A retrospective analysis of the prescribing patterns of hipolipidaemic drugs: A pharmacoeconomic approach

J. BLOEM

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12768340

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Supervisor: Mrs J.R. Burger

Co-supervisor: Prof. M.S. Lubbe

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IT IS OUR LIGHT NOT OUR DARKNESS THAT MOST FRIGHTENS US

Our deepest fear is not that we are inadequate.

Our deepest fear is that we are powerful beyond measure.

It is our light not our darkness that most frightens us.

We ask ourselves, who am I to be brilliant, gorgeous, talented and fabulous?

Actually, who are you not to be?

You are a child of God.

Your playing small does not serve the world.

There's nothing enlightened about shrinking so that other

people won't feel insecure around you.

We were born to make manifest the glory of God that is within us.

It's not just in some of us; it's in everyone.

And as we let our own light shine, we unconsciously give other people permission to do the same.

As we are liberated from our own fear, Our presence automatically liberates others.

MARIANNE WILLIAMSON

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ABSTRACT

Title: A retrospective analysis of the prescribing patterns of hipolipidaemic drugs: A pharmacoeconomic approach

Keywords: Dyslipidaemia, hipolipidaemic medicine, prevalence, total medicine cost, generic substitution, therapeutic substitution, age, sex, generic indicator, drug utilisation review

Background: More than 5.5 million South Africans aged 30 years and older are at risk of chronic disease by virtue of their triglyceride levels (Maritz, 2006:101). Dyslipidaemia is common in westernized and industrialized communities (Steyn *et al*., 2000:720), especially so for South Africa, where burden of disease data show dyslipidaemia to be the second most prevalent of all the chronic conditions in the country (Council for Medical Schemes, 2006:48). It is therefore no surprise that at 3.3 per cent hipolipidaemics ranked second highest based on prevalence percentage per therapeutic group in the 2005 Mediscor medicines review on South African medical claims data (Bester *et al*., 2005:8-11). Hipolipidaemic drugs subsequently also ranked second highest for expenditure per therapeutic group, achieving a total expenditure of 5.8 per cent.

Objective: The purpose of this study was to characterise the usage and cost of hipolipidaemic drugs in the private health care environment in South Africa based on various categories, including age, sex, prescriber type and generic indicator.

Methods: A quantitative retrospective drug utilisation review was performed using dispensing records from a medicine claims database. Data for a two-year period (1 Jan. 2005 to 31 Dec. 2006) were used. Hipolipidaemic medicine usage was analysed according to five patient age strata: patients younger than 9 years, 10≤ 19 years, 20 ≤ 45 years, 46 ≤ 59 years and older than 59 years.

Basic descriptive statistics such as frequencies and arithmetic mean (average) were used to characterise the study sample, and were calculated using the Statistical Analysis System (SAS®) for Windows 9.1® program (SAS Institute Inc., 2002-2003).

Results: The database consisted of 19 860 593 and 21 473 062 medicine item claims for 2005 and 2006 respectively, at a total cost of R 1 893 376 921.00 (for 2005) and R2 046 944 383.00 (for 2006). Patients receiving hipolipidaemic medicine items represented about 7.2% of the

total number of patients on the database in both 2005 and 2006. About 47% of the study population in both 2005 and 2006 was female, compared to 53% males.

Hipolipidaemics represented between 3.1% (N = 19 860 593) and 3.3% (N = 21 473 062) of the total number of items claimed during the study period. The total cost of hipolipidaemics accounted for between 5.6% (N = R1 893 376 921.00) and 5.8% (N = R2 046 944 383.00) of the total cost of all medications claimed during the study period. The average cost per item of hipolipidaemics was R170.63 ± 70.19 in 2005 compared to R167.08 ± 71.93) in 2006.

HMG-CoA reductase inhibitors formed the leading therapeutic class in hipolipidaemic medicine items in all age groups on the database, except for children aged 0≤ 9 years, where the "others" group, in particular cholestyramine (Questran Lite 4 mg) was claimed more frequently. Of the items claimed for both study periods, simvastatin was the most commonly claimed, accounting for 45.35% (n = 284 232) and 46.21% (n = 325 970) respectively of the number of hipolipidaemic items claimed, at a total cost of 30.97% (n = R33 119 294.18) and 31.38% (n = R36 983 938.41) for 2005 and 2006 respectively.

Non-substitutable and generic hipolipidaemic medicine items carried the largest percentage of prevalence and cost in both study periods for both sex categories and all age groups. The majority of claims for hipolipidaemic medicine items were prescribed by general medical practitioners, followed by "other prescribers" and then by cardiologists. Only a small number of prescriptions claimed were prescribed by thoracic surgeons and even fewer by pharmacotherapists and pharmacists. Trade name products that were mostly prescribed were Lipitor and Adco-Simvastatin.

Of all the hipolipidaemic drugs utilised on the database, only three active ingredients (bezafibrate, simvastatin and pravastatin) had generic equivalents available at the time of the study. With total substitution (100%) of these three drugs with the average price of the available generic hipolipidaemic equivalents on the database, a cost saving of R1 744 462.27 or 1.63% (N = R106 943 348.53) was possible in 2005. In 2006, a total cost saving of R1 526 985.79 or 1.30% (N = R117 862 631.87) was calculated.

Conclusion: The study highlighted the most commonly prescribed hipolipidaemics within a sub-population of South African patients. The high average cost per prescription of hipolipidaemic drugs indicates that they are relatively expensive in comparison to other medications. Generic (and therapeutic) substitution should be investigated as potential cost-saving mechanisms in the private health care sector of South Africa.

OPSOMMING

Titel: 'n Retrospektiewe ontleding van die voorskrifpatrone van hipolipidemiese middels: 'n farmako-ekonomiese benadering

Sleutelwoorde: dislipidemie, hipolipidemiese medisyne, voorkoms, totale koste van medisyne, generiese vervanging, terapeutiese vervanging, ouderdom, geslag, generiese aanwyser, medisyneverbruiksevaluering

Agtergrond: Meer as 5.5 milljoen Suid-Afrikaners van 30 jaar en ouer loop 'n risiko vir chroniese siektes vanweë hulle trigliseriedvlakke (Maritz, 2006:101). Dislipidemie kom algemeen in Westerse en geïndustrialiseerde gemeenskappe voor (Steyn *et al*., 2000:720), en veral in Suid-Afrika waar die oorwig van data oor siektes toon dat dislipidemie die tweede mees algemene chroniese toestand in die land is (Raad vir Mediese Skemas, 2006:48). Dit verbaas dus nie dat hipolipidemiese middels teen 3.3 persent die tweede grootste voorkoms per terapeutiese groep het in die databasis van Mediscor vir 2005 oor eise vir medisyne in Suid-Afrika nie (Bester *et al*., 2005:8-11). Hipolipidemiese medisyne is met 'n uitgawe van 5.8 persent gevolglik ook in die tweede plek vir die grootste uitgawe per terapeutiese groep.

Doel: Die doel van hierdie studie was om die gebruik en koste van hipolipidemiese medisyne in die private gesondheidsorgomgewing in Suid-Afrika op grond van verskillende kategorieë, waaronder ouderdom, geslag, tipe voorskrywer en generiese aanwyser, te karakteriseer.

Metodes: 'n Kwantitatiewe retrospektiewe studie van gebruik van medisyne is gedoen deur die voorskrifrekords uit 'n databasis van eise te gebruik. Data van 'n periode van twee jaar (1 Jan. 2005 tot 31 Des. 2006) is gebruik. Gebruik van hipolipidemiese medisyne is volgens vyf ouderdomsgroepe van pasiënte ontleed: jonger as 9 jaar, 10 ≤ 19 jaar, 20 ≤ 45 jaar, 46 ≤ 59 jaar en ouer as 59 jaar.

Basiese beskrywende statistiek, soos frekwensies en rekenkundige gemiddeld, is gebruik om die studiemonster te karakteriseer, en is met die Statistical Analysis System (SAS®) for Windows 9.1®-program bereken.

Resultate: Die databasis het 19 860 593 en 21 473 062 eise vir medisyne vir 2005 en 2006 onderskeidelik, met 'n totale koste van R 1 893 376 921.00 (vir 2005) en R2 046 944 383.00 (vir 2006) gehad. Pasiënte wat hipolipidemiese medisyne ontvang het, het vir sowel 2005 as 2006

7.2% van die totale aantal pasiënte in die databasis uitgemaak. Ongeveer 47% van die studiepopulasie in sowel 2005 as 2006 was vroulik en 53% manlik.

Hipolipidemiese middels het 3.1% (N = 19 860 593) tot 3.3% (N = 21 473 062) van die totale aantal items uitgemaak wat tydens die studieperiode geëis is. Die totale koste van hierdie middels was 5.6% (N = R1 893 376 921.00) tot 5.8% (N = R2 046 944 383.00) van die totale koste van alle medikasie wat tydens die studieperiode geëis is. Die gemiddelde koste van hipolipidemiese middels per item was R170.63 ± 70.19 in 2005 teenoor R167.08 ± 71.93 in 2006.

HMG-CoA-reduktaseremmers was die belangrikste klas terapeutiese hipolipidemiese middels vir alle ouderdomsgroepe in die databasis, behalwe vir kinders van 0 ≤ 9 jaar, waar die groep "ander", en veral cholestiramien (Questran Lite 4 mg), meer dikwels geëis is. Simvastatien met 45.35% (n = 284 232) en 46.21% (n = 325 970) onderskeidelik van die totale aantal hipolipidemiese middels, was die item wat in 2005 en 2006 die meeste geëis is met 'n totale koste van 30.97% (n = R33 119 294.18) en 31.38% (n = R36 983 938.41) onderskeidelik in die studieperiodes.

Nie-vervangbare en generiese hipolipidemiese medisyne het in albei studieperiodes die grootste persentasie van sowel voorkoms en koste vir albei geslagte en alle ouderdomsgroepe uitgemaak. Die meeste hipolipidemiese medisyne-items is deur algemene praktisyns voorgeskryf, gevolg deur "ander voorskrywers" en dan deur kardioloë. Slegs 'n klein aantal voorskrifte wat geëis is, is deur torakschirurge en nog minder deur farmakoterapeute en aptekers voorgeskryf. Die handelsname wat die meeste voorgeskryf was, was Lipitor en Adco-Simvastatin.

Van al die hipolipidemiese middels in die databasis, het slegs drie aktiewe bestanddele (besafibraat, simvastatien en pravastatien) ten tye van die studie generiese ekwivalente gehad. Met totale vervanging (100%) van hierdie drie middels met die gemiddelde prys van die beskikbare hipolipidemiese ekwivalente in die databasis was 'n kostebesparing van R1 744 462.27 of 1.63% (N = R106 943 348.53) in 2005 moontlik. Vir 2006 is 'n totale kostebesparing van R1 526 985.79 of 1.30% (N = R117 862 631.87) bereken.

Gevolgtrekking: Die studie het die mees algemeen voorgeskryfde hipolipidemiese middels vir 'n sub-populasie van Suid-Afrikaanse pasiënte uitgelig. Die hoë gemiddelde koste van hierdie middels per voorskrif toon dat hulle vergeleke met ander medisyne relatief duur is. Generiese (en terapeutiese) vervanging as moontlike meganismes vir kostebesparing in die private gesondheidsorgomgewing in Suid-Afrika moet ondersoek word.

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CHAPTER 1

INTRODUCTION AND PROBLEM STATEMENT

1.1 INTRODUCTION

This dissertation focuses on the prescribing patterns and cost of hipolipidaemic drugs in South Africa. In this chapter the problem statement, background and rationale for the study, research objective, research methodology, terms and definitions, abbreviations and the division of further chapters will be discussed. A layout of the division of chapters is given at the end of this chapter.

1.2 PROBLEM STATEMENT

Dyslipidaemia is common in westernised and industrialised communities (Steyn *et al.,* 2000:720), especially so for South Africa, where burden of disease data show dyslipidaemia to be the second most prevalent of all the chronic conditions in South Africa (Council for Medical Schemes, 2005:61). It is therefore no surprise that hipolipidaemics ranked second highest based on prevalence percentage per therapeutic group in the 2005 Mediscor medicines review on South African medical claims data at 3.3 per cent (Bester *et al*., 2005:8). Hipolipidaemic drugs subsequently ranked second highest for expenditure per therapeutic group, achieving a total expenditure of 5.8 per cent. Lipitor (atorvastatin) 10mg and 20mg ranked highest and second highest respectively on the top 50 list by contributing to total expenditure of 2005 in this report (Bester *et al*., 2005:8-11).

Drug utilisation review has emerged in response to the needs to control both cost and the quality of medication usage (Chrischilles *et al.,* 1996:172). The principal aim of drug utilisation research is to facilitate the rational use of drugs in populations (WHO, 2003a:9) and at the same time to reduce needless expenditure and improve the quality of care (Chrischilles *et al*., 1996:172). McMurray (1999:2) stated that pharmacoeconomic analysis of the management as well as impediment strategies for coronary heart diseases is a valuable tool for comparing the cost-effectiveness of new medical interventions allowing health care decision makers to contain cost by choosing those interventions that are most efficient. Intervention by means of medication / drugs is imperative and in the case of lowering cholesterol levels, it involves a large population of patients and potentially high costs (Johannesson *et al.,* 1997:332). Drug

utilisation review research and pharmacoeconomic studies conducted on the use of hipolipidaemics in the private health care sector of South Africa could therefore, potentially, aid in controlling the cost of hipolipidaemics, ensuring quality care and rational drug usage.

1.3 BACKGROUND AND RATIONALE FOR THE STUDY

Dyslipidaemia is defined as a disorder of the lipoprotein metabolism, described by an overproduction or deficiency in lipoprotein. Dyslipidaemias may manifest as an elevation of the total cholesterol (TC); or elevated low-density lipoprotein (LDL) cholesterol and triglyceride (TG) concentrations; or a decrease in the high-density lipoprotein (HDL) cholesterol concentrations in the blood (Ahmed *et al*., 1998; Berger & Marais, 2000:164).

Different types of dyslipidaemia can be identified, e.g. Type I to Type IV. These types include: dysbetalipoproteinaemia, exogenous hypertriglyceridaemia, familial hyperglyceridaemia, fat-induced hyperlipidaemia, familial hypercholesterolaemia, endogenous hypertriglyceridaemia, mixed hypertriglyceridaemia and mixed hyperlipidaemia (Anderson, 2002:845).

Familial hypercholesterolaemia (FH) is "*an autosomal dominant disorder that causes severe elevations in total cholesterol and low-density lipoprotein cholesterol*" (Citkowitz, 2006). Gender wise, the gene for FH is on the 19th chromosome, thus the inheritance pattern is the same for males and females although severe hypercholesterolaemia manifests earlier in males than in females. Non-familial hypercholesterolaemia, however, is more common in men younger than 55 and in women older than 55 years of age (Citkowitz, 2006).

Data that were collected by Maritz (2006:101) show that at least 1.5 million African people aged 30 years and older are hypercholesterolaemic. Familial Hypercholesterolaemia (FH) in particular, is very common in the Afrikaner (white) population group. Its prevalence is estimated to be 1:72 compared to 1:500 worldwide (Maritz, 2006:102). Older women were furthermore found to have hypercholesterolaemia more frequently than older men (Maritz, 2006:101).

The study conducted by Maritz (2006:101) indicates that more than 5.5 million South Africans aged 30 years and older carry a risk for chronic disease by virtue of their TC level. Dyslipidaemia also plays an important role in other diseases, e.g. diabetes mellitus (DM), hypertension, angina, stroke, cardiac ischemia, coronary artery disease (atherosclerosis) and pancreatitis (Kromhout, 1999:796-802).

Dyslipidaemia itself causes no symptoms though it can lead to symptomatic vascular disease (coronary artery disease and peripheral arterial disease), and high TGs (> 1000 mg/dℓ or > 11.3

mmol/ℓ) can cause acute pancreatitis (Baron; 2007:1276; Berger & Marais, 2000:168; Bhatnagar, 1998:213). High levels of LDL can cause eyelid xanthelasmas; arcus corneae; and tendinous xanthomas found at the achilles, elbow, and knee tendons and over metacarpophalangeal joints (Anon., 2005). Patients with homozygous familial hypercholesterolaemia may have the above findings plus planar or cutaneous xanthomas. Patients with severe elevations of TGs can have eruptive xanthomas over the trunk, back, elbows, buttocks, knees, hands, and feet (Anon., 2005). Patients with the rare dysbetalipoproteinaemia may manifest with palmar and tuberous xanthomas. Severe hypertriglyceridaemia (> 2000 mg/dℓ or > 22.6 mmol/ℓ) can give retinal arteries and veins a creamy white appearance (a condition called lipemia retinalis) (Anon., 2005). Extremely high lipid levels also give a lactescent appearance to blood plasma (Anon., 2005).

According to Gibbon (2008:164) HMG CoA reductase inhibitors (statins) are the foundation of treatment, as they are potent reducers of plasma LDL-cholesterol and have beneficial effects on HDL-cholesterol and triglycerides levels. According to Ridker *et al.* (1999:230-235) fenofibrate, gemfibrozil and niacin are the optimum treatment regimens in patients with elevated triglycerides and low HDL-cholesterol levels. Statins reduce triglycerides 30-40 per cent in general (Ridker *et al*., 1999:230-235). In patients with low HDL-cholesterol, the HDL-cholesterol will be raised 25-30 per cent with the treatment of niacin, compared to gemfibrozil, which raises HDL- cholesterol by 10-15 per cent.

A lowering (rate ratio [RR] 0.88, 95% CI 0.84-0.91; p<0.0001) in LDL- cholesterol is associated with a 12 per cent reduction in all-cause mortality; it has a 19 per cent reduction in cardiovascular heart disease (CHD) mortality and 21 per cent reduction in major vascular events (Baigent *et al.,* 2005:1273).

In developed countries such as Australia and America the treatment and prevention of cardiovascular diseases embody the highest proportion of the total health expenditure by disease group, consisting of hospitalisation and medication costs (American Heart Association, 2004). Hospitalisation contributed 45 per cent (US$109 billion ~ R907 billion)[1] of the estimated (US$241.9 billion ~ R2 trillion) spent on therapy in the United States and 46 per cent (A$2.5 billion ~ R10.8 billion) of the estimated A$5.5 billion (~R23 billion)[2] spent in Australia in 2000 to 2001.

In a recent report by Bester *et al.* (2005:8-11) conducted on South African medical claims data, hipolipidaemic drugs ranked second highest for expenditure per therapeutic group, achieving a

[1] US Dollar = R8.33 (2000 - 2001) (OANDA, 2009).
[2] Australian Dollar = R4.35 (2000 - 2001) (OANDA, 2009).

total expenditure of 5.8 per cent from a possible 74.6 per cent. Lipitor (atorvastatin) 10mg- and 20mg ranked highest and second highest respectively on the top 50 list by contributing to total expenditure of 2005 in this report (Bester *et al*., 2005:8-11).

McMurray (1999:100) stated that pharmacoeconomic analysis of the management as well as impediment strategies for coronary heart diseases is a valuable tool for comparing the cost-effectiveness of new medical interventions allowing health care decision makers to contain cost by choosing those interventions that are most efficient. Intervention by means of medication / drugs is imperative and in the case of lowering cholesterol levels, it involves a large population of patients and potentially high costs (Johannesson *et al.,* 1997:332).

A cost minimisation study that estimated the benefits of lowering cholesterol using data from the 4S-study (Scandinavian Simvastatin Survival Study) show that simvastatin therapy produced a 10 per cent decrease in length of hospital stay, a 26 per cent reduction in number of hospitalisation, a 31 per cent reduction in hospital costs and a 34 per cent reduction in total hospital days. As a result of these savings, the cost of simvastatin was reduced (Pedersen *et al.*, 1996:1796). In a treat-to-target pharmacoeconomic analysis of HMG-CoA reductase inhibitors in hypercholesterolaemia, Hilleman *et al.* (1999:536-562) showed that the most cost-effective treatment approach, was to individualise the selection of statins based on coronary risk.

Ballesteros *et al.* (2001:516) investigated the economic cost generated in one year in primary care because of inadequate (unnecessary) prescriptions of hipolipidaemic agents. It was found that the cost of inadequate prescription for hipolipidaemic drugs reached US$1.1 million (~ R9 million) for quality level one (patients whose age, risk factors, total cholesterol level and low-density lipoprotein cholesterol level were known before pharmacological intervention) and US$38 000 (~ R316 540) for level two (patients whose low-density lipoprotein levels and diet were unknown before pharmacological intervention). It was also found that 12.3 per cent of the health professionals ordered all their prescriptions inadequately. Of the total inadequate prescriptions expenditure, 20.4 per cent represented treatment initiated by family physicians and 35.3 per cent by specialists. Statins made up 78.2 per cent of the total cost and the inadequate expenditure for this therapeutic group reached US$89 000 ~ R741 370). Of the prescriptions for fibrates, 88 per cent were inadequate (Ballesteros *et al*., 2001:513).

Drug utilisation review has emerged in response to the needs to control both cost and the quality of medication usage (Chrischilles *et al.,* 1996:172). The principal aim of drug utilisation research is to facilitate the rational use of drugs in populations (WHO, 2003a:9) and at the same time to reduce needless expenditure and improve the quality of care (Chrischilles *et al*.,

1996:172). All of these can be achieved through the detection of drug interactions, contraindications, overdoses, over-utilisation and under-utilisation (Monane *et al*., 1998:51).

Based on the above discussion it is clear that treatment for lipid-deficiency in South Africa should be a very high priority with any health care organisation, and that such treatment calls for thorough and ongoing investigation and research. Drug utilisation review research and pharmacoeconomic studies conducted on the use of hipolipidaemics in the private health care sector of South Africa could, potentially, aid in controlling the cost of hipolipidaemics, ensuring quality care and providing rational drug usage.

The following questions can be formulated based on the foregoing discussion:

- What does dyslipidaemia entail and what is the significance thereof in the context of South Africa?
- What do drug utilisation review, pharmacoeconomics and managed health care entail, and what role can these play in the "rational" use of hipolipidaemic agents in the private health care sector of South Africa?

1.4 RESEARCH OBJECTIVES

The research of this study will include general and specific objectives.

1.4.1 General research objective

The general research objective of this study was to analyse the usage patterns and cost of hipolipidaemic drugs in South Africa, by utilising data from a South African Pharmaceutical Benefit Management company.

1.4.2 Specific research objectives

In order to achieve the general objective of the study, the following specific objectives needed attention:

- To describe and define the concepts of dyslipidaemia as well as the different types of dyslipidaemia.
- To describe the incidence and prevalence of dyslipidaemia, in worldwide countries as well as South Africa.

- To describe the pathophysiology and significance of dyslipidaemia including the risk for CVD and other diseases and the use of resources.
- To describe the diagnosis, signs and symptoms, as well as the clinical management (both non-pharmacological and pharmacological) of the disease.
- To define managed health care, describe the different types of managed health care plans and concepts within the managed health care framework as well as the application thereof in the South African health care environment.
- To define drug utilisation review and identify the different classifications of drug utilisation review and the types of drug utilisation review.
- To describe the process and units of measurement of drug utilisation review.
- To review the application of drug utilisation review in South Africa.
- To define pharmacoeconomics and the methodology of pharmacoeconomics.
- To describe the objectives of pharmacoeconomics as well the applications thereof in South Africa.
- To review evidence from pharmacoeconomical- and drug utilisation studies on the treatment of dyslipidaemia.
- To define and describe pharmacoepidemiology, the objectives, study designs as well as the application thereof.
- To define and describe evidence-based medicine, its objectives as well as the application thereof.
- To determine the prescribing patterns and cost associated with hipolipidaemic medicine within a section of the private health care sector of South Africa.
- To determine age and sex differences with regard to hipolipidaemic drug usage and cost medicine within a section of the private health care sector of South Africa.
- To determine the prevalence of original medicine items *vs*. generic medicine items for hipolipidaemic medicine within a section of the private health care sector of South Africa.
- To determine the prevalence and cost of the hipolipidaemic active ingredients based on prescribing patterns for the various age- and sex categories within a section of the private health care sector of South Africa.
- To determine the top ten hipolipidaemic trade name products for the various age- and sex categories as well as the type of prescriber within a section of the private health care sector of South Africa.
- To determine the potential cost-savings possible with generic and therapeutic substitution within a section of the private health care sector of South Africa.

1.5 RESEARCH METHODOLOGY

This research consisted of the literature review phase and the empirical investigation phase.

1.5.1 Phase 1: Literature review

According to Neuman (2003:96) a literature study (the use of relevant books, journals and articles) is conducted to express familiarity with a certain topic and to integrate what is already known in a particular field. The books and articles that were consulted for this study enclosed several fields of research, *i.e*. pharmacology (therapeutics and diseases), pharmacy practice (disease management, managed health care, drug utilisation review, pharmacoepidemiology evidence-based medicine) and economics (pharmacoeconomics).

