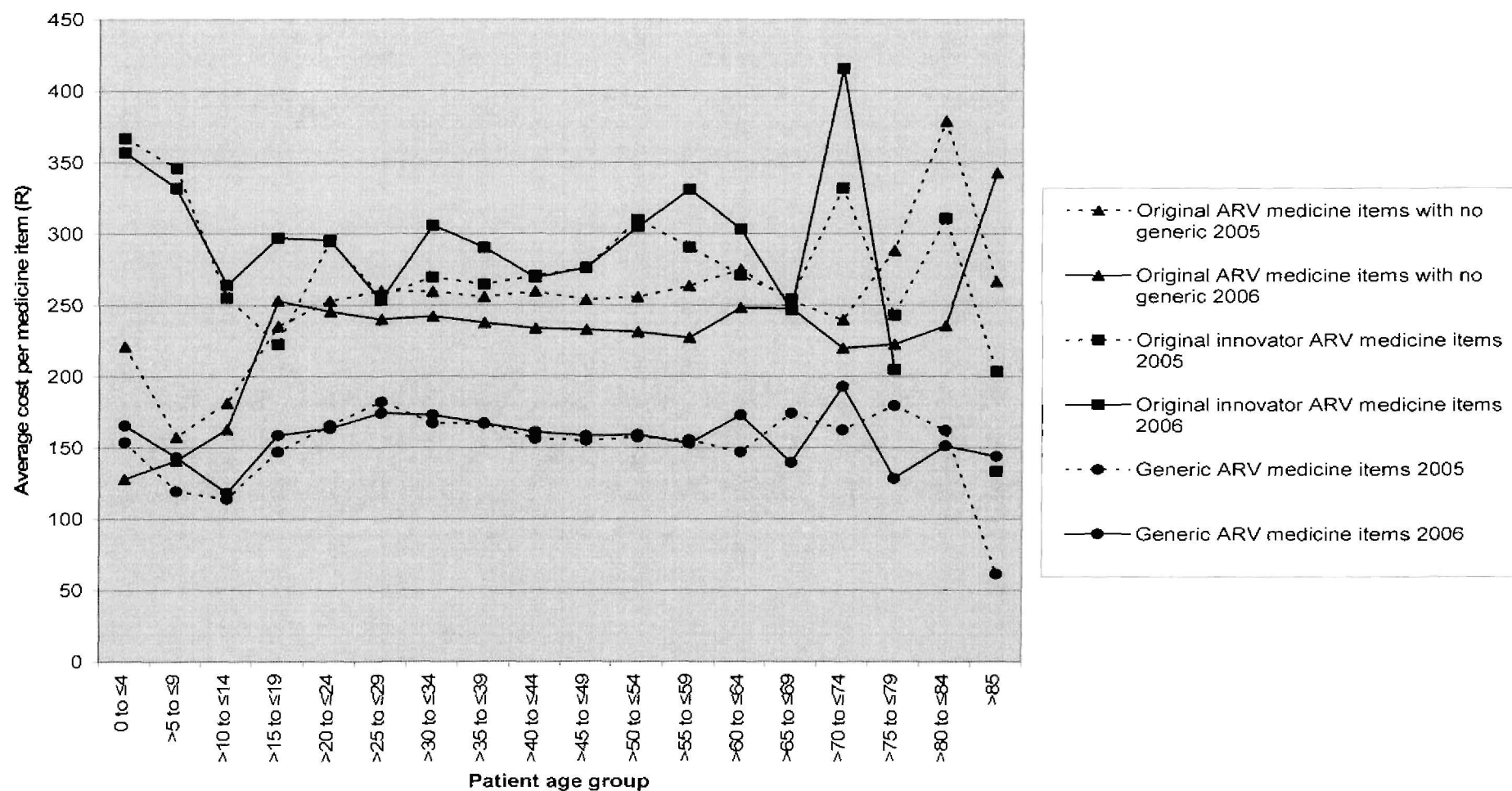


Figure 4.5 Average cost per ARV medicine item according to type of medicine and patient age group

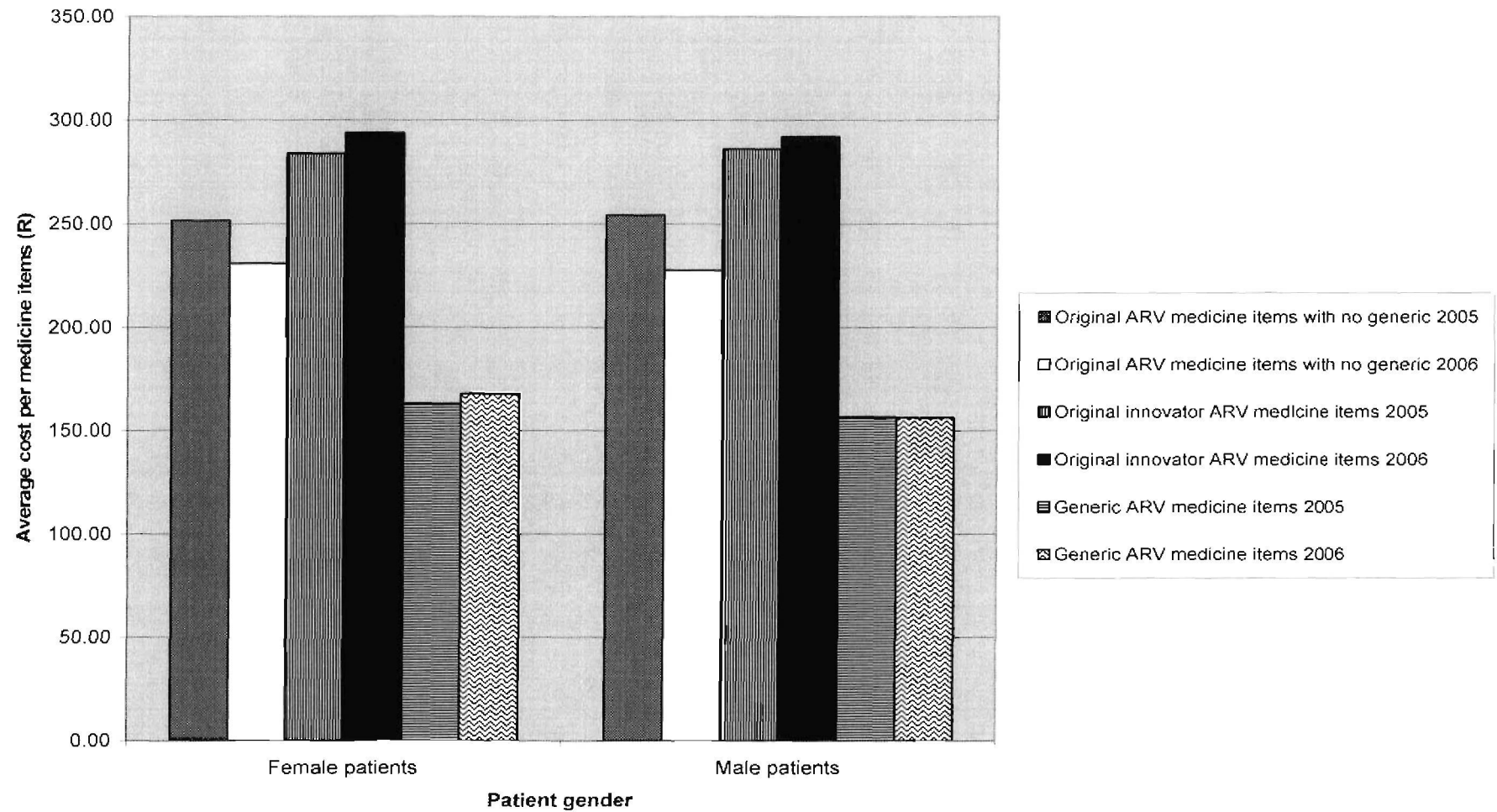


Figure 4.6 Average cost per ARV medicine item according to type of medicine and patient gender

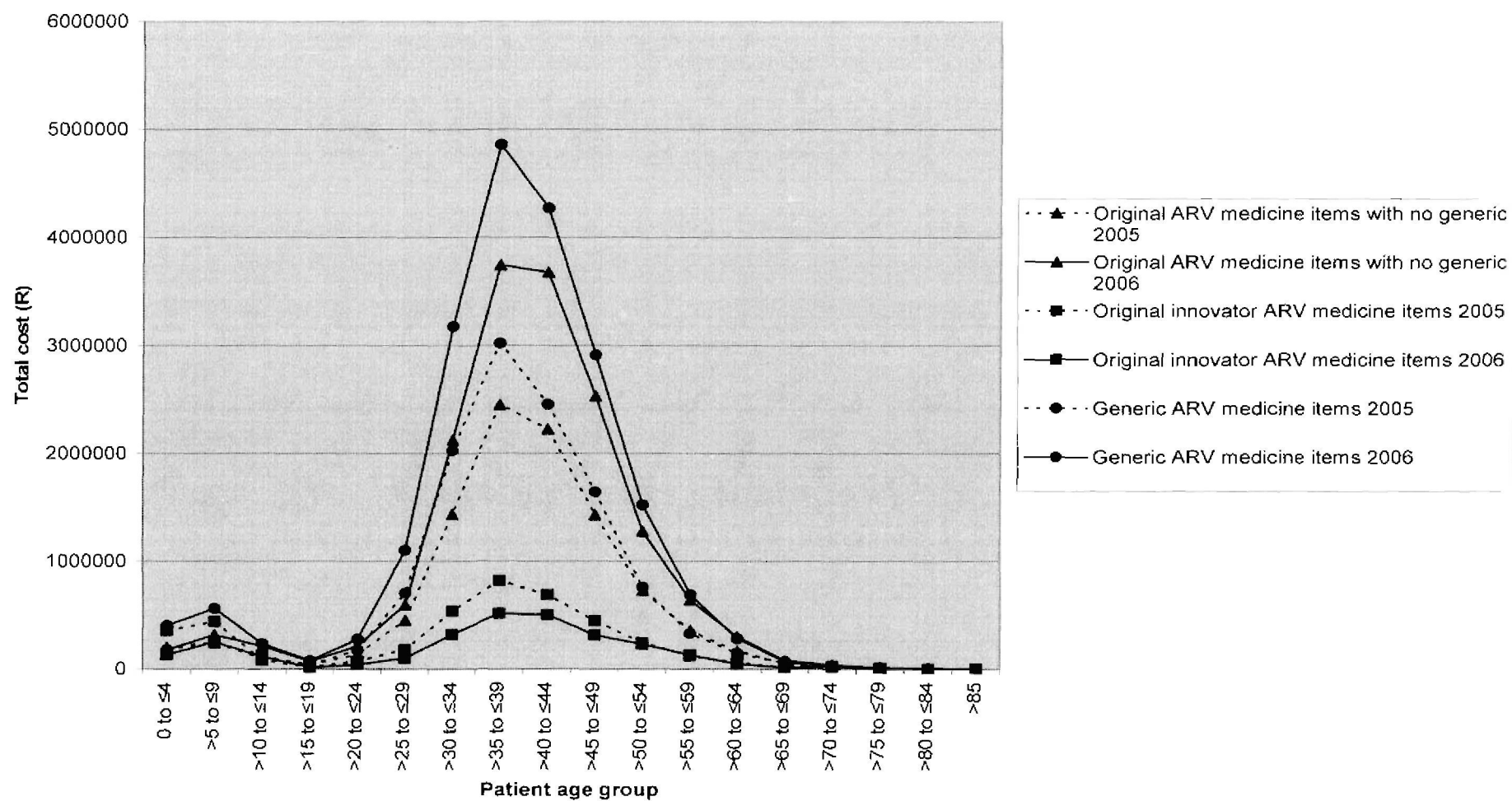


Figure 4.7 Total cost of ARV medicine items according to type of medicine and patient age group

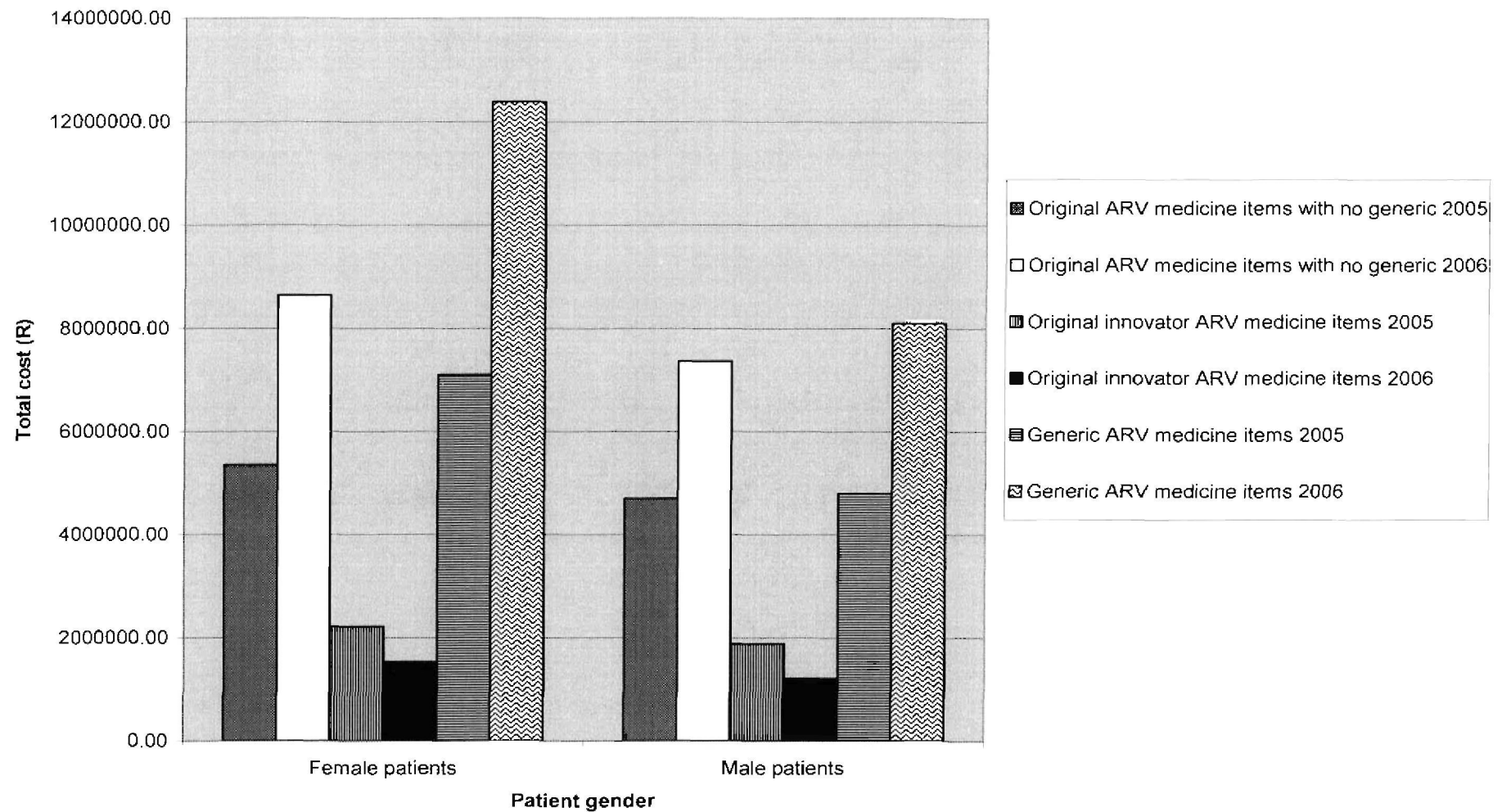


Figure 4.8 Total cost of ARV medicine items according to type of medicine and patient gender

4.10 Prescribing patterns according to combination of antiretroviral medicine items

The following trade name ARVs were included in the database, as listed here by active ingredient and classified by mechanism of action:

Table 4.43 Classification of antiretroviral medicine items (active ingredient and trade names) in the Top 20 ARV combinations

NRTI*	Abacavir	Ziagen® 300mg Tab Ziagen® 100mg/5ml Sol
	Didanosine	Videx® 150mg Chew Videx® 100mg Chew Videx® 50mg Chew Videx® 25mg Chew Videx® 250mg EC Cap Videx® 400mg EC Cap Aspen Didanosine® 100mg Aspen Didanosine® 25mg Aspen Didanosine® 50mg Aspen Didanosine® 150mg
		Aspen Lamivudine® 150mg Tab Aspen Lamivudine® 10mg/MI 3TC® 150mg Tab 3TC® Oral 10mg/MI Sol
		Aspen Stavudine® 40mg Cap Zerit® 40mg Cap Aspen Stavudine® 15mg Cap Aspen Stavudine® 20mg Cap Aspen Stavudine® 30mg Cap Aspen Stavudine® 40mg Cap Zerit® 5mg/5ml Sus Zerit® 20mg Cap Zerit® 30mg Cap
		Retrovir® S 50mg/5ml Syr Retrovir® 100mg Cap Retrovir® 200mg/20ml Inj Retrovir® 250mg Cap Aspen Zidovudine® Syr 50mg/5ml Aspen Zidovudine® 300mg Tab
		Aspen Lamzid® Tab Combivir® Tab Cipla Duovir® Tab
	NRTI**	Aspen Nevirapine® 200mg Tab Viramune® 200mg Tab Viramune® Oral Cipla Nevirapine® 200mg Tab
		Stocrin® 600mg Tab Stocrin® 200mg Cap Stocrin® 50mg Cap
	PI***	Crixivan® 400mg Cap Crixivan® 200mg Cap
		Norvir® 100mg Cap
		Kaletra® 80mg/20mg Cap Kaletra® 400/100mg/5ml

**NRTI = Nucleoside Reverse Transcriptase Inhibitor*

***NNRTI = Non-Nucleoside Reverse Transcriptase Inhibitor*

****PI = Protease Inhibitor*

(refer to section 2.6.1)

One would expect the majority of prescriptions to comply with the following National Antiretroviral treatment guidelines for adults as released by the South African Department of Health (South Africa, 2004b:4):

- Regimen 1A: Stavudine + Lamivudine + Efavirenz
- Regimen 1B: Stavudine + Lamivudine + Nevirapine
- Regimen 2: Zidovudine + Didanosine + Lopinavir/Ritonavir

Comparably, the World Health Organization recommends the following treatment regimens for adults (WHO, 2002: 14-18):

- Preferred first-line regimen: Nevirapine + 2 NRTI
- Preferred second-line regimen: Boosted PI + 2 NRTI

4.10.1 Prescribing patterns of ARV combination prescriptions according to frequency

Only the top 20 ARV prescriptions ranked according to frequency were analysed for each group of ARV combinations classified by the number of ARV medicine items in combination.

4.10.1.1 One antiretroviral medicine item per prescription

It has been established that monotherapy (treatment with only one antiretroviral agent) and dual therapy (treatment with two antiretroviral agents) fosters occurrence of resistance to ARV medication, leading to reduced efficiency of triple therapy (McLeod *et al.*, 2003:92-93) (refer to section 2.7.2).

According to the World Health Organization none of the existing antiretroviral agents at this time can sustainably and effectively suppress viral replication on its own. Monotherapy produces partial viral suppression for a very short period at best and inexorably leads to drug resistance and even cross-resistance to other antiretroviral agents. Consequently, monotherapy is not recommended for the management of HIV infection (Munderi *et al.*, 2000:21). The WHO still recommends short course monotherapy explicitly for prevention of mother to child transmission of HIV infection (Munderi *et al.*, 2000:21), although the South African Medicines Control Council retracted approval of nevirapine monotherapy for prevention of mother to child transmission during pregnancy in 2004 (MCC, 2004:2).

Table 4.44 Top 20 ARV monotherapy according to frequency for 2005

	ARV medicine item 1	N	Average cost (R)	Total cost (R)
1	Kaletra [®] 80mg/20mg Cap	491	347.10 ± 31.25	170 425.27
2	Aspen Lamzid [®] Tab	332	324.50 ± 47.59	107 734.47
3	Combivir [®] Tab	308	372.51 ± 87.53	114 732.66
4	Stocrin [®] 600mg Tab	299	240.72 ± 23.31	71 974.58
5	Norvir [®] 100mg Cap	97	218.36 ± 69.18	21 180.65
6	Aspen Nevirapine [®] 200mg Tab	78	210.43 ± 37.81	16 413.52
7	Aspen Lamivudine [®] 150mg Tab	73	97.26 ± 23.32	7 099.95
8	3TC [®] 150mg Tab	68	115.14 ± 39.01	7 829.36
9	Viramune [®] 200mg Tab	63	475.23 ± 101.02	29 939.71
10	Aspen Stavudine [®] 40mg Cap	54	49.76 ± 1.87	2 686.80
11	Stocrin [®] 200mg Cap	41	296.55 ± 68.91	12 158.35
12	Retrovir [®] S 50mg/5ml Syr	26	137.03 ± 89.28	3 562.90
13	Crixivan [®] 400mg Cap	24	256.48 ± 93.20	6 155.50
14	Kaletra [®] 400/100mg/5ml	20	285.70 ± 91.86	5 714.08
15	Zerit [®] 40mg Cap	20	53.37 ± 9.92	1 067.38
16	Videx [®] 150mg Chew	19	223.99 ± 23.94	4 255.88
17	Aspen Stavudine [®] 30mg Cap	18	46.76 ± 6.13	841.73
18	Aspen Zidovudine [®] Syr 50mg/5ml	17	104.83 ± 49.40	1 782.07
19	Videx [®] 100mg Chew	17	205.28 ± 81.45	3 489.81
20	3TC [®] Oral 10mg/MI Sol	15	118.09 ± 50.96	1 771.32

4.10.1.1.1 Top 20 ARV monotherapy according to frequency for 2005

As seen in table 4.44, ARV medicine items were prescribed as **monotherapy** with a frequency of 2 246 occurrences in total during 2005. **Kaletra® 80mg/20mg capsules** were prescribed at the highest frequency for all **prescriptions containing a single ARV medicine item**, and represented 0.98 per cent (n = 491) of the **total number of ARV prescriptions** (n = 49 995) claimed during 2005. The **top 20 ARV items** prescribed as **monotherapy** during 2005 comprised 4.16 per cent (n = 2 080) of the **total number of ARV prescriptions** for 2005.