Databases that were consulted during the literature search, included SABINET (SACat), PubMed, EBSCO Host, A-Z list of journals (NWU library), and Science Direct. Electronic search engines that were used included Yahoo (www.yahoo.com) and Google (www.google.com). Books that were used included the Merck manual, Goodman & Gilman's pharmacology, Monthly Index of Medical Specialities (MIMS), South African Medicines Formulary (SAMF), Pharmacotherapy handbook, Current Medical Diagnosis and Treatment, Textbook of Therapeutics, Clinical Pharmacy and Therapeutics, The Managed Health Care Dictionary, Managed Care - What it is and how it works, Introduction to applied Pharmacoeconomics, Case Management - A practical guide to success in managed care, Outcomes Management - Applications to clinical practice, and Fundamentals of Case Management - Guidelines for practicing Case Managers, Risk Management, Managed Care Beware, and Essentials of Managed Health Care.

The literature review is reflected in one of the chapters of this study (refer to paragraph 1.8).

1.5.2 Phase 2: Empirical investigation

The second phase of the research method (the empirical investigation) consisted of various elements, namely the research design, selection of the study population, data analysis, and ethical considerations (the empirical investigation is discussed in detail in chapter 3).

- Research design: a retrospective drug utilisation review was conducted on the data obtained from the database.

- Selection of the study population: The setting for the study was the private health care section of South Africa. The study population consisted of all patients on the database who had received a hipolipidaemic drug [based on MIMS classification (Snyman, 2007:12a)]. The study population was selected from data for a two-year period (starting 1 January 2005 and ending on 31 December 2006).

- Data analysis: The data were analysed by using the Statistical Analysis System® SAS 9.1® (SAS institute Inc., 2006-2007). Microsoft Word® 2000 and Microsoft Excel® 2000 were used in accordance with the SAS system for analysis and processing.

1.6 TERMS AND DEFINITIONS

The following terms (employed in this study) need to be explained:

- **Active ingredient**

An active ingredient is any component of a medicine item intended to provide a pharmacological activity or any other direct effect in the diagnosis, treatment, alleviation or prevention of disease, or to affect the structure or any function of the body of humans or other animals. Active ingredients include those components of the medicine item that may undergo chemical change during the manufacturing of the medicine item and that may be present in the medicine item in a modified form, intended to give the specified activity or effect (FDA, 2007).

- **Medicine item**

The term “medicine item” was used as a synonym for the term “medicine” in the study. Medicine is a substance, or mixture of substances which is accepted as being ethical by medical science and is registered with the South African Medicines Control Council, and it is to be administered or applied for the prevention, treatment or healing of an illness (Medihelp, 2007).

- **Original medicine items**

Original medicine items are the original patented pharmaceutical products (Ball *et al*., 2005). Original medicine items are generally the products that were first authorised worldwide for marketing on the basis of the documentation of their efficacy, safety and quality, according to requirements at the time of authorisation. The original product always has a brand name; this may, however, vary between countries (WHO, 2003b:116). In this study original medicine items may be classified into the following categories: Original patented drugs placed on the market for

further research ("M"), non-substitutable medicine items for which there are no generic items available ("N") and original medicine items, with available generics ("O) (refer to paragraph 4.4.3).

- **Generic medicine items**

Generic medicine items are pharmaceutical products intended to be interchangeable with the original medicine item, manufactured without a licence from the original manufacturer and marketed only after the expiry of the original patent or other exclusivity rights (WHO, 2003b:116). Generic medicine items are required to meet the same pharmacological requirements for the preparation as the original medicine item (Rognehaugh, 1998:91). In this study generic medicine items are classified in the "Y" (Yes, generic equivalent was dispensed) category (refer to paragraph 4.4.3).

- **Patient**

A patient is someone receiving medical attention, treatment, care or medication on prescription by a legal prescriber or another medical professional. The person is usually ill or has been injured and requires medical attention (OED, 2009).

- **Number of prescriptions**

A prescription is a written instruction from a legal prescriber. A "number of prescriptions", therefore, would refer to the number of written instructions from legal prescribers that were claimed during the specific study period. A prescription can contain one or more than one medicine item in South Africa.

- **Total database**

The total database consists of all the prescriptions on the database (containing all medicine items) that were issued to all patients on the database and that were claimed during the specific study periods.

- **Hipolipidaemic medicine**

Hipolipidaemic medicine includes all medicine that is used in the management of hipolipidaemic disorders, classified as pharmacological group 7.7 based on the MIMS® classification system. Hipolipidaemic agents / medicine can be divided into four categories/sub-pharmacological

groups namely: fibrates, HMG-CoA reductase inhibitors (statins), cholesterol absorption inhibitors and "others" (Snyman, 2007:12a).

1.7 ABBREVIATIONS

The following abbreviations are applicable to the study:

LDL = Low-density lipoprotein
HDL = High-density lipoprotein
VLDL = Very low-density lipoprotein
IDL = Intermediate-density lipoprotein
TC = Total cholesterol
TG = Triglycerides
DM = Diabetes Mellitus
CVD = Cardiovascular disease
CHD = Coronary heart disease
WHO = World Health Organization
CPI = Cost Prevalence Index
NCEP = National Cholesterol Education Program
ATP III = Adult Treatment Panel III

1.8 DIVISION OF CHAPTERS

This study was divided into five chapters. Chapter two (literature review) focuses on dyslipidaemia, types of dyslipidaemia and deals with the analysis of usage patterns and cost of hipolipidaemic drugs as well as the contributing factor dyslipidaemia has to other diseases. An overview of the definitions, signs and symptoms, prevalence, pathophysiology and complications of the disease are discussed. The second part of the chapter focuses on managed health care, pharmacoeconomics, drug utilisation review, pharmacoepidemiology and evidence-based medicine with reference to the usage patterns and cost of hipolipidaemic drugs.

Chapter three describes the research method followed in the empirical investigation. In this chapter, a detailed description of the variables and measures used, the analysis and processing of the data, ethical aspects regarding this study and the limitations concerning this study are given.

Chapter four provides an analysis and interpretation of the research results of the empirical investigation and chapter five provides the conclusions and recommendations arrived at.

1.9 CHAPTER SUMMARY

In this chapter the introduction, problem statement, background and rationale for the study, research objectives, research methodology, terms and definitions, abbreviations and the division of chapters have been discussed. The following chapter will entail the literature review for dyslipidaemia, various managed health care concepts, drug utilisation review, pharmacoeconomics, pharmacoepidemiology and evidence based medicine.

CHAPTER 2

DYSLIPIDAEMIA AND THE USE OF HIPOLIPIDAEMICS IN A MANAGED HEALTH CARE ENVIRONMENT

This chapter provides an overview of definitions, risk factors, the pathophysiology, diagnosis and the management of dyslipidaemia. The chapter furthermore reflects on the concepts of managed care, pharmacoeconomics and drug utilisation review, evidence-based medicine and pharmacoepidemiology as well as the application thereof in the treatment of dyslipidaemia.

2.1 DYSLIPIDAEMIA

2.1.1 Introduction

Coronary heart disease (CHD) is one of the primary causes of morbidity and mortality in Western countries (Rodonki, 1999:388). About 7.2 million people die from CHD in worldwide populations every year, more than from cancer, human immune virus (HIV) and infectious causes. In the United States of America (USA) alone, 640 000 deaths can be attributed to CHD (Farnier & Davignon, 1998:4J). Mortality from CVD was the third highest cause of mortality in the world in 1999 (WHO, 1999). Three of the treatable and preventable risk factors for CHD are hypertension, dyslipidaemia, and cigarette smoking. Between 1997 and 2004, 195 people died per day because of some form of heart and blood vessel disease in South Africa (Steyn, 2007:2).

Until the mid-1990s, the importance of dyslipidaemia as a risk factor for CHD was controversial, as was the use of lipid lowering treatment (Raynor & Scarborough, 2005:154). In recent years, more emphasis has been placed on the management of cholesterol, primarily through lifestyle modifications and drug therapy (Farnier & Davignon, 1998:4J).

While the number of individuals with dyslipidaemia is difficult to estimate, a national survey of approximately 10 000 individuals aged 16 years or over in the UK found that more than 67 per cent had total cholesterol ≥ 5 mmol/ℓ (193.5 mg/dℓ) and 27 per cent had a total cholesterol:HDL-cholesterol ratio of ≥ 5.0 (Primatesta & Poulter, 2000:1322). An estimated 98.6 million adults in the USA have total blood cholesterol values of 200 mg/dℓ and higher, and of these about 34.4 million American adults have levels of 240 or above (AHA, 2009).

Risks for the development of CHD from high total cholesterol levels are high; and especially so for high risk patients; *i.e.*, people who smoke; males over the age of 45, females over the age of 55, diabetics, people with high blood pressure and people with a personal or family history of heart disease (Anon., 2008).

In the subsequent paragraph the definition of dyslipidaemia will be given as well as the main type of lipids in dyslipidaemia.

2.1.2 Definition of dyslipidaemia

According to Berger and Marais (2000:164) and Thornton and Holt (2000:407), dyslipidaemia is the presence of an elevation of plasma cholesterol and / or triglyceride (TGs) or a low high-density lipoprotein (HDL) level that contributes to the development of atherosclerosis and related disorders. The causes may be primary (genetic) or secondary; and the diagnosis thereof is by measuring plasma levels of total cholesterol, TGs and individual lipoproteins (Mcelroy & Chorvat, 2007; Porter & Kaplan, 2008). The main types of lipids are presented and discussed in table 2.1.

Table 2.1: Main types of lipids (adapted from Anaizi, 2002; Walker, 2006:355)

Main types of lipids	
Cholesterol	• A steroid alcohol synthesised in the liver with variable amounts obtained from diet. • Average total body cholesterol = 150g of which 90% is part of cell membrane structures. • Necessary for the synthesis of steroid hormones.
Triglycerides (TGs)	• Sources: Saturated fat e.g. red meat, dairy products, coconut oil and palm oil. Unsaturated fat: omega-3: (fish oil, soybean, canola oil), omega-6: vegetable oils (corn, sunflower) and monounsaturated fat: olive oil. Trans-fatty acids: hydrogenated vegetable oils (margarine).
Very low–density lipoprotein (VLDL) (density <1 mmol/ℓ)	• Produced in the liver. • Rich in triglycerides (>65%) and cholesterol (20%). • Serves to transport endogenous lipids (particularly triglycerides) to extra-hepatic sites. • Hydrolysed by lipoprotein lipase (LPL) to intermediate density lipoprotein (IDL) and then to low density lipoprotein (LDL).
Low density lipoprotein (LDL) (density ~ 1 mmol/ℓ)	• Product of VLDL catabolism (catalysed by LPL). • Contains >60% cholesterol and accounts for >60% the total plasma cholesterol. • Taken up by hepatic and extra-hepatic tissue through receptor-mediated endocytosis triggered by apolipoprotein B100 (apo B100) - LDL receptor interaction. • Has a high atherogenic potential. • Oxidised LDL is a major source of cholesterol for macrophages in atheromatous plaques.

Table 2.1: Main lipids (adapted from Anaizi, 2002; Walker, 2006:355) (continued)

Intermediate density lipoprotein (IDL) (density ~ 1.05 mmol/ℓ)	• Derived from both VLDL and HDL. • The liver either takes up IDL particles, a process mediated by apoE or may be reduced to LDL (by losing apoE and more triglycerides).
High density lipoprotein (HDL) (density ~ 1.15 mmol/ℓ)	• Produced by extra-hepatic tissue and serves as a vehicle for the transfer of cholesterol from the peripheral tissues to the liver. • HDL takes up the cholesterol liberated in the course of normal cell membrane turnover. • Cholesterol esters are transferred form HDL to IDL, which are then converted to LDL or taken up by the liver directly.

According to Wells *et al.* (2003:71) the elevated total, low-density lipoprotein cholesterol (LDL) and reduced high-density cholesterol are associated with the development of coronary heart disease. LDL accounts for 60 to 70 per cent of total serum cholesterol, and when transformed from plasma to sub-endothelial tissue, becomes oxidised (Thornton & Holt, 2000:409). This oxidation causes LDL to become cytotoxic and therefore contributes to artherosclerosis development. HDL cholesterol accounts for 20 to 30 per cent of total serum cholesterol and these levels are inversely associated with risk of coronary heart disease (CHD) (Thornton & Holt, 2000:409). VLDL is mainly composed of triglycerides and make out 10 to 15 per cent of total serum cholesterol (Thornton & Holt, 2000:409).

It can be concluded from table 2.1 that all the main lipids form part of dyslipidaemia. Dyslipidaemia, however, is classified as primary or secondary dyslipidaemia, each with its own sub-classifications. The classification of dyslipidaemia with the sub-classifications will be discussed in the subsequent paragraphs.

2.1.3 Classification of dyslipidaemia

Dyslipidaemia is a heterogeneous disorder with multiple aetiologies (Kromhout, 1999:798), with modern diet and lifestyle (tobacco use, obesity, high fat intake, and sedentary activity) probably being the largest contributors to the current epidemic of atherosclerosis. There are primary causes of dyslipidaemia that occur rarely and demand the attention of a consulting lipidologist; e.g., table 2.2 (Gau & Wright, 2006:449). There also are many secondary causes (table 2.3) of dyslipidaemia that may exist in clinical practice that should be addressed concurrently with initiation of pharmacotherapy.

The great majority of cases encountered during the daily practice of medicine will be secondary aetiologies of dyslipidaemia (Gau & Wright, 2006:449). A short discussion of the primary- and secondary aetiologies in the development of dislipidaemia follows subsequently.

Table 2.2: Primary causes of dyslipidaemia (Gau & Wright, 2006:451)

Elevated LDL-cholesterol	Low HDL-cholesterol
• LDL receptor deficiency	• Apo A-1 deficiency
• Familial homozygous hyperlipidaemia	• Apo A-1 mutations
	• Lecithin-cholesterol acyltransferase (LCAT) deficiency (partial or complete)
	• Tangiers's disease
	• Familial hypoalpaliproteinemia

Table 2.3: Secondary causes of dyslipidaemia (Gau & Wright, 2006:451)

Elevated LDL-cholesterol	Low HDL-cholesterol
• Obesity	• Metabolic Syndrome
• High fat intake	• Diabetes Mellitus
• Hyperthyroidism	• Obesity or Weight gain
• Diabetes Mellitus	• Physical inactivity
• Nephrotic Syndrome	• Tobacco use
• Anabolic Steroids	• Beta Blocker therapy
• Progestins	• Low fat or High Polysaturated fat diets
• Obstructive Hepatobiliary Disease	• Anabolic Steroids
	• Progestins
	• Thiazide diuretics

2.1.3.1 Primary dyslipidaemia

Up to 60 per cent of the variability in serum fasting lipids may be genetically determined, though; expression is often influenced by interaction with environmental factors (Walker, 2006:355). Primary dyslipidaemia is a result of a confluence of factors affecting lipoprotein metabolism (Zanni & Wick, 2006) (refer to table 2.1 for the different patterns of lipoprotein distribution). Common familial disorders are classified in table 2.2 (adapted from Anaizi, 2002; Walker, 2006:355).

Table 2.4: The different classes of primary hyperlipidaemia (adapted from Anaizi, 2002; Walker, 2006:355)

Class	Cause	Abnormalities*
I: Familial Hyperchylomicronemia	LPL deficiency	⇧Chylomicrons; ⇧TGs; Pancreatitis, Diabetes Mellitus (DM)
IIa: Familial Hypercholesterolemia	LDL receptor deficiency	⇧LDL; ⇧TC
IIb: Familial Combined Hyperlipidaemia	High Apo B synthesis + defective Apo E	⇧VLDL, ⇧LDL, ⇧TC, ⇧TG.
III: Familial dysbetalipoproteinemia	Abnormal IDL metabolism	⇧IDL, ⇧TC, ⇧TGs
IV: Familial Hypertriglyceridaemia	Abnormal VLDL metabolism	⇧⇧ TGs + ⇧TC
V: Familial mixed Hypertriglyceridaemia	Abnormal VLDL & chylomicron metabolism	⇧⇧TGs + ⇧ TC. ⇧VLDL, ⇧chylomicron; ⇔ LDL.

* TGs = Triglycerides; TC = Total cholesterol; LDL = low-density lipoprotein; VLDL = very low density lipoprotein and IDL = Intermediate density lipoprotein; LPL = Lipoprotein lipase

The different types of primary dyslipidemias will be discussed in the following paragraphs.

2.1.3.1.1 Familial hyperchylomicronemia (F.CH)

Familial hyperchylomicronemia (type I hyperlipidaemia) is a rare (1/106 births) autosomal recessive disorder caused by a complete deficiency of lipoprotein lipase or its cofactor apolipoprotein CII (apo CII), and is characterised by elevated plasma chylomicrons and triglycerides, pancreatitis, cutaneous xanthomas, and hepatosplenomegaly (Anon., 2007b; Tzotzas *et al*., 2002:185). According To Berger and Marais (2000:169), familial hyperchylomicronemia often presents itself in childhood and has various patterns of inheritance.

2.1.3.1.2 Familial hypercholesterolaemia (FH)

Familial hypercholesterolemia (homozygous and heterozygous) is autosomal dominant disorders that cause severe elevations in total cholesterol and low-density lipoprotein cholesterol (Citkowitz, 2007). In this type of dyslipidaemia, the genetic abnormality is in the low-density lipoprotein receptor, which results in increased plasma low-density lipoprotein concentration (Berger & Marais, 2000:168).

Moderate hypercholesterolemia is a common finding in industrialised countries, with heterozygous FH occurring in approximately 1 per 500 persons worldwide, compared to homozygous FH, which occurs in 1 case per 1 million persons (Citkowitz, 2007). The latter type

of dyslipidaemia in adults is usually characterised by a plasma cholesterol level of more than 7.5 mmol/ℓ (LDL-cholesterol > 5) (often > 9 mmol/ℓ) before any dietary modification (Berger & Marais, 2000:168).

In South Africa, FH is prevalent mostly in European/white population groups (about 1 per cent of the population) as well as in other groups including Asians, Jews and Lebanese. Familial hypercholesterolaemia is also known to occur in the coloured and in Black populations (Berger & Marais, 2000:168).

2.1.3.1.3 Familial combined hyperlipidaemia (FCH)

Familial combined hyperlipidaemia is a new inherited lipid disorder, characterised by multiple lipoprotein phenotypes - strongly associated with premature cardiovascular disease (de Graaf *et al*., 2002:46). Accordingly, in the present, FCH is the most common inherited hyperlipidaemia in humans, affecting one to three per cent of the population and up to 20 per cent of patients with premature myocardial infarction. The genetic basis of this disorder has, however, not been defined yet (Berger & Marais, 2000:170).

2.1.3.1.4 Familial dysbetalipoproteinaemia

Dysbetalipoproteinemia is a genetic disorder, giving rise to severe disturbances of lipid homeostasis and premature atherosclerosis (Tremblay *et al*., 2006:203). This lipid disorder is characterised by the accumulation of abnormal β-migrating cholesterol enriched remnants of both intestinal and hepatic origin (β-VLDL) in the plasma, resulting in the elevation of plasma total cholesterol, triglycerides and apo-E. Apo E is the ligand that mediates binding of remnants to hepatic receptors involved in the clearance of these lipoproteins from the circulation (Maley & Rall, 1999:1953).

2.1.3.1.5 Familial hypertriglyceridaemia

Hypertriglyceridaemia is a commonly encountered but often overlooked component of dyslipidaemia. Hypertriglyceridaemia can occur as a primary disorder due to various genetic and/or ensymatic defects and can also occur as a secondary disorder that is associated with numerous medical conditions (Haymore *et al*., 2005:17). It often presents in childhood only and has variable patterns of inheritance (Berger & Marais, 2000:169). It further presents with tuberous xanthomata, which is associated with high intermediate density lipoprotein. Depending on the severity of the lipemia, eruptive xanthoma, lipemia retinalis, epigastric pain and overt pancreatitis are variably present (Malloy & Kane, 1998:568).

2.1.3.2 Secondary dyslipidaemia

Although most cases of dyslipidaemia have a primary genetic pathogenesis, a significant proportion of patients have a secondary cause that can be modified (Maritz, 2003:365).

Secondary dyslipidaemia stems from various pathologies, such as endocrine disorders, untreated hyperglycaemia, hypothyroidism, nephritic syndrome, chronic renal failure, or gastrointestinal disorders (Zanni & Wich, 2006); and is characterised by normal or only minor gene defects (Berger & Marais, 2000:170). According to Berger and Marais (2000:170) the environment, underlying incidental disease, drugs and several factors may also create secondary dyslipidaemia. Some of the causes of secondary dyslipidaemia and risk factors associated therewith are summarised in table 2.5.

Table 2.5: Causes of secondary dyslipidaemia and risk factors associated therewith (adapted from Maritz, 2003:367)

Secondary cause	High cholesterol (high LDL- C)*	TG excess mild to moderate (high VLDL)*	Low HDL –C*	Severe TG excess: chylomicronaemia syndrome*
Diet	• Saturated fats • Caloric excess • Anorexia	• Weight gain • Alcohol	• Low-fat diet	• Alcohol and fat with genetic lipid disorder
Drugs	• Diuretics • Glucocorticoids • Cyclosporine	• Retinoids • Beta-blockers • Oestrogen • Glucocorticoids	• Anabolic steroids • Progestin's • Beta-blockers • Cigarettes	• Glucocorticoids • Oestrogen • Genetic lipid disorder
Disorders of metabolism	• Diabetes poorly controlled • Hypothyroidism • Pregnancy	• Type 2 diabetes • Obesity • Pregnancy	• Type 2 diabetes • Obesity	• Diabetes poorly controlled • Hypothyroidism with genetic lipid disorder
Diseases	• Nephritic syndrome • Biliary obstruction	• Chronic renal failure with / without dialysis • Nephritic syndrome	• Chronic renal failure with / without dialysis	• SLE (rare)

* LDL-C = low-density lipoprotein cholesterol; TG = triglyceride; VLDL = very low-density lipoprotein; HDL-C = high-density lipoprotein cholesterol; SLE = systemic lupus erythematosus.

2.1.4 Incidence and the prevalence of dyslipidaemia

Data from the US National Health and Nutrition Examination Survey (NHANES) that was conducted in 1999–2000 found that 25 per cent of adults had total cholesterol greater than 5.2 mmol/ℓ or were taking a lipid lowering medication (Ford *et al.,* 2003:2185).

Data that were collected by Maritz (2006:101) show that at least 1.5 million African people aged 30 years and older are hypercholesterolaemic. This study indicates that more than 5.5 million South Africans aged 30 years and older carry a risk for chronic disease by virtue of their TC level (Maritz, 2006:101). Familial Hypercholesterolaemia (FH) is very common in the European/white population, and its prevalence is estimated to be 1:72 compared to 1:500 worldwide (Maritz, 2006:102). Older women were found to have hypercholesterolaemia more frequently than older men, in the middle age groups men and women tended to have equal rates of cholesterol and in the younger age groups, female frequency was much lower than that of the men (Maritz, 2006:101).

2.1.5 Pathophysiology of dyslipidaemia

Cholesterol is a lipid that is one of the primary components of cell membranes and a precursor in steroid hormone and bile acid metabolism (Thornton & Holt, 2000:409). Cholesterol, triglycerides and phospholipids are transported as lipids and apolipoproteins/lipoproteins (Wells *et al*., 2003:71). Lipoproteins divide into five categories: LDL, HDL, VLDL, chylomicrons and apolipoproteins (Thornton & Holt, 2000:409) (refer to table 2.1).

There are three main pathways responsible for the generation and transport of lipids within the body. These pathways include the exogenous pathway, the endogenous pathway, and the pathway of reverse cholesterol transport.

- **Exogenous (dietary) lipid pathway:** Following digestion and absorption of dietary fat, TG and cholesterol are packaged to form chylomicrons in the epithelial cells of the intestines. Chylomicrons circulate through the intestinal lymphatic system. In the blood, circulating chylomicrons interact at the capillaries of adipose tissue and muscle cells releasing TG to the adipose tissue to be stored and made available for the body's energy needs. The enzyme lipoprotein lipase (LPL) hydrolyses the TG and free fatty acids are released. Some of the components of the chylomicrons are "repackaged" into other lipoproteins (Shepherd, 2001:E2).

- **Endogenous pathway**: The endogenous pathway involves the liver synthesising lipoproteins. TG and cholesterol esters are generated by the liver and packaged into VLDL particles and then released into the circulation. VLDL is then processed by LPL in tissues to release fatty acids and glycerol. Once processed by LPL, the VLDL becomes a VLDL remnant. The majority of the VLDL remnants are taken up by the liver *via* the LDL receptor, and the remaining remnant particles become IDL, a smaller, denser lipoprotein than VLDL. The fat of some of the IDL particles requires them to be reabsorbed by the liver (again by the LDL receptor); however, other IDL particles are hydrolysed by hepatic-triglyceride lipase to form LDL, a smaller, denser particle than IDL. LDL is the main carrier of circulating cholesterol within the body (Shepherd, 2001:E3).

- **Reverse cholesterol transport:** Reverse cholesterol transport refers to the process by which cholesterol is removed from the tissues and returned to the liver. HDL is the key lipoprotein involved in reverse cholesterol transport and the transfer of cholesterol esters between lipoproteins.

These aforementioned discussions are illustrated in figure 2.1 (Shepherd, 2001:E3):

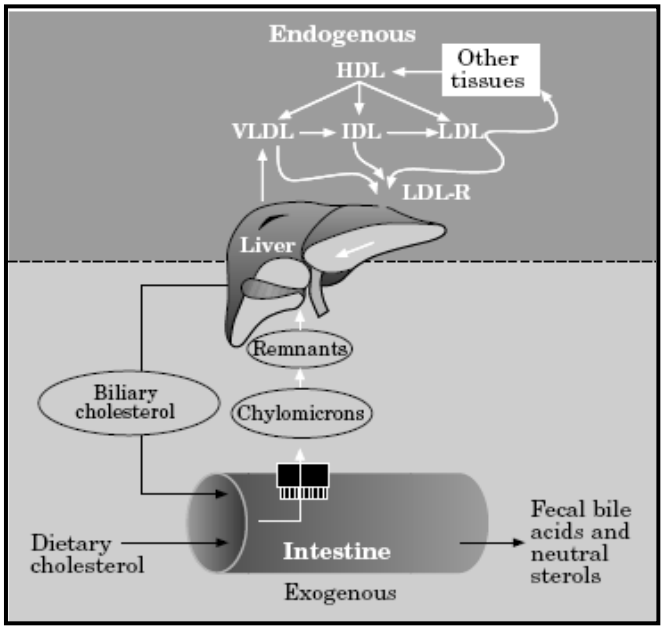

Figure 2.1: The endogenous and exogenous lipid pathways (Shepherd, 2001:E3)

2.1.6 Significance of dyslipidaemia

According to Wells *et al*. (2003:71) the elevated total, low-density lipoprotein cholesterol and reduced high-density cholesterol are associated with the development of coronary heart disease. Dyslipidaemia also carries a high risk for other diseases, as well as a risk in terms of

health care utilisation and scarce resource consumption/utilisation. These risk factors are discussed in the subsequent paragraphs.

2.1.6.1 Risk for the development of cardiovascular- and other diseases

HDL-cholesterol makes up 20 to 30 per cent of total serum cholesterol and plays several critical roles in maintaining a healthy vasculature and preventing cardiovascular events (Toth, 2008:488). Approximately 54 to 77 per cent of type 2 diabetics have a borderline-high to high total cholesterol (Harris, 1991:366). The rate of atherogenesis is proportional to the severity of ambient risk factors including serum cholesterol levels (Vega, 2001:1109).

There are some other factors also involved other than high LDL levels that add to the risk of developing secondary diseases from dyslipidaemia. These factors are shown in table 2.6 (Anaizi, 2002; Berger & Marais, 2000:168; Thornton & Holt, 2000:413).

Table 2.6: Contributing risk factors

Positive lifestyle and behavioural factors	Positive other modifiable risk factors	Positive non-modifiable risk factors
• Cigarette smoking • Lack in physical exercise • Artherogenic diet • Alcohol and Anabolic steroids (Drug abuse)	• Hypertension • Obesity • Diabetes Mellitus • Low HDL-cholesterol • Hypertriglyceridaemia	• ≥ 45 years old male • ≥ 55 years old female • Female without oestrogen therapy that is postmenopausal • Family history of CHD • Personal history of CHD
Negative Risk Factors		
HDL level ≥ 1.6 mmol/ℓ		
Subtract Positive Risk Factor if there is a Negative Risk Factor present		

Patients are placed (categorised) in one of three risk categories (table 2.6), whereby the most appropriate treatment/intervention for the patient's needs and the specific goals of that intervention are determined (Thornton & Holt, 2000:411). Patients with two or more risk factors are further stratified by evaluating their 10-year risk of developing CHD using the model Framingham 10-year risk for CHD (refer to appendix A.1).

According to Fodor *et al*. (2000:1443) the Framingham scoring system is very effective but does not apply to patients with extreme or unusual risk factors like severe hypercholesterolaemia, and also in patients with very low HDL levels. Patients with very high risk of cardiovascular disease's therapeutic management show good improvement through using the Framingham scoring system (Irons *et al*., 2002:1617).

According to Baigent *et al.* (2005:1267) a lowering in LDL-cholesterol is associated with a 12 per cent reduction in all-cause mortality; it has a 19 per cent reduction in cardiovascular heart disease mortality and a 21 per cent reduction in major vascular events.

2.1.6.2 Influence on health care and scarce resource utilisation

Dyslipidaemia is a significant contributor to cardiovascular morbidity and mortality in the industrialised world. This impact ensures that dyslipidaemia carries a high cost in terms of human life and health care expenditures.

In developed countries such as Australia and America the treatment or prevention of cardiovascular diseases embodies the highest proportion of the total health expenditure by disease group, consisting of hospitalisation and medication costs (AHA, 2004). Hospitalisation contributed 45 per cent (US$109 billion ~ R907 billion)[1] of the estimated (US$241.9 billion ~ R2 trillion) spent on therapy in the United States and 46 per cent (A$2.5 billion ~ R10.8 million)[2] of the estimated A$5.5 billion (~R23 billion) spent in Australia in 2000 to 2001.

According to the World Health Report of 1999, ischaemic heart disease was the leading single cause of death in the world, the leading single cause of death in high income countries, and second only to lower respiratory tract infections in low and middle income countries (WHO, 1999). In 1998 it was also the leading cause of death, with nearly 7.4 million estimated deaths a year in member states of the World Health Organization and causing the eighth highest burden of disease in the low and middle income countries (30.7 million disability adjusted life years) (WHO, 1999). It is estimated that that ischaemic heart disease will be the largest single cause of disease burden globally by the year 2020 (WHO, 1999).

There has been a rapid and significant growth in the measurement of quality of life as an indicator of health outcome in patients with coronary heart disease (Treasure, 1999:331). In the clinical course of CHD, there are many aspects that may affect a patients' quality of life. These include symptoms of angina and heart failure, limited exercise capacity of the aforementioned symptoms, the physical debility caused, and psychological stress associated with the chronic stress. Modern treatments nowadays focus not only on improving life expectancy, symptoms and functional status, but also quality of life. Thus, an improvement in health-related quality of life (HRQL) is considered to be important as a primary outcome and in the determination of therapeutic benefit (Treasure, 1999:332).

[1] US Dollar = R8.33 (2000 - 2001) (OANDA, 2009).
[2] Australian Dollar = R4.35 (2000 - 2001) (OANDA, 2009).

2.1.7 Diagnosis of dyslipidaemia

Wells *et al.* (2003:72) recommend that a fasting lipid profile including total cholesterol, HDL cholesterol, LDL cholesterol and triglycerides should be measured in adults 20 years of age and older at least once every 5 years. A full serum lipoprotein profile and/or a plasma lipoprotein profile should be performed on patients that have hypercholesterolaemia (cholesterol levels greater than 5 mmol/ℓ on screening) and also have physical signs of a lipid disorder (Berger & Marais, 2000:166). Measurement of plasma cholesterol, triglyceride and HDL-cholesterol levels should be conducted after at least 12 hours of fasting, since triglycerides may be elevated in non-fasting patients (Wells *et al.,* 2003:72). Measurement should also be repeated once or more for patients with suspected elevated LDL cholesterol levels (Baron, 2007:1270).

There are appropriate and desirable levels for lipids and triglycerides as presented in table 2.7. Decisions on the type of treatment are based on a patient's LDL-cholesterol level, his or her risk factor status and the presence of known CHD or artherosclerotic disease (Baron, 2007:1274; Thornton & Holt, 2000:411). It is suggested that cholesterol is not a risk factor for CHD in patients over 75 years of age, and it is preferable for clinicians to stop screening for such patients (Baron, 2007:1272).

The National Cholesterol Education Program adult treatment panel (NCEP ATP III) that lays forth treatment options and opinions based on cholesterol and cholesterol-related diseases/sicknesses. The classification of cholesterol and triglyceride levels as based on the National Cholesterol Education Program-Adult Treatment Panel III (NCEP-ATP III) guidelines is depicted in table 2.7.

Table 2.7: Classification of cholesterol and triglyceride levels based on NCEP-ATP III guidelines (adapted from Thornton & Holt, 2000:412).

Type	Desirable	Borderline	High Risk
Total cholesterol	< 5.2 mmol/ℓ (200 mg/dℓ)	5.2 – 6.2 mmol/ℓ (200 – 239 mg/dℓ)	> 6.2 mmol/ℓ (240 mg/dℓ)
LDL	< 3.4 mmol/ℓ (130 mg/dℓ)	3.4 – 4.1 mmol/ℓ (130 - 159 mg/dℓ)	> 4.1 mmol/ℓ (160 mg/dℓ)
HDL	> 1.5 mmol/ℓ (60 mg/dℓ)	–	< 0.9 mmol/ℓ (35 mg/dℓ)
Triglycerides	< 2.3 mmol/ℓ (200 mg/dℓ)	2.3 - 4.5 mmol/ℓ (200 - 400 mg/dℓ)	4.5 - 11.3 mmol/ℓ (400 - 1000 mg/dℓ)

2.1.8 Signs and symptoms of dyslipidaemia

Dyslipidaemia itself causes no symptoms, though it can lead to symptomatic vascular disease (coronary artery disease and peripheral arterial disease) (Baron; 2007:1276; Berger & Marais, 2000:168; Bhatnagar, 1998:213). High TGs (> 1000 mg/dℓ or > 11.3 mmol/ℓ) can cause acute pancreatitis (Baron; 2007:1276; Berger & Marais, 2000:168; Bhatnagar, 1998:213). High levels of LDL can also cause eyelid xanthelasmas; arcus cornea; and tendinous xanthomas found at the achilles, elbow, and knee tendons and over metacarpophalangeal joints (Porter & Kaplan, 2008).

Patients with homozygous familial hypercholesterolaemia may also have planar or cutaneous xanthomas. Patients with severe elevations of triglycerides can have eruptive xanthomas over the trunk, back, elbows, buttocks, knees, hands, and feet (Porter & Kaplan, 2008).

Patients with the rare dysbetalipoproteinaemia may manifest with palmar and tuberous xanthomas (Porter & Kaplan, 2008). Severe hypertriglyceridaemia (> 2000 mg/dℓ or > 22.6 mmol/ℓ) can give retinal arteries and veins a creamy white appearance (a condition called lipemia retinalis) (Porter & Kaplan, 2008). Extremely high lipid levels also give a lactescent appearance to blood plasma (Porter & Kaplan, 2008; Marks *et al.*, 2003:4). The signs associated with disorders of lipoprotein metabolism are summarised according to the area it affects, in table 2.8.

Table 2.8: Signs associated with disorders in lipoprotein metabolism (Bhatnagar, 1998:207)

Eyes	Skin	Systemic
• Corneal arcus • Corneal opacities	• Xanthelasmata • Tendon xanthomata • Eruptive xanthomata • Tubero-eruptive xanthomata • Planar xanthomata • Palmar xanthomata	• Aortic stenosis • Ataxia • Lipemia retinalis • Peripheral neuropathy • Hepatosplenomegaly

2.1.9 Clinical management of dyslipidaemia

The South African lipid guidelines for the treatment of hyperlipidaemia are based on the revised American NCEP-ATP III guidelines (Raal, 2004:53). The ATP III guidelines recommend a two-step approach to cholesterol management with priority to attaining the goal for LDL cholesterol.

The emphasis thereafter shifts to management of the metabolic syndrome and other lipid risk factors (NIH, 2002).

After an appropriate trial of dietary therapy to reduce LDL cholesterol (~ 3 months), two additional therapeutic decisions may be required. Firstly, if the LDL cholesterol goal has not been achieved, consideration may be given to initiating drug therapy. Secondly, if the metabolic syndrome is present, additional lifestyle changes (i.e., weight reduction and increased physical activity) will be needed. Later, if lifestyle therapies do not alleviate, drug therapy for treatment of the metabolic risk factors may be required (NIH, 2002) (refer to appendix A.2 for the treatment algorithm of hyperlipidaemia).

Two treatment strategies, *inter alia* non-pharmacological treatment and pharmacological treatment, will now be discussed.

2.1.9.1 Non-pharmacological treatment of dyslipidaemia

According to Berger and Marais (2000:171) one of the two key fundamentals in the management of dyslipidaemia is lifestyle modifications. The patient's lifestyle should be thoroughly assessed, with simple methods of reducing cholesterol levels and risk of CHD as the main focus (Berger & Marais, 2000:171; Raal, 2003:378).

Epidemiological and clinical trial evidence evaluating diet and CAD prevention shows that dietary strategies are effective; together with this the NCEP-ATP III has recommended a multifaceted lifestyle approach to reduce risk for CHD. This approach includes designated therapeutic lifestyle changes (TLC). Its essential features are (NIH, 2002; Raal, 2003:378):

- Reduced intake of saturated fats (<7% of total calories) and cholesterol (<200 mg/day).
- Therapeutic options for enhancing LDL lowering such as plant stanols/sterols and increased viscous fibres.
- Weight reduction.
- Increased physical activity.

The following model demonstrates a step by step programme of dietary therapy and therapeutic lifestyle changes (adapted from NIH, 2002).

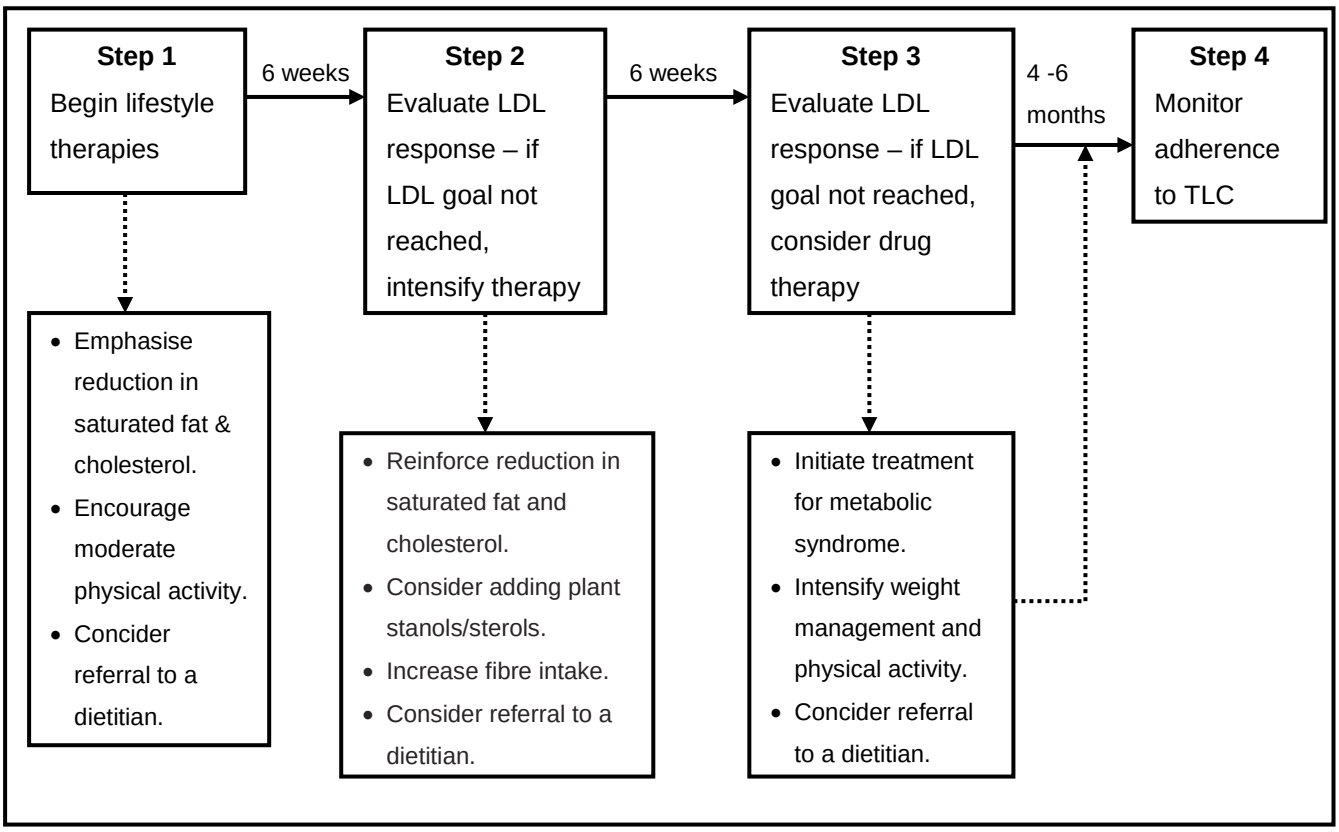

Figure 2.2: A step by step programme of dietary therapy and TLC (adapted from NIH, 2002)

In most patients, TLC is implemented before initiating drug therapy. However, in high-risk patients, drug therapy may be initiated simultaneously with TLC. If the patient does not achieve the LDL-cholesterol goal within 12 weeks after starting the TLC programme, then drug therapy / pharmacological treatment may be started.

2.1.9.2 Pharmacological treatment of dyslipidaemia

The main indication for lipid-modifying medication is to reduce cardiovascular risk. LDL cholesterol is the primary target of treatment in clinical lipid management. The use of therapeutic lifestyle changes, including LDL-lowering dietary options (plant stanols/sterols and increased viscous fibre) will usually achieve the therapeutic goal. Nonetheless, some patients' short-term and/or long-term risk for CHD will require LDL lowering medicine to reach the prescribed goal for LDL cholesterol. Drug therapy should be considered when non-pharmacological means fail to reduce the lipid levels until within the target range specified in table 2.9 (NIH, 2002; Raal, 2003:380).

Table 2.9: Optimal fasted lipid profiles (NIH, 2002; Raal, 2003:380)

Type of lipoprotein	Lipoprotein level
• Total cholesterol	• </= 5 mmol/ℓ
• Triglycerides	• </= 1.5 mmol/ℓ
• HDL cholesterol	• >/= 1.2 mmol/ℓ
• LDL cholesterol	• >/= 3 mmol/ℓ

There are four main classes of lipid-lowering drugs (Snyman, 2007:12a):

- Fibrates.
- HMG – CoA reductase inhibitors (Statins).
- Cholesterol absorption inhibitors (Ezetimibe).
- Others (Acipimox, cholestyramine).

In the subsequent paragraphs, the main classes of lipid-lowering drugs will be discussed.

2.1.9.2.1 Fibric acid derivates / Fibrates

Newer fibrates on the market such as bezafibrate, fenofibrate and gemfibrozil are suitable for the treatment of hypercholesterolaemia especially with low HDL levels and/or increased triglyceride levels (Gibbon *et al*., 2008:169). Fibrates lower triglycerides by increasing lipoprotein lipase activity, which is responsible for the hydrolysis of triglycerides from VLDL and IDL (Thornton & Holt, 2000:420). Fibrates effectively reduce LDL levels by 10 to 15 per cent; triglycerides by up to 40 per cent, and increase HDL levels effectively by 15 to 20 per cent (Gibbon *et al*., 2008:169; Thornton & Holt, 2000:420).

Table 2.11 gives the complete layout of fibrates, including the available agents, side effects, their effects on lipids / lipoproteins, contra-indications and clinical trial results.

2.1.9.2.2 HMG-CoA reductase inhibitors (statins)

When used as monotherapy, 3-hydroxy-3-methylglutaryl coenzyme A (statins) are the most potent agent to lower total cholesterol and also LDL levels (Wells *et al*., 2003:79). Statins are therefore regarded as the drugs of choice for the management of the most dyslipidaemias (primary and secondary), and they also are the most cost-effective agents (Gibbon *et al*., 2008:164; Walker, 2006:365).

Statins competitively inhibits the enzyme HMG-CoA reductase, which is the responsible enzyme in the conversion from HMG-CoA to mevalonic acid (Thornton & Holt, 2000:419). Mevalonic acid is a precursor to cholesterol in its synthesis, and when this process is inhibited it lowers the

production of cholesterol which results in an up-regulation of LDL receptors and also further reduction of freely -circulating cholesterol.

Statins were introduced in the United Kingdom in the order of simvastatin, pravastatin, fluvastatin and atorvastatin (Walker, 2006:365). The indications and relative efficacy of statins in terms of reducing total cholesterol (TC) and low-density lipoprotein cholesterol are laid out in table 2.10.

The effectiveness of statins in reducing low-density lipoprotein cholesterol concentration is highly predictable and this makes comparisons of statins easy and reliable (Stein, 2002:51c). Atorvastatin 10 mg to 40 mg/day is associated with significant greater reductions in low-density lipoprotein cholesterol than simvastatin 10mg to 40 mg/day, lovastatin 20 mg to 40 mg/day, fluvastatin 20 mg to 40 mg/day and pravastatin 20 mg to 40 mg/day (Lopez, 2002:1175). It appears that there is a possibility that all these statins would achieve greater reduction in low-density lipoprotein cholesterol levels if doses were doubled. The limiting factor, preventing doubling of doses, is an increase in hepatic toxicity and/or muscle toxicity which is observed with increased doses of these drugs (Stein, 2002:51c).

Table 2.10 gives the complete layout of HMG-CoA reductase inhibitors (statins) including the available agents and their effects on lipids / lipoproteins, contra-indications and clinical trial results.

Table 2.10: Comparison of statins (adapted from Berger & Marias, 2000:174; Gibbon et al., 2008:165; Walker, 2006:366)

Drug	Indication	Daily dose	Mean TC reduction	Mean LDL reduction
Atorvastatin	• Primary hypercholesterolaemia • Familial hypercholesterolaemia • Mixed hyperlipidaemia	10 mg 20 mg 40 mg 40 mg BD 80 mg BD	28 % 35 % 40 % 42 % 46 %	38 % 46 % 51 % 54 % 61 %
Simvastatin	• Primary hypercholesterolaemia • Heterozygous & Homozygous familial hypercholesterolaemia • Mixed hyperlipidaemia • CHD prevention in hypercholesterolaemia	10 mg 20 mg 40 mg 80 mg	21 % 26 % 30 % 37 %	28 % 35 % 41 % 48 %
Pravastatin	• Primary hypercholesterolaemia • CHD prevention in hypercholesterolaemia • Hypercholesterolaemia & CHD	10 mg 20 mg 40 mg	13 % 18 % 24 %	19 % 24 % 34 %

Table 2.10: Comparison of statins (adapted from Berger & Marias, 2000:174; Gibbon et al., 2008:165; Walker, 2006:366) (continued)

Fluvastatin	• Primary hypercholesterolaemia • Mixed hyperlipidaemia • CHD prevention in hypercholesterolaemia	20 mg 40 mg 40 mg BD 80 mg D	13 % 19 % 25 %	17 % 23 % 34 %
Rosuvustatin	• Primary hypercholesterolaemia • Heterozygous & Homozygous familial hypercholesterolaemia • Mixed Hyperlipidaemia • Hypertriglyceridaemia	10 mg 20mg	27% 33%	45 % 52 %
Lovastatin	• CHD prevention • Primary hypercholesterolaemia • Familial Hypertriglyceridaemia	10 mg 20 mg 40 mg 40 mg BD	24% 27%	21 % 27 % 31 % 42 %

2.1.9.2.3 Cholesterol absorption inhibitors

Ezetimibe is a lipid-lowering drug that blocks the passage across the intestinal wall by inhibiting a newly discovered cholesterol transporter and thus it inhibits intestinal absorption of dietary and biliary cholesterol (Baron, 2007:1276). According to Gibbon *et al.* (2008:170) ezetimibe would lower LDL cholesterol by approximately 15 per cent.

Dietary and biliary cholesterol in the lumen of the small intestine is packaged into micelles that diffuse across a thin mucus layer to the surface of the intestinal epithelial cells (enterocytes) (Turley, 1999:S29). Upon reaching the enterocyte, cholesterol is released from the micelle. The cholesterol then passes through the mucosal membrane of the enterocyte by a mechanism that is thought to be mediated by a transporter within the brush border.

Soon after administration, the majority of ezetimibe and the active metabolite localise in the enterocyte brush border, with the remainder passing through the portal circulation and returning to the intestines *via* the bile (Catapano, 2001:E6). The localisation of ezetimibe in the brush border is thought to inhibit a cholesterol transport protein called Niemann-Pick C1 Like1 (NPC1L1), thus preventing biliary and dietary cholesterol from entering the bloodstream. Consequently, less cholesterol is delivered to the liver, which causes a reduction of hepatic cholesterol stores and increases clearance of cholesterol from the blood (Altman *et al*., 2004:1201; van Heek *et al*., 2000:1748).

Table 2.11 gives the complete layout of cholesterol absorption inhibitors, including the available agents, side effects, their effects on lipids / lipoproteins, contra-indications and clinical trial results.

2.1.9.2.4 Others

The action of bile-acid sequestrants (cholestyramine) is primarily to bind bile acids in the intestinal lumen, with a concurrent interruption of enterohepatic circulation of bile acids, which decreases the bile acid pool size and stimulates hepatic synthesis of bile acids from cholesterol (Gibbon *et al*., 2008:167; Wells *et al*., 2003:78). This depletion of the hepatic pool of cholesterol will result in an increase in cholesterol biosynthesis and also an increase in the number of LDL receptors on the hepatocyte membrane. Therefore a directly stimulated enhanced rate of catabolism from plasma takes place and lowers LDL levels (Wells *et al*., 2003:78).