The **top 20 monotherapy ARV prescriptions** (n = 2 080) represented 92.61 per cent of the **total number of prescriptions for one ARV** claimed during 2005 (n = 2 246). The **total number of prescriptions for one ARV** claimed during 2005 represented 4.49 per cent, and the **top 20 monotherapy ARV prescriptions** represented 4.16 per cent of the **total number of ARV prescriptions** (n = 49 995) claimed during 2005.

Of the ARV prescriptions containing one ARV claimed during 2005, prescriptions containing **two PIs** (n = 2) represented 10 per cent, and prescriptions for **one PI** (n = 2) also represented 10 per cent of the top 20 ARV monotherapy prescriptions according to frequency during 2005. Prescriptions containing **two NRTIs** (n = 2) represented 10 per cent, and prescriptions for **one NRTI** (n = 10) represented 50 per cent of the top 20 ARV monotherapy prescriptions according to frequency during 2005. Prescriptions for **one NNRTI** (n = 4) accounted for 20 per cent of the top 20 ARV monotherapy prescriptions according to frequency during 2005.

4.10.1.1.2 Top 20 ARV monotherapy according to frequency for 2006

During 2006 ARV medicine items were prescribed as **monotherapy** at a frequency of 3 301 occurrences in total (*Refer to table 4.45*). As in 2005, **Kaletra® 80mg/20mg capsules** were also prescribed showing the highest frequency for all **prescriptions containing a single ARV medicine item**, and represented 1.35 per cent (n = 1 091) of the **total number of ARV prescriptions** (n = 81 096) claimed during 2006. The **top 20 ARV items** prescribed as **monotherapy** during 2006 comprised 3.82 per cent (n = 3 100) of the **total number of ARV prescriptions** for 2006.

The **top 20 ARV prescriptions containing one ARV** (n = 3 100) represented 93.91 per cent of the **total number of prescriptions for ARV monotherapy** claimed during 2006 (n = 3 301). The **total number of ARV monotherapy prescriptions** claimed during 2006 represented 4.07 per cent, and the **top 20 monotherapy ARV prescriptions** represented 3.82 per cent of the **total number of ARV prescriptions** (n = 81 096) claimed during 2006.

Of the ARV monotherapy prescriptions claimed during 2006, prescriptions containing **two PIs** (n = 2) represented 10 per cent, and prescriptions for **one PI** (n = 1) represented 5 per cent of the top 20 ARV monotherapy prescriptions according to frequency during 2006. Prescriptions containing **two NRTIs** (n = 2) represented 10 per cent, and prescriptions for **one NRTI** (n = 10) represented 50 per cent of the top 20 ARV monotherapy prescriptions according to frequency during 2006. Prescriptions for **one NNRTI** (n = 5) accounted for 25 per cent of the top 20 ARV monotherapy prescriptions according to frequency during 2006.

Table 4.45 Top 20 ARV monotherapy according to frequency for 2006

	ARV medicine item 1	N	Average cost (R)	Standard deviation (R)	Total cost (R)
1	Kaletra [®] 80mg/20mg Cap	1091	354.05	32.09	386 272.79
2	Stocrin [®] 600mg Tab	438	218.20	22.06	95 569.72
3	Aspen Lamzid [®] Tab	436	326.11	31.19	142 182.39
4	Combivir [®] Tab	259	380.15	78.34	98 459.50
5	Aspen Nevirapine [®] 200mg Tab	165	226.47	12.93	37 366.99
6	Norvir [®] 100mg Cap	105	147.60	107.41	15 498.19
7	Aspen Lamivudine [®] 150mg Tab	101	95.37	23.15	9 632.63
8	Aspen Stavudine [®] 40mg Cap	78	50.41	6.21	3 931.59
9	3TC [®] 150mg Tab	66	109.25	33.96	7 210.25
10	Aspen Zidovudine [®] Syr 50mg/5ml	61	96.24	34.43	5 870.67
11	Viramune [®] 200mg Tab	55	430.65	60.40	23 685.65
12	Retrovir [®] S 50mg/5ml Syr	43	192.70	169.69	8 286.06
13	Stocrin [®] 200mg Cap	35	205.46	81.19	7 190.95
14	Videx [®] 400mg EC Cap	29	232.02	0.00	6 728.58
15	Aspen Lamivudine [®] 10mg/MI	27	108.70	57.48	2 934.94
16	Kaletra [®] 400/100mg/5ml	27	253.38	81.66	6 841.28
17	Aspen Stavudine [®] 30mg Cap	26	41.26	3.63	1 072.80
18	3TC [®] Oral 10mg/MI Sol	24	146.38	56.81	3 513.21
19	Viramune [®] Oral	19	833.64	202.77	15 839.16
20	Aspen Didanosine [®] 100mg	15	191.36	78.32	2 870.33

4.10.1.2 Two antiretroviral medicine items per prescription

The World Health Organization claims that there is some benefit to be derived from dual nucleoside regimens (as presently used in certain resource limited countries), but that these regimens fail to accomplish or sustain suppression of HIV replication to the same degree as the triple drug regimens (Munderi *et al.*, 2000:22).

4.10.1.2.1 Top 20 combinations of 2 ARVs per prescription according to frequency for 2005

Table 4.46 illustrated that **Aspen Lamzid[®] tablets** in combination with **Stocrin[®] 600mg tablets** were prescribed at the highest frequency (n = 10 077), and represented 46.03 per

cent of all prescriptions containing combinations of **two ARVs** during 2005 (n = 21 890). Prescriptions for **Aspen Lamzid® tablets** in combination with **Stocrin® 600mg tablets** represented 20.16 per cent of the **total number of ARV prescriptions** claimed during 2005 (49 995). The **top 20** combinations of **two ARVs** prescribed during 2005 (n = 21 109) represented 42.22 per cent of the **total number of ARV prescriptions** for 2005.

The **top 20 prescriptions of two ARVs** in combination (n = 21 109) represented 96.42 per cent of the **total number of prescriptions for two ARVs** claimed during 2005 (n = 21 892). The **total number of prescriptions for two ARVs** claimed during 2005 represented 43.79 per cent, and the **top 20 ARV prescriptions for two ARVs** represented 42.22 per cent of the **total number of ARV prescriptions** (n = 49 995) claimed during 2005.

Prescriptions containing the combinations **2PI + NNRTI** (n = 1), **2PI + NRTI** (n = 1), and **2NRTI + PI** (n = 1) all represented 5 per cent of the top 20 prescriptions for two ARVs claimed during 2005 respectively. Prescriptions for **2NRTI + 2PI** (n = 2) represented 10 per cent, **NRTI + NNRTI** (n = 3) represented 15 per cent, **NRTI + NRTI** (n = 4) represented 20 per cent, and **2NRTI + NNRTI** (n = 8) represented 40 per cent of the top 20 prescriptions for two ARVs claimed during 2005.

4.10.1.2.2 Top 20 combinations of 2 ARVs per prescription according to frequency for 2006

Table 4.47 illustrated that **Aspen Lamzid® tablets** in combination with **Stocrin® 600mg tablets** were prescribed at the highest frequency (n = 18 819), and represented 54.96 per cent of all prescriptions containing combinations of **two ARVs** during 2006 (n = 34 243). Prescriptions for **Aspen Lamzid® tablets** in combination with **Stocrin® 600mg tablets** represented 23.21 per cent of the **total number of ARV prescriptions** claimed during 2006 (n = 81 096). The **top 20** combinations of **two ARVs** prescribed during 2006 (n = 34 243) represented 42.23 per cent of the **total number of ARV prescriptions** for 2006.

The **top 20 prescriptions of two ARVs** in combination (n = 34 243) represented 96.93 per cent of the **total number of prescriptions for two ARVs** claimed during 2006 (n = 35 328). The **total number of prescriptions for two ARVs** claimed during 2006 represented 43.56 per cent, and the **top 20 ARV prescriptions for two ARVs** represented 42.23 per cent of the **total number of ARV prescriptions** (n = 81 096) claimed during 2006.

Prescriptions containing the combinations **PI + 2PI**: (n = 1) and **NRTI + 2PI** (n = 1) both represented 5 per cent of the top 20 prescriptions for two ARVs claimed during 2006. Prescriptions for **NRTI + NRTI** (n = 2), **2NRTI + 2PI** (n = 2), and **2PI + NNRTI** (n = 2) all represented 10 per cent of the top 20 prescriptions for two ARVs claimed during 2006.

Prescriptions for **NRTI + NNRTI** ($n = 3$) represented 15 per cent, and prescriptions for the combination **2NRTI + NNRTI** ($n = 9$) represented 45 per cent of the top 20 prescriptions for two ARVs claimed during 2006.

Table 4.46 Top 20 combinations of 2 ARVs per prescription according to frequency for 2005

	ARV medicine item 1	ARV medicine item 2	N	Average cost (R)	Standard deviation (R)	Total cost (R)
1	Aspen Lamzid [®] Tab	Stocrin [®] 600mg Tab	10 077	571.12	24.71	5 755 153.41
2	Aspen Lamzid [®] Tab	Aspen Nevirapine [®] 200mg Tab	5 470	555.76	20.16	3 040 006.65
3	Combivir [®] Tab	Stocrin [®] 600mg Tab	1 650	639.92	60.20	1 055 875.45
4	Aspen Lamzid [®] Tab	Kaletra [®] 80mg/20mg Cap	1 182	676.36	28.74	799 456.49
5	Combivir [®] Tab	Viramune [®] 200mg Tab	965	854.22	66.04	824 320.56
6	Combivir [®] Tab	Stocrin [®] 200mg Cap	402	722.78	29.98	290 557.90
7	Combivir [®] Tab	Kaletra [®] 80mg/20mg Cap	281	752.26	47.30	211 384.52
8	Kaletra [®] 80mg/20mg Cap	Stocrin [®] 600mg Tab	217	599.68	57.07	130 129.99
9	Aspen Lamzid [®] Tab	Stocrin [®] 200mg Cap	180	629.04	45.02	113 227.26
10	Aspen Nevirapine [®] 200mg Tab	Combivir [®] Tab	136	614.13	20.61	83 522.12
11	Aspen Lamzid [®] Tab	Viramune [®] 200mg Tab	123	772.87	19.26	95 062.45
12	3TC [®] 150mg Tab	Stocrin [®] 600mg Tab	84	380.10	32.35	31 928.27
13	Aspen Lamivudine [®] 150mg Tab	Aspen Stavudine [®] 40mg Cap	80	160.97	3.12	12 877.36
14	Aspen Lamivudine [®] 150mg Tab	Stocrin [®] 600mg Tab	52	350.51	15.24	18 226.33
15	Aspen Lamivudine [®] 150mg Tab	Aspen Stavudine [®] 30mg Cap	46	151.12	15.31	6 951.35
16	Combivir [®] Tab	Crixivan [®] 400mg Cap	42	718.59	164.58	30 180.64
17	Aspen Stavudine [®] 40mg Cap	Stocrin [®] 600mg Tab	38	287.52	11.56	10 925.93
18	3TC [®] 150mg Tab	Retrovir [®] 100mg Cap	29	402.45	203.11	11 670.98
19	Kaletra [®] 80mg/20mg Cap	Ziagen [®] 300mg Tab	28	1 352.02	21.42	37 856.47
20	Videx [®] 100mg Chew	Zerit [®] 40mg Cap	27	324.93	62.11	8 773.20

Table 4.47 Top 20 combinations of 2 ARVs per prescription according to frequency for 2006

	ARV medicine item 1	ARV medicine item 2	N	Average cost (R)	Standard deviation (R)	Total cost (R)
1	Aspen Lamzid [®] Tab	Stocrin [®] 600mg Tab	18 819	547.24	42.16	10 298 552.61
2	Aspen Lamzid [®] Tab	Aspen Nevirapine [®] 200mg Tab	8 597	554.04	32.58	4 763 064.96
3	Aspen Lamzid [®] Tab	Kaletra [®] 80mg/20mg Cap	2 563	679.73	36.22	1 742 156.51
4	Combivir [®] Tab	Stocrin [®] 600mg Tab	1 753	615.38	52.96	1 078 766.40
5	Combivir [®] Tab	Viramune [®] 200mg Tab	531	840.23	53.73	446 162.21
6	Kaletra [®] 80mg/20mg Cap	Stocrin [®] 600mg Tab	507	598.96	56.81	303 671.91
7	Combivir [®] Tab	Kaletra [®] 80mg/20mg Cap	314	749.63	78.35	235 382.69
8	Aspen Lamivudine [®] 150mg Tab	Stocrin [®] 600mg Tab	173	331.19	28.49	57 296.62
9	Aspen Lamzid [®] Tab	Viramune [®] 200mg Tab	141	779.45	69.83	109 902.09
10	Aspen Nevirapine [®] 200mg Tab	Combivir [®] Tab	134	622.77	37.36	83 450.88
11	Aspen Lamivudine [®] 150mg Tab	Aspen Stavudine [®] 40mg Cap	133	142.13	37.06	18 902.68
12	Combivir [®] Tab	Stocrin [®] 200mg Cap	122	682.94	43.15	83 318.44
13	Aspen Lamivudine [®] 150mg Tab	Aspen Stavudine [®] 30mg Cap	82	153.53	3.96	12 589.54
14	Aspen Lamzid [®] Tab	Stocrin [®] 200mg Cap	71	581.76	62.31	41 304.81
15	Aspen Nevirapine [®] 200mg Tab	Kaletra [®] 80mg/20mg Cap	63	678.47	34.29	42 743.58
16	Aspen Stavudine [®] 40mg Cap	Stocrin [®] 600mg Tab	58	266.67	25.71	15 466.94
17	Crixivan [®] 400mg Cap	Kaletra [®] 80mg/20mg Cap	49	653.91	39.96	32 041.37
18	3TC [®] 150mg Tab	Stocrin [®] 600mg Tab	46	353.88	26.69	16 278.60
19	Aspen Zidovudine [®] 300mg Tab	Kaletra [®] 80mg/20mg Cap	44	625.57	29.77	27 525.25
20	Cipla Duovir [®] Tab	Cipla Nevirapine [®] 200mg Tab	43	479.90	1.37	20 635.52

Table 4.48 Top 20 combinations of 3 ARVs per prescription according to frequency for 2005

	ARV medicine item 1 ^o	ARV medicine item 2 ^o	ARV medicine item 3 ^o	N	Average cost (R)	Standard deviation (R)	Total cost (R)
1	Aspen Lamivudine [®] 150mg Tab	Aspen Stavudine [®] 40mg Cap	Stocrin [®] 600mg Tab	9 334	403.60	13.75	3 767 208.41
2	Aspen Lamivudine [®] 150mg Tab	Aspen Stavudine [®] 30mg Cap	Stocrin [®] 600mg Tab	5 039	394.91	13.35	1 989 958.46
3	Aspen Lamivudine [®] 150mg Tab	Aspen Nevirapine [®] 200mg Tab	Aspen Stavudine [®] 40mg Cap	1 254	387.87	13.50	486 391.79
4	Aspen Lamivudine [®] 150mg Tab	Aspen Nevirapine [®] 200mg Tab	Aspen Stavudine [®] 30mg Cap	752	379.54	11.35	285 417.71
5	Aspen Lamivudine [®] 150mg Tab	Aspen Stavudine [®] 40mg Cap	Kaletra [®] 80mg/20mg Cap	303	513.84	55.15	155 694.62
6	3TC [®] 150mg Tab	Aspen Stavudine [®] 40mg Cap	Stocrin [®] 600mg Tab	272	437.54	24.14	119 009.94
7	Aspen Lamivudine [®] 10mg/MI	Viramune [®] Oral	Zerit [®] 5mg/5ml Sus	233	906.17	240.67	211 136.65
8	3TC [®] 150mg Tab	Stocrin [®] 600mg Tab	Zerit [®] 40mg Cap	209	435.98	34.27	91 119.31
9	Aspen Lamivudine [®] 150mg Tab	Aspen Nevirapine [®] 200mg Tab	Retrovir [®] 100mg Cap	199	514.17	59.19	102 319.28
10	Aspen Lamivudine [®] 10mg/MI	Aspen Zidovudine [®] Syr 50mg/5ml	Viramune [®] Oral	189	976.56	197.34	184 569.37
11	3TC [®] Oral 10mg/MI Sol	Retrovir [®] S 50mg/5ml Syr	Viramune [®] Oral	184	1 169.98	331.32	215 277.16
12	3TC [®] 150mg Tab	Stocrin [®] 600mg Tab	Zerit [®] 30mg Cap	147	441.80	16.12	64 944.01
13	Aspen Lamivudine [®] 150mg Tab	Aspen Stavudine [®] 30mg Cap	Kaletra [®] 80mg/20mg Cap	134	497.37	14.28	66 647.72
14	Stocrin [®] 600mg Tab	Videx [®] 100mg Chew	Zerit [®] 40mg Cap	107	574.29	30.23	61 449.32
15	3TC [®] 150mg Tab	Viramune [®] 200mg Tab	Zerit [®] 40mg Cap	93	616.83	41.03	57 364.80
16	Aspen Lamivudine [®] 10mg/MI	Kaletra [®] 400/100mg/5ml	Zerit [®] 5mg/5ml Sus	92	393.79	130.52	36 228.96
17	Crixivan [®] 400mg Cap	Norvir [®] 100mg Cap	Stocrin [®] 600mg Tab	92	588.66	51.86	54 156.97
18	Aspen Lamivudine [®] 10mg/MI	Aspen Nevirapine [®]	Zerit [®] 5mg/5ml Sus	83	410.70	98.64	34 087.88
19	Aspen Stavudine [®] 40mg Cap	Stocrin [®] 600mg Tab	Videx [®] 100mg Chew	83	554.87	63.12	46 054.47
20	3TC [®] Oral 10mg/MI Sol	Viramune [®] Oral	Zerit [®] 5mg/5ml Sus	76	904.41	319.73	68 734.94

4.10.1.3 Three antiretroviral medicine items per prescription

Antiretroviral treatment regimens containing three ARVs are very efficient and can reduce the HIV viral load to undetectable levels (McLeod *et al.*, 2003:92-93), thus triple combination therapy (entailing two NRTIs in combination with a PI or a NNRTI) is the recommended treatment approach in ARV-naïve patients (Sendi *et al.*, 2001:709).

4.10.1.3.1 Top 20 combinations of 3 ARVs per prescription according to frequency for 2005

Combinations **1, 2, 6, 8 and 12** were compliant with the **National Antiretroviral Treatment guidelines** first-line **Regimen 1A**, consisting of stavudine + lamivudine + efavirenz. There were 15 001 occurrences of Regimen 1A combination prescriptions and five Regimen 1A combinations, which represented 79 per cent of the total number of top 20 triple ARV prescriptions according to frequency ($n = 18\,875$) and 25 per cent of the top 20 combinations of three ARVs per prescription according to frequency during 2005 (*refer to table 4.48*).

Combinations **3, 4, 7, 15, 18 and 20** were compliant with **Regimen 1B** of the **National ART guidelines**, consisting of stavudine + lamivudine + nevirapine. There were 2 491 occurrences of prescriptions with six different Regimen 1B combinations, which represented 13.20 per cent of the total number of top 20 triple ARV prescriptions according to frequency and 30 per cent of the top 20 combinations of three ARVs per prescription according to frequency during 2005 (*refer to table 4.48*).

Combinations **5, 9, 10, 11, 13, 14, 16, 17 and 19** were **not compliant** with the **National ART guidelines**, with 1 249 prescriptions representing 6.62 per cent of the total number of prescriptions for three ARVs in the top 20 according to frequency, and these nine combinations represented 45 per cent of the top 20 combinations of three ARVs per prescription. These non-compliant combinations represented 11.39 per cent ($n = R922\,397.87$) of the total cost of the top 20 triple ARV prescriptions according to frequency ($n = R8\,097\,771.77$) during 2005 (*refer to table 4.48*).

When compared to the **World Health Organization's** recommended ART regimens for adults, combinations **3, 4, 7, 9, 10, 11, 15, 18 and 20** complied with the **preferred first line regimen** of nevirapine + 2 NRTI. A total of 3 063 prescriptions for first line ART occurred which represented 16.23 per cent of the total number of top 20 triple ARV prescriptions according to frequency during 2005. These prescriptions consisted of 9 different first-line regimen combinations which represented 45 per cent of the top 20 combinations of 3 ARVs according to frequency during 2005 (*refer to table 4.48*).

Combinations **5**, **13** and **16** were in accordance with the **WHO's preferred second-line regimen** of a ritonavir-boosted PI + 2 NRTI. A total of 529 prescriptions for second-line ART occurred which represented 2.80 per cent of the total number of top 20 triple ARV prescriptions according to frequency during 2005. These prescriptions consisted of three different second-line regimen combinations which represented 15 per cent of the top 20 combinations of 3 ARVs according to frequency during 2005 (*refer to table 4.48*).