Bile-acid sequestrants or resins lower total cholesterol and LDL by 15 to 30 per cent; simultaneously increasing HDL by 3 to 5 per cent and also decreases triglycerides by 2 to 3 per cent with prolonged therapy (Thornton & Holt, 2000:422).

Table 2.11 gives the complete layout of these medicines, the available agents, side effects, their effects on lipids / lipoproteins, contra-indications and clinical trial results.

2.1.9.2.5 Niacin

Niacin / Nicotinic acid was the first lipid lowering agent that was associated with a reduction in total mortality (Baron, 2007:1274). Niacin lowers both VLDL and LDL and increases HDL in pharmacological doses (1.5 g – 6 g) (Walker, 2006:369) by reducing the release of VLDL which in turn leads to decreased levels of IDL and LDL. Studies have shown that VLDL and LDL are lowered by mainly two mechanisms which include firstly, the modulation of liver triglycerides synthesis which results in increased intracellular apo B degradation, and secondly, the modulation of triglyceride lipolysis in adipose tissue (Kamanna & Kashyap, 2008:21B). By a mechanism of decreased HDL-apo A-1 catabolism, HDL half-life would be increased as well as lipoprotein (A-1) HDL subfractions, thus augmenting cholesterol efflux and reverse cholesterol transport which will cause an increase in residence time and thus allow HDL size to increase (Kamanna & Kashyap, 2008:23B).

Niacin is widely recommended as the first choice in almost all dyslipidaemias as it is very effective and inexpensive (Gibbon *et al*., 2008:168; Kamanna & Kashyap, 2008:20B). Research in hypercholesterolaemic patients show niacin to have the potential to reduce total cholesterol by up to 20 per cent (Gibbon *et al*., 2008:168; Walker, 2006:365). Niacin also has the effect when used in a full dose (3 g - 4.5 g) to lower LDL by 15 to 25 per cent, triglycerides by up to 15 per cent and increases HDL by 15 to 35 per cent (Gibbon *et al*., 2008:168; Walker, 2006:365).

Table 2.11 gives the complete layout of niacin and its derivates, the available agents, side effects, its effects on lipids / lipoproteins, contra-indications and clinical trial results.

Table 2.11: Layout of the various drug classes, available agents, indications, its effects and side effects, contraindications and interactions (Anaizi, 2002; Berger & Marais, 2000:164-176; Gibbon *et al*., 2008:163-171; Snyman, 2007:164-170)

Drug class	Agents	Indications	Lipid / Lipoprotein effect	Major side-effects	Contraindications	Drug interactions	Clinical trial results
• **HMG-CoA reductase inhibitors (Statins)**	• Simvastatin • Atorvastatin • Fluvastatin • Pravastatin • Lovastatin • Rosuvastatin	• Lowering of LDL and total cholesterol in dyslipidaemias • Reduction of risk of cardiovascular disease	• **LDL** ↓ 18% - 55% • **HDL** ↑ 5% - 15% • **TG** ↓ 7% - 30%	• Myopathy • Increased liver enzymes • Gastrointestinal distress • Headache • Insomnia • Skin rash • Angioedema	**Absolute:** • Active or chronic liver disease **Relative:** • Concomitant use of certain drugs	• **Alcohol:** Abuse potentiates hepatotoxicity • **Warfarin:** Enhanced anticoagulant effect • **Cyclosporine:** cyclosporine levels increase • **Cholestyramine:** Statin should be administered 1 hour before or 4 after Colestyramine	• Reduced major coronary events • CHD deaths • Need for coronary procedures • Stroke • Total mortality
• **Bile-Acid Sequestrants / Resins**	• Cholestyramine	• Hypercholesterolaemia	• **LDL** ↓ 15% - 30% • **HDL** ↑ 3% - 5% • **TG** – No change	• Gastrointestinal distress • Constipation • Decreased absorption of other drugs	**Absolute:** • Dysbetalipo-proteinemia • TG > 400mg/dℓ **Relative:** • TG > 200 mg/dℓ	• **Fat-soluble vitamins:** Cholestyramine may interfere with vitamin absorption. • **Absorption is reduced with:** Warfarin Digoxin Thiazides Barbiturates Aspirin Tetracyclines Thyroxine	• Reduced major coronary events • CHD deaths

Table 2.11: Layout of the various drug classes, available agents, indications, its effects and side effects, contraindications and interactions (Anaizi, 2002; Berger & Marais, 2000:164-176; Gibbon *et al*., 2008:163-171; Snyman, 2007:164-170) (continued)

Drug class	Agents	Indications	Lipid / Lipoprotein effect	Major side-effects	Contraindications	Drug interactions	Clinical trial results
• **Niacin / Nicotinic Acid**	• Nicotinic acid (niacin) • Acipimox	• Hyperlipidaemia type II, III, IV & V • Triglyceride-related disorders	• **LDL** ↓ 5% - 25% • **HDL** ↑ 15% - 35% • **TG** ↓ 20% - 50%	• Flushing • Hyperglycaemia; hyperuricemia (gout) • Upper gastrointestinal distress • Hepatotoxicity	**Absolute:** • Chronic liver disease • Severe gout **Relative:** • Diabetes hyper-uricemia • Peptic ulcer disease	• **HMG-CoA reductase inhibitors (Statins):** Enhanced risk of rhabdo-myolysis • **Antihyper-tensives:** Hypotensive effect is potentiated	• Reduced major coronary events • Possible total mortality
• **Fibric-Acid Derivatives / Fibrates**	• Bezafibrate • Gemfibrozil	• Hyperlipidaemia • Type IIb & type IV hyperlipidaemia (Gemfibrozil)	• **LDL** ↓ 5% - 20% (May be increased in patients with high TG) • **HDL** ↑ 10% - 20% • **TG** ↓ 20% - 50%	• Dyspepsia • Gallstones • Myopathy • Unexplained non-CHD deaths in WHO study	**Absolute:** • Severe renal disease • Severe hepatic disease	• **Warfarin:** Increased anticoagulant effect • **Statins:** Additive muscle effect • **Phenytoin:** Increased level of phenytoin • **Sulphonyl-ureas:** Hypogly-caemia	• Reduced major coronary events

Table 2.11: Layout of the various drug classes, available agents, indications, its effects and side effects, contraindications and interactions (Anaizi, 2002; Berger & Marais, 2000:164-176; Gibbon *et al*., 2008:163-171; Snyman, 2007:164-170) (continued)

Drug class	Agents	Indications	Lipid / Lipoprotein effect	Major side-effects	Contraindications	Drug interactions	Clinical trial results
• **Other**	• Ezetimibe	• Primary Hypercholesterola-emia	• **LDL** ↓ 17% - 25% (primary) • **TG** ↓ (Minimal) • **HDL** ↑ (Minimal, but up to 25 % in combination with statin)	• Headache • Fatigue • Gastro-intestinal disturbances • Headache	• Pregnancy and lactation • Children under 10 years of age • Moderate to severe hepatitis	• Bioavailability decreases with cholestyramine • Cyclosporin increases bioavailability	• Reduced major cornary events

The use of lipid-lowering drugs is associated with the development of side-effects and that poses a more frequent cause of referral to the specialist. The most common side-effect is indigestion, which can be combated before initiating therapy by starting treatment alongside antacid. Other side-effects are diarrhoea, nausea, skin rash, fatigue, worsening of eczema and generalised aches and pains. When such side-effects are encountered treatment with lipid lowering drugs should be stopped for two to three weeks until the condition has been settled completely (Bhatnagar, 1998:221).

2.1.10 Discussion and conclusion

The following applications can be made for this study from the above-mentioned discussions:

- Dyslipidaemia can lead to coronary heart disease, which, in turn, can lead to sudden death.
- Dyslipidaemia can be classified as primary or secondary, each depending on specific signs and symptoms.
- The complications caused by dyslipidaemia are severe and should be prevented or treated aggressively.
- Treatment of dyslipidaemia can be pharmacological or non-pharmacological, with the latter being the first line of treatment.

It can be concluded that dyslipidaemia is diagnosed according to specific signs and symptoms and can be primary or secondary. The incidence of dyslipidaemia is infuenced by genetics, lifestyle habits such as lack of exercise, smoking and diet. The general aim of the management of dyslipidaemia is to reduce symptoms, risk factors, clinical course and to prevent possible complications, which in turn would have a direct influence on utilisation and cost of treatment.

2.1.11 Section summary

This section focused on the introduction and defining of dyslipidaemia as well as on the classification of dyslipidaemia (primary and secondary), the incidence and prevalence of dyslipidaemia, the pathophysiology, significance thereof, diagnosis, signs and symptoms together with the management of dyslipidaemia, including pharmacological and non-pharmacological treatment.

Managed health care and what it entails will be discussed in the following section.

2.2 MANAGED HEALTH CARE (MHC)

2.2.1 Introduction

Managed care has a long history. Over an extended period a hostile regulatory environment discouraged this form of organisation (Glied, 1999). However, since early 1980, managed care has grown dramatically (Glied, 1999). The growth may be due to this organisational form's relative success in responding to underlying market failures in the health care system – asymmetric information about health risks, moral hazard, limited information on quality and limited industrial competitiveness. Luiz and Wessels (2004:10) stated that South Africa is taking the USA-MHC model and changing it to fit the South African structure, but fortunately South Africa can observe the mistakes made in the USA regarding the implementation process of MHC and may choose to apply the best practices only according to that which had proved to be successful in the USA.

2.2.2 Definition of managed health care

Over the years many definitions of managed health care have been developed. These definitions differ in focus point and target strategy.

Powell (2000:3) defined managed health care as a collection or group of techniques used by or on behalf of purchasers of health care benefits to manage health care costs by influencing patient care decision making through case-by-case assessments of the appropriateness of care prior to its provision. In 2004, Kongstvedt (2004:285) defined managed care as "*a system of health care delivery that tries to control the cost of health care services while regulating access to those services and maintaining or improving their quality"*. Anon. (2007a) is furthermore of the opion that managed care is the enrolment of patients into a plan that makes capitated payments to health care providers on behalf of its members, thus shifting the financial risk for health care from patients and payers, to providers. The intent of this shift is to provide incentives to health care professionals to reduce their utilisation of resources, ideally through measures such as health promotion and disease prevention among the group's members.

Managed health care was defined in the Regulations published in terms of the Medical Schemes Act (131/1998) of South Africa as the "*clinical and financial risk assessment and management of health care, with a view to facilitating appropriateness and cost effectiveness of relevant health services within the constraints of what is affordable, through the use of rules-based and clinical management based programs [cit]".*

A new set of activities governing managed health care in South Africa started being used as from the 1st of January 2003 (Council for Medical Schemes, 2003:1). According to the Council for Medical Schemes (2003:19) managed care within South Africa refers to a diverse range of health care organisational strategies that are aimed at containing cost, improving access and assuring the quality of care provided to the beneficiaries of the medical schemes.

The Council of Medical Schemes (2003:3) gave some advantages of managed health care that include (but are not limited to) the following:

- To promote the use of the most cost-effective health care delivery mechanisms, thereby achieving cost reduction.
- To align the financial incentives of providers and financiers to reduce unreasonable incentives for unnecessary care.
- To strongly establish mechanisms to maintain or improve the quality of health care.
- To encourage the development of standardised treatment protocols.
- To support members in gaining access to the most suitable treatment interventions.
- To promote an integrated and holistic approach to manage the health care needs of patients.

Based on these statements it can be reasoned that managed care is a process that is used to deliver cost-effective care to patients without limiting access or quality. This can be achieved by controlled access to providers, comprehensive regulatory controls, emphasis on preventative care, risk sharing, quality and behaviour modification of both the participants and the providers.

2.2.3 Types of managed care plans

Defining the different types of managed care organisations (MCOs) is an ever-evolving challenge (Kongstvedt, 2004:25). It is also said that it is a generic term that describes organisations that manage and control costs and quality related to health care (Harvey & Shapiro, 1997a:270). The Integrated Healthcare Association (IHA) (2001) indicates that a broad array of health insurers, medical groups, hospitals and health systems are considered as managed care organisations. There are various types of MCOs that are being used, *inter alia* the following: health maintenance organisation (HMO), preferred provider organisation (PPO) and exclusive provider organisation (EPO) (Fincham, 2006).

2.2.3.1 Health Maintenance Organisations (HMOs)

An HMO is defined by Al-Assaf (1998:3) as a health care system that provides comprehensive health services to the enrolled persons living within a specific geographic region. This type of MCO provides a form of health care insurance coverage that is fulfilled by hospitals, doctors and other providers with which the HMO has a contract (Kongstvedt, 2004:26). Five different HMO models exist *i.e.* group model, staff model, network model, direct contract model and independent practice associations (IPA) which will be discussed shortly in table 2.12.

Table 2.12: Different types of Health Maintenance Organisations (HMOs)

Type of HMO model	Description
• **Group model**	Group model HMO contracts with a multispeciality physician group practice to provide all physician services to the HMO members (Kongstvedt, 1997:44). These physicians are employed by the group practice and not by the HMO. The medical groups may be organised as a partnership, professional corporation, or an association; the health plan compensates the medical group for covered services at a contracted rate and arranges hospital service agreements for the inpatient or ancillary care needs (Rognehaugh, 1998:95).
• **Staff model**	In this closed-panel HMO, physicians are employees of the HMO (Rognehaugh, 1998:234). Accordingly all premiums and other revenues accrue to the HMO, which, in turn, compensates physicians. Very much like the group model, except the doctors are employees of the HMO.
• **Network model**	This type of HMO contracts with more than one physician group and may contract with single or multi-specialty groups as well as hospitals and other health care providers (Pohly, 2007). When these services are bought, network HMOs sub-capitates the primary care doctor, which in return becomes responsible for providing most of the members' care (Harvey & Shapiro, 1997b:14).
• **Direct contract model**	In this model the practitioners have a direct contract with the HMO but are free to see non-HMO patients. The practitioners provide services to the enrolled population. The practitioners are compensated according to a fee for service plan or on a capitation basis (Kongstvedt, 1997:47).
• **Independent practice association (IPA)**	The HMO contracts with a physician organisation, which in turn contracts with individual physicians, known as a delivery model. The HMO reimburses the IPA on a capitated basis; however, the IPA may reimburse the physicians on a capitated basis (Pohly, 2007).

All the HMOs have certain specific features in common such as that they tolerate risks, have lower premiums, they are less comprehensive and also have a responsibility to deliver a certain stated service for a fixed rate to an enrolled patient (Managed Care Organisations, 2007). Members of an HMO must receive their medical treatment from specific physicians and facilities within the HMO network (Mamdami & Mamdami, 2001:96).

2.2.3.2 Preferred Provider Organisations (PPOs)

Preferred Provider Organisations (PPOs) enter into contract with a private insurer and therefore particular services are rendered through an agreed combination of physicians and hospitals (Pohly, 2007; Rickel & Wise, 2000:105). Accordingly it is a health care delivery system that hold a contract with providers of medical care to provide services at discounted fees to members.

PPOs limit the size of participating provider panels and also provide incentives for their covered individuals to use these participating providers instead of other providers (Kongstvedt, 1997:38). Generally PPOs will offer more choice for the patient and will provide higher reimbursement to the providers (Pohly, 2007).

2.2.3.3 Exclusive Provider Organisations (EPOs)

Wagner (1997:39) states that the EPO is very similar to the PPO. The difference, however, is that payment is provided to contracted providers only and this agreement limits beneficiaries to participating health care providers. PPOs extend their coverage to non-preferred providers as well as preferred providers and their services.

2.3 MANAGED HEALTH CARE AND PRESCRIBED MINIMUM BENEFITS IN SOUTH AFRICA

In South Africa there is no true form of a specific HMO currently in use. The HMO models that do exist are merely extensions of a combination of models (Serfontein, 2008).

According to the Council for Medical Schemes (CMS, 2007), South Africa currently has about sixty (60) different MCOs together with about one hundred and sixty (160) different medical aid schemes, totalling close to seven million medical schemes. From these 160 beneficiaries, there are only about 40 open to the South African public.

Prescribed minimum benefits (PMB) represent the scope of level of benefits that are available to beneficiaries as prescribed by the Medical Schemes Act (131/1998). Any benefit that is offered by the medical scheme must pay in full, without payment sharing or the use of deductibles, the diagnosis, treatment and care costs of the prescribed minimum benefit conditions. However, the co-payment or deductibles may be forced on members who have received their health care from persons other than their designated service providers (Regulations for Medical Schemes Act (Act 131/1998).

Designated health provider is defined according to the Regulations publicised for the Medical Schemes Act (Act 131/1998) as *"a health care provider or group of providers selected by the medical schemes as the preferred provider or providers to provide to its members diagnosis treatment and care in respect of one or more of the prescribed minimum benefit conditions"*.

There are three sets of prescribed minimum benefits applicable to South Africa which include (Still, 2008:115):

- A list of 271 conditions.
- The chronic disease list.
- Emergencies.

Each one of these PMB has a set of minimum treatment standards which have been published in the Regulations for the Medical Schemes Act (Act 131/1998).

The PMB system has been introduced into the South African health care system to avoid incidences where individuals are put at serious financial risk due to unfunded usage of medical services. The list of the PMB consists of disease conditions that all medical schemes are obliged to cover. In addition to that a chronic disease list (CDL) that consists of 26 chronic disease conditions has been attached. All the medical schemes are also obligated to pay for these. Hyperlipidaemia is one of the conditions listed on the CDL (Regulations for the Medical Schemes Act) (Act 131/1998).

The introduction of Prescribed Minimum Benefits aims to attain the following (Medikredit, 2009; Qualsa, 2008):

- Provide treatment access even where members do not have medical scheme coverage due to their plan benefits or limits having been exceeded/depleted.
- Avoid excess pressure on the limited resources of public hospitals as the state would have to manage these patients.
- Encourage more efficient use of the limited health care resources of the public and private sectors.

The PMB cover offered by the medical scheme should be managed under an insured benefit pool and coverage must be offered even if

- there are specified scheme exclusions;
- waiting periods apply; or
- a limit for a specific benefit has been depleted.

In order to contain costs of PMB, medical schemes may assign designated service providers and apply managed care protocols to ensure a cost-effective and efficient health care service to their members (Medikredit, 2009).

2.4 MANAGED HEALTH CARE CONCEPTS

Managed health care consists of certain information systems and techniques. These systems and techniques are laid out in figure 2.3.

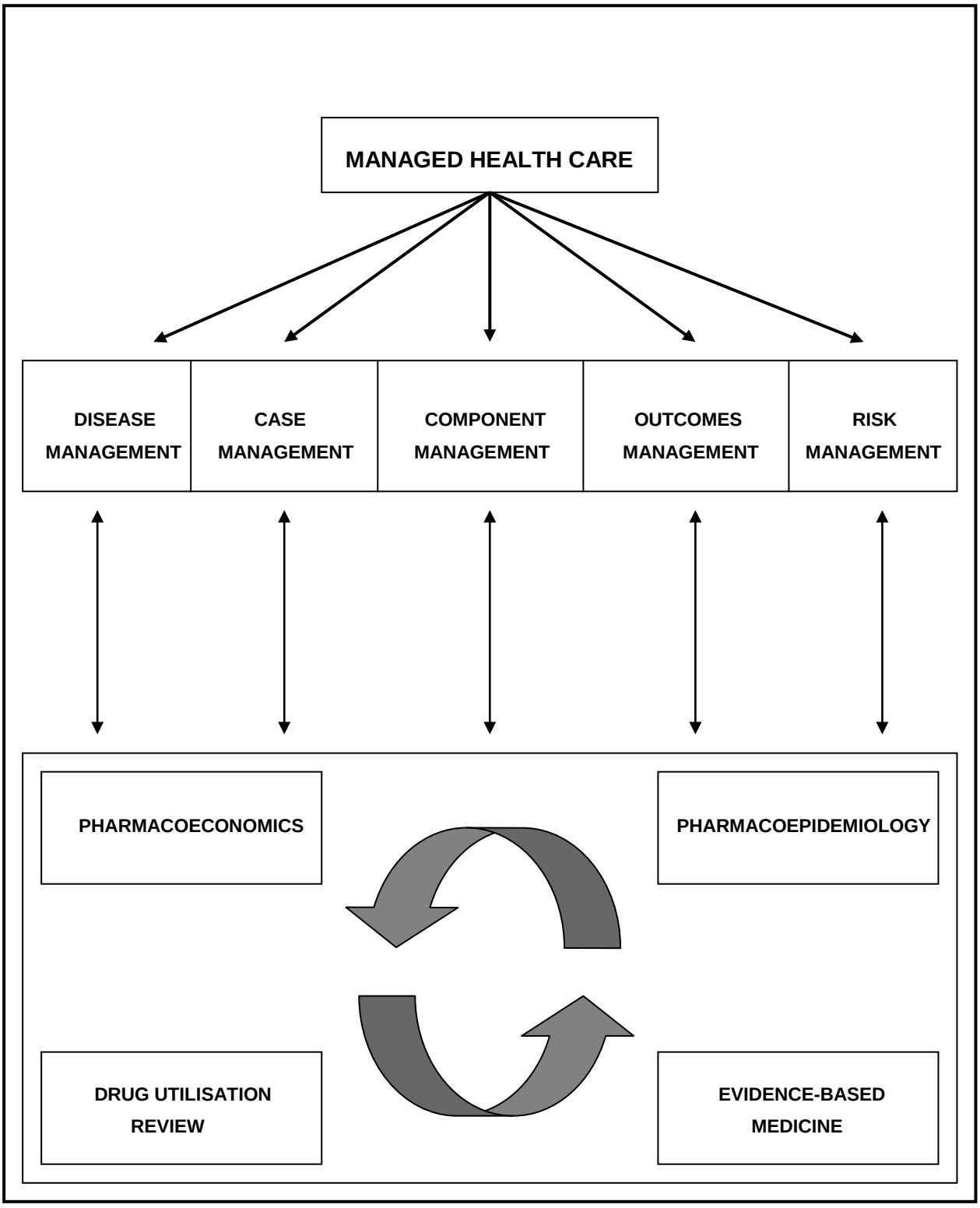

Figure 2.3: Relationship between different concepts of managed health care (adapted from Serfontein & Hein, 1999)

The various components of managed health care as illustrated in figure 2.7 will be discussed in the subsequent paragraphs.

2.4.1 Disease management

In 1996, Wynn (1996:19) stated that disease management is "*a system that integrates and coordinates all providers and facilities that ordinarily deal with the patient (i.e. physician, pharmacist, nurse, hospital, laboratory, managed-care organisation, drug manufacturer, etc.) to provide cost-effective patient care based on the clinical outcomes*". Another definition to be used is the definition of Pasternak and Harris (1996:28), which states that disease management is "*a systematic approach to a health condition or a health care intervention that organises preventative, interventional and care approaches throughout the continuum of care and which measures outcomes in terms of population, not individuals*". The latter two definitions have the same goal even though they differ in focus. Pasternak and Harris (1996:28) focus on the population where Wynn (1996:19) focuses on the patient.

Disease management is thus an approach to strategic management, using inter-disciplinary clinical terms, continuous analysis of data and cost- effective technology to improve the health outcomes of a patient or population.

In disease management, the focus may very well be on quality of care as well as overall cost. Disease management is also proactive since it focuses on the prevention aspects as well as health promotion. The goal of disease management is to decrease health care costs and utilisation over the life of the patient regardless of the short term impact or whether drug benefit costs increase as a result of more aggressive management (Olson, 2002:253). Disease management in South Africa is still at the beginning of implementation, though some guidelines have been set out for certain chronic diseases such as cholesterol / dyslipidaemia. The basic premise of disease management is that there may be a more optimal way to manage patients that could result in lowered costs, and it is possible to develop and implement a system of care that improves health outcomes (van der Merwe, 2002:24). Figure 2.4 illustrates a disease management programme for dyslipidaemia.