The **top 20 triple combination ARV prescriptions** (n = 18 875) represented 86.08 per cent of the **total number of prescriptions for three ARVs** claimed during 2005 (n = 21 927). The **total number of prescriptions for three ARVs** claimed during 2005 represented 43.86 per cent, and the **top 20 triple therapy ARV prescriptions** represented 37.75 per cent of the **total number of ARV prescriptions** (n = 49 995) claimed during 2005.

Prescriptions for the combination **2PI + NNRTI** (n = 1) represented 5 per cent of the top 20 triple combination ARV prescriptions claimed during 2005. Prescriptions for **2NRTI + 2PI** (n = 3) represented 15 per cent, and **2NRTI + NNRTI** (n = 16) represented 80 per cent of the top 20 combination prescriptions for three ARVs claimed during 2005.

Table 4.49 Top 20 combinations of 3 ARVs per prescription according to frequency for 2006

	ARV medicine item 1	ARV medicine item 2	ARV medicine item 3	N	Average cost (R)	Standard deviation (R)	Total cost (R)
1	Aspen Lamivudine® 150mg Tab	Aspen Stavudine® 40mg Cap	Stocrin® 600mg Tab	15 195	378.74	25.13	5 754 959.81
2	Aspen Lamivudine® 150mg Tab	Aspen Stavudine® 30mg Cap	Stocrin® 600mg Tab	11 403	370.38	20.87	4 223 406.95
3	Aspen Lamivudine® 150mg Tab	Aspen Nevirapine® 200mg Tab	Aspen Stavudine® 40mg Cap	2 101	387.87	27.79	814 918.81
4	Aspen Lamivudine® 150mg Tab	Aspen Nevirapine® 200mg Tab	Aspen Stavudine® 30mg Cap	1 714	379.24	13.59	650 017.16
5	Aspen Stavudine® 40mg Cap	Stocrin® 600mg Tab	Videx® 400mg EC Cap	1 099	497.85	23.95	547 132.77
6	Aspen Lamivudine® 150mg Tab	Aspen Stavudine® 40mg Cap	Kaletra® 80mg/20mg Cap	535	511.06	30.67	273 415.52
7	Aspen Lamivudine® 10mg/MI	Aspen Nevirapine®	Zerit® 5mg/5ml Sus	371	437.11	111.05	162 168.72
8	Aspen Lamivudine® 10mg/MI	Aspen Nevirapine®	Aspen Zidovudine® Syr 50mg/5ml	360	711.25	129.76	256 050.67
9	3TC® 150mg Tab	Aspen Stavudine® 40mg Cap	Stocrin® 600mg Tab	339	409.25	21.76	138 737.12
10	Aspen Nevirapine® 200mg Tab	Aspen Stavudine® 40mg Cap	Videx® 400mg EC Cap	311	507.80	10.62	157 926.23
11	Aspen Stavudine® 30mg Cap	Stocrin® 600mg Tab	Videx® 250mg EC Cap	305	441.02	16.47	134 510.74
12	3TC® 150mg Tab	Stocrin® 600mg Tab	Zerit® 40mg Cap	274	412.17	33.55	112 935.35
13	Aspen Lamivudine® 150mg Tab	Aspen Stavudine® 30mg Cap	Kaletra® 80mg/20mg Cap	274	501.36	46.24	137 371.60
14	Aspen Lamivudine® 10mg/MI	Kaletra® 400/100mg/5ml	Zerit® 5mg/5ml Sus	250	313.81	82.75	78 452.06
15	Aspen Didanosine® 100mg	Aspen Stavudine® 40mg Cap	Stocrin® 600mg Tab	154	519.62	42.35	80 021.06
16	3TC® 150mg Tab	Stocrin® 600mg Tab	Zerit® 30mg Cap	146	410.50	16.73	59 932.44
17	Aspen Lamivudine® 150mg Tab	Aspen Nevirapine® 200mg Tab	Aspen Stavudine® 20mg Cap	140	284.62	39.41	39 846.10
18	Aspen Stavudine® 40mg Cap	Kaletra® 80mg/20mg Cap	Videx® 400mg EC Cap	140	635.20	24.68	88 927.49
19	Aspen Lamivudine® 10mg/MI	Aspen Zidovudine® Syr 50mg/5ml	Kaletra® 400/100mg/5ml	130	536.11	97.21	69 694.50
20	Aspen Lamivudine® 150mg Tab	Aspen Stavudine® 30mg Cap	Stocrin® 200mg Cap	130	349.43	28.96	45 425.68

4.10.1.3.2 Top 20 combinations of 3 ARVs per prescription according to frequency for 2006

Combinations **1, 2, 9, 12, 16** and **20** were compliant with the **National Antiretroviral Treatment guidelines** first-line **Regimen 1A**, consisting of stavudine + lamivudine + efavirenz. There were 27 487 occurrences of Regimen 1A combination prescriptions and six Regimen 1A combinations, which represented 77.71 per cent of the total number of top 20 triple ARV prescriptions according to frequency ($n = 35\,371$) and 30 per cent of the top 20 combinations of three ARVs per prescription according to frequency during 2006 (*refer to table 4.49*).

Combinations **3, 4, 7** and **17** were compliant with **Regimen 1B** of the **National ART guidelines**, consisting of stavudine + lamivudine + nevirapine. There were 4 326 occurrences of prescriptions with four Regimen 1B combinations, which represented 12.23 per cent of the total number of top 20 triple ARV prescriptions according to frequency and 20 per cent of the top 20 combinations of three ARVs per prescription according to frequency during 2006 (*refer to table 4.49*).

Combinations **5, 6, 8, 10, 11, 13, 14, 15, 18** and **19** were **not compliant** with the **National ART guidelines**, with 2 749 prescriptions representing 7.77 per cent of the total number of prescriptions for three ARVs in the top 20 according to frequency, and these ten combinations represented 50 per cent of the top 20 combinations of three ARVs per prescription. These non-compliant combinations represented 9.71 per cent ($n = R1\,343\,021.02$) of the total cost of the top 20 triple ARV prescriptions according to frequency ($n = R13\,825\,850.78$) during 2006 (*refer to table 4.49*).

When compared to the **World Health Organization's** recommended ART regimens for adults, combinations **3, 4, 7, 8, 10** and **17** complied with the **preferred first-line regimen** of nevirapine + 2 NRTI. A total of 4 997 prescriptions for first-line ART represented 14.13 per cent of the total number of top 20 triple ARV prescriptions according to frequency during 2006. These prescriptions consisted of six different first-line regimen combinations which represented 30 per cent of the top 20 combinations of 3 ARVs according to frequency during 2006 (*refer to table 4.49*).

Combinations **6, 13, 14** and **19** were in accordance with the **WHO's preferred second-line regimen** of a ritonavir-boosted PI + 2 NRTI. A total of 1 189 prescriptions for second-line ART represented 3.36 per cent of the total number of top 20 triple ARV prescriptions according to frequency during 2006. These prescriptions consisted of four different second-line regimen combinations which represented 20 per cent of the top 20 combinations of 3 ARVs according to frequency during 2006 (*refer to table 4.49*).

The **top 20 triple combination ARV prescriptions** (n = 35 371) represented 88.00 per cent of the **total number of prescriptions for three ARVs** claimed during 2006 (n = 40 195). The **total number of prescriptions for three ARVs** claimed during 2006 represented 49.56 per cent, and the **top 20 triple therapy ARV prescriptions** represented 43.62 per cent of the **total number of ARV prescriptions** (n = 81 096) claimed during 2006.

Prescriptions for **2NRTI + 2PI** (n = 5) represented 25 per cent, and **2NRTI + NNRTI** (n = 15) represented 75 per cent of the top 20 combination prescriptions for three ARVs claimed during 2006.

Table 4.50 Top 20 combinations of 4 ARVs per prescription according to frequency for 2005

	ARV medicine item 1	ARV medicine item 2	ARV medicine item 3	ARV medicine item 4	N	Average cost (R)	Standard deviation (R)	Total cost (R)
1	Aspen Lamivudine® 150mg Tab	Retrovir® 100mg Cap	Stocrin® 200mg Cap	Stocrin® 50mg Cap	150	539.13	50.09	80 868.85
2	Aspen Lamivudine® 150mg Tab	Aspen Stavudine® 20mg Cap	Stocrin® 200mg Cap	Stocrin® 50mg Cap	106	277.61	19.70	29 426.48
3	Aspen Lamivudine® 10mg/MI	Aspen Stavudine® 20mg Cap	Stocrin® 200mg Cap	Stocrin® 50mg Cap	55	417.08	24.67	22 939.30
4	Aspen Lamivudine® 150mg Tab	Aspen Stavudine® 30mg Cap	Stocrin® 200mg Cap	Stocrin® 50mg Cap	33	363.46	20.35	11 994.06
5	Aspen Lamivudine® 10mg/MI	Stocrin® 200mg Cap	Stocrin® 50mg Cap	Zerit® 5mg/5ml Sus	19	517.38	164.36	9 830.28
6	Aspen Lamivudine® 10mg/MI	Aspen Stavudine® 30mg Cap	Kaletra® 400/100mg/5ml	Ziagen® 100mg/5ml Sol	17	1 021.23	72.83	17 360.84
7	Aspen Didanosine® 100mg	Aspen Stavudine® 20mg Cap	Stocrin® 200mg Cap	Stocrin® 50mg Cap	15	360.55	14.03	5 408.19
8	Aspen Lamivudine® 150mg Tab	Stocrin® 200mg Cap	Stocrin® 50mg Cap	Zerit® 5mg/5ml Sus	13	611.72	132.24	7 952.42
9	Aspen Lamivudine® 10mg/MI	Aspen Zidovudine® Syr 50mg/5ml	Stocrin® 200mg Cap	Stocrin® 50mg Cap	12	584.15	23.60	7 009.80
10	3TC® Oral 10mg/MI Sol	Aspen Stavudine® 20mg Cap	Stocrin® 200mg Cap	Stocrin® 50mg Cap	11	409.90	17.47	4 508.94
11	Aspen Lamivudine® 10mg/MI	Stocrin® 200mg Cap	Stocrin® 50mg Cap	Ziagen® 100mg/5ml Sol	11	1 249.27	192.68	13 741.95
12	Aspen Didanosine® 100mg	Aspen Didanosine® 150mg	Aspen Nevirapine® 200mg Tab	Aspen Stavudine® 30mg Cap	10	436.29	0.00	4 362.90
13	Aspen Didanosine® 100mg	Aspen Didanosine® 150mg	Aspen Stavudine® 20mg Cap	Kaletra® 80mg/20mg Cap	8	547.99	0.00	4 383.92
14	3TC® 150mg Tab	Retrovir® 100mg Cap	Stocrin® 200mg Cap	Stocrin® 50mg Cap	7	568.97	3.28	3 982.80
15	3TC® Oral 10mg/MI Sol	Stocrin® 200mg Cap	Stocrin® 50mg Cap	Zerit® 20mg Cap	7	439.60	14.39	3 077.22
16	3TC® Oral 10mg/MI Sol	Retrovir® 250mg Cap	Stocrin® 200mg Cap	Stocrin® 50mg Cap	6	754.61	57.55	4 527.63
17	Aspen Lamivudine® 10mg/MI	Retrovir® 100mg Cap	Stocrin® 200mg Cap	Stocrin® 50mg Cap	6	480.48	35.22	2 882.88
18	Aspen Stavudine® 20mg Cap	Kaletra® 400/100mg/5ml	Videx® 25mg Chew	Videx® 50mg Chew	6	655.38	0.00	3 932.28
19	3TC® Oral 10mg/MI Sol	Stocrin® 200mg Cap	Stocrin® 50mg Cap	Zerit® 30mg Cap	5	524.00	0.00	2 620.00
20	Aspen Stavudine® 20mg Cap	Kaletra® 80mg/20mg Cap	Videx® 100mg Chew	Videx® 150mg Chew	5	486.00	0.00	2 430.00

4.10.1.4 Four antiretroviral medicine items per prescription

These prescriptions contained four antiretroviral medicine items (trade name items) in combination.

4.10.1.4.1 Top 20 combinations of 4 ARVs per prescription according to frequency for 2005

Combinations **2, 3, 4, 5, 8, 10, 15** and **19** were compliant with the **National Antiretroviral Treatment guidelines** first-line **Regimen 1A**, consisting of stavudine + lamivudine + efavirenz. There were 249 occurrences of Regimen 1A combination prescriptions and eight Regimen 1A combinations, which represented 49.60 per cent of the total number of top 20 ARV prescriptions with 4 ARVs in combination according to frequency ($n = 502$) and 40 per cent of the top 20 combinations of four ARVs per prescription according to frequency during 2005 (*refer to table 4.50*).

None of the top 20 combination prescriptions of four ARVs according to frequency for 2005 was compliant with **Regimen 1B** of the **National ART guidelines**, consisting of stavudine + lamivudine + nevirapine (*refer to table 4.50*).

Combinations **1, 6, 7, 9, 11, 12, 13, 14, 16, 17, 18** and **20** were **not compliant** with the **National ART guidelines**, with 253 prescriptions representing 50.40 per cent of the total number of prescriptions for four ARVs in the top 20 according to frequency, and these twelve combinations represented 60 per cent of the top 20 combinations of three ARVs per prescription. These non-compliant combinations represented 62.03 per cent ($n = R150\ 892.04$) of the total cost of the top 20 ARV prescriptions with 4 ARVs in combination according to frequency ($n = R243\ 240.74$) during 2005 (*refer to table 4.50*).

When compared to the **World Health Organization's** recommended ART regimens for adults, only combination **12** complied with the **preferred first-line regimen** of nevirapine + 2 NRTI. A total of 10 prescriptions for first-line ART represented 1.99 per cent of the total number of top 20 ARV prescriptions with 4 ARVs in combination according to frequency during 2005. There was only one first-line regimen combination which represented 5 per cent of the top 20 combinations of four ARVs according to frequency during 2005 (*refer to table 4.50*).

Combinations **13, 18** and **20** were in accordance with the **WHO's preferred second-line regimen** of a ritonavir-boosted PI + 2 NRTI. A total of 19 prescriptions for second-line ART represented 3.78 per cent of the total number of top 20 ARV prescriptions with 4 ARVs in combination according to frequency during 2006. These prescriptions consisted of three

different second-line regimen combinations which represented 15 per cent of the top 20 combinations of four ARVs according to frequency during 2006 (*refer to table 4.50*).

The **top 20 prescriptions with four ARVs in combination** (n = 502) represented 78.92 per cent of the **total number of prescriptions for four ARVs** claimed during 2005 (n = 571). The **total number of prescriptions for four ARVs** claimed during 2005 represented 1.14 per cent, and the **top 20 prescriptions for four ARVs** represented 1.00 per cent of the **total number of ARV prescriptions** (n = 49 995) claimed during 2005.

Prescriptions for the combination **3NRTI + 2PI** (n = 1) represented 5 per cent of the top 20 combination prescriptions for 4 ARVs claimed during 2005. Prescriptions for **2NRTI + 2PI** (n = 3) represented 15 per cent, and **2NRTI + NNRTI** (n = 16) represented 80 per cent of the top 20 combination prescriptions for four ARVs claimed during 2005.

Table 4.51 Top 20 combinations of 4 ARVs per prescription according to frequency for 2006

	ARV medicine item 1	ARV medicine item 2	ARV medicine item 3	ARV medicine item 4	N	Average cost (R)	Standard deviation (R)	Total cost (R)
1	Aspen Didanosine® 100mg	Aspen Didanosine® 150mg	Aspen Stavudine® 40mg Cap	Stocrin® 600mg Tab	294	534.12	30.48	157 030.23
2	Aspen Lamivudine® 150mg Tab	Aspen Stavudine® 20mg Cap	Stocrin® 200mg Cap	Stocrin® 50mg Cap	250	280.26	36.52	70 066.23
3	Aspen Lamzid® Tab	Aspen Zidovudine® Syr 50mg/5ml	Kaletra® 80mg/20mg Cap	Retrovir® 200mg/20ml Inj	207	938.74	57.81	194 318.19
4	Aspen Lamivudine® 10mg/MI	Aspen Stavudine® 20mg Cap	Stocrin® 200mg Cap	Stocrin® 50mg Cap	159	399.49	36.24	63 518.20
5	Aspen Lamivudine® 150mg Tab	Aspen Zidovudine® 300mg Tab	Stocrin® 200mg Cap	Stocrin® 50mg Cap	96	378.56	28.84	36 341.52
6	Aspen Lamivudine® 150mg Tab	Retrovir® 100mg Cap	Stocrin® 200mg Cap	Stocrin® 50mg Cap	94	551.92	66.76	51 880.23
7	Aspen Didanosine® 100mg	Aspen Didanosine® 150mg	Aspen Stavudine® 30mg Cap	Stocrin® 600mg Tab	86	457.11	47.63	39 311.32
8	Aspen Didanosine® 100mg	Aspen Didanosine® 150mg	Aspen Nevirapine® 200mg Tab	Aspen Stavudine® 40mg Cap	83	537.13	21.09	44 582.04
9	Aspen Lamzid® Tab	Aspen Nevirapine® 200mg Tab	Aspen Zidovudine® Syr 50mg/5ml	Retrovir® 200mg/20ml Inj	74	809.10	49.85	59 873.13
10	Aspen Lamivudine® 150mg Tab	Aspen Stavudine® 30mg Cap	Stocrin® 200mg Cap	Stocrin® 50mg Cap	72	356.11	19.76	25 640.02
11	Aspen Lamivudine® 10mg/MI	Aspen Zidovudine® 300mg Tab	Stocrin® 200mg Cap	Stocrin® 50mg Cap	67	546.29	78.06	36 601.40
12	Aspen Lamivudine® 10mg/MI	Aspen Stavudine® 15mg Cap	Stocrin® 200mg Cap	Stocrin® 50mg Cap	64	317.04	22.08	20 290.33
13	Aspen Lamivudine® 10mg/MI	Stocrin® 200mg Cap	Stocrin® 50mg Cap	Zerit® 5mg/5ml Sus	52	390.11	28.87	20 285.50
14	Aspen Lamzid® Tab	Kaletra® 80mg/20mg Cap	Retrovir® 200mg/20ml Inj	Retrovir® S 50mg/5ml Syr	42	983.15	76.54	41 292.14
15	Aspen Lamivudine® 150mg Tab	Aspen Stavudine® 40mg Cap	Crixivan® 400mg Cap	Norvir® 100mg Cap	23	514.61	37.15	11 836.10
16	Aspen Didanosine® 100mg	Aspen Didanosine® 25mg	Aspen Stavudine® 30mg Cap	Stocrin® 600mg Tab	18	523.99	108.36	9 431.78
17	Aspen Lamivudine® 150mg Tab	Aspen Stavudine® 15mg Cap	Stocrin® 200mg Cap	Stocrin® 50mg Cap	18	245.82	14.51	4 424.69
18	Stocrin® 600mg Tab	Videx® 100mg Chew	Videx® 25mg Chew	Zerit® 30mg Cap	18	563.31	23.70	10 139.59
19	Aspen Didanosine® 100mg	Aspen Didanosine® 25mg	Aspen Zidovudine® 300mg Tab	Kaletra® 80mg/20mg Cap	17	850.42	36.12	14 457.13
20	Aspen Lamzid® Tab	Aspen Nevirapine® 200mg Tab	Retrovir® 200mg/20ml Inj	Retrovir® S 50mg/5ml Syr	16	847.69	91.13	13 563.06

4.10.1.4.2 Top 20 combinations of 4 ARVs per prescription according to frequency for 2005

Combinations **2, 4, 10, 12, 13** and **17** were compliant with the **National Antiretroviral Treatment guidelines** first-line **Regimen 1A**, consisting of stavudine + lamivudine + efavirenz. There were 615 occurrences of Regimen 1A combination prescriptions and six Regimen 1A combinations, which represented 35.14 per cent of the total number of top 20 ARV prescriptions with 4 ARVs in combination according to frequency ($n = 1\,750$) and 30 per cent of the top 20 combinations of four ARVs per prescription according to frequency during 2006 (*refer to table 4.51*).

None of the top 20 combination prescriptions of four ARVs according to frequency for 2006 was compliant with **Regimen 1B** of the **National ART guidelines**, consisting of stavudine + lamivudine + nevirapine (*refer to table 4.51*).

Combination **19** was compliant with Regimen 2 of the National ART guidelines, consisting of zidovudine + didanosine + lopinavir/ritonavir. There were 17 Regimen 2 prescriptions of only one Regimen 2 combination, which represented 0.97 per cent of the total number of top 20 ARV prescriptions with four ARVs in combination according to frequency and 5 per cent of the top 20 combinations of four ARVs per prescription according to frequency during 2006 (*refer to table 4.51*).

Combinations **1, 3, 5, 6, 7, 8, 9, 11, 14, 15, 16, 18** and **20** were **not compliant** with the **National ART guidelines**, with 1 118 prescriptions representing 63.89 per cent of the total number of prescriptions for four ARVs in the top 20 according to frequency, and these 13 combinations represented 65 per cent of the top 20 combinations of four ARVs per prescription. These non-compliant combinations represented 77.22 per cent ($n = R706\,200.73$) of the total cost of the top 20 ARV prescriptions with four ARVs in combination according to frequency ($n = R914\,582.83$) during 2006 (*refer to table 4.51*).