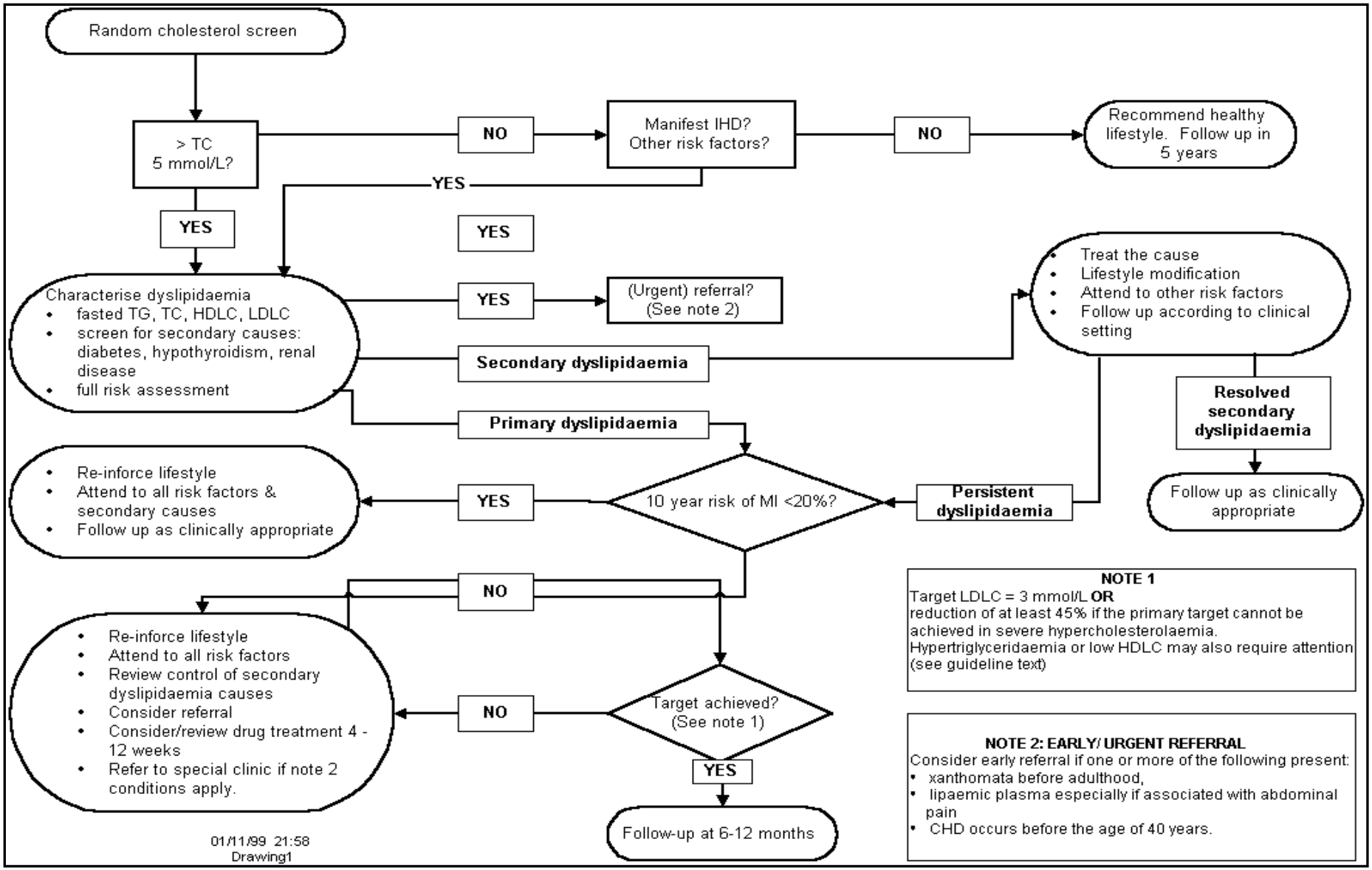

Figure 2.4: Disease management programme for dyslipidaemia (Berger & Marias, 2000:167)

There are three essential elements in disease management (van der Merwe, 2002:25):

- A knowledge base that quantifies the economic structure of the disease problem and describes care guidelines.
- A delivery system that co-ordinates all cares.
- A quality improvement system to audit performance against evolving standards.

Disease management should be a system of care which focuses on the patient and compartmentalisation of care should be avoided, thus providing preventative medicine rather than reactive medicine and poor patient care (McDonald *et al*., 2004:72).

McDonald *et al*. (2004:75) further state that a disease management programme aims to accomplish the following:

- Contain cost.
- Improve health outcomes.
- Reduce variations in health care.
- Improve the quality of care provided.
- Maintain or increase drug sales.

The new model for the management of disease includes population-based risk and disease assessment, systems of disease prevention and health promotion, community-based intervention and provider's network, evidence-based medicine and defined protocols of care with measurement of outcomes. The application of outcomes assessment to the practice of medicine through disease management has already begun (van der Merwe, 2002:26).

2.4.2 Case management

Case management originated in response to movements toward controlling the spiralling costs of health care in accident and health insurance (Siefker *et al*., 1998:3).

According to Al-Assaf (1998:3) case management is defined as "*the process by which an individual patient's care is managed by a plan to assure appropriate, cost-effective treatment in a timely approach"*. Case management is also an element of the utilisation management process and it controls the costs of health insurances (Siefker *et al*., 1998:4). It is therefore a process which assesses, plans, implements, coordinates, monitors, and evaluates options and services to meet an individual's health care needs through communication and available resources (Powell, 2000:5).

Case management is a process which is intended to assist patients in the ongoing process to improve and maintain optimum health (Fraser & Strang, 2004:32). According to Fraser and Strang (2004:32) a personalised case management process is needed since every patient has his/her own unique problems. A standard guideline should be used in every patient's specific case, though, thus case managers must use creativity to add uniqueness to each individuals case management process (Fraser & Strang, 2004:32).

2.4.3 Component management

Component management is a traditional approach to managing health care cost, where the individual health transaction (the doctor's consultation or procedures) is viewed as a relevant unit of service and cost. The duration of treatment, various transactions, and component categories are analysed to establish norms for unit of cost. The unit of cost of each component is then driven as low as possible through aggressive contracting, utilisation management, case management and other cost controlling techniques. Component management provided one of the very first tools for addressing the increased growth of health care costs (Tremonti, 1998).

2.4.4 Outcomes management

Outcomes management (OM) is the "*enhancement of physiologic and psychosocial patient outcomes through development and implantation of exemplary health practices and services, driven by outcomes assessment*" (Marcus, 2000:10). OM is a research-based process that consists of a never-ending cycle of measurement and continuous quality improvement (CQI) of clinical practice (Wojner, 2001:5). OM facilitates dissemination of health outcomes information to patients, providers, and payers of health services (Wojner, 2001:5).

South Africa has entered into an era of unprecedented growth in activity directed at the assessment of outcomes, the analysis of effectiveness and quality assurance in health care (van der Merwe, 2002:27). According to van der Merwe (2002:29), outcomes management is a technology of patient experience designed to help patients, providers and payers make rational medical care-related choices based on better insight into the effect of these choices on the patient's life and quality of life.

Outcomes management is based on the dependence of clinical standards and guidelines that doctors can use to select interventions. It is also a programme in which clinical standards and guidelines are based systematically on patient outcomes where it routinely and systematically measures the functioning and well-being of patients by means of specific clinical outcomes (van der Merwe, 2002:29).

Outcomes measurement represents an objective way to measure the end result of a health care intervention and health payers are demanding efficiency and value for their health care cost.

Table 2.13 presents different outcomes, types and examples thereof.

Table 2.13: Types of outcomes (van der Merwe, 2002:28)

Outcomes	Types	Example
Clinical	• Clinical events • Physiologic and metabolic measures • Morbidity and mortality rates	• Blood pressure and measurement of cholesterol levels • Death (cardiovascular) and all causes and complications • Measures if group patients lived longer and improve in their health status
Economic	• Direct medical • Indirect medical	• Hospitalisations and outpatient visits • Work loss and restricted activity days
Humanistic	• Symptoms • Quality of life • Fuctional status • Patient satisfaction • Disability	• Quality of life lost, life years affected

The addition of outcomes management to practices of health care has resulted in efforts to implement disease management programmes. These efforts are based on systematic population-based approaches in identifying patients at risk, intervening with specific programmes of care and measuring clinical and other outcomes (van der Merwe, 2002:28).

2.4.5 Risk management

Risk management is a term that was first coined by insurance companies in the United States during the 1960s to describe the control of expenditure on the generality of claims (van der Merwe, 2002:13).

According to Rognehaugh (1998:221) risk management is "*a health care function or discipline that executes one or more strategies to limit the organisation to the financial risk associated with delivering care; which may include the strategy of reviewing the actuarial risk of a given enrolment population toward catastrophic care, purchasing insurance or self-insuring to protect against risk, associated medico-legal factors to protect against undue risk, or organisational programs [cit] to preclude the occurrence of health events that typically lead to legal claims*". Risk management is defined by van der Merwe (2002:13) as the systematic process of

identifying and evaluating together with addressing actual risk through a well-designed programme that prevents, controls and minimises risk exposure.

The increase of medical malpractice lawsuits led the insurance companies to apply the same techniques to the health sector. Public and private health care providers developed risk management programmes to prevent injury to patients, visitors and staff to control liability of costs (van der Merwe, 2002:13).

Risk management is thus the application of skills, knowledge and risk management tools and techniques to a project in order to reduce threats to an acceptable level while maximising opportunities (Heldman, 2005:214).

2.4.6 Conclusion of the different instruments used in managed health care

Disease management, case management, risk management and outcomes management are different management strategies which can be used in managed health care. Wojner (2001:178) explains that the different instruments used in managed health care have a constricted relationship. Outcomes management can always be seen as the central part of the connection between the different instruments.

Disease management incorporates outcome research technology into outcomes measurement and creates management programmes. Disease management and outcomes management are separated by only a technical distinction (van der Merwe, 2002:26). Wojner (2001:178) added that case management can be seen as an opposite outcomes to disease management with outcomes management being the core, this is illustrated in figure 2.5. In this study risk management plays a part in all of the different managed care instruments.

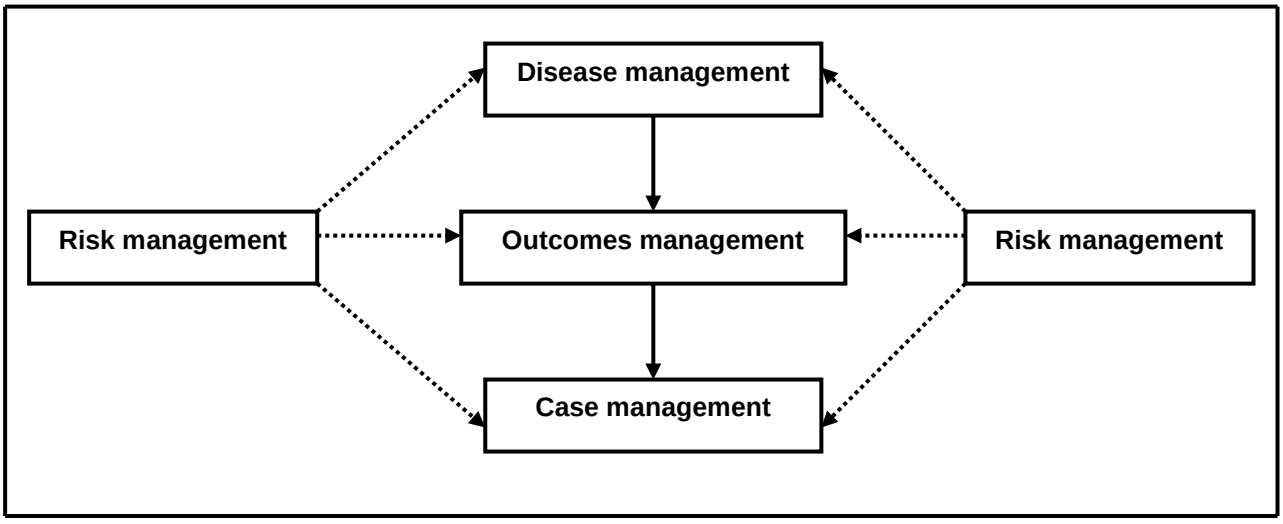

Figure 2.5: The relationship between the health care instruments (adapted from van der Merwe, 2002:27; Wojner, 2001:178)

In the next section the different information systems for managed health care such as drug utilisation review (DUR), pharmacoeconomics, pharmacepidemiology and evidence-based medicine will be discussed as well as the different measurement tools within the framework of these systems (refer to paragraphs 2.5.1 and 2.5.2).

2.5 INFORMATION SYSTEMS FOR MANAGED HEALTH CARE

2.5.1 DRUG UTILISATION REVIEW (DUR)

Drug utlisation review (DUR) as information system for managed health care and its measurement tools within the framework will briefly be discussed in the subsequent paragraphs.

2.5.1.1 Defining drug utilisation review

Kreling and Mott (1993:415) refer to the definition of the secretary of the Health, Education and Welfare Task Force that defined DUR as a "*dynamic process aimed at the consequent improvement in the quality of health care and minimising needless expenditure*".

Drug utilisation was defined in 1977 by the World Health Organization (WHO) as the "*marketing, distribution, prescription, and use of drugs in a society, with special emphasis on the resulting medical, social and economic consequences*" (WHO, 2003a:8). A good DUR programme will look at all processes involved in the rendering of a pharmaceutical service (Serfontein & Hendriks, 2001:3).

Walters and Smart (1994:821) formulated a definition for the South African situation as follows: "*A DUR program [cit] is an authorised, structured, ongoing system for the monitoring of drug use through comparisons with specific standards and initiating of corrective action when drug-use patterns are inconsistent with these standards*". In this definition Walters and Smart neglected the cost aspect and focused on the rational medicine use. In the Republic of South Africa (RSA) the cuttings of health care cost without compromising the quality of the health care are contentious issues being addressed in both the private and public sectors (Serfontein & Hendriks, 2001:3).

DUR is a process specifically formulated to improve safe, effective and appropriate drug therapy by detecting widespread variations from prescribing drug utlilisation (Jones & Radloff, 2007:32). With this in mind, a definition for the purpose of this study can then be seen as a structured system to determine whether the usage patterns of hipolipidaemic medicine is safe, effective and appropriate in a specific sex or age group, compared to standard criteria and prescribed drug treatment.

2.5.1.2 Rationale for drug utilisation research

The principal aim of drug utilisation research is to determine whether the use of drugs in populations is rational or not (WHO, 2003a:9). For the individual patient, the rational use of a drug implies the prescription of a well-documented drug at an optional dose, together with the correct information, at an affordable price (WHO, 2003a:9). Without knowledge of how drugs are being prescribed and used, it is difficult to initiate a discussion on rational drug use or to suggest measures to improve prescribing habits. Information on the past performance of prescribers is the linchpin of any auditing system (Sjöqvist & Birkett, 2003:78). Drug utilisation research in itself does not necessarily provide answers, but contributes to rational use in important ways (WHO, 2003a:9).

2.5.1.3 The drug utilisation review process

DUR systems include an input (the health care system and data structure), the process (criteria, application, intervention and evaluation), and end with an output (specified percentage of decreased costs, hospitalisations or drugs per patient) (Jones, 1991:620).

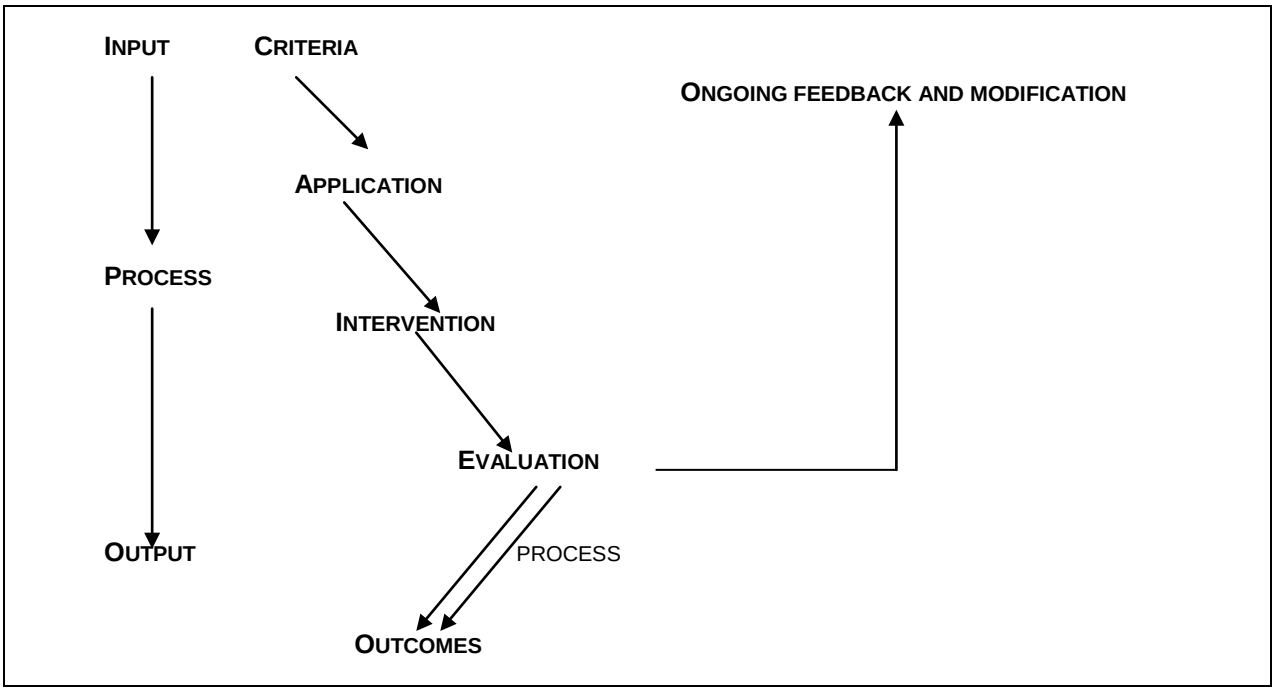

Figure 2.6: The system's view of drug utilisation review (Jones, 1991:621)

In the following section the classification, nature and type of DUR-studies will be discussed and related examples as applied to dyslipidaemia will be presented (refer to paragraph 2.5.1.8).

2.5.1.4 Classification of drug utilisation review

Drug utilisation reviews can be divided into “quantitative” or “qualitative” (Kongstvedt, 1993:154). Both of these studies as classification systems for DUR will be discussed respectively in the subsequent paragraphs.

2.5.1.4.1 Quantitative drug utilisation review studies

According to Iñesta (1992:353) and Sjöqvist and Birkett (2003:80) quantitative data may be used to describe the present state and trends in drug prescribing and drug use at various levels of the health care system. Quantitative data are usually obtained from routinely collected data or from surveys (Sjöqvist & Birkett, 2003:80), and can be used to process the following (Iñesta, 1992:353; Lee *et al*., 2006:400; Sacristan & Soto, 1994:300):

- Analyse the amount of drugs consumed in a specific area.
- Identify over- and under-prescribing areas.
- Estimate the misuse of drugs.
- Compare consumption or prescribing patterns of drugs in specific areas.
- Calculate the utilisation of drugs in accordance to demographical features.
- Observe the impact of informational or regulatory activities on drug use patterns.

2.5.1.4.2 Qualitative drug utilisation review studies

Qualitative studies assess the appropriateness of drug utilisation and generally link prescribing data to reasons (indications) for prescribing (Lee & Bergman, 1994:380; Sjöqvist & Birkett, 2003:80). Qualitative DUR studies include the collecting, organising, analysing and reporting of information on the rationality of drug use and can be used to accomplish the following (Kreling & Mott, 1993:416; Lee *et al*., 2006:400):

- Assess the daily dosage suitability.
- Analyse the time period of therapy.
- Identify potential drug interactions.
- Establish the most suitable dosage per indication.
- Assess the fixed combination of drugs.
- Establish an indication of use for a specific drug or non-drug regimen.

2.5.1.5 Nature of drug utilisation review studies

Based on their nature, drug utilisation studies are divided into prospective, retrospective and concurrent reviews which will be described in table 2.14.

Table 2.14: The nature of drug utilisation reviews (compiled and adapted from Blackburn, 1993; Krawleski *et al*., 1994; Kreling & Mott, 1993; Wertheimer & Navarro, 1999; Powell, 2000).

Type	Description
Prospective reviews	• Prospective review has the greatest potential benefit for the patient, because it identifies drug therapy problems and corrects them before they can occur. It relies on criteria from published literature, clinical experience and basic pharmacological principles to provide an evaluation of drug therapy (Krawleski *et al*., 1994:425; Kreling & Mott, 1993:417). • The Drug utilisation review (DUR) procedure is usually achieved through computer linkages between the DUR company and the network of participating pharmacies and it is accomplished through prior authorisation programmes, which require physicians to obtain approval before prescribing certain medications (Wertheimer & Navarro, 1999:379).
Retrospective reviews	• Retrospective review is a programme that is largely focused on preventing recurrence of a problem and is a structured ongoing initiative that interprets patterns of drug use in relation to predetermined criteria therefore attempt to minimise inappropriate prescribing (Hennessy *et al.*, 2003:1494; Krawleski *et al.*, 1994:431). Retrospective DUR has a number of advantages: o By using a data base from a medical aid it can be performed effortlessly. o Inappropriate prescribing practices can be identified and through educational interventions with the doctor these problems can be eradicated (which will lead to rational prescribing and better quality treatment for the patient). o Drug therapy trends and information in certain geographical areas can be analysed and if required to, can be changed by using suitable interventions. o Relatively it is an inexpensive type of DUR method with a variety of interesting applications.
Concurrent reviews	• Concurrent review concentrates on the appropriateness and correctness of the drugs prescribed while the patient is in the facility. • Concurrent review is very limited and only used for patients on chronic medication and certain institutionalised patients. If the desired effect (therapeutic outcome) is not achieved, this review therefore allows for the changing of therapy (Blackburn, 1993:15; Powell, 2000:502).

2.5.1.6 Types of drug utilisation review studies

There are various types of DUR studies, cross-sectional, longitudinal or continuous longitudinal and these will be described in table 2.15.

Table 2.15: Types of drug utilisation review studies (adapted from WHO, 2003a)

Cross-sectional studies	• According to The World Health Organization (2003a:17) cross-sectional studies is "data, which provided a 'snapshot' of drug use at a particular time (e.g. over a year, month or a day)". • Comparisons can be made with data collected over the same time period in another health facility. Such data can be drug-, problem-, indication-, prescriber-, or patient-based. • A cross-sectional study can measure drug use or be criterion-based to assess drug use in relation to guidelines or limitations (WHO, 2003a:17). • A cross-sectional study can be carried out before and after an educational or any other intervention (WHO, 2003a:17).
Longitudinal studies	• According to the WHO (2003a:17) longitudinal data is a necessity to public health authorities to study the trends in drug use. • This data can be on total drug use as obtained through a database or it can be on a statistically valid sample of pharmacies / medical practices (WHO, 2003a:17). • Data used in longitudinal studies are often obtained from cross-sectional surveys, and although data collection is a constant and continuous process, the practices and patients surveyed are constantly changing (WHO, 2003a:17). • Prescribing trends of individual practitioners and practices cannot be obtained from longitudinal data.
Continuous longitudinal studies	• Continuous longitudinal data can be collected at individual practitioners and patient levels (WHO, 2003a:17). Through a unique identifier claims databases are able to follow individual patients. • Information about concordance with treatment based on the period among prescriptions, co-prescribing, duration of treatment and prescribed daily doses (PDDs) can be provided through continuous longitudinal data (WHO, 2003a:17).

2.5.1.7 Drug utilisation review units of measurement

The units of measurement used in DUR will be discussed in table 2.16.

Table 2.16: Units of measurement in drug utilisation review (compiled and adapted from Sjöqvist & Birkett, 2003; WHO, 2003a)

Defined daily dose (DDD)	• The WHO (2003a:38) defines DDD as "*the assumed average maintenance dose per day for a drug used for its main indication in adults*." • The defined daily dose is a unit of measurement and does not necessarily agree with the recommended or prescribed daily dose (PDD) (Sjöqvist & Birkett, 2003:83). • The doses for individual patients and patient groups will often differ from the DDD and have to be based on individual characteristics (e.g. age and weight) as well as pharmacokinetic and pharmacogenetic considerations. • The DDD is often a compromise based on a review of the available information about doses used in various countries (WHO, 2003a:38). • The DDD may even be a dose that is seldom prescribed, because it is an average of two or more commonly used dose sizes (WHO, 2003a:38).

Table 2.16: Units of measurement in drug utilisation review (compiled and adapted from Sjöqvist & Birkett, 2003; WHO, 2003a) (continued)

Prescribed daily dose (PDD)	• According to The World Health Organization (2003a:38) PDD can be defined as "*the average dose prescribed according to a representative sample of prescriptions.*" • Studies of prescriptions or medical-/ pharmacy records can establish the PDD. • PDD does not necessarily reflect actual drug utilisation since the patient does not always take all the prescribed medication that has been dispensed (Sjöqvist & Birkett, 2003:84).
Cost	• According to the WHO (2003a:39) drug use can be expressed in terms of costs. Cost figures are appropriate for an in general analysis of expenditure on drugs. • International comparisons based on cost parameters can be misleading and have limited value in the evaluation of drug use (WHO, 2003a:39). • Long-term studies are difficult due to fluctuations in currency and changes in prices (Sjöqvist & Birkett, 2003:83; WHO, 2003a:40). • When cost data are used, an increase in the use of cheaper drugs may have little influence on the total level of expenditure on drugs, while a shift to more expensive drugs is more noticeable (WHO, 2003a:40).
Other units for presentation of volume	• Grams of active ingredient. • Number of tablets. • Number of prescriptions (WHO, 2003a:39).

2.5.1.8 Application of drug utilisation reviews to the use of statins

Numerous studies have been conducted using drug utilisation review on hipolipidaemics. Examples of such studies are outlined in table 2.17.