Combinations **8, 9** and **20** complied with the **WHO's preferred first-line regimen** of nevirapine + 2 NRTI. A total of 173 prescriptions for first-line ART represented 9.89 per cent of the total number of top 20 ARV prescriptions with four ARVs in combination according to frequency during 2005. These prescriptions consisted of three different first-line regimen combinations which represented 15 per cent of the top 20 combinations of four ARVs according to frequency during 2006 (*refer to table 4.51*).

Combinations **3, 14** and **19** were in accordance with the **WHO's preferred second-line regimen** of a ritonavir-boosted PI + 2 NRTI. A total of 266 prescriptions for second line ART represented 15.20 per cent of the total number of top 20 ARV prescriptions with 4 ARVs in

combination according to frequency during 2006. These prescriptions consisted of three different second-line regimen combinations which represented 15 per cent of the top 20 combinations of four ARVs according to frequency during 2006 (*refer to table 4.51*).

The **top 20 prescriptions with four ARVs in combination** (n = 1 750) represented 77.61 per cent of the **total number of prescriptions for four ARVs** claimed during 2006 (n = 2 255). The **total number of prescriptions for four ARVs** claimed during 2006 represented 2.78 per cent, and the **top 20 prescriptions for four ARVs** represented 2.16 per cent of the **total number of ARV prescriptions** (n = 81 096) claimed during 2006.

Prescriptions for the combination **3NRTI + 2PI** (n = 1) represented 5 per cent of the top 20 prescriptions for 4 ARVs claimed during 2006. Prescriptions for **2NRTI + 2PI** (n = 3) represented 15 per cent, and **2NRTI + NNRTI** (n = 16) represented 80 per cent of the top 20 combination prescriptions for four ARVs claimed during 2006.

Table 4.52 Top 16 combinations of 5 ARVs per prescription according to frequency for 2005

	ARV medicine item 1	ARV medicine item 2	ARV medicine item 3	ARV medicine item 4	ARV medicine item 5	N	Average cost (R)	Standard deviation (R)	Total cost (R)
1	Aspen Didanosine [®] 100mg	Aspen Didanosine [®] 150mg	Aspen Stavudine [®] 40mg Cap	Crixivan [®] 400mg Cap	Norvir [®] 100mg Cap	7	648.74	5.97	4 541.20
2	3TC [®] Oral 10mg/MI Sol	Aspen Stavudine [®] 20mg Cap	Stocrin [®] 200mg Cap	Stocrin [®] 50mg Cap	Ziagen [®] 100mg/5ml Sol	4	1 133.84	0.00	4 535.36
3	Aspen Stavudine [®] 40mg Cap	Crixivan [®] 400mg Cap	Norvir [®] 100mg Cap	Videx [®] 100mg Chew	Videx [®] 150mg Chew	4	679.28	0.00	2 717.12
4	Kaletra [®] 80mg/20mg Cap	Stocrin [®] 600mg Tab	Videx [®] 100mg Chew	Videx [®] 150mg Chew	Zerit [®] 40mg Cap	4	931.72	20.70	3 726.88
5	Aspen Lamivudine [®] 150mg Tab	Aspen Nevirapine [®] 200mg Tab	Aspen Stavudine [®] 40mg Cap	Aspen Zidovudine [®] Syr 50mg/5ml	Retrovir [®] 200mg/20ml Inj	3	628.74	0.00	1 886.22
6	Aspen Didanosine [®] 100mg	Aspen Didanosine [®] 150mg	Aspen Stavudine [®] 30mg Cap	Crixivan [®] 400mg Cap	Norvir [®] 100mg Cap	2	547.48	0.00	1 094.96
7	Aspen Stavudine [®] 30mg Cap	Crixivan [®] 400mg Cap	Norvir [®] 100mg Cap	Videx [®] 100mg Chew	Videx [®] 150mg Chew	2	572.96	0.00	1 145.92
8	Aspen Stavudine [®] 40mg Cap	Crixivan [®] 200mg Cap	Norvir [®] 100mg Cap	Videx [®] 100mg Chew	Videx [®] 150mg Chew	2	739.27	0.00	1 478.54
9	3TC [®] 150mg Tab	Combivir [®] Tab	Kaletra [®] 80mg/20mg Cap	Stavir [®] 40mg Cap	Stocrin [®] 600mg Tab	1	1 151.16	-	1 151.16
10	Aspen Didanosine [®] 100mg	Aspen Stavudine [®] 30mg Cap	Crixivan [®] 400mg Cap	Norvir [®] 100mg Cap	Videx [®] 150mg Chew	1	572.88	-	572.88
11	Aspen Didanosine [®] 25mg	Aspen Didanosine [®] 50mg	Aspen Stavudine [®] 20mg Cap	Stocrin [®] 200mg Cap	Stocrin [®] 50mg Cap	1	438.18	-	438.18
12	Aspen Lamivudine [®] 150mg Tab	Aspen Nevirapine [®] 200mg Tab	Aspen Stavudine [®] 30mg Cap	Aspen Stavudine [®] 40mg Cap	Viramune [®] 200mg Tab	1	866.91	-	866.91
13	Aspen Lamivudine [®] 150mg Tab	Aspen Nevirapine [®] 200mg Tab	Aspen Stavudine [®] 30mg Cap	Aspen Zidovudine [®] Syr 50mg/5ml	Retrovir [®] 200mg/20ml Inj	1	621.20	-	621.20
14	Aspen Lamivudine [®] 150mg Tab	Aspen Stavudine [®] 20mg Cap	Aspen Stavudine [®] 30mg Cap	Stocrin [®] 200mg Cap	Stocrin [®] 50mg Cap	1	358.16	-	358.16
15	Aspen Lamizid [®] Tab	Aspen Nevirapine [®] 200mg Tab	Combivir [®] Tab	Retrovir [®] S 50mg/5ml Syr	Viramune [®] 200mg Tab	1	1 494.58	-	1 494.58
16	Aspen Stavudine [®] 40mg Cap	Kaletra [®] 80mg/20mg Cap	Stocrin [®] 600mg Tab	Videx [®] 100mg Chew	Videx [®] 150mg Chew	1	939.41	-	939.41

4.10.1.5 Five antiretroviral medicine items per prescription

These prescriptions contained five antiretroviral medicine items (trade name items) in combination.

4.10.1.5.1 Top 16 combinations of 5 ARVs per prescription according to frequency for 2005

Combination **14** was compliant with the **National Antiretroviral Treatment guidelines** first-line **Regimen 1A**, consisting of stavudine + lamivudine + efavirenz. There was one Regimen 1A combination prescription with one Regimen 1A combination, which represented 2.78 per cent of the total number of top 16 ARV prescriptions with five ARVs in combination according to frequency ($n = 36$) and 6.25 per cent of the top 16 combinations of five ARVs per prescription according to frequency during 2005 (*refer to table 4.52*).

Combination **12** was compliant with **Regimen 1B** of the **National ART guidelines**, consisting of stavudine + lamivudine + nevirapine. There was one prescription with one Regimen 1B combination, which represented 2.78 per cent of the total number of top 16 ARV prescriptions with five ARVs in combination according to frequency and 6.25 per cent of the top 16 combinations of five ARVs per prescription according to frequency during 2005 (*refer to table 4.52*).

Combinations **1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 13, 15** and **16** were **not compliant** with the **National ART guidelines**, with 34 prescriptions representing 94.44 per cent of the total number of prescriptions for five ARVs in the top 16 according to frequency, and these 14 combinations represented 87.50 per cent of the top 16 combinations of five ARVs per prescription. These non-compliant combinations represented 95.56 per cent ($n = R26\ 343.61$) of the total cost of the top 16 ARV prescriptions with five ARVs in combination according to frequency ($n = R27\ 568.68$) during 2005 (*refer to table 4.52*).

When compared to the **World Health Organization's** recommended ART regimens for adults, combinations **12** and **15** complied with the **preferred first-line regimen** of nevirapine + 2 NRTI. A total of 2 prescriptions for first-line ART represented 5.56 per cent of the total number of top 16 ARV prescriptions with five ARVs in combination according to frequency during 2005. These prescriptions consisted of two different first-line regimen combinations which represented 12.5 per cent of the top 16 combinations of five ARVs according to frequency during 2005 (*refer to table 4.52*).

None of the top 20 combination prescriptions of five ARVs according to frequency for 2006 was compliant with the **WHO's preferred second-line regimen** of a ritonavir-boosted PI + 2 NRTI (*refer to table 4.52*).

Only 16 different combinations for **five ARVs** were claimed during 2005 ($n = 36$). These 36 **prescriptions with combinations of five ARVs** represented 0.07 per cent of the total number of ARV prescriptions ($n = 49\,995$) claimed during 2005.

Prescriptions for the combination **3NRTI + 2PI + NNRTI** ($n = 1$) represented 6.25 per cent, **2PI + 2NRTI + NNRTI** ($n = 2$) represented 12.5 per cent, **3NRTI + NNRTI** ($n = 3$) represented 18.75 per cent, and **2NRTI + NNRTI** ($n = 4$) represented 25 per cent of the total number of prescriptions for five ARVs claimed during 2005. Prescriptions for **2NRTI + 2PI** ($n = 6$) constituted 37.5 per cent of the total number of prescriptions for combinations of five ARVs claimed during 2005.

Table 4.53 Top 16 combinations of 5 ARVs per prescription according to frequency for 2006

	ARV medicine item 1	ARV medicine item 2	ARV medicine item 3	ARV medicine item 4	ARV medicine item 5	N	Average cost (R)	Standard deviation (R)	Total cost (R)
1	Aspen Lamivudine® 150mg Tab	Aspen Nevirapine® 200mg Tab	Aspen Stavudine® 30mg Cap	Aspen Zidovudine® Syr 50mg/5ml	Retrovir® 200mg/20ml Inj	9	621.20	0.00	5 590.80
2	Aspen Lamivudine® 150mg Tab	Aspen Nevirapine® 200mg Tab	Aspen Stavudine® 40mg Cap	Aspen Zidovudine® Syr 50mg/5ml	Retrovir® 200mg/20ml Inj	9	697.94	83.38	6 281.50
3	Aspen Lamivudine® 10mg/MI	Aspen Stavudine® 15mg Cap	Stocrin® 200mg Cap	Stocrin® 50mg Cap	Ziagen® 100mg/5ml Sol	6	1 031.45	6.53	6 188.69
4	Aspen Stavudine® 20mg Cap	Stocrin® 200mg Cap	Stocrin® 50mg Cap	Videx® 25mg Chew	Videx® 50mg Chew	6	492.30	11.30	2 953.80
5	Aspen Didanosine® 100mg	Aspen Didanosine® 150mg	Aspen Stavudine® 40mg Cap	Crixivan® 400mg Cap	Norvir® 100mg Cap	5	638.10	2.13	3 190.49
6	Aspen Lamivudine® 150mg Tab	Aspen Stavudine® 30mg Cap	Aspen Zidovudine® Syr 50mg/5ml	Kaletra® 80mg/20mg Cap	Retrovir® 200mg/20ml Inj	3	739.55	0.00	2 218.65
7	Aspen Lamivudine® 150mg Tab	Aspen Stavudine® 40mg Cap	Aspen Zidovudine® Syr 50mg/5ml	Kaletra® 80mg/20mg Cap	Retrovir® 200mg/20ml Inj	3	778.02	26.79	2 334.06
8	Aspen Lamivudine® 150mg Tab	Aspen Stavudine® 30mg Cap	Stocrin® 200mg Cap	Stocrin® 50mg Cap	Ziagen® 100mg/5ml Sol	2	1 457.89	23.62	2 915.78
9	3TC® 150mg Tab	Aspen Nevirapine® 200mg Tab	Retrovir® 200mg/20ml Inj	Retrovir® S 50mg/5ml Syr	Zerit® 40mg Cap	1	824.15	-	824.15
10	Aspen Didanosine® 100mg	Aspen Didanosine® 150mg	Aspen Nevirapine® 200mg Tab	Aspen Stavudine® 40mg Cap	Videx® 250mg EC Cap	1	715.26	-	715.26
11	Aspen Lamivudine® 150mg Tab	Aspen Nevirapine® 200mg Tab	Aspen Stavudine® 40mg Cap	Retrovir® 200mg/20ml Inj	Retrovir® S 50mg/5ml Syr	1	842.55	-	842.55
12	Aspen Lamivudine® 150mg Tab	Aspen Stavudine® 40mg Cap	Aspen Zidovudine® Syr 50mg/5ml	Retrovir® 200mg/20ml Inj	Stocrin® 600mg Tab	1	622.93	-	622.93
13	Aspen Lamzid® Tab	Aspen Nevirapine®	Aspen Nevirapine® 200mg Tab	Aspen Zidovudine® 300mg Tab	Aspen Zidovudine® Syr 50mg/5ml	1	474.03	-	474.03
14	Aspen Lamzid® Tab	Aspen Zidovudine® Syr 50mg/5ml	Kaletra® 80mg/20mg Cap	Retrovir® 200mg/20ml Inj	Retrovir® S 50mg/5ml Syr	1	1 239.08	-	1 239.08
15	Aspen Stavudine® 40mg Cap	Aspen Zidovudine® Syr 50mg/5ml	Kaletra® 80mg/20mg Cap	Retrovir® 200mg/20ml Inj	Ziagen® 300mg Tab	1	1 637.50	-	1 637.50
16	Aspen Stavudine® 40mg Cap	Kaletra® 80mg/20mg Cap	Norvir® 100mg Cap	Videx® 100mg Chew	Videx® 150mg Chew	1	908.06	-	908.06

4.10.1.5.2 Top 16 combinations of 5 ARVs per prescription according to frequency for 2006

Combination **8** was compliant with the **National Antiretroviral Treatment guidelines** first-line **Regimen 1A**, consisting of stavudine + lamivudine + efavirenz. There was one Regimen 1A combination prescription with one Regimen 1A combination, which represented 1.96 per cent of the total number of top 16 ARV prescriptions with five ARVs in combination according to frequency ($n = 51$) and 6.25 per cent of the top 16 combinations of five ARVs per prescription according to frequency during 2006 (*refer to table 4.53*).

None of the top 16 combination prescriptions of five ARVs according to frequency for 2006 was compliant with **Regimen 1B** of the **National ART guidelines**, consisting of stavudine + lamivudine + nevirapine (*refer to table 4.53*).

Combinations **1, 2, 3, 4, 5, 6, 7, 9, 10, 11, 12, 13, 14, 15** and **16** were **not compliant** with the **National ART guidelines**, with 50 prescriptions representing 98.04 per cent of the total number of prescriptions for five ARVs in the top 16 according to frequency, and these 15 combinations represented 93.75 per cent of the top 16 combinations of five ARVs per prescription. These non-compliant combinations represented 92.51 per cent ($n = R36\ 021.55$) of the total cost of the top 16 ARV prescriptions with 5 ARVs in combination according to frequency ($n = R38\ 937.33$) during 2006 (*refer to table 4.53*).

When compared to the **World Health Organization's** recommended ART regimens for adults, combinations **10** and **13** complied with the **preferred first-line regimen** of nevirapine + 2 NRTI. A total of 2 prescriptions for first-line ART represented 3.92 per cent of the total number of top 16 ARV prescriptions with 5 ARVs in combination according to frequency during 2006. These prescriptions consisted of two different first-line regimen combinations which represented 12.50 per cent of the top 16 combinations of 5 ARVs according to frequency during 2006 (*refer to table 4.53*).

Combinations **14** and **16** were in accordance with the **WHO's preferred second-line regimen** of a ritonavir-boosted PI + 2 NRTI. A total of 2 prescriptions for second-line ART represented 3.92 per cent of the total number of top 16 ARV prescriptions with 5 ARVs in combination according to frequency during 2006. These prescriptions consisted of two different second-line regimen combinations which represented 12.5 per cent of the top 16 combinations of five ARVs according to frequency during 2006 (*refer to table 4.53*).

Only 16 different **combinations** for **five ARVs** were claimed during 2006 ($n = 51$). The total of 51 **prescriptions** with combinations of **five ARVs** represented 0.10 per cent of the total number of ARV prescriptions ($n = 81\ 096$) claimed during 2006.

Prescriptions for **2NRTI + NNRTI** (n = 3), **2NRTI + 2PI** (n = 3), and **3NRTI + 2PI** (n = 3) all represented 18.75 per cent of the total number of prescriptions for five ARVs claimed during 2006. Prescriptions for **3NRTI + NNRTI** (n = 7) constituted 43.75 per cent of the total number of prescriptions for combinations of five ARVs claimed during 2006.

Table 4.54 Top 2 combinations of 6 ARVs per prescription according to frequency for 2005

ARV medicine item 1	ARV medicine item 2	ARV medicine item 3	ARV medicine item 4	ARV medicine item 5	ARV medicine item 6	N	Average cost (R)	Standard deviation (R)	Total cost (R)
Aspen Didanosine® 100mg	Aspen Didanosine® 25mg	Aspen Stavudine® 30mg Cap	Kaletra® 80mg/20mg Cap	Videx® 100mg Chew	Videx® 25mg Chew	1	913.84	-	913.84
Aspen Lamivudine® 10mg/MI	Aspen Lamzid® Tab	Cipla Zidovudine® 100mg Cap	Stocrin® 200mg Cap	Stocrin® 50mg Cap	Stocrin® 600mg Tab	1	1 188.27	-	1 188.27

4.10.1.6 Six antiretroviral medicine items per prescription

These prescriptions contained six antiretroviral medicine items (trade name items) in combination.

4.10.1.6.1 Top 2 combinations of 6 ARVs per prescription according to frequency for 2005

None of the top 2 combination prescriptions of six ARVs according to frequency for 2005 were compliant with **Regimen 1A** of the **National ART guidelines**, consisting of stavudine + lamivudine + efavirenz (*refer to table 4.54*).

None of the top 2 combination prescriptions of six ARVs according to frequency for 2005 were compliant with **Regimen 1B** of the **National ART guidelines**, consisting of stavudine + lamivudine + nevirapine (*refer to table 4.54*).

Combinations **1** and **2** were **not compliant** with the **National ART guidelines**, with 2 prescriptions representing 100.00 per cent of the total number of prescriptions for six ARVs in the top 2 according to frequency, and these two combinations represented 100.00 per cent of the top 2 combinations of six ARVs per prescription. These non-compliant combinations represented 100.00 per cent (n = R2 102.11) of the total cost of the top 20 ARV prescriptions with six ARVs in combination according to frequency (n = R2 102.11) during 2005 (*refer to table 4.54*).

None of the top 2 combination prescriptions of six ARVs according to frequency during 2005 was in accordance with the **WHO's preferred first-line regimen** of nevirapine + 2 NRTI (*refer to table 4.54*).

Combination **2** was in accordance with the **WHO's preferred second-line regimen** of a ritonavir-boosted PI + 2 NRTI. There was a total of one prescription for second-line ART which represented 50 per cent of the total number of top 2 ARV prescriptions with six ARVs in combination according to frequency ($n = 2$) during 2005, with one second-line regimen combination which represented 50 per cent of the top 2 combinations of six ARVs according to frequency during 2005 (*refer to table 4.54*).

Only two different combinations for **six ARVs** were claimed during 2005 ($n = 2$). These two **prescriptions with combinations of six ARVs** represented 0.004 per cent of the total number of ARV prescriptions ($n = 49\,995$) claimed during 2005.

Combination prescriptions for **2NRTI + NNRTI** ($n = 1$), and **2NRTI + 2PI** ($n = 1$) both represented 50.00 per cent of the total number of prescriptions for six ARVs claimed during 2005.

4.10.2 Prescribing patterns of ARV combination prescriptions according to total cost

The top 20 ARV prescriptions ranked according to total cost were analysed for each group of ARV combinations classified by the number of ARV medicine items in combination. These combinations are not reviewed comprehensively, and only certain key points are discussed.

Table 4.55 Top 20 ARV monotherapy according to total cost for 2005

ARV medicine item	N	Average cost (R)	Standard deviation (R)	Total cost (R)
Kaletra [®] 80mg/20mg Cap	491	347.10	31.25	170 425.27
Combivir [®] Tab	308	372.51	87.53	114 732.66
Aspen Lamzid [®] Tab	332	324.50	47.59	107 734.47
Stocrin [®] 600mg Tab	299	240.72	23.31	71 974.58
Viramune [®] 200mg Tab	63	475.23	101.02	29 939.71
Norvir [®] 100mg Cap	97	218.36	69.18	21 180.65
Aspen Nevirapine [®] 200mg Tab	78	210.43	37.81	16 413.52
Stocrin [®] 200mg Cap	41	296.55	68.91	12 158.35
3TC [®] 150mg Tab	68	115.14	39.01	7 829.36
Aspen Lamivudine [®] 150mg Tab	73	97.26	23.32	7 099.95
Crixivan [®] 400mg Cap	24	256.48	93.20	6 155.50
Kaletra [®] 400/100mg/5ml	20	285.70	91.86	5 714.08
Viramune [®] Oral	11	469.30	303.77	5 162.28
Videx [®] 150mg Chew	19	223.99	23.94	4 255.88
Ziagen [®] 300mg Tab	4	1 002.37	2.23	4 009.49
Retrovir [®] S 50mg/5ml Syr	26	137.03	89.28	3 562.90
Videx [®] 100mg Chew	17	205.28	81.45	3 489.81
Retrovir [®] 250mg Cap	9	306.09	95.46	2 754.79
Aspen Stavudine [®] 40mg Cap	54	49.76	1.87	2 686.80
Retrovir [®] 300mg (Azt)	9	296.68	80.11	2 670.15

4.10.2.1 One antiretroviral medicine item per prescription

4.10.2.1.1 Top 20 ARV monotherapy according to total cost for 2005

The combinations **Zerit[®] 40mg cap** (R53.37 ± R9.92), **Aspen Stavudine[®] 30mg cap** (R46.76 ± R6.13), **Aspen Zidovudine[®] syr 50mg/5ml** (R104.83 ± R49.40), and **3TC[®] oral 10mg/ml sol** (R118.09 ± R50.96) were present among the top 20 according to frequency, but were absent from the top 20 monotherapy prescriptions ranked according to total cost during 2005 (*refer to table 4.55*).

Viramune[®] oral (R469.30 ± R303.77), **Ziagen[®] 300mg tab** (R1002.37 ± 2.23), **Retrovir[®] 250mg cap** (R306.09 ± R95.46), and **Retrovir[®] 300mg (AZT)** (R296.68 ± R80.11) did not feature among the top 20 monotherapy prescriptions according to frequency, but were

included in the top 20 monotherapy prescriptions according to total cost during 2005 (*refer to table 4.55*).

The monotherapy prescription that had the highest total cost was **Kaletra® 80mg/20mg cap** at R170 425.27, which represented 28.41 per cent of the total cost of the top 20 monotherapy prescriptions (n = R599 950.20) during 2005 (*refer to table 4.55*).

The **top 20 monotherapy ARV prescriptions** (n = 2 043) represented 92.61 per cent of the **total number of prescriptions for one ARV** claimed during 2005 (n = 2 246). The **top 20 monotherapy ARV prescriptions** represented 4.16 per cent of the **total number of ARV prescriptions** (n = 49 995) claimed during 2005.

Of the ARV prescriptions containing one ARV claimed during 2005, prescriptions containing **two PIs** (n = 2) represented 10 per cent, and prescriptions for **one PI** (n = 2) also represented 10 per cent of the top 20 ARV monotherapy prescriptions according to total cost during 2005. Prescriptions containing **two NRTIs** (n = 2) represented 10 per cent, and prescriptions for **one NRTI** (n = 9) represented 45 per cent of the top 20 ARV monotherapy prescriptions according to total cost during 2005. Prescriptions for **one NNRTI** (n = 5) accounted for 25 per cent of the top 20 ARV monotherapy prescriptions according to total cost during 2005.

Table 4.56 Top 20 ARV monotherapy according to total cost for 2006

ARV medicine item	N	Average cost (R)	Standard deviation (R)	Total cost (R)
Kaletra® 80mg/20mg Cap	1 091	354.05	32.09	386 272.79
Aspen Lamzid® Tab	436	326.11	31.19	142 182.39
Combivir® Tab	259	380.15	78.34	98 459.50
Stocrin® 600mg Tab	438	218.20	22.06	95 569.72
Aspen Nevirapine® 200mg Tab	165	226.47	12.93	37 366.99
Viramune® 200mg Tab	55	430.65	60.40	23 685.65
Viramune® Oral	19	833.64	202.77	15 839.16
Norvir® 100mg Cap	105	147.60	107.41	15 498.19
Aspen Lamivudine® 150mg Tab	101	95.37	23.15	9 632.63
Retrovir® S 50mg/5ml Syr	43	192.70	169.69	8 286.06
3TC® 150mg Tab	66	109.25	33.96	7 210.25
Stocrin® 200mg Cap	35	205.46	81.19	7 190.95
Kaletra® 400/100mg/5ml	27	253.38	81.66	6 841.28
Videx® 400mg EC Cap	29	232.02	0.00	6 728.58
Aspen Zidovudine® Syr 50mg/5ml	61	96.24	34.43	5 870.67
Ziagen® 300mg Tab	5	904.99	217.77	4 524.94
Aspen Stavudine® 40mg Cap	78	50.41	6.21	3 931.59
3TC® Oral 10mg/MI Sol	24	146.38	56.81	3 513.21
Aspen Lamivudine® 10mg/MI	27	108.70	57.48	2 934.94
Aspen Zidovudine 300mg Tab	13	222.70	66.94	2 895.11

4.10.2.1.2 Top 20 ARV monotherapy according to total cost for 2006

Aspen Stavudine® 30mg cap (R41.26 ± 3.63) and **Aspen Didanosine® 100mg** (R191.36 ± R78.32) were present among the top 20 according to frequency, but were absent from the top 20 monotherapy prescriptions ranked according to total cost during 2006 (*refer to table 4.56*).

Ziagen® 300mg tab (R904.99 ± R217.77) and **Aspen Zidovudine® 300mg tab** (R222.70 ± R66.94) did not feature among the top 20 monotherapy prescriptions according to frequency, but were included in the top 20 monotherapy prescriptions according to total cost during 2006 (*refer to table 4.56*).

The monotherapy prescription that had the highest total cost was **Kaletra® 80mg/20mg cap** at R386 272.79, which represented 43.67 per cent of the total cost of the top 20 monotherapy prescriptions (n = R884 434.60) during 2006 (*refer to table 4.56*).

The **top 20 monotherapy ARV prescriptions** (n = 3 077) represented 93.21 per cent of the **total number of prescriptions for one ARV** claimed during 2006 (n = 3 301). The **top 20 monotherapy ARV prescriptions** according to total cost represented 3.79 per cent of the **total number of ARV prescriptions** (n = 81 096) claimed during 2006.

Of the ARV prescriptions containing one ARV claimed during 2006, prescriptions containing **two PIs** (n = 2) represented 10 per cent, and prescriptions for **one PI** (n = 1) represented 5 per cent of the top 20 ARV monotherapy prescriptions according to total cost during 2006. Prescriptions containing **two NRTIs** (n = 2) represented 10 per cent, and prescriptions for **one NRTI** (n = 10) represented 50 per cent of the top 20 ARV monotherapy prescriptions according to frequency during 2006. Prescriptions for **one NNRTI** (n = 5) accounted for 25 per cent of the top 20 ARV monotherapy prescriptions according to frequency during 2006.

Table 4.57 Top 20 combinations of 2 ARVs per prescription according to total cost for 2005

ARV medicine item 1	ARV medicine item 2	N	Average cost (R)	Standard deviation (R)	Total cost (R)
Aspen Lamzid [®] Tab	Stocrin [®] 600mg Tab	10 077	571.12	24.71	5 755 153.41
Aspen Lamzid [®] Tab	Aspen Nevirapine [®] 200mg Tab	5 470	555.76	20.16	3 040 006.65
Combivir [®] Tab	Stocrin [®] 600mg Tab	1 650	639.92	60.20	1 055 875.45
Combivir [®] Tab	Viramune [®] 200mg Tab	965	854.22	66.04	824 320.56
Aspen Lamzid [®] Tab	Kaletra [®] 80mg/20mg Cap	1 182	676.36	28.74	799 456.49
Combivir [®] Tab	Stocrin [®] 200mg Cap	402	722.78	29.98	290 557.90
Combivir [®] Tab	Kaletra [®] 80mg/20mg Cap	281	752.26	47.30	211 384.52
Kaletra [®] 80mg/20mg Cap	Stocrin [®] 600mg Tab	217	599.68	57.07	130 129.99
Aspen Lamzid [®] Tab	Stocrin [®] 200mg Cap	180	629.04	45.02	113 227.26
Aspen Lamzid [®] Tab	Viramune [®] 200mg Tab	123	772.87	19.26	95 062.45
Aspen Nevirapine [®] 200mg Tab	Combivir [®] Tab	136	614.13	20.61	83 522.12
Kaletra [®] 80mg/20mg Cap	Ziagen [®] 300mg Tab	28	1 352.02	21.42	37 856.47
3TC [®] 150mg Tab	Stocrin [®] 600mg Tab	84	380.10	32.35	31 928.27
Combivir [®] Tab	Crixivan [®] 400mg Cap	42	718.59	164.58	30 180.64
Aspen Lamivudine [®] 150mg Tab	Stocrin [®] 600mg Tab	52	350.51	15.24	18 226.33
Norvir [®] 100mg Cap	Ziagen [®] 300mg Tab	13	1 309.55	78.73	17 024.15
Aspen Nevirapine [®] 200mg Tab	Kaletra [®] 80mg/20mg Cap	22	661.67	30.70	14 556.66
Hivid [®] Combo Tab	Ziagen [®] 300mg Tab	10	1 421.76	88.75	14 217.61
Crixivan [®] 400mg Cap	Kaletra [®] 80mg/20mg Cap	21	674.55	70.44	14 165.62
Aspen Lamivudine [®] 150mg Tab	Aspen Stavudine [®] 40mg Cap	80	160.97	3.12	12 877.36

4.10.2.2 Two antiretroviral medicine items per prescription

4.10.2.2.1 Top 20 combinations of 2 ARVs per prescription according to total cost for 2005

The combinations **Aspen Lamivudine[®] 150mg tab + Aspen Stavudine[®] 30mg cap** (R151.12 ± R15.31), **Aspen Stavudine[®] 40mg cap + Stocrin[®] 600mg tab** (R287.52 ± R11.56), **3TC[®] 150mg tab + Retrovir[®] 100mg cap** (R402.45 ± R203.11) and **Videx[®] 100mg chew + Zerit[®] 40mg cap** (R324.93 ± R62.11) were present among the top 20 according to frequency, but were absent from the top 20 prescriptions with two ARVs in combination ranked according to total cost during 2005 (*refer to table 4.57*).

Norvir[®] 100mg cap + Ziagen[®] 300mg tab (R1 309.55 ± R78.73), **Aspen Nevirapine[®] 200mg tab + Kaletra[®] 80mg/20mg cap** (R661.67 ± R30.70), **Hivid[®] Combo tab + Ziagen[®] 300mg tab** (R1 421.76 ± R88.75) and **Crixivan[®] 400mg cap + Kaletra[®] 80mg/20mg cap** (R674.55 ± R70.44) did not feature among the top 20 prescriptions with two ARVs in combination according to frequency, but were included among the top 20 prescriptions according to total cost during 2005 (*refer to table 4.57*).

The combination prescription of two ARVs that had the highest total cost was **Aspen Lamzid[®] tab + Stocrin[®] 600mg tab** at R5 755 153.41, which represented 45.71 per cent of the total cost of the top 20 prescriptions with two ARVs in combination ($n = R12\ 589\ 729.91$) during 2005 (*refer to table 4.57*).

The **top 20 prescriptions of two ARVs in combination** ($n = 21\ 035$) represented 96.09 per cent of the **total number of prescriptions for two ARVs** claimed during 2005 ($n = 21\ 892$). The **top 20 dual therapy ARV prescriptions** represented 42.07 per cent of the **total number of ARV prescriptions** ($n = 49\ 995$) claimed during 2005.

Prescriptions containing the combinations **2NRTI + PI** ($n = 1$), **2PI + NRTI** ($n = 1$), **PI + NRTI** ($n = 1$), **2NRTI** ($n = 1$), **3PI** ($n = 1$), and **NRTI + OTHER** ($n = 1$) all individually represented 5 per cent of the top 20 prescriptions for two ARVs claimed during 2005. Prescriptions for **2PI + NNRTI** ($n = 2$), **2NRTI + 2PI** ($n = 2$), **NRTI + NNRTI** ($n = 2$) represented 10 per cent each of the top 20 prescriptions for two ARVs claimed during 2005. Prescriptions for the combination **2NRTI + NNRTI** ($n = 8$) represented 40 per cent of the top 20 prescriptions for two ARVs claimed during 2005.

Table 4.58 Top 20 combinations of 2 ARVs per prescription according to total cost for 2006

ARV medicine item 1	ARV medicine item 2	N	Average cost (R)	Standard deviation (R)	Total cost (R)
Aspen Lamzid [®] Tab	Stocrin [®] 600mg Tab	18 819	547.24	42.16	10 298 552.61
Aspen Lamzid [®] Tab	Aspen Nevirapine [®] 200mg Tab	8 597	554.04	32.58	4 763 064.96
Aspen Lamzid [®] Tab	Kaletra [®] 80mg/20mg Cap	2 563	679.73	36.22	1 742 156.51
Combivir [®] Tab	Stocrin [®] 600mg Tab	1 753	615.38	52.96	1 078 766.40
Combivir [®] Tab	Viramune [®] 200mg Tab	531	840.23	53.73	446 162.21
Kaletra [®] 80mg/20mg Cap	Stocrin [®] 600mg Tab	507	598.96	56.81	303 671.91
Combivir [®] Tab	Kaletra [®] 80mg/20mg Cap	314	749.63	78.35	235 382.69
Aspen Lamzid [®] Tab	Viramune [®] 200mg Tab	141	779.45	69.83	109 902.09
Aspen Nevirapine [®] 200mg Tab	Combivir [®] Tab	134	622.77	37.36	83 450.88
Combivir [®] Tab	Stocrin [®] 200mg Cap	122	682.94	43.15	83 318.44
Aspen Lamivudine [®] 150mg Tab	Stocrin [®] 600mg Tab	173	331.19	28.49	57 296.62
Kaletra [®] 80mg/20mg Cap	Ziagen [®] 300mg Tab	33	1 350.14	16.56	44 554.70
Aspen Nevirapine [®] 200mg Tab	Kaletra [®] 80mg/20mg Cap	63	678.47	34.29	42 743.58
Aspen Lamzid [®] Tab	Stocrin [®] 200mg Cap	71	581.76	62.31	41 304.81
Crixivan [®] 400mg Cap	Kaletra [®] 80mg/20mg Cap	49	653.91	39.96	32 041.37
Aspen Zidovudine [®] 300mg Tab	Kaletra [®] 80mg/20mg Cap	44	625.57	29.77	27 525.25
Aspen Lamzid [®] Tab	Cipla Nevirapine [®] 200mg Tab	37	561.95	130.94	20 792.21
Cipla Duovir [®] Tab	Cipla Nevirapine [®] 200mg Tab	43	479.90	1.37	20 635.52
Aspen Lamivudine [®] 150mg Tab	Aspen Stavudine [®] 40mg Cap	133	142.13	37.06	18 902.68
Aspen Lamzid [®] Tab	Crixivan [®] 400mg Cap	27	670.80	194.09	18 111.67

4.10.2.2.2 Top 20 combinations of 2 ARVs per prescription according to total cost for 2006

The combinations **Aspen Lamivudine® 150mg tab + Aspen Stavudine® 30mg cap** (R153.53 ± R3.96), **Aspen Stavudine® 40mg cap + Stocrin® 600mg tab** (R266.67 ± R25.71), and **3TC® 150mg tab + Stocrin® 600mg tab** (R353.88 ± R26.69) were present among the top 20 prescriptions with 2 ARVs in combination according to frequency, but were absent from the top 20 prescriptions ranked according to total cost during 2006 (*refer to table 4.58*).

Kaletra® 80mg/20mg cap + Ziagen® 300mg tab (R1 350.14 ± R16.56), **Aspen Lamzid® tab + Cipla Nevirapine® 200mg** (R561.95 ± R130.94), and **Aspen Lamzid® tab + Crixivan® 400mg cap** (R670.80 ± R194.09) did not feature among the top 20 prescriptions with 2 ARVs in combination according to frequency, but were included among the top 20 prescriptions according to total cost during 2006 (*refer to table 4.58*).

The combination prescription of two ARVs that had the highest total cost was **Aspen Lamzid® tab + Stocrin® 600mg tab** at R10 298 552.61, which represented 52.90 per cent of the total cost of the top 20 prescriptions with 2 ARVs in combination ($n = R19\ 468\ 337.11$) during 2006 (*refer to table 4.58*).

The top 20 prescriptions of **two ARVs in combination** ($n = 34\ 154$) represented 96.68 per cent of the **total number of prescriptions for two ARVs** claimed during 2006 ($n = 35\ 328$). The **top 20 dual therapy ARV prescriptions** represented 42.12 per cent of the **total number of ARV prescriptions** ($n = 81\ 096$) claimed during 2006.

Prescriptions containing the combinations **NRTI + NNRTI** ($n = 1$), **2NRTI + PI** ($n = 1$), **3PI** ($n = 1$) and **2NRTI** ($n = 1$) all individually represented 5 per cent of the top 20 prescriptions for two ARVs claimed during 2006. Prescriptions for **2PI + NRTI** ($n = 2$), **2PI + NNRTI** ($n = 2$), and **2NRTI + 2PI** ($n = 2$) represented 10 per cent each of the top 20 prescriptions for two ARVs claimed during 2006. Prescriptions for the combination **2NRTI + NNRTI** ($n = 10$) represented 50 per cent of the top 20 prescriptions for two ARVs claimed during 2006.

Table 4.59 Top 20 combinations of 3 ARVs per prescription according to total cost for 2005

ARV medicine item 1	ARV medicine item 2	ARV medicine item 3	N	Average cost (R)	Standard deviation (R)	Total cost (R)
Aspen Lamivudine® 150mg Tab	Aspen Stavudine® 40mg Cap	Stocrin® 600mg Tab	9 334	403.60	13.75	3 767 208.41
Aspen Lamivudine® 150mg Tab	Aspen Stavudine® 30mg Cap	Stocrin® 600mg Tab	5 039	394.91	13.35	1 989 958.46
Aspen Lamivudine® 150mg Tab	Aspen Nevirapine® 200mg Tab	Aspen Stavudine® 40mg Cap	1 254	387.87	13.50	486 391.79
Aspen Lamivudine® 150mg Tab	Aspen Nevirapine® 200mg Tab	Aspen Stavudine® 30mg Cap	752	379.54	11.35	285 417.71
3TC® Oral 10mg/MI Sol	Retrovir® S 50mg/5ml Syr	Viramune® Oral	184	1 169.98	331.32	215 277.16
Aspen Lamivudine® 10mg/MI	Viramune® Oral	Zerit® 5mg/5ml Sus	233	906.17	240.67	211 136.65
Aspen Lamivudine® 10mg/MI	Aspen Zidovudine® Syr 50mg/5ml	Viramune® Oral	189	976.56	197.34	184 569.37
Aspen Lamivudine® 150mg Tab	Aspen Stavudine® 40mg Cap	Kaletra® 80mg/20mg Cap	303	513.84	55.15	155 694.62
3TC® 150mg Tab	Aspen Stavudine® 40mg Cap	Stocrin® 600mg Tab	272	437.54	24.14	119 009.94
Aspen Lamivudine® 150mg Tab	Aspen Nevirapine® 200mg Tab	Retrovir® 100mg Cap	199	514.17	59.19	102 319.28
3TC® 150mg Tab	Stocrin® 600mg Tab	Zerit® 40mg Cap	209	435.98	34.27	91 119.31
3TC® Oral 10mg/MI Sol	Viramune® Oral	Zerit® 5mg/5ml Sus	76	904.41	319.73	68 734.94
Aspen Lamivudine® 150mg Tab	Aspen Stavudine® 30mg Cap	Kaletra® 80mg/20mg Cap	134	497.37	14.28	66 647.72
3TC® 150mg Tab	Stocrin® 600mg Tab	Zerit® 30mg Cap	147	441.80	16.12	64 944.01
Stocrin® 600mg Tab	Videx® 100mg Chew	Zerit® 40mg Cap	107	574.29	30.23	61 449.32
3TC® 150mg Tab	Viramune® 200mg Tab	Zerit® 40mg Cap	93	616.83	41.03	57 364.80
Crixivan® 400mg Cap	Norvir® 100mg Cap	Stocrin® 600mg Tab	92	588.66	51.86	54 156.97
Aspen Lamivudine® 150mg Tab	Kaletra® 80mg/20mg Cap	Ziagen® 300mg Tab	33	1 464.54	23.65	48 329.90
Aspen Stavudine® 40mg Cap	Stocrin® 600mg Tab	Videx® 100mg Chew	83	554.87	63.12	46 054.47
Aspen Lamivudine® 150mg Tab	Aspen Nevirapine® 200mg Tab	Retrovir® 250mg Cap	71	602.58	52.24	42 782.86

4.10.2.3 Three antiretroviral medicine items per prescription

4.10.2.3.1 Top 20 combinations of 3 ARVs per prescription according to total cost for 2005

The combinations **Aspen Lamivudine[®] 150mg tab + Aspen Stavudine[®] 30mg cap + Kaletra[®] 80mg/20mg cap** (R497.37 ± R14.28), **Aspen Lamivudine[®] 10mg/ml + Kaletra[®] 400mg/100mg/5ml + Zerit[®] 5mg/5ml sus** (R393.79 ± R130.52), and **Aspen Lamivudine[®] 10mg/ml + Aspen Nevirapine[®] + Zerit[®] 5mg/5ml sus** (R410.70 ± R98.64) were present among the top 20 triple therapy prescriptions according to frequency, but were absent from the top 20 triple therapy prescriptions ranked according to total cost during 2005 (*refer to table 4.59*).

Aspen Lamivudine[®] 150mg tab + Kaletra[®] 80mg/20mg tab + Ziagen[®] 300mg tab (R1 464.54 ± R23.65), and **Aspen Lamivudine[®] 150mg tab + Aspen Nevirapine[®] 200mg tab + Retrovir[®] 250mg cap** (R602.58 ± R52.24) did not feature among the top 20 triple combination prescriptions according to frequency, but were included among the top 20 prescriptions according to total cost during 2005 (*refer to table 4.59*).