Table 2.17: Examples of drug utilisation studies on hipolipidaemic medicine items

Author & Year	Description	DUR classification, type and nature	DUR measurement unit	Outcome
Hartz *et al*. (2007)	Estimates for all statins consumed in Norway, with focus on atorvastatin *vs* simvastatin.	Cross-sectional and longitudinal; quantitive and qualitative; prospective / longitudinal	PDDs; DDDs; number of prescriptions	Atorvastatin and simvastatin were dispensed in 79 – 87% of all statin users, and the proportion was significantly higher in the high consumption county. The estimated PDDs were higher than the DDDs, up to twice the DDD for atorvastatin. The high consumption county had the highest PDD for simvastatin (25.9 mg) and atorvastatin (21.9 mg), and more users received tablets in the upper range of available strengths. Continuity of therapy was similar in the three counties in Norway.

Table 2.17: Examples of drug utilisation studies on hipolipidaemic medicine items (continued)

Tabata *et al*. (2007)	Determine and define the renoprotective effect of preoperative statin use in coronary artery bypass grafting.	Retrospective cohort; longitudinal; quantitative	Number of prescriptions; DDDs	The statin group had a lower incidence of new renal insufficiency than the non-statin group (1.6% *vs* 3.9%, odds ratio 0.39, 95% confidential interval 0.18 to 0.82). Multivariate logistic regression analysis including all patients also showed that preoperative statin use (odds ratio 0.54, 95% confidence interval 0.30 to 0.99) was significantly associated with low incidence of new postoperative renal insufficiency. In conclusion, preoperative statin use may be renoprotective after coronary artery bypass grafting.
Savoie & Kazanjian (2001)	Study on the utilisation of lipid-lowering drugs in men and women in Canada.	Retrospective; longitudinal; quantitative	Number of prescriptions	The results indicated that, 74.7 per cent of individuals on statins had no reported history of coronary heart disease. Women without coronary heart disease formed 23.1 per cent of statins recipients and were aged 70 and over. Only 15.3% of men with CHD had been prescribed a statin. Based on the systematic review, 88.7% of the utilisation of statins in this Canadian province was not supported by the results of the systematic review. Considering baseline lipid-levels does not substantially alter these findings. This study concludes that statins prescribing practices need to be realigned with research evidence. This implies refocusing utilisation away from women and the elderly, towards men with CHD.
Straus *et al*. (1999)	Use of a tiered review for evaluation of appropriate drug use of HMG-CoA reductase inhibitor therapy.	Longitudinal; quantitative and qualitative; concurrent review	PDDs; DDDs; number of prescriptions	The pharmacy reviewer judged 57 (48%) of the 118 high-dose cases and 47 (47%) of the 100 standard-dose cases to be questionable; these were subsequently reviewed by the physician reviewer, who found that 43 (75%) of the 57 questionable high dose cases and 38 (81%) of the 47 questionable standard-dose cases involved suboptimal prescribing practices. Overall, the physician's review determined that 36% of the high-dose cases and 38% of the standard-dose cases reviewed involved suboptimal prescribing practices.
Raymond *et al*. (2007)	The purpose of this research was to measure prevalent and incident statin use in the population of British Columbia from 1996 to 2004 across specific patient characteristics (sociodemographic and clinical).	Quantitative and qualitative; continuous longitudinal studies; retrospective review	PDDs; DDDs; number of prescriptions	Prevalent use (1996-2004) and incident use (1999-2004) of statins in an entire population have increased dramatically. Although many statin users (60.19%) had evidence of medical conditions that indicate appropriate statin use, 39.91% of users were at low risk for cardiovascular disease, and therefore the benefit of statins in this group remains small.

Table 2.17: Examples of drug utilisation studies on hipolipidaemic medicine items (continued)

Cooke & Hammerash (2006)	The objective of this study was to evaluate the treatment of dyslipidemia in patients with CHD and determine if sex differences exist.	Retrospective, quantitative and qualitative	Number of claims (dianostic codes)	The majority of CHD patients from a Maryland-based health maintenance organization had elevated LDL-C values, despite a lipid-lowering prescription rate of 68.6%. A significant gap in dyslipidaemia treatment in these CHD patients remained, particularly for women.

Most DUR studies as respected in table 2.17 have been done in retrospect with PDDs and DDDs as the unit of measurement. Looking at the outcomes as reported in table 2.17, it is clear that DUR is very effective in the health care environment and provides valuable answers.

2.5.1.9 Drug utilisation review in South Africa

The National Drug Policy of South Africa (1996) has some specific aims, policies and strategies that include the following:

- Drug selection: To promote the rational choice of drugs and associated items to be used in South Africa, in accordance with the Essential Drugs concept. Essential drugs are drugs that are required to treat the majority of conditions that are prevalent in a country in a cost-effective and efficient manner. The concept does not imply that no other drugs are useful, but that these drugs are the most needed for the health care of the majority of the population. They should therefore be available at all times, in adequate amounts and in the proper dosage forms (Department of Health, 1996:18).

- Procurement and distribution: To ensure an adequate supply of effective and safe drugs of good quality to all people in South Africa. Standard Operating Procedures (SOP) will be developed with practical guidelines to cover all administrative procedures to manage and control effectively the storage and distribution of drugs (Department of Health, 1996:18)

- Rational use of drugs: To promote the rational prescribing, dispensing and use of drugs by medical, paramedical and pharmaceutical personnel and to support the informed and appropriate use of drugs by the community (Department of Health, 1996:18).

These aims are combined in the definition of drug utilisation of the WHO. Drug utilisation reviews may be used to reach these aims of the National Drug Policy.

Venter (2009) stated that millions of DURs are annually performed in South Africa by PBMs. Examples of DUR studies conducted on hipolipidaemic medicine items in South Africa are presented in table 2.18:

Table 2.18: Examples of drug utilisation studies on hipolipidaemic medicine items performed in South Africa

Author & Year	Description	DUR classification, type and nature	DUR measurement unit	Outcome
Truter & Kotze (1996)	To estimate average prescribed daily doses (PDDs) for selected hipolipidaemics available on the South African market, compared to the estimated PDDs with established DDDs and international dosage ranges. To investigate the age and sex of the hipolipidaemic users.	Retrospective drug utilisation study using data from an organisation.	PDDs and DDDs.	The PDDs used in the patient population studied were within locally and internationally acceptable dosage ranges, but were generally lower than established DDDs for lipid-lowering drugs. Prescription differences occured between female and male patients and between age groups with regard to chronic medication.
Truter & Kotze (1997)	To investigate the variability of prescribed daily doses (PDDs) with respect to sex and age categories in the usage of simvastatin in South Africa.	Retrospective drug utilisation study using prescription data from various medical schemes..	PDDs and DDDs.	Average PDDs were in all cases lower than the DDD of 15mg, except for females aged 30 to 39 years. In almost all sex and age categories, a dose of 10mg was the median as well as the mode and the standard deviation of the PDD for females and males decreased age the age of 40 to 49 years. Variation existed in the dosage regimen of simvastatin which depended on a multitude of factors, such as the severity of the disease state, sex and age.

Both these studies were conducted in retrospect with PDDs and DDDs as the unit of measurement.

2.5.1.10 Conclusion to drug utilisation review

There is a definite and compelling need for drug utilisation in South Africa. Drug utilisation research is a multidisciplinary activity and the results of drug utilisation studies can be used for various purposes. It can, for example, be a part of an academic investigation, a management initiative or an audit of the performance of a drug or group of drugs. Drug utilisation research is a valuable component of quality assurance for medicine usage. It should thus be formally recognised and encouraged, and the necessary infrastructure for this type of research needs to be established in South Africa.

According to Sacristan and Soto (1994:299) the concomitant use of drug utilisation review with pharmacoeconomics can result in improved cost-effective utilisation of medicines and a better utilisation of pharmacoeconomic methods, both of which contribute to a more rational use of drugs. This in turn, can help to achieve at least one of the economic objectives of the National Drug Policy for South Africa, namely the promotion of the cost-effective and rational use of drugs (Truter, 1997:20).

The concomitant use of drug utilisation review with pharmacoeconomics can result in a more cost-effective utilisation of medicines and a better utilisation of pharmacoeconomic methods, both of which contribute to a more rational use of drugs (Sacristan & Soto, 1994:299). Pharmacoeconomics and its contents will be discussed in the subsequent paragraphs.

2.5.2 PHARMACOECONOMICS

2.5.2.1 Introduction

Pharmacoeconomics is particularly relevant when managing the health of a group or a population and any organisation that makes use of pooled resources to pay for the health services e.g. managed health care organisations, government programmes and insurance plans (Vogenberg, 2001:2).

The proportion of prescriptions costs paid for by public financed schemes has been increasing steadily and there are also concerns about the quality of prescribing patterns as well as the effectiveness of many drugs, with some preparations having little or even no proven therapeutic value (Robays, 1999).

The treatment of coronary heart diseases places a substantial financial burden on health care resources (McMurray, 1999:100). This is because the cost of coronary heart disease is the sum of three components: (1) the medical resources used to treat the illness, (2) the non-medical resources associated with it, and (3) lost productivity due to illness (Larson, 1996:46). As a result, pharmacoeconomic analysis of the management and impediment strategies for coronary heart diseases is a valuable tool for comparing the cost-effectiveness of new medical interventions allowing health care decision makers to contain cost by choosing those interventions that are most efficient (McMurray, 1999:100). This is imperative especially because intervention to lower cholesterol levels with drugs involves large populations of patients and potentially high costs (Johannesson *et al*., 1997:332).

Economics of health care includes not merely an assessment of the cost of a new therapy, but also an assessment of its overall economic and clinical impact. The discipline of pharmacoeconomics is developed to fulfil this role (Li, 2003:192).

2.5.2.2 Defining pharmacoeconomics

Pharmacoeconomics identifies, measures and compares costs and consequences of medicine therapy to health care systems and the society (Carriere & Huang, 2001:19; Sanchez, 2005:1). Cantor (2002:S29) furthermore stated that pharmacoeconomics is an interdisciplinary science that incorporates elements from pharmacies, clinical medicines, clinical epidemiology, statistics, psychology, economics and ethics. More recently, Jones (2006:96) described pharmacoeconomics as an evidence-based approach that assesses whether the additional benefits associated with a medicine or medicine therapy are worth the additional costs associated with the treatment.

Pharmacoeconomics can thus be seen as a simultaneous comparison of medicines against alternative treatments (medicine based or non-medicine based) with reference to both the costs and outcomes.

2.5.2.3 Objectives of pharmacoeconomics

The primary objective of pharmacoeconomic analysis is to identify measures and compare the costs and consequences of pharmaceutical interventions (Venturini & Johnson, 2002). A pharmacoeconomic study is thus intended to apprise the decision maker (whether it is the patient, family, provider, a third party payer, or the policy maker) about the balance between the cost and effects of a new health care practice in comparison with an established method (Rajagopalan *et al*., 1996:1298).

Health care costs are increasing rapidly and the ageing of populations in developed countries has contributed significantly to the need for consideration of effectiveness in the evaluation of any health care treatment, especially in pharmaceuticals (Li, 2003:192). The ultimate objective of pharmacoeconomic evaluation is to compare costs and outcomes of alternative regimens, ideally by generating a single index or cost-outcome ratio (Li, 2003:194). This ratio can be generated by using the process as shown in figure 2.7.

A properly constructed pharmacoeconomic evaluation will provide valuable insights that will allow for the selection of options representing the best value for money, without compromising the quality of care that will be received (Li, 2003:199).

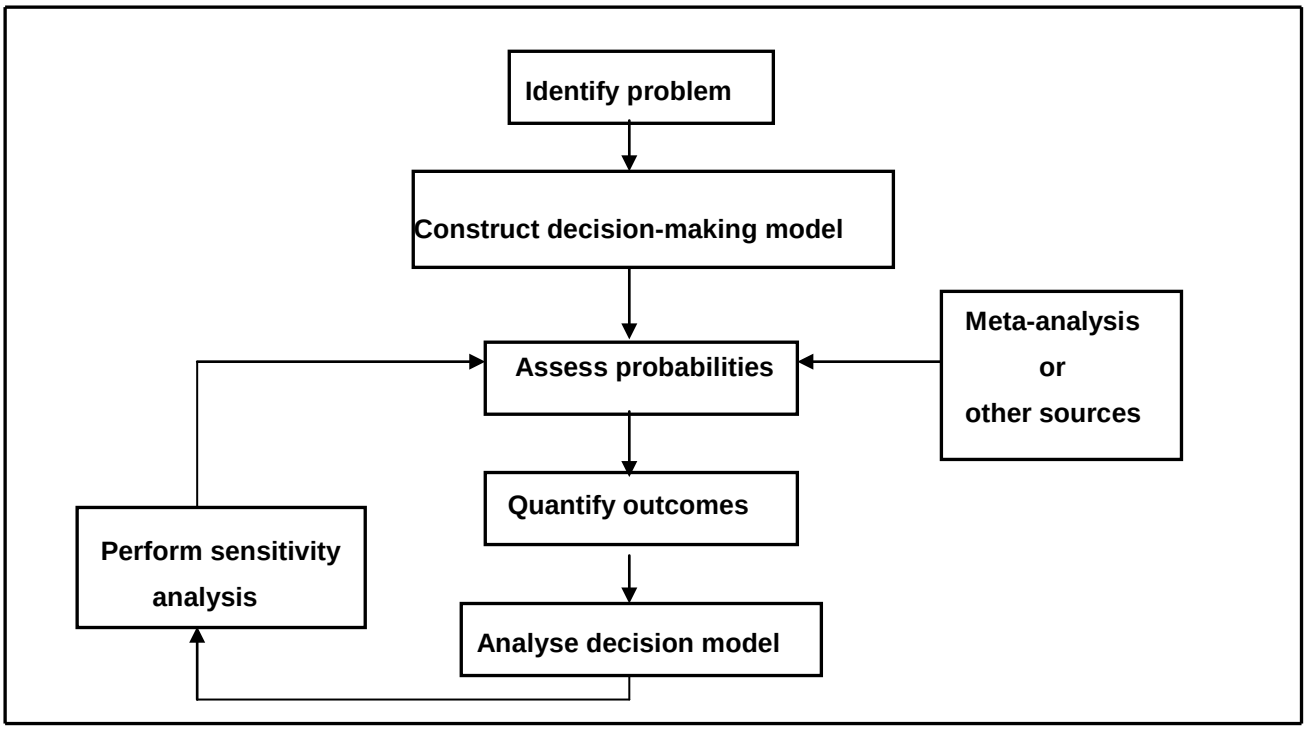

Figure 2.7: Overview of the process of pharmacoeconomic evaluation (Li, 2003:194)

In accordance with the pharmacoeconomic evaluation by Li (2003:194), the WHO (2000) formulated the following main steps in conducting a pharmacoeconomic evaluation:

- Define the economic question and the perspective of the study.
- Determine the treatments that need to be evaluated.
- Choose the study design.
- Identify, measure and value the costs of the alternative treatments.
- Identify, measure and value the benefits associated with the alternative treatments.
- Adjust costs and benefits for differential timing.
- Measure the incremental costs and benefits.
- Combine costs and benefits and analyse the results.
- Test the sensitivity of the results.

2.5.2.4 Application of pharmacoeconomics

The proper application of a pharmacoeconomic model in clinical medicine would necessitate a multidisciplinary approach that requires expertise and inputs from clinical medicine practitioners, biostatistics and psychometrics, among others. Li (2003:192) is also of the opinion that a properly conducted pharmacoeconomic evaluation will provide valuable insight for clinicians to allow them to choose from the options that represent the best value-for-money without compromising the quality of care delivered.

Pharmacoeconomics has been lauded to be of great value in the following areas of health care delivery:

- To improve public and individual health through improved rational decision making.
- To determine relative values among alternative therapies.
- To improve system resource allocation.
- To determine whether interventions work in practice.
- To assess whether the care is of high quality.
- To assess new diagnostic tests.
- To determine whether a programme represents good value-for-money (Li, 2003:194).

To date, the most successful application of the principles of pharmacoeconomics is in the areas of purchase decision, subsidy decision, establishing practice standards and the assessment of technologies (Li, 2003:192).

2.5.2.5 Methodology of pharmacoeconomics and cost-analysis

The term cost-analysis is used widely and is therefore sometimes abused (Beyea & Nicoll, 1999:1). Cost analysis is a process that examines cost-related aspects of a specific clinical process or event (Beyea & Nicoll, 1999:1). Accordingly, cost-analysis is performed to provide information that will help decision makers determine how a resource or resources will be allocated. Expenses may include direct and indirect costs and outcomes and benefits may be reflected by clinical measures or financial calculations based on the projected benefit of outcome.

There are different methodologies that exist in a pharmacoeconomic analysis such as cost-benefit analysis (CBA), cost-minimisation analysis (CMA), cost-effectiveness analysis (CEA) and cost-utility analysis (CUA) (Walley *et al*., 2004:108). In table 2.19 the different methodologies and the criteria for selecting different methodologies are compared.

In subsequent paragraphs examples of the application of pharmacoeconomic studies as related to dyslipidaemia/hyperlipidaemic will be given (refer to paragraph 2.5.2.6).

Table 2.19: Different methodologies and criteria for selecting pharmacoeconomic study methods (compiled from Chang & Nash, 1998:13; Walley *et al*., 2004:108)

Method of evaluation	Aim of evaluation	Costs and benefits
• **Cost-benefit analysis (CMA)**	Comparison of different programmes with different outcomes.	Costs and benefits are measured in pecuniary units to determine a cost benefit ratio.
• **Cost-minimalisation analysis (CMA)**	Comparison of similar therapies producing essentially identical outcomes.	The cost is measured for additional cost to therapy A relative to therapy B.
• **Cost-effectiveness analysis (CEA)**	Comparison of different therapies resulting in clinically different patient outcomes.	Measures the cost per life saved, cost per patient cured or cost per life year gained.
• **Cost-utility analysis (CUA)**	Comparison of similar therapies affecting quality of life.	Measures cost per Quality Adjusted Life Years (QALY) gained.
• **Cost-of-illness evaluation**	Compares prevention / treatment options.	Estimates the cost of a defined population.

A discussion of these methods of pharmacoeconomics will follow subsequently.

2.5.2.5.1 Cost-benefit analysis (CBA)

Cost-benefit analysis (CBA) is a type of clinical economic evaluation of the outcomes of a programme or an intervention (Carriere & Huang, 2001:19). CBA measures both the costs and the benefits in monetary terms by net benefits (total benefits - total cost) or by benefits-to-cost ratio (total benefits/total cost) (Bungay & Sanchez, 2003:32; Carriere & Huang, 2001:19).

According to Bungay and Sanchez (2003:32), in a CBA, the benefits acquired from a programme or an intervention, and all the costs of providing that programme or intervention are identified and converted into equivalent dollars in the year in which they will occur.

The consequences of CBA should be measured as the willingness-to-pay of the individuals who bear the consequences (Barner & Rascati, 2003:115; Carrier & Huang, 2001:19). These consequences include direct and indirect benefits such as explained below (Bootman *et al*., 1996:63):

- Direct benefits

  Direct benefits include the portion of averted costs currently borne that are associated with spending for health services; they represent potential savings in the avoided use of health resources (Bootman *et al*., 1996:63).

- Indirect benefits

  Indirect benefits include the potential increased earnings of productivity gains that would not have been possible without the particular health care programme (Bootman *et al*., 1996:63).

There are five steps in conducting a CBA and they are depicted in figure 2.8.

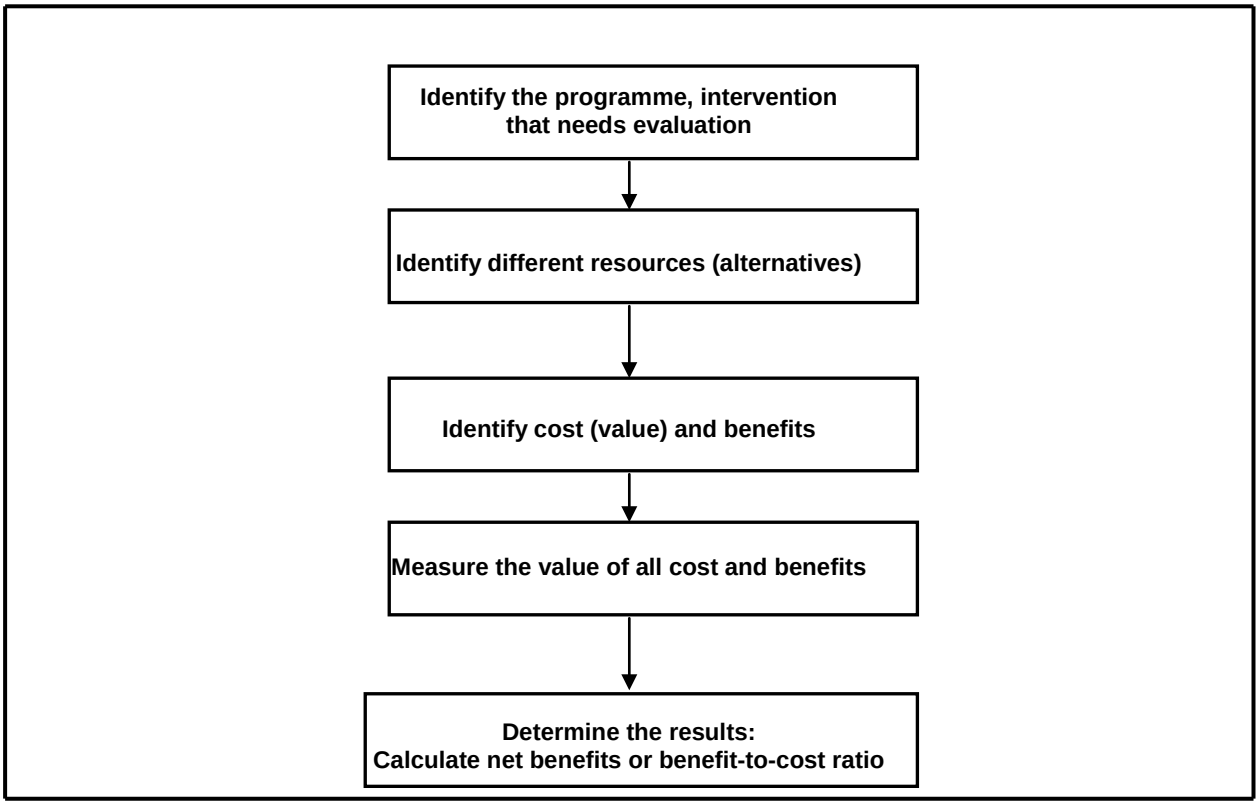

Figure 2.8: Steps in conducting a cost-benefit analysis (Barner & Rascati, 2003:120; McGhan & Kitz, 1996:65)

2.5.2.5.2 Cost-minimisation analysis (CMA)

CMA is a technique designed to identify the preferred choice among possible alternatives with equivalent outcomes or consequences by examining the cost associated with each of those alternatives (Carriere & Haung, 2001:19). According to Bungay and Sanchez (2003:32) cost-minimalisation analysis is used to compare two or more treatment alternatives that are both equal in efficacy, and treatment alternatives are measured in monetary terms.

2.5.2.5.3 Cost-effectiveness analysis (CEA)

Cost-effectiveness analysis (CEA) compares the costs of medical interventions based on their effectiveness, in monetary terms. The effectiveness is determined independently and is measured in terms of clinical meaningfulness (e.g., life years gained) (Strom & Kimmel, 2006:474).

After a CEA an incremental cost-effectiveness ratio is calculated as in figure 2.9.

$$\text{ICER} = \frac{\text{(Cost of treatment A) – (Cost of treatment B)}}{\text{(Effectiveness of treatment A) – (Effectiveness of treatment B)}}$$

Figure 2.9: Formula for an incremental cost-effectiveness ratio (Venturi & Johnson, 2002)

The results express the cost that - on average - needs to be sustained to obtain "an additional success" if treatment A is chosen instead of B (e.g., cost per avoided recurrence, cost to avoid a complication, cost to avoid an adverse event, etc.) (Venturini & Johnson, 2002).

According to Edejer *et al*. (2003:5) CEAs have two main uses namely:

- CEA of a wide range of interventions can be performed to inform a specific decision maker.
- CEA of a wide range of interventions can be performed to provide general information on the relative costs and health benefits of different technologies or strategies, which contribute through multiple channels to a more informed debate on resource priorities.

The steps in performing a CEA are described in figure 2.10.