The combination prescription of three ARVs that had the highest total cost was **Aspen Lamivudine[®] 150mg tab + Aspen Stavudine[®] 40mg cap + Stocrin[®] 600mg tab** at R3 767 208.41, which represented 46.40 per cent of the total cost of the top 20 triple therapy prescriptions (n = R8 118 567.69) during 2005 (*refer to table 4.59*).

The top 20 prescriptions of **three ARVs in combination** (n = 18 804) represented 85.76 per cent of the **total number of prescriptions for three ARVs** claimed during 2005 (n = 21 927). The **top 20 triple therapy ARV prescriptions** represented 37.61 per cent of the **total number of ARV prescriptions** (n = 49 995) claimed during 2005.

Prescriptions for **2PI + NNRTI** (n = 1) represented 5 per cent of the top 20 prescriptions for three ARVs claimed during 2005. Prescriptions for the combination **2NRTI + 2PI** (n = 3) represented 15 per cent of the top 20 prescriptions for three ARVs claimed during 2005. Prescriptions for **2NRTI + NNRTI** (n = 16) represented 80 per cent of the top 20 prescriptions for three ARVs claimed during 2005.

Table 4.60 Top 20 combinations of 3 ARVs per prescription according to total cost for 2006

ARV medicine item 1	ARV medicine item 2	ARV medicine item 3	N	Average cost (R)	Standard deviation (R)	Total cost (R)
Aspen Lamivudine [®] 150mg Tab	Aspen Stavudine [®] 40mg Cap	Stocrin [®] 600mg Tab	15195	378.74	25.13	5754959.81
Aspen Lamivudine [®] 150mg Tab	Aspen Stavudine [®] 30mg Cap	Stocrin [®] 600mg Tab	11403	370.38	20.87	4223406.95
Aspen Lamivudine [®] 150mg Tab	Aspen Nevirapine [®] 200mg Tab	Aspen Stavudine [®] 40mg Cap	2101	387.87	27.79	814918.81
Aspen Lamivudine [®] 150mg Tab	Aspen Nevirapine [®] 200mg Tab	Aspen Stavudine [®] 30mg Cap	1714	379.24	13.59	650017.16
Aspen Stavudine [®] 40mg Cap	Stocrin [®] 600mg Tab	Videx [®] 400mg EC Cap	1099	497.85	23.95	547132.77
Aspen Lamivudine [®] 150mg Tab	Aspen Stavudine [®] 40mg Cap	Kaletra [®] 80mg/20mg Cap	535	511.06	30.67	273415.52
Aspen Lamivudine [®] 10mg/MI	Aspen Nevirapine [®]	Aspen Zidovudine [®] Syr 50mg/5ml	360	711.25	129.76	256050.67
Aspen Lamivudine [®] 10mg/MI	Aspen Nevirapine [®]	Zerit [®] 5mg/5ml Sus	371	437.11	111.05	162168.72
Aspen Nevirapine [®] 200mg Tab	Aspen Stavudine [®] 40mg Cap	Videx [®] 400mg EC Cap	311	507.80	10.62	157926.23
3TC [®] 150mg Tab	Aspen Stavudine [®] 40mg Cap	Stocrin [®] 600mg Tab	339	409.25	21.76	138737.12
Aspen Lamivudine [®] 150mg Tab	Aspen Stavudine [®] 30mg Cap	Kaletra [®] 80mg/20mg Cap	274	501.36	46.24	137371.60
Aspen Stavudine [®] 30mg Cap	Stocrin [®] 600mg Tab	Videx [®] 250mg EC Cap	305	441.02	16.47	134510.74
3TC [®] 150mg Tab	Stocrin [®] 600mg Tab	Zerit [®] 40mg Cap	274	412.17	33.55	112935.35
Aspen Zidovudine [®] 300mg Tab	Kaletra [®] 80mg/20mg Cap	Videx [®] 400mg EC Cap	130	853.96	85.55	111015.22
3TC [®] Oral 10mg/MI Sol	Retrovir [®] S 50mg/5ml Syr	Viramune [®] Oral	78	1260.79	302.11	98341.23
Aspen Stavudine [®] 40mg Cap	Kaletra [®] 80mg/20mg Cap	Videx [®] 400mg EC Cap	140	635.20	24.68	88927.49
Aspen Didanosine [®] 100mg	Aspen Stavudine [®] 40mg Cap	Stocrin [®] 600mg Tab	154	519.62	42.35	80021.06
Aspen Lamivudine [®] 10mg/MI	Kaletra [®] 400/100mg/5ml	Zerit [®] 5mg/5ml Sus	250	313.81	82.75	78452.06
Aspen Lamzid [®] Tab	Aspen Zidovudine [®] Syr 50mg/5ml	Kaletra [®] 80mg/20mg Cap	98	761.10	19.66	74587.59
Aspen Lamivudine [®] 10mg/MI	Viramune [®] Oral	Zerit [®] 5mg/5ml Sus	85	833.39	166.38	70837.83

4.10.2.3.2 Top 20 combinations of 3 ARVs per prescription according to total cost for 2006

The combinations **3TC[®] 150mg tab + Stocrin[®] 600mg tab + Zerit[®] 30mg cap** (R410.50 ± R16.73), **Aspen Lamivudine[®] 150mg tab + Aspen Nevirapine[®] 200mg tab + Aspen Stavudine[®] 20mg cap** (R284.62 ± R39.41), **Aspen Lamivudine[®] 10mg/ml + Aspen Zidovudine[®] syr 50mg/5ml + Kaletra[®] 400mg/100mg/5ml** (R536.11 ± R97.21), and **Aspen Lamivudine[®] 150mg tab + Aspen Stavudine[®] 30mg cap + Stocrin[®] 200mg cap** (R349.43 ± R28.96) were present among the top 20 triple therapy prescriptions according to frequency, but were absent from the top 20 prescriptions with 3 ARVs in combination ranked according to total cost during 2006 (*refer to table 4.60*).

Aspen Zidovudine[®] 300mg tab + Kaletra[®] 80mg/20mg cap + Videx[®] 400mg EC cap (R853.96 ± R85.55), **3TC[®] oral 10mg/ml sol + Retrovir[®] S 50mg/5ml syr + Viramune[®] oral** (R1 260.79 ± R302.11), **Aspen Lamzid[®] tab + Aspen Zidovudine[®] syr 50mg/5ml + Kaletra[®] 80mg/20mg cap** (R761.10 ± R19.66), and **Aspen Lamivudine[®] 10mg/ml + Viramune[®] oral + Zerit[®] 5mg/5ml sus** (R833.39 ± R166.38) did not feature among the top 20 triple therapy prescriptions according to frequency, but were included among the top 20 prescriptions with 3 ARVs in combination according to total cost during 2006 (*refer to table 4.60*).

The combination prescription of three ARVs that had the highest total cost was **Aspen Lamivudine[®] 150mg tab + Aspen Stavudine[®] 40mg cap + Stocrin[®] 600mg tab** at R5 754 959.81, which represented 41.21 per cent of the total cost of the top 20 triple therapy prescriptions (n = R13 965 733.93) during 2006 (*refer to table 4.60*).

The top 20 prescriptions of **three ARVs in combination** (n = 35 216) represented 87.61 per cent of the **total number of prescriptions for three ARVs** claimed during 2006 (n = 40 195). The **top 20 triple therapy ARV prescriptions** represented 43.43 per cent of the **total number of ARV prescriptions** (n = 81 096) claimed during 2006.

Prescriptions for the combination **2NRTI + 2PI** (n = 6) represented 30 per cent of the top 20 prescriptions for three ARVs claimed during 2006. Prescriptions for **2NRTI + NNRTI** (n = 14) represented 70 per cent of the top 20 prescriptions for three ARVs claimed during 2006.

Table 4.61 Top 20 combinations of 4 ARVs per prescription according to total cost for 2005

ARV medicine item 1	ARV medicine item 2	ARV medicine item 3	ARV medicine item 4	N	Average cost (R)	Standard deviation (R)	Total cost (R)
Aspen Lamivudine [®] 150mg Tab	Retrovir [®] 100mg Cap	Stocrin [®] 200mg Cap	Stocrin [®] 50mg Cap	150	539.13	50.09	80868.85
Aspen Lamivudine [®] 150mg Tab	Aspen Stavudine [®] 20mg Cap	Stocrin [®] 200mg Cap	Stocrin [®] 50mg Cap	106	277.61	19.70	29426.48
Aspen Lamivudine [®] 10mg/MI	Aspen Stavudine [®] 20mg Cap	Stocrin [®] 200mg Cap	Stocrin [®] 50mg Cap	55	417.08	24.67	22939.30
Aspen Lamivudine [®] 10mg/MI	Aspen Stavudine [®] 30mg Cap	Kaletra [®] 400/100mg/5ml	Ziagen [®] 100mg/5ml Sol	17	1021.23	72.83	17360.84
Aspen Lamivudine [®] 10mg/MI	Stocrin [®] 200mg Cap	Stocrin [®] 50mg Cap	Ziagen [®] 100mg/5ml Sol	11	1249.27	192.68	13741.95
Aspen Lamivudine [®] 150mg Tab	Aspen Stavudine [®] 30mg Cap	Stocrin [®] 200mg Cap	Stocrin [®] 50mg Cap	33	363.46	20.35	11994.06
Aspen Lamivudine [®] 10mg/MI	Stocrin [®] 200mg Cap	Stocrin [®] 50mg Cap	Zerit [®] 5mg/5ml Sus	19	517.38	164.36	9830.28
Aspen Lamivudine [®] 150mg Tab	Stocrin [®] 200mg Cap	Stocrin [®] 50mg Cap	Zerit [®] 5mg/5ml Sus	13	611.72	132.24	7952.42
Aspen Lamivudine [®] 10mg/MI	Aspen Zidovudine [®] Syr 50mg/5ml	Stocrin [®] 200mg Cap	Stocrin [®] 50mg Cap	12	584.15	23.60	7009.80
Aspen Didanosine [®] 100mg	Aspen Stavudine [®] 20mg Cap	Stocrin [®] 200mg Cap	Stocrin [®] 50mg Cap	15	360.55	14.03	5408.19
3TC [®] Oral 10mg/MI Sol	Retrovir [®] 250mg Cap	Stocrin [®] 200mg Cap	Stocrin [®] 50mg Cap	6	754.61	57.55	4527.63
3TC [®] Oral 10mg/MI Sol	Aspen Stavudine [®] 20mg Cap	Stocrin [®] 200mg Cap	Stocrin [®] 50mg Cap	11	409.90	17.47	4508.94
Aspen Didanosine [®] 100mg	Aspen Didanosine [®] 150mg	Aspen Stavudine [®] 20mg Cap	Kaletra [®] 80mg/20mg Cap	8	547.99	0.00	4383.92
Aspen Didanosine [®] 100mg	Aspen Didanosine [®] 150mg	Aspen Nevirapine [®] 200mg Tab	Aspen Stavudine [®] 30mg Cap	10	436.29	0.00	4362.90
3TC [®] 150mg Tab	Retrovir [®] 100mg Cap	Stocrin [®] 200mg Cap	Stocrin [®] 50mg Cap	7	568.97	3.28	3982.80
Aspen Stavudine [®] 20mg Cap	Kaletra [®] 400/100mg/5ml	Videx [®] 25mg Chew	Videx [®] 50mg Chew	6	655.38	0.00	3932.28
3TC [®] Oral 10mg/MI Sol	Stocrin [®] 200mg Cap	Stocrin [®] 50mg Cap	Zerit [®] 20mg Cap	7	439.60	14.39	3077.22
Aspen Lamivudine [®] 10mg/MI	Retrovir [®] 100mg Cap	Stocrin [®] 200mg Cap	Stocrin [®] 50mg Cap	6	480.48	35.22	2882.88
3TC [®] Oral 10mg/MI Sol	Stocrin [®] 200mg Cap	Stocrin [®] 50mg Cap	Zerit [®] 30mg Cap	5	524.00	0.00	2620.00
Aspen Stavudine [®] 20mg Cap	Kaletra [®] 80mg/20mg Cap	Videx [®] 100mg Chew	Videx [®] 150mg Chew	5	486.00	0.00	2430.00

4.10.2.4 Four antiretroviral medicine items per prescription

4.10.2.4.1 Top 20 combinations of 4 ARVs per prescription according to total cost for 2005

The same combinations that were present among the top 20 prescriptions with 4 ARVs in combination according to frequency were also present among the top 20 prescriptions ranked according to total cost during 2005 (*refer to table 4.61*).

The combination prescription of four ARVs that had the highest total cost was **Aspen Lamivudine® 150mg tab + Retrovir® 100mg cap + Stocrin® 200mg cap + Stocrin® 50mg cap** at R80 868.85, which represented 33.25 per cent of the total cost of the top 20 prescriptions with 4 ARVs in combination (n = R243 240.74) during 2005 (*refer to table 4.61*).

The **top 20 prescriptions of four ARVs** in combination (n = 502) represented 87.92 per cent of the **total number of prescriptions for four ARVs** claimed during 2005 (n = 571). The **top 20 ARV prescriptions for four ARVs** represented 1.00 per cent of the **total number of ARV prescriptions** (n = 49 995) claimed during 2005.

Prescriptions for the combination **2NRTI + 2PI** (n = 4) represented 20 per cent of the top 20 prescriptions for four ARVs claimed during 2005. Prescriptions for **2NRTI + NNRTI** (n = 16) represented 80 per cent of the top 20 prescriptions for four ARVs claimed during 2005.

Table 4.62 Top 20 combinations of 4 ARVs per prescription according to total cost for 2006

ARV medicine item 1	ARV medicine item 2	ARV medicine item 3	ARV medicine item 4	N	Average cost (R)	Standard deviation (R)	Total cost (R)
Aspen Lamzid [®] Tab	Aspen Zidovudine [®] Syr 50mg/5ml	Kaletra [®] 80mg/20mg Cap	Retrovir [®] 200mg/20ml Inj	207	938.74	57.81	194318.19
Aspen Didanosine [®] 100mg	Aspen Didanosine [®] 150mg	Aspen Stavudine [®] 40mg Cap	Stocrin [®] 600mg Tab	294	534.12	30.48	157030.23
Aspen Lamivudine [®] 150mg Tab	Aspen Stavudine [®] 20mg Cap	Stocrin [®] 200 Cap	Stocrin [®] 50 Cap	250	280.26	36.52	70066.23
Aspen Lamivudine [®] 10mg/MI	Aspen Stavudine [®] 20mg Cap	Stocrin [®] 200 Cap	Stocrin [®] 50 Cap	159	399.49	36.24	63518.20
Aspen Lamzid [®] Tab	Aspen Nevirapine [®] 200mg Tab	Aspen Zidovudine [®] Syr 50mg/5ml	Retrovir [®] 200mg/20ml Inj	74	809.10	49.85	59873.13
Aspen Lamivudine [®] 150mg Tab	Retrovir [®] 100mg Cap	Stocrin [®] 200 Cap	Stocrin [®] 50 Cap	94	551.92	66.76	51880.23
Aspen Didanosine [®] 100mg	Aspen Didanosine [®] 150mg	Aspen Nevirapine [®] 200mg Tab	Aspen Stavudine [®] 40mg Cap	83	537.13	21.09	44582.04
Aspen Lamzid [®] Tab	Kaletra [®] 80mg/20mg Cap	Retrovir [®] 200mg/20ml Inj	Retrovir [®] S 50mg/5ml Syr	42	983.15	76.54	41292.14
Aspen Didanosine [®] 100mg	Aspen Didanosine [®] 150mg	Aspen Stavudine [®] 30mg Cap	Stocrin [®] 600mg Tab	86	457.11	47.63	39311.32
Aspen Lamivudine [®] 10mg/MI	Aspen Zidovudine [®] 300mg Tab	Stocrin [®] 200 Cap	Stocrin [®] 50 Cap	67	546.29	78.06	36601.40
Aspen Lamivudine [®] 150mg Tab	Aspen Zidovudine [®] 300mg Tab	Stocrin [®] 200 Cap	Stocrin [®] 50 Cap	96	378.56	28.84	36341.52
Aspen Lamivudine [®] 150mg Tab	Aspen Stavudine [®] 30mg Cap	Stocrin [®] 200 Cap	Stocrin [®] 50 Cap	72	356.11	19.76	25640.02
Aspen Lamivudine [®] 10mg/MI	Aspen Stavudine [®] 15mg Cap	Stocrin [®] 200 Cap	Stocrin [®] 50 Cap	64	317.04	22.08	20290.33
Aspen Lamivudine [®] 10mg/MI	Stocrin [®] 200 Cap	Stocrin [®] 50 Cap	Zerit [®] 5mg/5ml Sus	52	390.11	28.87	20285.50
Aspen Lamivudine [®] 10mg/MI	Stocrin [®] 200 Cap	Stocrin [®] 50 Cap	Ziagen [®] 100mg/5ml Sol	12	1 310.76	195.52	15729.12
Aspen Didanosine [®] 100mg	Aspen Didanosine [®] 25mg	Aspen Zidovudine [®] 300mg Tab	Kaletra [®] 80mg/20mg Cap	17	850.42	36.12	14457.13
Aspen Lamzid [®] Tab	Aspen Nevirapine [®] 200mg Tab	Retrovir [®] 200mg/20ml Inj	Retrovir [®] S 50mg/5ml Syr	16	847.69	91.13	13563.06
Aspen Lamivudine [®] 150mg Tab	Aspen Stavudine [®] 40mg Cap	Crixivan [®] 400mg Cap	Norvir [®] 100mg Cap	23	514.61	37.15	11836.10
Stocrin [®] 600mg Tab	Videx [®] 100mg Chew	Videx [®] 25mg Chew	Zerit [®] 30mg Cap	18	563.31	23.70	10139.59
Kaletra [®] 80mg/20mg Cap	Videx [®] 100mg Chew	Videx [®] 150mg Chew	Ziagen [®] 300mg Tab	6	1 608.39	0.03	9650.34

4.10.2.4.2 Top 20 combinations of 4 ARVs per prescription according to total cost for 2006

Aspen Didanosine® 100mg + Aspen Didanosine® 25mg + Aspen Stavudine® 30mg cap + Stocrin® 600mg tab (R523.99 ± R108.36), and **Aspen Lamivudine® 150mg tab + Aspen Stavudine® 15mg cap + Stocrin® 200mg cap + Stocrin® 50mg cap** (R245.82 ± R14.51) were present among the top 20 prescriptions with 4 ARVs in combination according to frequency, but were absent from the top 20 prescriptions ranked according to total cost during 2006 (*refer to table 4.62*).

Aspen Lamivudine® 10mg/ml + Stocrin® 200mg cap + Stocrin® 50mg cap + Ziagen® 100mg/5ml sol (R1 310.76 ± R195.52), and **Kaletra® 80mg/20mg cap + Videx® 100mg chew + Videx® 150mg chew + Ziagen® 300mg chew** (R1 608.39 ± R0.03) did not feature among the top 20 prescriptions with 4 ARVs in combination according to frequency, but were included among the top 20 prescriptions according to total cost during 2006 (*refer to table 4.62*).

The combination prescription of four ARVs that had the highest total cost was **Aspen Lamzid® tab + Aspen Zidovudine® syr 50mg/5ml + Kaletra® 80mg/20mg cap + Retrovir® 200mg/20ml inj** at R194 318.19, which represented 20.75 per cent of the total cost of the top 20 prescriptions with four ARVs in combination ($n = R936\ 405.82$) during 2006 (*refer to table 4.62*).

The **top 20 prescriptions of four ARVs** in combination ($n = 1\ 732$) represented 76.81 per cent of the **total number of prescriptions for four ARVs** claimed during 2006 ($n = 2\ 255$). The **top 20 prescriptions for four ARVs** represented 2.14 per cent of the total number of ARV prescriptions ($n = 81\ 096$) claimed during 2006.

Prescriptions for the combination **2NRTI + 2PI** ($n = 5$) represented 25 per cent of the top 20 prescriptions for four ARVs claimed during 2006. Prescriptions for **2NRTI + NNRTI** ($n = 15$) represented 75 per cent of the top 20 prescriptions for four ARVs claimed during 2006.

Table 4.63 Top 16 combinations of 5 ARVs per prescription according to total cost for 2005

ARV medicine item 1	ARV medicine item 2	ARV medicine item 3	ARV medicine item 4	ARV medicine item 5	N	Average cost (R)	Standard deviation (R)	Total cost (R)
Aspen Didanosine® 100mg	Aspen Didanosine® 150mg	Aspen Stavudine® 40mg Cap	Crixivan® 400mg Cap	Norvir® 100mg Cap	7	648.74	5.97	4 541.20
3TC® Oral 10mg/MI Sol	Aspen Stavudine® 20mg Cap	Stocrin® 200mg Cap	Stocrin® 50mg Cap	Ziagen® 100mg/5ml Sol	4	1 133.84	0.00	4 535.36
Kaletra® 80mg/20mg Cap	Stocrin® 600mg Tab	Videx® 100mg Chew	Videx® 150mg Chew	Zerit® 40mg Cap	4	931.72	20.70	3 726.88
Aspen Stavudine® 40mg Cap	Crixivan® 400mg Cap	Norvir® 100mg Cap	Videx® 100mg Chew	Videx® 150mg Chew	4	679.28	0.00	2 717.12
Aspen Lamivudine® 150mg Tab	Aspen Nevirapine® 200mg Tab	Aspen Stavudine® 40mg Cap	Aspen Zidovudine® Syr 50mg/5ml	Retrovir® 200mg/20ml Inj	3	628.74	0.00	1 886.22
Aspen Lamivudine® Tab	Aspen Nevirapine® 200mg Tab	Combivir® Tab	Retrovir® S 50mg/5ml Syr	Viramune® 200mg Tab	1	1 494.58	-	1 494.58
Aspen Stavudine® 40mg Cap	Crixivan® 200mg Cap	Norvir® 100mg Cap	Videx® 100mg Chew	Videx® 150mg Chew	2	739.27	0.00	1 478.54
3TC® 150mg Tab	Combivir® Tab	Kaletra® 80mg/20mg Cap	Stavir® 40mg Cap	Stocrin® 600mg Tab	1	1 151.16	-	1 151.16
Aspen Stavudine® 30mg Cap	Crixivan® 400mg Cap	Norvir® 100mg Cap	Videx® 100mg Chew	Videx® 150mg Chew	2	572.96	0.00	1 145.92
Aspen Didanosine® 100mg	Aspen Didanosine® 150mg	Aspen Stavudine® 30mg Cap	Crixivan® 400mg Cap	Norvir® 100mg Cap	2	547.48	0.00	1 094.96
Aspen Stavudine® 40mg Cap	Kaletra® 80mg/20mg Cap	Stocrin® 600mg Tab	Videx® 100mg Chew	Videx® 150mg Chew	1	939.41	-	939.41
Aspen Lamivudine® 150mg Tab	Aspen Nevirapine® 200mg Tab	Aspen Stavudine® 30mg Cap	Aspen Stavudine® 40mg Cap	Viramune® 200mg Tab	1	866.91	-	866.91
Aspen Lamivudine® 150mg Tab	Aspen Nevirapine® 200mg Tab	Aspen Stavudine® 30mg Cap	Aspen Zidovudine® Syr 50mg/5ml	Retrovir® 200mg/20ml Inj	1	621.20	-	621.20
Aspen Didanosine® 100mg	Aspen Stavudine® 30mg Cap	Crixivan® 400mg Cap	Norvir® 100mg Cap	Videx® 150mg Chew	1	572.88	-	572.88
Aspen Didanosine® 25mg	Aspen Didanosine® 50mg	Aspen Stavudine® 20mg Cap	Stocrin® 200mg Cap	Stocrin® 50mg Cap	1	438.18	-	438.18
Aspen Lamivudine® 150mg Tab	Aspen Stavudine® 20mg Cap	Aspen Stavudine® 30mg Cap	Stocrin® 200mg Cap	Stocrin® 50mg Cap	1	358.16	-	358.16

4.10.2.5 Five antiretroviral medicine items per prescription

4.10.2.5.1 Top 16 combinations of 5 ARVs per prescription according to total cost for 2005

The same combinations that were present among the top 16 according to frequency were also present among the top 16 prescriptions with 5 ARVs in combination ranked according to total cost during 2005 (*refer to table 4.63 and table 4.52*).

The combination prescription of five ARVs that had the highest total cost was Aspen Didanosine[®] 100mg + Aspen Didanosine[®] 150mg + Aspen Stavudine[®] 40mg cap + Crixivan[®] 400mg cap + Norvir[®] 100mg cap at R4 541.20, which represented 16.47 per cent of the total cost of the top 16 prescriptions with 5 ARVs in combination (n = R27 568.68) during 2005 (*refer to table 4.63*).

Only 16 different **combinations for five ARVs** were claimed through 36 prescriptions during 2005 (*refer to section 4.9.1.5.1*).

Prescriptions for the combinations **3NRTI + 2PI + NNRTI** (n = 1) and **3NRTI + PI** (n = 1) represented 6.25 per cent each of the top 16 prescriptions for five ARVs claimed during 2005. Prescriptions for **2NRTI + 2PI + NNRTI** (n = 2) represented 12.5 per cent, **3NRTI + NNRTI** (n = 3) represented 18.75 per cent, and **2NRTI + NNRTI** (n = 4) represented 25 per cent of the top 16 prescriptions for five ARVs claimed during 2005. Prescriptions for the combination **2NRTI + 2PI** (n = 5) constituted 31.25 per cent of the top 16 prescriptions for five ARVs claimed during 2005.

Table 4.64 Top 16 combinations of 5 ARVs per prescription according to total cost for 2006

ARV medicine item 1 [®]	ARV medicine item 2 [®]	ARV medicine item 3 [®]	ARV medicine item 4 [®]	ARV medicine item 5 [®]	N	Average cost (R)	Standard deviation (R)	Total cost (R)
Aspen Lamivudine [®] 150mg Tab	Aspen Nevirapine [®] 200mg Tab	Aspen Stavudine [®] 40mg Cap	Aspen Zidovudine [®] Syr 50mg/5ml	Retrovir [®] 200mg/20ml Inj	9	697.94	83.38	6 281.50
Aspen Lamivudine [®] 10mg/MI	Aspen Stavudine [®] 15mg Cap	Stocrin [®] 200mg Cap	Stocrin 50mg Cap	Ziagen [®] 100mg/5ml Sol	6	1 031.45	6.53	6 188.69
Aspen Lamivudine [®] 150mg Tab	Aspen Nevirapine [®] 200mg Tab	Aspen Stavudine [®] 30mg Cap	Aspen Zidovudine [®] Syr 50mg/5ml	Retrovir [®] 200mg/20ml Inj	9	621.20	0.00	5 590.80
Aspen Didanosine [®] 100mg	Aspen Didanosine [®] 150mg	Aspen Stavudine [®] 40mg Cap	Crixivan [®] 400mg Cap	Norvir [®] 100mg Cap	5	638.10	2.13	3 190.49
Aspen Stavudine [®] 20mg Cap	Stocrin [®] 200mg Cap	Stocrin [®] 50mg Cap	Videx [®] 25mg Chew	Videx [®] 50mg Chew	6	492.30	11.30	2 953.80
Aspen Lamivudine [®] 150mg Tab	Aspen Stavudine [®] 30mg Cap	Stocrin [®] 200mg Cap	Stocrin [®] 50mg Cap	Ziagen [®] 100mg/5ml Sol	2	1 457.89	23.62	2 915.78
Aspen Lamivudine [®] 150mg Tab	Aspen Stavudine [®] 40mg Cap	Aspen Zidovudine [®] Syr 50mg/5ml	Kaletra [®] 80mg/20mg Cap	Retrovir [®] 200mg/20ml Inj	3	778.02	26.79	2 334.06
Aspen Lamivudine [®] 150mg Tab	Aspen Stavudine [®] 30mg Cap	Aspen Zidovudine [®] Syr 50mg/5ml	Kaletra [®] 80mg/20mg Cap	Retrovir [®] 200mg/20ml Inj	3	739.55	0.00	2 218.65
Aspen Stavudine [®] 40mg Cap	Aspen Zidovudine [®] Syr 50mg/5ml	Kaletra [®] 80mg/20mg Cap	Retrovir [®] 200mg/20ml Inj	Ziagen [®] 300mg Tab	1	1 637.50	-	1 637.50
Aspen Lamzid [®] Tab	Aspen Zidovudine [®] Syr 50mg/5ml	Kaletra [®] 80mg/20mg Cap	Retrovir [®] 200mg/20ml Inj	Retrovir [®] S 50mg/5ml Syr	1	1 239.08	-	1 239.08
Aspen Stavudine [®] 40mg Cap	Kaletra [®] 80mg/20mg Cap	Norvir [®] 100mg Cap	Videx [®] 100mg Chew	Videx [®] 150mg Chew	1	908.06	-	908.06
Aspen Lamivudine [®] 150mg Tab	Aspen Nevirapine [®] 200mg Tab	Aspen Stavudine [®] 40mg Cap	Retrovir [®] 200mg/20ml Inj	Retrovir [®] S 50mg/5ml Syr	1	842.55	-	842.55
3TC [®] 150mg Tab	Aspen Nevirapine [®] 200mg Tab	Retrovir [®] 200mg/20ml Inj	Retrovir [®] S 50mg/5ml Syr	Zerit [®] 40mg Cap	1	824.15	-	824.15
Aspen Didanosine [®] 100mg	Aspen Didanosine [®] 150mg	Aspen Nevirapine [®] 200mg Tab	Aspen Stavudine [®] 40mg Cap	Videx [®] 250mg EC Cap	1	715.26	-	715.26
Aspen Lamivudine [®] 150mg Tab	Aspen Stavudine [®] 40mg Cap	Aspen Zidovudine [®] Syr 50mg/5ml	Retrovir [®] 200mg/20ml Inj	Stocrin [®] 600mg Tab	1	622.93	-	622.93
Aspen Lamzid [®] Tab	Aspen Nevirapine [®]	Aspen Nevirapine [®] 200mg Tab	Aspen Zidovudine [®] 300mg Tab	Aspen Zidovudine [®] Syr 50mg/5ml	1	474.03	-	474.03

4.10.2.5.2 Top 16 combinations of 5 ARVs per prescription according to total cost for 2006

The same combinations that were present among the top 16 according to frequency were also present among the top 16 prescriptions with 5 ARVs in combination ranked according to total cost during 2006 (*refer to table 4.64 and table 4.53*).

The combination prescription of five ARVs that had the highest total cost was Aspen Lamivudine[®] 150mg tab + Aspen Nevirapine[®] 200mg tab + Aspen Stavudine[®] 40mg cap + Aspen Zidovudine[®] syr 50mg/5ml + Retrovir[®] 200mg/20ml inj at R6 281.50, which represented 16.13 per cent of the total cost of the top 16 prescriptions with 5 ARVs in combination (n = R38 937.33) during 2006 (*refer to table 4.64*).

Only 16 different **combinations for five ARVs** were claimed through 51 prescriptions during 2006 (*refer to section 4.9.1.5.2*).

Prescriptions for the combination **2NRTI + 3PI** (n = 1) represented 6.25 per cent, and **2NRTI + 2PI** (n = 2) represented 12.5 per cent of the top 16 prescriptions for five ARVs claimed during 2006. Prescriptions for **2NRTI + NNRTI** (n = 3) and **3NRTI + 2PI** (n = 3) each represented 18.75 per cent of the top 16 prescriptions for five ARVs claimed during 2006. Prescriptions for the combination **3NRTI + NNRTI** (n = 7) constituted 43.75 per cent of the top 16 prescriptions for five ARVs claimed during 2006.

Table 4.65 Top 2 combinations of 6 ARVs per prescription according to total cost for 2005

ARV medicine item 1	ARV medicine item 2	ARV medicine item 3	ARV medicine item 4	ARV medicine item 5	ARV medicine item 6	N	Average cost (R)	Standard deviation	Total cost (R)
Aspen Lamivudine® 10mg/ml	Aspen Lamzid® Tab	Cipla Zidovudine® 100mg Cap	Stocrin® 200mg Cap	Stocrin® 50mg Cap	Stocrin® 600mg Tab	1	1188.27	-	1188.27
Aspen Didanosine® 100mg	Aspen Didanosine® 25mg	Aspen Stavudine® 30mg Cap	Kaletra® 80mg/20mg Cap	Videx® 100mg Chew	Videx® 25mg Chew	1	913.84	-	913.84

4.10.2.6 Six antiretroviral medicine items per prescription

4.10.2.6.1 Top 2 combinations of 6 ARVs per prescription according to total cost for 2005

The same combinations that were present among the top 2 prescriptions with 6 ARVs in combination according to frequency were also present among the top 2 prescriptions ranked according to total cost during 2005 (*refer to table 4.65 and table 4.54*).

The combination prescription of six ARVs that had the highest total cost was **Aspen Lamivudine® 10mg/ml + Aspen Lamzid® tab + Cipla Zidovudine® 100mg cap + Stocrin® 200mg cap + Stocrin® 50mg cap + Stocrin® 600mg tab** at R1 188.27, which represented 56.53 per cent of the total cost of the top 2 prescriptions with 6 ARVs in combination ($n = R2\ 102.11$) during 2005 (*refer to table 4.65*).

Only 2 different **combinations for six ARVs** were claimed through 2 prescriptions during 2005 (*refer to section 4.9.1.6.1*).

Prescriptions for the combinations **2NRTI + NNRTI** ($n = 1$) and **2NRTI + 2PI** ($n = 1$) both represented 50 per cent of the top 2 combinations of six ARVs claimed during 2005.

CHAPTER 5: CONCLUSIONS AND RECOMMENDATIONS

5.1 Introduction

In this chapter the conclusions of the study will be discussed, based on the results of the literature review and the empirical investigation. Recommendations resulting from this study will also be discussed, as well as limitations encountered during the study.

5.2 Conclusions

5.2.1 Literature review

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

*The **first research objective** was to conceptualise the HIV/AIDS pandemic from available literature.*

This was done via systematic appraisal of the literature (*refer to chapter 2*). The extent of the HIV/AIDS epidemic in South Africa, including the spread of the epidemic and the impact of HIV on society (impact on population growth, and social and economic effects) were investigated (*refer to section 2.2*). It was found that HIV has had a progressively severe impact on all sectors of local society from the onset of the South African epidemic, causing major socio-economic problems with far-reaching consequences.

Clinical aspects of HIV were discussed, including the transmission of HIV, patterns of HIV spread, and the stages of HIV disease and disease progression to full-blown AIDS (*refer to sections 2.3, 2.4 and 2.5*). It was established that HIV/AIDS is a devastating disease which may take years to fulminate but inevitably leads to the death of the patient. The nature of HIV makes it a very difficult disease to prevent and treat.

*The **second research objective** was to describe HIV/AIDS treatment protocols and the antiretroviral drugs involved therein.*

A literature study was done reviewing antiretroviral drugs and their classification and mechanism of action. Treatment protocols and indications for ARV therapy were discussed, as well as a brief overview of ARV-ARV interactions (*refer to sections 2.6 to 2.9*). It can be concluded that, even though much progress has been made in developing treatment for HIV/AIDS, no vaccine or cure has been discovered. Presently recommended antiretroviral regimens only suppress viral replication for a limited period of time and currently available therapy is plagued by many factors like drug interactions, side-effects and resistance.

*The **third research objective** was to conceptualise from the literature some pharmacoeconomic principles involved in the South African health care system.*

This was done via an overview of the literature regarding pharmacoeconomic principles such as the classification of cost, types of pharmacoeconomic analyses, quality of life, and drug utilisation review (DUR) (*refer to section 2.11*). It can be concluded that pharmacoeconomics is an extensive subject that has valuable applications in health care, e.g. analysing costs and benefits involved in HIV/AIDS treatment through drug utilisation review.

*The **fourth research objective** was to study the health care system of South Africa and ascertain through the literature how South African medical aid funds approach and manage antiretroviral therapy.*

The literature was investigated on the subject of the South African health care system, health care expenditure in South Africa, and health care concepts. Health insurance and South African medical scheme legislation regarding prescribed minimum benefits and ART were also discussed (*refer to section 2.10*). It was found that there are imbalances between the public and private health care sectors in South Africa regarding distribution of human resources and funding. It can also be concluded that important legislation transformed medical schemes' discriminatory approach to members with HIV/AIDS, preventing rejection of membership on grounds of HIV status and introducing prescribed minimum benefits for the treatment of HIV/AIDS patients.

5.2.2 Empirical investigation

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

*The **fifth research objective** was to determine the usage patterns and cost of drugs in general according to all medicine items and prescriptions in the total medicine claims database for the study period 2005 to 2006.*

General prescribing patterns of ARV medicine items

From 2005 to 2006 there was an increase in the total number of patients, both for the total database and patients receiving antiretroviral therapy (*refer to table 4.1*). The average number of prescriptions per patient per year also showed an increase (practically insignificant) during the two study years for both patients in the total database and patients receiving antiretroviral treatment (*refer to table 4.2*). An increase in the total number of prescriptions was also observed for prescriptions claimed through the total database as well as ARV prescriptions from 2005 to 2006. The average number of medicine items per

prescription claimed through the total database increased during the study period, while the average number of ARV medicine items per prescription decreased from 2005 to 2006 (no practical significance). An increase was also observed in the total number of medicine items claimed for both the total database and ARV medicine items (*refer to table 4.1 and section 4.2.1*).

Both the average cost per ARV medicine item and the average cost per ARV prescription decreased during the study period. However, the average cost per medicine item claimed through the total database stayed unchanged and the average cost per prescription claimed through the total database increased during the two study years (no practical significance) (*refer to table 4.1*). Total prescription cost increased for both the total database and ARV prescriptions from 2005 to 2006. The CPI values of ARV medicine items in comparison with all medicine items indicate that ARV medicine items are relatively expensive (*refer to section 4.2.1*).

It can be concluded that both the prevalence and total medicine cost of ARV medicine items in general have increased during the study period, even though the average number of ARV medicine items per prescription as well as both the average cost per ARV medicine item and the average cost per ARV prescription decreased during the study period.

*The **sixth research objective** was to investigate generic substitution of innovator antiretroviral drugs as well as the costs and possible cost-savings associated with these drugs for the two study years.*

The percentage that original innovator ARV medicine items represented of all ARV medicine items decreased from 2005 to 2006. The percentage that original ARV medicine items with no generic represented of all ARV medicine items increased from 2005 to 2006 and the percentage that generic ARV medicine items represented of all ARV medicine items also increased from 2005 to 2006 (*refer to table 4.4*). It can be concluded that the prevalence of both original ARV medicine items with no generic and generic ARV medicine items increased from 2005 to 2006, while the prevalence of original innovator ARV medicine items decreased during the study period (*refer to section 4.2.2*).

Original innovator ARV medicine items demonstrated the highest average cost per medicine item during 2006 and the average cost per original innovator ARV medicine item increased during the study period. The average cost per generic medicine item also showed an increase during the study period. However, the average cost per original medicine item with no generic decreased during the two study years (none of these changes were practically significant). It can be concluded that the average cost per medicine item of both original

innovator ARV medicine items and generic ARV medicine items increased from 2005 to 2006, while the average cost per medicine item of original ARV medicine items with no generic decreased during the two study years (*refer to section 4.2.2*).

Generic ARV medicine items represented the highest total medicine cost during both study years and an increase was observed in the percentage that generic ARV medicine items represented of total medicine cost (*refer to table 4.4*). An increase was also noticed in the percentage that original ARV medicine items with no generic represented of total medicine cost. Original innovator ARV medicine items represented the lowest total medicine cost during both study years, and a decrease was noted in the percentage that original innovator ARV medicine items represented of total medicine cost (*refer to section 4.2.2*).

It can be concluded that original innovator ARV medicine items and original ARV medicine items with no generic are relatively expensive in comparison with ARV medicine items in general (*refer to table 4.5*). Generic ARV medicine items are relatively inexpensive in comparison with ARV medicine items in general, as indicated by the CPI values. Consequently, generic substitution of ARV medicine items would decrease the total medicine cost.

*The **seventh research objective** was to analyse utilisation patterns and cost of antiretroviral agents and antiretroviral prescriptions in the medicine claims database according to gender, age group, prescriber and provider for the two study years.*

Utilisation patterns and cost of antiretroviral agents and antiretroviral prescriptions in the medicine claims database according to patient gender

The average number of prescriptions per patient per year increased (practically insignificant) for patients of both genders in the total database as well as patients receiving antiretroviral therapy from 2005 to 2006 (*refer to table 4.6*). Female patients received a higher average number of ARV prescriptions per year during the two study years than male patients. The same trend was observed with prescriptions claimed through the total database, as a higher average number of prescriptions per year were claimed for female patients during the study period in comparison with male patients (*refer to section 4.3*).

The total number of prescriptions for female and male patients claimed through the total database showed an increase from 2005 to 2006, and a similar increase was observed for the total number of ARV prescriptions claimed for patients of both genders during the study period (*refer to table 4.6*). The average number of medicine items per prescription decreased (no practical significance) for patients of both genders during the study period. This trend

was observed for both medicine items claimed through the total database as well as ARV medicine items. The total number of medicine items claimed through the total database, as well as ARV medicine items, increased from 2005 to 2006 for both female and male patients (*refer to section 4.3*).

The average cost per medicine item claimed through the total database for female patients decreased during the two study years, while the average cost per medicine item claimed through the total database for male patients increased from 2005 to 2006 (*refer to table 4.6*). In comparison, the average cost of ARV medicine items decreased for patients of both genders during the study period (no practical significance). Interestingly, the average ARV prescription cost decreased for patients of both genders during the study period, while the average cost per prescription claimed through the total database increased from 2005 to 2006 for both female and male patients (practically insignificant). The total cost of all medicine items as well as ARV medicine items increased for patients of both genders 2005 to 2006 (*refer to table 4.6*). CPI values indicated that ARV medicine items are relatively expensive for patients of both genders, albeit marginally more expensive for female patients (*refer to section 4.3 and table 4.7*).

It can be concluded that the average cost of ARV medicine items and prescriptions for both genders decreased from 2005 to 2006, while there was an increase in the prevalence of medicine items and prescriptions claimed for both female and male patients. There was also an increase in the total ARV medicine cost during the study period regarding patients of both genders.

Utilisation patterns and cost of antiretroviral agents and antiretroviral prescriptions in the medicine claims database according to patient age

The largest total number of patients in the total database was represented by the age group >40 to ≤44 years during both 2005 and 2006 (*refer to table 4.16*), while the age group >35 to ≤39 years embodied the largest total number of patients receiving antiretroviral therapy (*refer to table 4.15*) during both study years (*refer to section 4.4*).