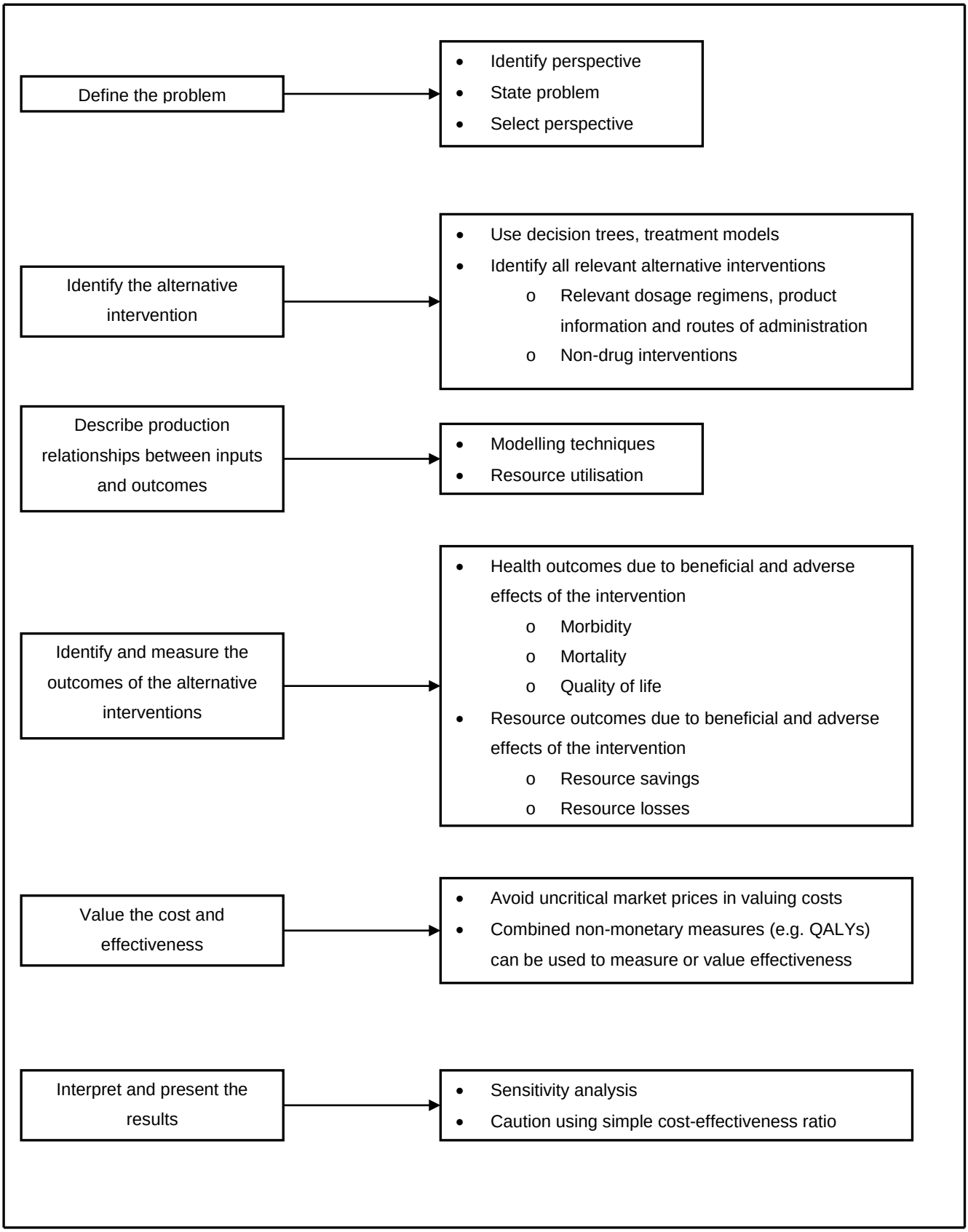

Figure 2.10: Steps in performing cost-effectiveness analysis (Bootman *et al*., 1996:80)

After performing a CEA there are four possible results as illustrated in Figure 2.11.

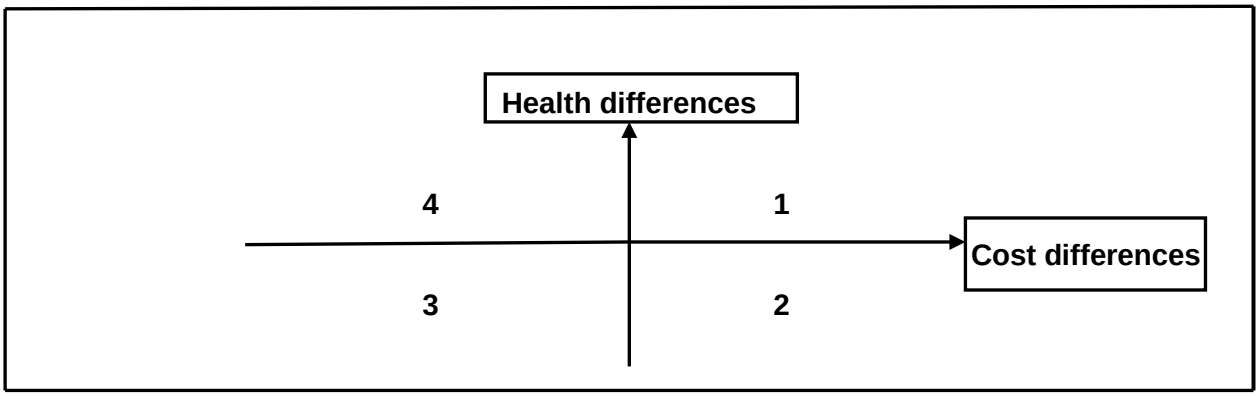

Figure 2.11: Four possible results of a cost-effectiveness analysis (Walley *et al*., 2004:112)

In figure 2.11 the four quadrants represent the following (Walley *et al*., 2004:112):

- **1** = the new treatment is more effective and more expensive.
- **2** = the new treatment is less effective and more expensive.
- **3** = the new treatment is less effective and less expensive.
- **4** = the new treatment is more effective and less expensive.

2.5.2.5.4 Cost-utility analysis (CUA)

Cost-utility analysis (CUA) is an economic tool in which the intervention or cost of a treatment alternative is expressed in monetary terms and the outcomes or consequences in terms of patient preference or quality-adjusted-life-years gained (QALYs) (Bungay & Sanchez, 2003:33). CUA is controversial because it is difficult to place a value on health status or on an improvement in health status as perceived by different individuals or societies (WHO, 2003a:27). CUA can compare cost, quality and quantity of patient years (Bungay & Sanchez, 2003:33).

Health-related quality of life is a specific area of investigation within the field of health services and quality of life (Bungay & Sanchez, 2003:40). Quality of life (QoL) is the description of aspects or areas of physical, social and emotional health that are important and relevant to the patient (Strom & Kimmel, 2006:478).

2.5.2.5.5 Cost-of-illness analysis (COI)

Bungay and Sanchez (2003:32) refer to cost-of-illness as an examination of the overall costs (direct and indirect) of a particular disease in a specific or defined population. These costs of an

illness can be used to determine the value of a treatment or a prevention strategy.
The following costs are examined in a cost-of-illness study:

- Direct costs - direct costs are the responsibility of the health care system, community and family in directly addressing the problem (Jefferson *et al*., 2000:18).

    - Direct non-medical costs - the costs caused by the illness, disease or need to seek medical care (Strom & Kimmel, 2006:474).
    - Direct medical costs - the costs included in providing medical care (Strom & Kimmel, 2006:474).

- Indirect costs - these costs do not stem directly from the transactions for services (Strom & Kimmel, 2006:474). These costs are made up from productivity losses due to the illness or disease (Jefferson *et al*., 2000:18).

- Intangible costs - these are costs of pain, suffering, grief and loss of leisure time (Jefferson *et al*., 2000:18).

2.5.2.6 Application of pharmacoeconomics on hipolipidaemics

Numerous studies on the application of pharmacoeconomics with hipolipidaemic agents have been conducted. Examples of such studies are presented in table 2.20.

Table 2.20: Pharmacoeconomic studies on hipolipidaemics

Author & Year	Description	Study population	Type of study	Measuring unit	Outcomes / Foundings
Chaiyakunapruk *et al*. (2000)	The pharmacoeconomic impact of HMG-CoA reductase inhibitors (statins) in type II diabetes mellitus.	Patients with type II diabetes mellitus.	Cost-effectiveness analysis.	Measures the cost per life saved, cost per patient cured or cost per life year gained.	In the secondary prevention, statins have been shown to be well-tolerated, efficacious and cost-effective means of reducing cardiovascular risk.
Hilleman *et al*. (1999)	A population - based treat - to - target pharmacoeconomic analysis of HMG-CoA reductase inhibitors in hypercholesterolaemia.	Patients who is on HMG-CoA reductase inhibitors in Omaha, Nebraska.	Cost of illness.	Estimates the cost of a defined population.	The most cost-effective treatment approach is to individualise the selection of statins based on coronary risk and it was further recommended that atorvastatin and fluvastatin should be available in the national formulary.

Table 2.20: Pharmacoeconomic studies on hipolipidaemics (continued)

Crouch (2000)	To determine the effective use of statins to prevent coronary heart disease.	Middle-aged patients with CHD (secondary prevention)	Cost-benefit analysis.	Pecuniary units to determine a cost benefit ratio.	Lipid-lowering therapy is relatively cost-effective compared with other interventions. In middle-aged patients with CHD (secondary prevention), the estimated cost per year of life saved as a result of statin therapy is between $4,500 and $14,000. The cost for primary prevention of CHD with a statin in middle-aged patients is about $20,000 to $40,000 per year of life saved. These figures compare with a cost of $40,000 per year of life saved for haemodialysis and $70,000 per year of life saved for coronary artery bypass surgery for one-vessel coronary disease.
Pedersen *et al*. (1996)	To estimate the benefits of lowering cholesterol using data from the 4S (Scandinavian simvastatin survival study).	A group of 4444 patients with coronary heart disease in Scandinavia, aged between 35 and 70 years.	Cost-minimisation analysis.	The cost is measured for additional cost to therapy A relative to therapy B.	Simvastatin therapy, produced a 10 per cent decrease in length of hospital stay, a 26 per cent reduction in number of hospitalisation events, a 31 per cent reduction in hospital costs and a 34 per cent reduction in total hospital days. As a result of these savings the cost of simvastatin was reduced.
Attansio *et al*. (2001)	To compare the average annual maintenance costs for simvastatin and atorvastatin in hipolipidaemic patients.	Patients being treated with statin therapy in Western Europe countries.	Cost-minimisation analysis.	The cost is measured for additional cost to therapy A relative to therapy B.	There was no significant difference between groups in the percentage of patients reaching their LDL-cholesterol goal over the study period (80% for simvastatin-treated patients versus 89 per cent for atorvastatin-treated patients. However, the cost of maintaining a similar percentage of patients at their appropriate LDL-cholesterol levels was significantly lower in the simvastatin group compared to the atorvastatin group in 13 of the 17 countries assessed. In the remaining 4 countries, there was a cost advantage for simvastatin, but it did not reach statistical significance.

Table 2.20: Pharmacoeconomic studies on hipolipidaemics (continued)

Johannesson *et al*. (1997)	To evaluate the cost-effectiveness of treatment with simvastatin in male and female patients with coronary heart disease aged 35 – 70 years of age.	Male and female patients aged 35 – 70 years of age with coronary heart disease	Cost-effectiveness analysis.	Measures the cost per life saved, cost per patient cured or cost per life year gained.	Simvastatin was cost-effective in patients with coronary heart disease among both men and women at the ages (from 35 to 70 years) and with cholesterol levels (< 5.2mmol/ to >6.2mmol/ℓ).
Huse *et al*. (1998)	To calculated the cost-effectiveness of HMG-CoA reductase inhibitors (Statins) in both primary and secondary prevention of cardiovascular heart diseases.	Patients at risk of cardiovascular heart diseases on HMG-CoA reductase inhibitor (statin) therapy.	Cost-effectiveness analysis.	Measures the cost per life saved, cost per patient cured or cost per life year gained.	Statins (simvastatin, fluvastatin, atorvastatin, lovastatin, pravastatin) included in the study were cost-effective in prevention of cardiovascular heart diseases and atorvastatin was the most cost-effective.
Tonkin *et al.* (2006)	Determining the cost-effectiveness on lipid-lowering therapy with statins (pravastatin) in patients with previous coronary syndromes aged 65 - 74 years of age.	Patients with previous coronary syndromes aged 65 – 75 years of age.	Cost-effectiveness analysis.	Measures the cost per life saved, cost per patient cured or cost per life year gained.	All cause mortality was lowered by 4.3 per cent in the older patients compared to a reduction of 2.3 per cent in younger patients.

From the discussion depicted in table 2.20, most of the pharmacoeconomic studies evaluated HMG-CoA reductase inhibitors (statins), more specifictly pravastatin, simvastatin and atorvastatin. Also from table 2.20, most of these were CEA pharmacoeconomic studies.

2.5.2.7 Application of pharmacoeconomics in South Africa

In 2006 Jones (2006:96) stated that the full implementation of pharmacoeconomics in South Africa would not properly take place for the next two to five years since the full implementation would also require the development of capacity-building within the Department of Health and the industry. However, pharmacoeconomics is currently growing in South Africa since the International Society of Pharmacoeconomics and Outcomes Research South Africa (ISPOR) has been established in South Africa in May 2007 with the following objectives (ISPOR, 2008):

- To provide an environment and opportunity where researchers, health care practitioners and decision makers can share their views at a national and international level.
- To serve as a neutral forum in bringing together researchers, health care practitioners, and decision makers interested in pharmacoeconomics, the pharmaceutical industry, health-related organisations, public health and academia.
- To act as a facilitator together with improving the implementation of educational programmes in pharmacoeconomics and outcomes research for all members of the health care community.

2.5.2.8 Conclusion to pharmacoeconomics

Bruckner *et al*. (2000) came to the conclusion that pharmacoeconomics does not give one the correct answer, nor does it take away the use of common sense, it merely introduces one to the necessary scepticism and aids in the process of decision making. Pharmacoeconomics is thus not about saving money, but rather on focusing on how to spend money so that money is saved in the process to gain advantage in reaching the endpoint.

Pharmacoepidemiology will be discussed in the subsequent section.

2.5.3 PHARMACOEPIDEMIOLOGY

In the subsequent paragraphs, the introduction to pharmacoepidemiology, the definition thereof and the objectives and methods of pharmacoepidemiology will be dicussed.

2.5.3.1 Introduction to pharmacoepidemiology

Epidemiology is the study of the occurrence and transmission of diseases in human population and therefore epidemiological studies of drug use make use of the methods and statistical measures to study the occurrence and distribution of drug use and its associated problems (Waning & Montagne, 2001:1-2). Pharmacoepidemiology is derived from the Greek words *(pharmakon, epi, demos and logos)* meaning the study of poison (drugs/medicine) in a population (Chauvin *et al.,* 2002:455). It sums up two different areas: pharmacology (the study of interactions between drugs and living organisms) and epidemiology (Ley, 2001:386).

2.5.3.2 Defining pharmacoepidemiology

Pharmacoepidemiology is defined according to Chauvin *et al.* (2002:455) as "*the application of epidemiological reasoning, methods and knowledge to the study of the uses and effects*

(beneficial and adverse) of drugs within a large consumer population". *A* more recent and clearer definition of pharmacoepidemiology was put forward by the World Health Organization (2003a:8) as the study of the use and effects / side-effects of drugs in large numbers of people with the purpose of supporting the rational and cost-effective use of drugs in the population thereby improving health outcomes.

Strom (2006:3) defines pharmacoepidemiology as the study of the use and effects of medicine in large numbers of people. Pharmacoepidemiologal studies have the ability to find associations between a drug/drug class and one or more clinical events that had been missed under the strictly controlled conditions of therapeutic trials (Fautrel, 2004:175).

Pharmacoepidemiological studies often make useful contributions to our knowledge about effectiveness and safety, because unlike clinical trials, they assess drug effects in large, heterogenous populations of patients over longer periods of time (WHO, 2003a:9). With the rapidly growing use of epidemiological techniques, came the recognition of pharmacoepidemiology as a new discipline (Bergman, 2001:31).

2.5.3.3 Focus and objectives of pharmacoepidemiology

Initially the basic focus of pharmacoepidemiology was on the safety of individual drug products (pharmacosurveillance), but now it also includes studies on their beneficial effects (WHO, 2003a:9). As a result, pharmacoepidemiology focuses on pharmaceutical care outcomes and the identification of potential and realised drug-related problems. Though it has been used to examine drug epidemics, it can also be used to study illicit drug use. The idea of pharmacoepidemiology is to measure the source, diffusion, use and effects of drug use in a population and to determine the frequency and distribution of drug use outcomes in that population (Waning & Montagne, 2001:4).

Stewart (1978:122) indicates that pharmacoepidemiology has the following objectives:

- Assess medicine use patterns.
- Document prescriber physicians' prescribing habits.
- Assess toxicity of chronic medications.
- Monitor a patient using medication.
- Monitor why medicine is being used.
- Perform drug cost analysis.
- Document clinical efficacy of medicines.
- Collect information on new uses of a medicine.

- Alert health care systems of possible medicine-related problems.

2.5.3.4 Pharmacoepidemiological study designs and research methods

A brief description of the different pharmacoepidemiological study designs and research methods will now be discussed in table 2.21.

Table 2.21: Different pharmacoepidemiological study designs and research methods

Type of pharmacoepidemiological study	Description of the type of pharmacoepidemiological study
• **Cross-sectional study**	A prevalence survey of health and illness in the population at one point in time (Waning & Montagne, 2001:5).
• **Case-control study**	A retrospective analysis comparing subjects with the condition (referred to as cases) to those without it (referred to as controls) with respect to possible risk of getting the disease or causative factors for the diseases (Strom, 2006:19; Waning & Montagne, 2001:5).
• **Cohort study**	An incidence study that is usually prospective or longitudimal. This incidence study follows a population free of health problems over time, examining subsequent development of problems and factors associated with them (Strom, 2006:19; Waning & Montagne, 2001:5).
• **Clinical trials**	An experimental approach that tests the value of a new treatment or intervention and compares it with the standard treatment or a placebo. This investigator controls the therapy that each participant receives (Strom, 2006:21; Waning & Montagne, 2001:5).
• **Case reports**	These are reports of events that are observed in patients and not in groups. It describes a single patient who was exposed to a drug and who experienced an adverse outcome (Strom, 2006:18).

Based on the aforementioned discussions, Chaunvin *et al*. (2002:456) presented the types of epidemiological studies as illustrated in figure 2.12.

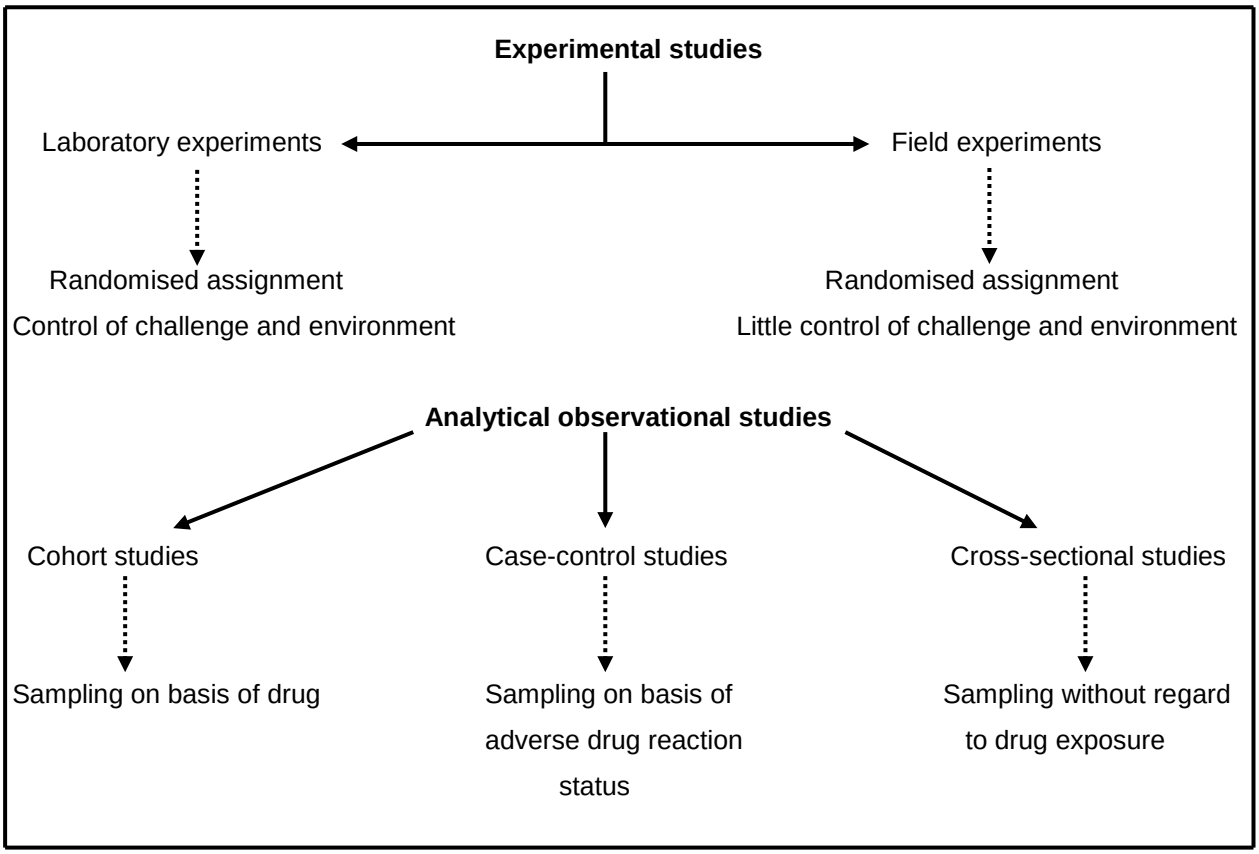

Figure 2.12: Types of epidemiological studies (Chauvin *et al.,* 2002:456)

2.5.3.5 Application of pharmacoepidemiology

In a population-based, case-control study by Meier *et al.* (2000:3205) whose objective was to determine whether statins, fibrates, or other lipid-lowering drugs were associated with reduced bone fracture risk, it was found that current exposure to statins is associated with a decreased risk of fractures in individuals aged 50 years and older.

Eaton *et al.* (2002:1389) quantified the effect of statins on 1-year mortality, hospitalisations and decline in physical functions among patients with cardiovascular disease aged 65 and older in nursing homes. In this retrospective cohort study it was found that the prevalence of statins was 2.6 per cent. Statin use was varied according to gender, age, comorbid condition, medication use, and cognitive and physical function. It was concluded that statin therapy improved clinical outcomes; including reduction in 1-year all cause mortality. Statin therapy also decreased death and hospitalisation in older population groups presenting with cardiovascular diseases.

A pharmacoepidemiological investigation into the drug management of four chronic disease states in South Africa was conducted by Truter in 1999 (also refer to table 2.15).

In the subsequent section, evidence-based medicine will be discussed.

2.5.4 EVIDENCE-BASED MEDICINE

Evidence-based medicine remains a much debated topic for clinicians, purchasers, planners and the public (van der Merwe, 2002:11). Dickersin *et al*. (2007:334) stated that the term 'evidence-based medicine' was coined in 1991 by a group at McMaster University, Ontario, and it arose from a confluence of events and changes in culture.

2.5.4.1 Defining the concept evidence-based medicine

Evidence-based medicine is the conscientious, explicit and judicious use of current best evidence in making decisions about the care of individual patients, which means integrating individual clinical evidence with the best available clinical external evidence obtained from systematic research (Bedenoch & Heneghan, 2002:1; van der Merwe, 2002:11). Dickersin *et al*. (2007:334) define evidence-based medicine as a part of the health care practice that is based on integrating knowledge which is gained from clinical expertise, research evidence and the patients' values and circumstances.

It can thus be concluded that evidence-based medicine is part of an integrated health system which gains knowledge from the analytical clinical research of evidence, which they use for formulating standard criteria for patient treatment.

2.5.4.2 Objectives and steps in evidence-based medicine

Since evidence-based medicine arose from a confluence of events and changes in culture, Dickersin *et al*. (2007:334) further state that there is a growing recognition which includes the following:

- The systematic synthesis of dependable information on a topic has greater value than conventional reviews.
- Tragedy can result from paying attention to poor quality evidence instead of good quality evidence.
- Results in many individual studies can be explained with bias, and randomised clinical trials are now recognised as the study design that is best suited for avoiding bias in questions of intervention effectiveness.
- Medical literature is growing exponentially.
- Clinicians need information and they do not get enough from the sources they use.

- Undesirable gaps and variation may or do exist in practice.

There are 5 steps in the evidence-based medicine process according to Meyrs (2002:47) namely: formulation of a clear clinical question about the patient's problem, searching the literature for relevant clinical questions, evaluating the evidence for its validity and usefulness, implementing useful findings in clinical practice and evaluating the entire process. These steps can be explained with the usage of the three-loop cycle as illustrated in figure 2.13, which will be discussed subsequently.