The highest total number of ARV prescriptions claimed through the total database was found for patients in the age group >45 to ≤49 years during both study years (*refer to table 4.17*). The age group >35 to ≤39 years represented the highest total number of ARV prescriptions for both study years (*refer to table 4.15*). The lowest total number of ARV prescriptions was found in age group >80 to ≤84 years (*refer to table 4.24*) during 2005 and age group >85 years (*refer to table 4.25*) during 2006 (*refer to section 4.4*).

The age group >45 to ≤49 represented the highest total number of medicine items claimed through the total database during the study period (*refer to table 4.17*). The highest total number of ARV medicine items was claimed for the age group >35 to ≤39 years (*refer to table 4.15*) during the two study years (*refer to section 4.4*).

The highest average number of ARV medicine items per prescription was found in the age group >5 to ≤9 years for both study years (*refer to table 4.9*). The age group >5 to ≤9 years was also representative of the highest average number of ARV prescriptions per patient per year during 2005 and 2006 (*refer to section 4.4*).

The highest average cost per medicine item was denoted by age group >70 to ≤74 years for medicine items claimed through the total database during both study years (*refer to table 4.22*). The highest average cost per ARV medicine item was found in age group >80 to ≤84 years during 2005 (*refer to table 4.24*) and age group >70 to ≤74 years during 2006 (*refer to table 4.22*). The age group >5 to ≤9 years represented the lowest average cost per medicine item claimed through the total database during 2005 (*refer to table 4.9*), and the age group 0 to ≤4 years denoted the lowest average cost per medicine item claimed through the total database during 2006 (*refer to table 4.8*). Age group >10 to ≤14 years represented the lowest average cost per ARV medicine item during both study years (*refer to table 4.10*). The percentage that ARVs claimed for patients in the age group >35 to ≤39 years (*refer to table 4.15*) represented of the total medicine cost was the highest of all the patient age groups for both 2005 and 2006 (*refer to section 4.4*).

The highest average cost per prescription claimed through the total database was represented by the age group >75 to ≤79 years during 2005 (*refer to table 4.23*) and the age group >70 to ≤74 years during 2006 (*refer to table 4.22*). The highest average cost per ARV prescription was found in age group 0 to ≤4 years during 2005 (*refer to table 4.8*) and age group >70 to ≤74 years during 2006 (*refer to table 4.22*). The lowest average cost per prescription claimed through the total database was denoted by age group 0 to ≤4 years during the study period (*refer to table 4.8*). Age group >85 years (*refer to table 4.25*) represented the lowest average cost per ARV prescription during both study years (*refer to section 4.4*).

ARVs were found to be the most expensive for patients in the age group 0 to ≤4 years for both study years according to the CPI values calculated for ARV medicine items claimed for patients in the different age groups (*refer to table 4.26*). The lowest CPI value was shared by the age group >75 to ≤79 years during 2005 and >80 to ≤84 years during 2006, implying that

antiretroviral medicine items were relatively inexpensive for patients in these age groups in comparison with patients in other age groups (*refer to section 4.4*).

It can also be concluded that the prevalence of patients receiving antiretroviral treatment in the private health care sector peaks at the age of >30 to ≤44 years, in comparison with the lower age of >25 to ≤39 years in the public health care sector (*refer to section 4.4*).

Utilisation patterns and cost of antiretroviral agents and antiretroviral prescriptions in the medicine claims database according to the type of prescriber

The highest total number of medicine items was prescribed by general medical practitioners during both study years (*refer to table 4.28*) for all medicine items claimed through the total database as well as ARV medicine items (*refer to section 4.5*).

The highest total number of prescriptions claimed through the total database as well as ARV prescriptions was prescribed by general medical practitioners during both study years (*refer to table 4.28*). General medical practitioners also tended to prescribe the highest average number of medicine items per prescription, for prescriptions claimed through the total database as well as ARV prescriptions during the study period (*refer to section 4.5*).

Medicine items prescribed by other practitioners had the highest average cost of medicine items claimed through the total database during both study years (*refer to table 4.29*). During 2005 ARV medicine items prescribed by other practitioners (e.g. specialists) had the highest average cost per medicine item (*refer to table 4.29*) but during 2006 ARV medicine items prescribed by pharmacies represented the highest average cost per medicine item (*refer to table 4.30*). The average cost of ARV medicine items prescribed by general medical practitioners as well as other practitioners decreased during the study period, however ARV medicine items prescribed by pharmacies showed an increase in the average cost per item during 2005 and 2006 (no practical significance) (*refer to section 4.5*).

Prescriptions claimed through the total database as well as ARV prescriptions representing the highest average cost per prescription were prescribed by other practitioners during both study years (*refer to section 4.5*).

General medical practitioners represented the type of prescriber that denoted the highest total medicine cost during the study period for medicine items claimed through the total database as well as ARV medicine items. The total ARV medicine cost prescribed by general medical practitioners and other prescribers, and the percentage that those ARVs represented of the total medicine cost increased from 2005 to 2006, but the total ARV medicine cost prescribed by general pharmacies and the percentage that those ARVs represented of the

total medicine cost decreased during the study period (*refer to section 4.5*). The CPI values of ARVs calculated according to prescriber illustrate that ARV medicine items prescribed by pharmacies are relatively expensive compared to ARV medicine items prescribed by general medical practitioners and other practitioners (*refer to table 4.31*).

General medical practitioners prescribed the highest average number of prescriptions claimed through the total database per patient per year during both study years, while the highest average number of ARV prescriptions per patient per year was prescribed by other prescribers during the study period (*refer to table 4.32*). The highest total number of ARV prescriptions was prescribed by general medical practitioners during both study years. The percentage that ARVs prescribed by general medical practitioners and other practitioners represented of all prescriptions increased during the study period. In turn, the percentage that ARVs prescribed by pharmacies represented of all prescriptions decreased during the study period (*refer to section 4.5*).

Thus it can be concluded that the majority of ARV medicine items are prescribed by general medical practitioners, and that the (illegal) practice of ARV medicine items being prescribed by pharmacies is decreasing (this should be further investigated).

Utilisation patterns and cost of antiretroviral agents and antiretroviral prescriptions in the medicine claims database according to the type of provider

The highest total number of both medicine items claimed through the total database and ARV medicine items was provided by pharmacies during both study years (*refer to table 4.35*). The percentage of all medicine items represented by ARV medicine items provided by general medical practitioners increased during the study period (*refer to table 4.33*) and the percentage of all medicine items represented by ARV medicine items provided by pharmacies increased during the two study years (*refer to table 4.35*). In contrast, the percentage that ARV medicine items provided by other providers (*refer to table 4.34*) represented of all medicine items decreased (*refer to section 4.6*).

The highest average number of medicine items per prescription claimed through the total database was provided by general medical practitioners during both study years (*refer to table 4.33*). In contrast, pharmacies provided the highest average number of ARV medicine items per prescription during the study period (*refer to table 4.35*).

The highest average cost per medicine item claimed through the total database during 2005 was found for prescriptions provided by other practitioners (no ARV medicine items were provided by other practitioners during 2006), and during 2006 the highest average cost per

medicine item claimed through the total database was found for prescriptions provided by pharmacies. The highest average cost per ARV medicine item during 2005 was also found for prescriptions provided by other practitioners, but during 2006 the highest average cost per ARV medicine item was found for prescriptions provided by general medical practitioners (*refer to section 4.6*).

The highest average cost per prescription claimed through the total database was observed for prescriptions provided by other practitioners during both study years (*refer to table 4.34*). The highest average cost per ARV prescription was represented by prescriptions provided by other practitioners during 2005 (*refer to table 4.34*) and pharmacies during 2006 (*refer to table 4.35*).

Pharmacies represented the type of provider that denoted the highest total medicine cost during the study period for medicine items claimed through the total database as well as ARV medicine items. The total medicine cost for ARVs provided by general medical practitioners and pharmacies, and the percentage that those ARVs represented of the total medicine cost increased from 2005 to 2006, but the total ARV medicine cost provided by other practitioners and the percentage that those ARVs represented of the total medicine cost decreased during the study period, since no ARV medicine items were provided by other practitioners during 2006 (*refer to section 4.6*). The CPI values of ARVs calculated according to provider demonstrate that ARV medicine items provided by general medical practitioners are relatively expensive compared to ARV medicine items prescribed by pharmacies and other practitioners (*refer to table 4.36*).

Pharmacies provided the highest average number of prescriptions claimed through the total database per patient per year during the study period. The highest average number of ARV prescriptions per patient per year was provided by general medical practitioners during 2005 and by pharmacies during 2006 (*refer to table 4.38*).

The highest total number of prescriptions was provided by pharmacies during both study years (both for prescriptions claimed through the total database as well as ARV prescriptions). The percentage that ARVs provided by pharmacies and general medical practitioners represented of all prescriptions increased during the study period. In turn, the percentage that ARVs provided by other practitioners represented of all prescriptions decreased during the study period, given that no ARVs were provided by other practitioners during 2006 (*refer to section 4.6*).

Thus it can be concluded that the majority of ARV medicine items were dispensed by pharmacies (community or private institutional pharmacies).

Utilisation patterns and cost of antiretroviral agents and antiretroviral prescriptions in the medicine claims database according to the type of medicine and patient age group

The lowest percentage of original ARV medicine items with no generic was found in both the age groups >80 to ≤84 years and >85 years during 2005. During 2006 the lowest percentage of original ARV medicine items with no generic was found in the age group >85 years (*refer to table 4.39*). The lowest percentage of original innovator ARV medicine items was found in the age groups >80 to ≤84 years during 2005. During 2006 the lowest percentage of original innovator ARV medicine items was found in the age group >75 to ≤79 years (*refer to table 4.40*). The lowest percentage of generic ARV medicine items was found in the age group >80 to ≤84 years during 2005. During 2006 the lowest percentage of generic ARV medicine items was found in the age group >85 years (*refer to table 4.41*). It can be concluded that the prevalence of all types of ARV medicine items was the lowest in the geriatric age groups ranging from >75 to >85 years (*refer to section 4.4*).

The highest percentage of original ARV medicine items with no generic was found in the age group >35 to ≤39 years during 2005. During 2006 the highest percentage of original ARV medicine items with no generic was also found in the age group >35 to ≤39 years (*refer to table 4.39*). The highest percentage of original innovator ARV medicine items was found in the age group >35 to ≤39 years during 2005. During 2006 the highest percentage of original innovator ARV medicine items was found in the age group >40 to ≤44 years (*refer to table 4.40*). The highest percentage of generic ARV medicine items was found in the age group >35 to ≤39 years during 2005. During 2006 the highest percentage of generic ARV medicine items was also found in the age group >35 to ≤39 years (*refer to table 4.41*). It can be concluded that the prevalence of all types of ARV medicine items was the highest in the age group ranging from >35 to ≤44 years (*refer to section 4.4*).

ARV medicine items claimed for patients in the age group >35 to ≤39 years represented the highest percentage of the total medicine cost incurred during both study years for all ARV medicine types.

Utilisation patterns and cost of antiretroviral agents and antiretroviral prescriptions in the medicine claims database according to the type of medicine and patient gender

The highest percentage of all types of ARV medicine items was observed for female patients during the study period (*refer to table 4.42*). ARV medicine items claimed for female patients also represented the highest total cost of all types of ARV medicine items (*refer to section 4.3*).

It can be concluded that the prevalence and the cost of all types of ARV medicine items are higher for female patients in general.

*The **eighth research objective** was to identify combination therapy of antiretroviral drugs and determine the costs associated with these combinations for 2005 and 2006.*

Prescriptions for one NRTI were dominant, representing 50 per cent of the top 20 prescriptions for one ARV medicine item during both 2005 and 2006 (*refer to section 4.9.1.1*). The combination 2NRTI + NNRTI represented 40 per cent and 45 per cent of the top 20 prescriptions for two ARVs claimed during 2005 and 2006 respectively (*refer to section 4.9.1.2*). Prescriptions for 2NRTI + NNRTI in combination represented 80 per cent and 75 per cent of the top 20 prescriptions for three ARVs claimed during 2005 and 2006 respectively (*refer to section 4.9.1.3*). Prescriptions for the combination 2NRTI + NNRTI represented 80 per cent of the top 20 prescriptions for four ARVs claimed during both study years (*refer to section 4.9.1.4*). Prescriptions for 2NRTI + 2PI combinations represented 37.50 per cent of the top 16 prescriptions for five ARVs claimed during 2005, while combinations of 3NRTI + NNRTI represented 43.75 per cent of the top 16 prescriptions for five ARVs claimed during 2006 (*refer to section 4.9.1.5*). The combination 2NRTI + NNRTI represented 50 per cent and 2NRTI + 2PI also represented 50 per cent of the top 2 prescriptions for six ARVs claimed during 2005 (*refer to section 4.9.1.6*).

It can be concluded that combinations of 2NRTI + NNRTI are prescribed at the highest frequency, which is in accordance with traditional HAART or 'triple therapy' (*refer to section 2.7.3.1*).

Combination prescription compliance with the South African National Antiretroviral Treatment Guidelines for adults

None of the top 20 prescriptions for one ARV medicine item was compliant with the National Antiretroviral Treatment Guidelines, thus implying that the totals of R590 815.99 and R880 957.68 (representing 100.00 per cent of the top 20 prescriptions for one ARV medicine item claimed during both study years) were claimed for noncompliant prescriptions (*refer to tables 4.44 and 4.45*).

None of the top 20 prescriptions for two ARV medicine items was compliant with the National Antiretroviral Treatment Guidelines, thus implying that the totals of R12 568 087.33 and R19 429 213.61 (representing 100.00 per cent of the top 20 prescriptions for two ARVs claimed during both study years) were claimed for noncompliant prescriptions (*refer to tables 4.46 and 4.47*).

Of the top 20 prescriptions for three ARV medicine items, 92.67 per cent (n = 17 492) and 89.94 per cent (n = 31 813) were compliant with the National Antiretroviral Treatment Guidelines during 2005 and 2006, thus implying that the totals of R922 397.87 and R1 343 021.02 (representing 11.39 per cent and 9.71 per cent of the top 20 prescriptions for three ARVs claimed during 2005 and 2006) were claimed for noncompliant prescriptions (*refer to tables 4.48 and 4.49*).

Of the top 20 prescriptions for four ARV medicine items, 49.60 per cent and 36.11 per cent were compliant with the National Antiretroviral Treatment Guidelines during the two study years, thus implying that the totals of R150 892.04 and R706 200.73 (representing 62.03 per cent and 77.22 per cent of the top 20 prescriptions for four ARVs claimed during 2005 and 2006) were claimed for noncompliant prescriptions (*refer to tables 4.50 and 4.51*).

Of the top 16 prescriptions for five ARV medicine items, 5.56 per cent and 3.92 per cent were compliant with the National Antiretroviral Treatment Guidelines during the two study years, thus implying that the totals of R26 343.61 and R36 021.55 (representing 95.56 per cent and 92.51 per cent of the top 16 prescriptions for five ARVs claimed during 2005 and 2006) were claimed for noncompliant prescriptions (*refer to tables 4.52 and 4.53*).

None of the top 2 prescriptions for six ARV medicine items was compliant with the National Antiretroviral Treatment Guidelines, thus implying that a total of R2 102.11 (representing 100.00 per cent of the top 2 prescriptions for six ARVs claimed during 2005) was claimed for noncompliant prescriptions (*refer to table 4.54*).

ARV combinations ranked number one according to frequency and total cost

The same ARV medicine item combinations were ranked first (top) according to frequency and total cost (*refer to table 5.1*) for prescriptions for one, two and three ARV medicine items respectively during both study years, demonstrating an increase in the percentage the combinations represented of the total ARV medicine cost as well as the total number of ARV prescriptions claimed during the specific study year (*refer to sections 4.9.1.1 to 4.9.1.3 and 4.9.2.1 to 4.9.2.3*).

For prescriptions containing four ARV medicine items, the same combination was ranked first according to both frequency and total cost during 2005 (*refer to table 5.1*). However, two different combinations were ranked first according to frequency and total cost during 2006 (*refer to sections 4.9.1.4 and 4.9.2.4*).

The same combination of five ARV medicine items in combination which ranked highest according to frequency during 2005 also ranked highest according to total cost during 2005,

and a different combination ranked highest according to both frequency and total cost during 2006 (*refer to table 5.1 as well as sections 4.9.1.5 and 4.9.2.5*).

During 2005 the same combination of six ARV medicine items was ranked highest according to both frequency and total cost (*refer to table 5.1 and sections 4.9.1.6 and 4.9.2.6*).

Table 5.1 ARV combinations ranked number one according to frequency and total cost for 2005 and 2006

Number of ARV medicine items in combination per prescription	2005				2006			
	First ranking combination according to frequency	%*	First ranking combination according to total cost	%**	First ranking combination according to frequency	%*	First ranking combination according to total cost	%**
1	Kaletra® 80mg/20mg Cap	0.98	Kaletra® 80mg/20mg Cap	0.65	Kaletra® 80mg/20mg Cap	1.35	Kaletra® 80mg/20mg Cap	0.98
2	Aspen Lamzid® tab Stocrin® 600mg tab	20.16	Aspen Lamzid® tab Stocrin® 600mg tab	22.08	Aspen Lamzid® tab Stocrin® 600mg tab	23.21	Aspen Lamzid® tab Stocrin® 600mg tab	26.25
3	Aspen Lamivudine® 150mg tab Aspen Stavudine® 40mg cap Stocrin® 600mg tab	18.67	Aspen Lamivudine® 150mg tab Aspen Stavudine® 40mg cap Stocrin® 600mg tab	14.45	Aspen Lamivudine® 150mg tab Aspen Stavudine® 40mg cap Stocrin® 600mg tab	18.74	Aspen Lamivudine® 150mg tab Aspen Stavudine® 40mg cap Stocrin® 600mg tab	14.68
4	Aspen Lamivudine® 150mg tab Retrovir® 100mg cap Stocrin® 200mg cap Stocrin® 50mg cap	0.30	Aspen Lamivudine® 150mg tab Retrovir® 100mg cap Stocrin® 200mg cap Stocrin® 50mg cap	0.31	Aspen Didanosine® 100mg Aspen Didanosine® 150mg Aspen Stavudine® 40mg cap Stocrin® 600mg tab	0.36	Aspen Lamzid® tab Aspen Zidovudine® syr 50mg/5ml Kaletra® 80mg/20mg cap Retrovir® 200mg/20ml inj	0.50
5	Aspen Didanosine® 100mg Aspen Didanosine® 150mg Aspen Stavudine® 40mg cap Crixivan® 400mg cap Norvir® 100mg cap	0.014	Aspen Didanosine® 100mg Aspen Didanosine® 150mg Aspen Stavudine® 40mg cap Crixivan® 400mg Norvir® 100mg cap	0.017	Aspen Lamivudine® 150mg tab Aspen Nevirapine® 200mg tab Aspen Stavudine® 30mg cap Aspen Zidovudine® syr 50mg/5ml Retrovir® 200mg/20ml inj	0.011	Aspen Lamivudine® 150mg tab Aspen Nevirapine® 200mg tab Aspen Stavudine® 40mg cap Aspen Zidovudine® syr 50mg/5ml Retrovir® 200mg/20ml inj	0.016
6	Aspen Didanosine® 100mg Aspen Didanosine® 25mg Aspen Stavudine® 30mg cap Kaletra® 80mg/20mg cap Videx® 100mg chew Videx® 25mg chew	0.002	Aspen Lamivudine® 10mg/ml Aspen Lamzid® tab Cipla Zidovudine® 100mg cap Stocrin® 200mg cap Stocrin® 50mg cap Stocrin® 600mg tab	0.005				

* percentage of the total number of ARV prescriptions claimed during the specific study year

** percentage of total ARV medicine cost during the specific study year

5.3 Limitations and shortcomings of this study

The following limitations and shortcomings should be taken into account when evaluating the results and conclusions of this study:

- All the data obtained from the pharmacy benefit management company database were considered to be accurate and correct.
- External validity is limited, implying that the results can only be generalised to the specific database and study population.
- Demographic data were limited to patient age and gender.
- Certain patients were not classified in age groups as their age was not recorded in the data, and those “unknown” patient data were excluded from calculations.
- Certain patients’ gender was not recorded in the data, and those “unknown” patient data were excluded from calculations.
- Results regarding ARV medicine item combinations were discussed based only on adult antiretroviral treatment guidelines and the possible clinical effectiveness of noncompliant combinations was not investigated or taken into account.

5.4 Recommendations

Due to the limited nature, extent and scope of this study it is recommended that the following issues should be addressed:

- Detailed analysis of ARV prescribing patterns according to patient demographic factors such as age and gender fall outside the scope of this study, and should be further investigated.
- A more detailed study regarding prescribing of combinations of ARV medicine items should be conducted. Possible angles to be investigated could include cost-savings, patient age group and appropriate dosage, drug-drug interactions and overlapping side-effects.
- A more in-depth analysis should be done which takes into account recommended paediatric treatment guidelines and treatment guidelines for patients with concomitant conditions or adverse drug reactions.

- Appropriate data systems and strategies to monitor ARV usage and prescribing patterns should be developed and implemented in the South African public and private health care sectors.
- Corrective intervention strategies for prescribers and providers should be formulated and put into practice to ensure appropriate prescribing and dispensing of antiretroviral therapy.

5.5 Chapter summary

The conclusions and recommendations resulting from this study were outlined in this chapter. Limitations and shortcomings encountered during the study were conveyed, and recommendations that were derived after completion of the study were suggested.

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