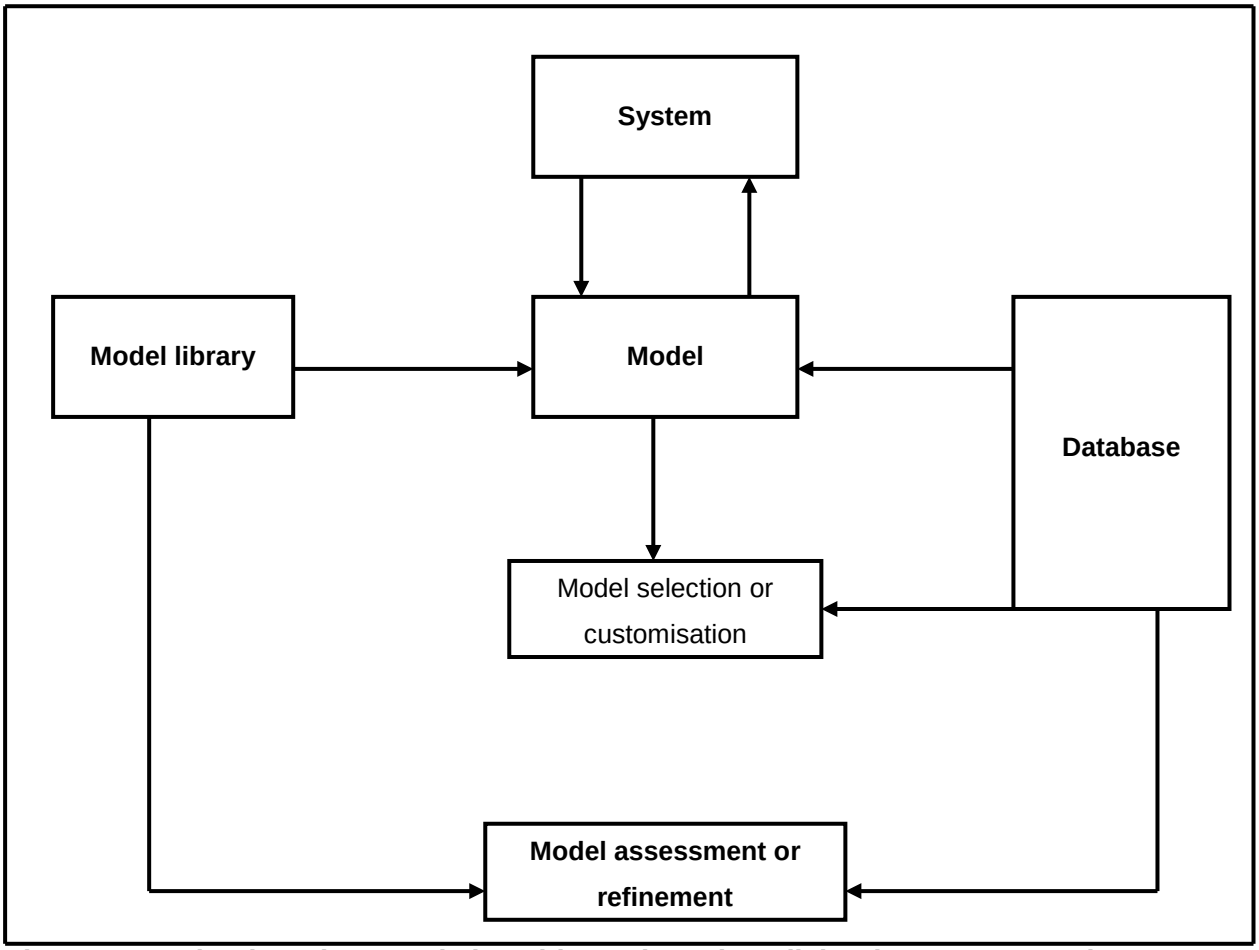

Figure 2.13: The three-loop cycle in evidence-based medicine (Meyrs, 2002:48)

- **Formulating a clear clinical question about a patient's problem (Step 1)**

The clinical question can be related to the specific diagnosis, prognosis, treatment, iatrogenic harm and the quality of care. The question must be specific and must contain the following three essential aspects (Meyrs, 2002:61):

  - The type of patient.
  - The clinical intervention.
  - The clinical outcome.

- **Searching the literature for relevant clinical articles (Step 2)**

This is done in order to find the most relevant studies in the literature on the internet or on the database. The evidence, however, must be concrete and medically correct (Meyrs, 2002:61).

- **Evaluating the evidence for validity and usefulness (Step 3)**

With this step it is essential to ensure that the evidence is valid for clinical use, and if this article is relevant the clinicians can rely on the content to provide guidance for an intervention (Meyrs, 2002:61).

- **Implementing useful findings in clinical practice (Step 4)**

The founded evidence can be implemented into the health care sector; the clinician can then implement it into the patient's care protocol which can be used as a guideline for future care programmes (Meyrs, 2002:61).

- **Evaluating the entire process (Step 5)**

The evidence-based medicine process as a whole should be re-evaluated regularly to determine shortcomings, thus the process will regularly be updated and improved (Meyrs, 2002:61).

2.5.4.3 Evidence-based medicine in South Africa and the future

Evidence-based medicine has not yet been fully implemented in South Africa, though some studies have been done with great findings and results which proved that implementation of evidence-based medicine in South Africa can lead to improved quality of care, as well as improved cost of care. Craig *et al*. (2001:254) state that evidence-based medicine as part of a health care organisation has three tasks for the future namely:

- To implement the evidence summaries in the clinical practice.
- To continuously develop and update the systematic reviews or evidence-based guidelines in their area of knowledge.
- To encourage patients to take part in studies of treatment, diagnosis and prognosis on which the medical practice is based.

2.6 CHAPTER SUMMARY

In this chapter the following aspects were discussed: dyslipidaemia, managed health care, drug utilisation review (DUR), pharmacoeconomics, pharmacoepidemiology and evidence-based medicine. These discussions correlate with general and specific goals and aims of this study as had been presented previously.

Chapter 3 will provide a gereral layout of the empirical investigation of this study.

CHAPTER 3

EMPIRICAL INVESTIGATION

3.1 INTRODUCTION

The general research objective of this study was to analyse the usage patterns and cost of hipolipidaemic medicine (agents) in the private health care sector of South Africa utilising data from a South African Pharmaceutical Benefit Management (PBM) company. In this chapter empirical research methodology employed during the study will be discussed in detail. The chapter concludes with a discussion of the study limitations.

3.2 RESEARCH METHOD

The study consisted of two phases (refer to paragraphs 1.4.1 - 1.4.2). Phase one of the study (literature review) was documented in chapter 2 of this dissertation. The details of the second phase (empirical investigation) are reported here. Included are a description of the research design, data source and study population, data analysis, variables and measures, statistics used in the data analysis as well as certain ethical aspects.

3.2.1 Research design

The data were obtained from a South African PBM's medicine claims database. The data were collected after the medicine had been dispensed and this study could, therefore, be defined as a retrospective utilisation study.

3.2.2 The data source and study population

Data were obtained directly (refer to paragraph 3.4.5 for validity and reliability aspects) from a South African Pharmaceutical Benefit Management company, which manages the benefits of medical schemes and -insurance companies in South Africa by providing a real-time auditing process to claims from pharmacies and other service providers.

In 2005-6, this company provided pharmaceutical benefit management services to 38 medical schemes[1] and four capitation provider clients, administered by 17 different health care administrators. The claims database's sample was therefore considered representative of the average patient served by the private health care sector of South Africa, given his/her choice of medical insurance.

The study population consisted of all prescriptions for hipolipidaemic medicine items on the PBM's database for the study period 1 January 2005 to 31 December 2006. The 2005-dataset consisted of data from 1 January 2005 to 31 December 2005. It contained 604 824 records of prescriptions, 626 759 items at R106 943 348.53. The 2006-dataset consisted of data form 1 January 2006 to 31 December 2006. It contained 678 297 records of prescriptions, 705 424 items at R117 862 631.87.

The fields used in the study were as follows:

- NAPPI[2] codes, NAPPI code description and NAPPI code extension:

The NAPPI code is a unique nine digit number implemented with electronic transactions in mind. This code is unique for each product for its product name, pack size, strength, manufacturer plus exclusions of the dispensed product (Snyman, 2007:6a). For example, the NAPPI code for Lipitor 10mg (pack size 30) is 831484006. The first 6 digits (NAPPI code) identify the product and strength and the last 3 digits the pack size.

- Trade names:

The MIMS (Monthly Index of Medical Specialities) is a monthly index of product active ingredients/trade names compiled from package inserts supplied by pharmaceutical companies. The MIMS classification system classifies pharmaceutical products based on specific pharmacological action into their appropriate pharmaceutical group or sub-pharmaceutical group (Snyman, 2007:11a). Figure 3.1 presents the MIMS classification system as applicable to this specific study.

1 South Africa has about 160 medical schemes totaling around seven million beneficiaries; of which only about 40 are open to the public (Anon., 2008).

2 NAPPI = National Approved Product Pricing Index

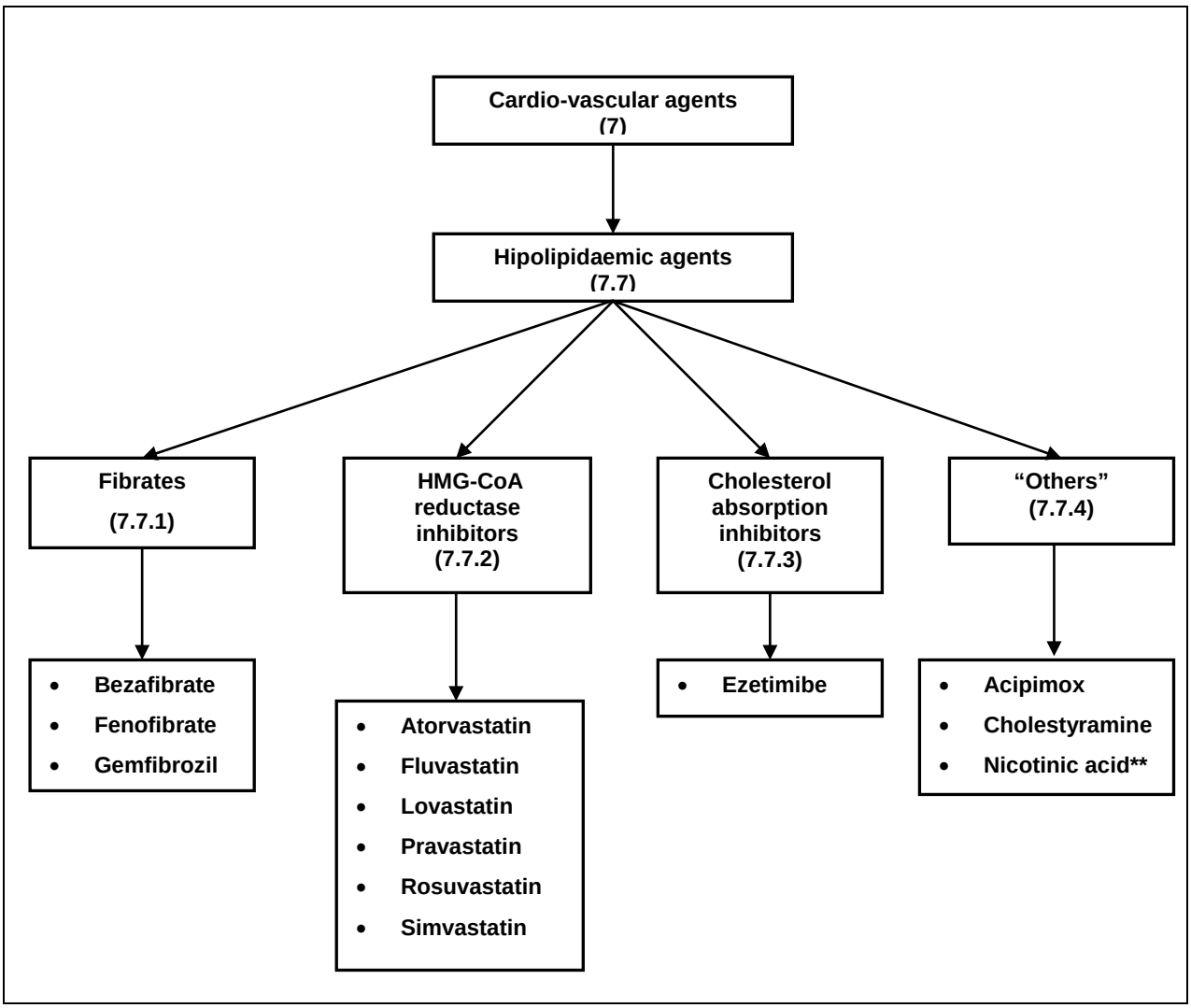

Figure 3.1: The MIMS classification system as applicable to this study

** Refer to paragraph 2.1.8.2.5.

- Quantity of medicine items dispensed:

Prevalence or frequency of the amount of the medicine dispensed to the patient (e.g., 30 or 60).

According to Waning and Montagne (2001:21) prevalence is defined as "*the probability that a condition exists in a specific population or the probability of the occurrence of a condition*".

Prevalence is a statistic of primary interest in public health since it identifies the level of burden of disease or any health-related events on the population and the health care system (NCI, 2007). Prevalence represents new and pre-existing cases alive on a certain date, in contrast to incidence which reflects new cases of a condition diagnosed during a given period of time. Prevalence is a function of both the incidence of the disease and survival (NCI, 2007).

For the purpose of this study prevalence was seen as the number of times a patient received a specific hipolipidaemic medicine item.

- Final prescription cost, Final amount paid by medical scheme and Final levy amount for the patient.

Cost is defined as the total value of all the resources that are consumed in the productions of a product or a service (Struwig, 2005:58).

Total cost in this study (i.e., the final prescription cost) was determined by adding the totals of the final scheme amount and final levy. For the purpose of this study cost is expressed as a Rand-value (R).

- Sex of the patient

The World Health Organization (WHO, 2007) defines the sex of an individual as the biological and physiological characteristics that define men and women; and gender as the socially constructed roles, behaviours, activities, and attributes that society considers appropriate for men and women. In other words male and female are sex categories and masculine and feminine are gender categories (WHO, 2007).

The three sex categories in the context of this study were: female (F), male (M) and unknown (U).

- The prescriber type

Data recorded on the PBM's database regarding the prescribers of specific medicine items made it possible to analyse the prescribing patterns of the prescribers. The different prescriber categories available on the database were as follows:

o Cardiology: This group includes all the cardiologists registered with the Health Professions Council of South Africa (HPCSA).

o General medical practitioner: This group includes all the medical prescribers that are registered with the Health Professions Council of South Africa (HPCSA) as general medical practitioners.

o Other: This group includes all the following prescribers:

Anaesthesiology, approved day clinics, cardiology paediatrician, clinical haematology, community dentistry, community health, dermatology, diagnostic radiology, gastroenterology, general dental practice, group practices, group practices/hospitals, homeopaths, maxillor-facial & oral surgery, neurology, neurosurgery, nuclear medicine, obstetrics & gynaecology, oncology, ophthalmology, oral pathology, orthodontics, orthopaedics, otorhinolaryngology, paediatrics, pathology, periodontics, urology, surgery / paediatric surgery, radiothology / oncology, psychiatry, private hospital (A tariff), private hospital (B tariff), physician / immunologist / rheumatologist / nephrotologist / diabetologist / endocrinologist, physical medicine, plastic & reconstructive surgery, prosthodontics, provincial hospital, pulmonology, radiography, rheumatology, unatt operating theatre / day.

- Pharmacotherapists: This group includes all the pharmacotherapists that are registered with the South African Pharmacy Council (SAPC).

- Pharmacists: This group includes all the pharmacists (including pharmacist interns, pharmacist assistants and nurses) registered with the South African Pharmacy Council.

- Thoracic surgeons: This group includes all the thoracic surgeons registered with the Health Professions Council of South Africa (HPCSA).

- Date of birth and treatment date

Age is generally derived from the date of birth of a person and is an indication of the completed life years of that person (Kids' well-being indicators Clearinghouse, 2007). The age of a patient in this study was determined according to the date of treatment for the patient minus the date of birth of the specific patient.

In this study, the ages of patients who received hipolipidaemic prescriptions were divided into the following five categories as set out in table 3.1.

Table 3.1: Five age group categories

Age group	Years	Description
1	• 0 ≤ 9 years	• Children between 0 and 9 years of age.
2	• 10 ≤ 19 years	• Adolescents between 10 and 19 years of age.
3	• 20 ≤ 45 years	• Young adults between 20 and 45 years of age.
4	• 46 ≤ 59 years	• Adults between 46 and 59 years of age.
5	• > 59 years	• Adults older than 59 years of age.

3.2.3 Variables and measures

Variables such as prevalence, cost, age, sex, provider and prescriber were used in the analysis of the prescribing patterns of hipolipidaemic drugs.

3.2.3.1 Prevalence

In this study the prevalence of medicine items was determined according to the following categories:

- The prevalence of all medicine items claimed through the database for the study period 2005 and 2006.
- The prevalence of hipolipidaemic medicine for the study period 2005 and 2006.
- The prevalence of original patented medicine items, placed on the market for further research (M), non-substitutable medicine items (N), original medicine items (O) and generic medicine items (Y) specifically focused on hipolipidaemic medicine.
- The prevalence of hipolipidaemic medicine according to age and sex for the study period 2005 and 2006.
- The prevalence of hipolipidaemic medicine according to active ingredient for the study period 2005 and 2006.

3.2.3.2 Cost

In this study the total medicine cost and the average cost per medicine item were analysed in the following categories as follows:

- The total cost and average cost of all medicine items claimed on the database as well as the average cost per prescription for the study period 2005 and 2006.
- The cost of hipolipidaemic medicine for the study period 2005 and 2006.
- The cost of original patented medicine items, placed on the market for further research (M), non-substitutable medicine items (N), original medicine items (O) and generic medicine items (Y) specifically focused on hipolipidaemic medicine.
- The cost of hipolipidaemic medicine according to age and sex for the study period 2005 and 2006.
- The cost of hipolipidaemic medicine according to active ingredient for the study period 2005 and 2006.

- Cost analysis was used to determine potential cost savings through generic substitution and/or therapeutic substitution of hipolipidaemic medicine.

3.2.3.3 Age

Age categories in this study were used to describe the various hipolipidaemic usage (prescribing) patterns during the two study periods for each age group, the total number of patients per age group, the average number of prescriptions per age group, the total number of prescriptions per age group, the average number of hipolipidaemic medicine items per age group, the total number of hipolipidaemic medicine items per age group, the average cost per prescription per age group, and the total cost per prescription per age group. All of the variables for the various age groups were calculated for each study period.

3.2.3.4 Sex

Sex categories in this study were used to describe the various hipolipidaemic usage (prescribing) patterns during the two study periods for each sex category, the total number of patients per sex category, the average number of prescriptions per sex category, the total number of prescriptions per sex category, the average number of hipolipidaemic medicine items per sex category, the total number of hipolipidaemic medicine items per sex category, the average cost per prescription per sex category, and the total cost per prescription per sex category. All of the variables for the various sex categories were calculated for each study period.

3.2.3.5 Prescriber

Data from the various prescribers on the PBM's database were used during the two study periods to determine the average number of hipolipidaemic medicine items per prescriptions, average cost per hipolipidaemic prescription prescribed by a specific prescriber, the number of patients per prescriber during each of the two study periods and the various prescribed hipolipidaemic trade name products prescribed by each prescriber during each of the two study period.

3.3 DATA PROCESSING AND ANALYSIS

3.3.1 Data analysis and programmes

The data were analysed using the Statistical Analysis System® SAS 9.1® (SAS Institute Inc., 2006-2007). Microsoft Word® 2000 and Microsoft Excel® 2000 were used in accordance with the SAS system for analysis and processing.

3.3.2 Descriptive statistics

The following descriptive statistics were used to describe the variables (measures) during the analysis of the data in this study.

3.3.2.1 Frequency

Prevalence was discussed (3.2.3.1) and for the purpose of this study prevalence and frequency will refer to the number of times that a trade name product was dispensed.

3.3.2.2 Arithmetic mean (AM)

The arithmetic mean can be defined as the average of all the numbers. The value of the arithmetic mean is always between the least and the greatest of the numbers. Mathematically the arithmetic mean can be defined as (Banerjee, 2003:3; Steyn *et al*., 2004:99):

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

Key to symbols:

- x = the values of the variable.
- $\sum$ = the sum of.
- *n* = the number of observations (Steyn *et al*., 2004:99).

3.3.2.3 Standard deviation (SD)

According to Brase and Brase (1999:103) the standard deviation can be defined as a measurement that indicates how the data entries differ from the mean, or it is the most frequent calculated measure of variability (Barlo, 2007). Mathematically the standard deviation can be expressed as (Barlo, 2007; Steyn *et al*., 2004:131).

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

Key to symbols:

- n = the number of observations
- s = the standard deviation
- $\bar{x}$ = the arithmetic mean
- x = any value in the data set

3.3.3 Inferential statistics

3.3.3.1 Effect sizes / *d*-values

According to Thalheimer and Cook (2002) an effect size is the difference between two means (e.g., treatment minus control) divided by the largest standard deviation of the two conditions. It is the division by the standard deviation that enables us to compare the effect sizes across experiments. The effect size (*d*) was calculated as follows:

$$d = \frac{\overline{x_t} - \overline{x_c}}{s_{\max}}$$

Key to symbols:

- d = effect size
- $\bar{x}$ = the average medicine treatment cost of a
- $\bar{x}$ = the average medicine treatment cost of b
- s max = the maximum standard deviation between a and b

The d-value can be interpreted as follows (Steyn, 1999:3; Thalheimer & Cook, 2002):

- d = 0.2 Small effect, with no practical significant difference.
- d = 0.5 Medium effect, which is observable and may be significant.
- d = 0.8 Large effect, which is significant and of practical importance.
- d > 0.8 Assumed to have practical importance.

3.3.3.2 Cost prevalence index (CPI)

According to Serfontein (1989:180) the cost prevalence index can be used as an indication to show the relationship between the total number of medicine items prescribed and the total medicine cost. The cost prevalence index was calculated as follows:

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

For study purposes the cost index can be analysed as follows:

- If cost index <1 the drug utilised is relatively inexpensive.
- If cost index = 1 there is an equilibrium between the cost and prevalence of the product.

- If cost index > 1 the product utilised is relatively expensive.

3.3.4 Cost calculations and potential cost savings

Potential cost savings were calculated for all original hipolipidaemic medicine item(s) available on the database that had an equivalent generic(s) available. The same formula was used in calculating potential cost saving in scenarios with therapeutic substitution.

The formula for potential cost saving is as follows (adapted from van der Westhuizen, 2007:68).

$$\text{Cost saving} = n_O \times [\text{Average cost}_O \times \text{Average cost}_G]$$

Key to symbols:

- Total $cost_O$ = Total cost of the original product.
- Average $cost_G$ = Average cost of the generic equivalent per item.
- N_O = frequency of the original product.

3.3.5 Reliability and validity of the data

It was assumed that all data were reliable and valid. The datasets were, however, verified by testing for outlying data, as well as by performing random data checks.

All non-medical supplies such as diagnostic material, special foods, needles, syringes, gauss, etc. were excluded from the study, thus focusing specifically on direct medicine costs.

Incomplete data fields were designated as “unknown” (e.g., age and sex of patients). These records were not removed from the database as the prevalence of these unknown groups was very small, and of no practical significance.

3.4 ETHICAL ASPECTS

The South African Pharmaceutical Benefit Management company's board of directors gave permission for the data to be used in this study, and the ethical committee of the North-West University approved the study as a sub-project within the "Investigation of medicine usage patterns in a section of the private health care sector utilising data from a Pharmaceutical Benefit Management (PBM) in South Africa" project (NWU-0046-08-S5).
Each prescription record contained an 11-digit reference number to link each patient, medical practice, pharmacy or medical scheme to line items. This number is a time stamp of when the transaction was adjudicated. The patient was allocated a random, "dummy" member number by the PBM, thus ensuring confidentiality.

In this study only 'type of prescriber' was used (refer to paragraph 3.2.2) thus ensuring confidentiality with regard to the prescribers.

Furthermore, the PBM's name was not reported anywhere in this dissertation, nor the medical aids contracted by this PBM, thus ensuring confidentiality as far as the data source is concerned.

3.5 LIMITATIONS OF THE STUDY

The following limitations to the study were identified:

- Medical aid claims data were used in the study – there are therefore no guarantees that the patient actually took the medicines, or that the medicines were dispensed to the right patient.
- The lack of reliable diagnosis on the database – the reason for the prescribing of the specific medicines is therefore not known, and the rationality of certain prescribing patterns could therefore not be ascertained.
- Only one PBM's data were used in the study therefore no cost or prevalence comparisons could be made.
- Only direct cost of medicine was used throughout the study.
- External validity is limited, implying that the results can be generalised to the specific database and study population only.

3.6 CHAPTER SUMMARY

In this chapter the research methodology of the empirical investigation was discussed. This included the introduction, research method, data processing and analysis, ethical aspects regarding this study. The limitations to the study were also listed.

The results of the empirical investigation will be discussed and documented in Chapter 4 and in the Appendix (refer to Appendix A and B).

The conclusions and recommendation based on the results of the literature review (phase 1 of the research) and the empirical investigation will be discussed in Chapter 5.

CHAPTER 4

RESULTS AND DISCUSSION

4.1 INTRODUCTION

In this chapter the results of the empirical investigation with regard to prescribing patterns and cost of hipolipidaemic drugs, for the study period of two consecutive years (1st January 2005 to 31st December 2005 and 1st January 2006 to 31st December 2006), will be outlined and discussed.

The total database was analysed and the hipolipidaemic medicine items have been referred to as medicine items of the main pharmacological group 7.7 according to the MIMS classification system (Snyman, 2007:12a). This main pharmacological group has been divided into four categories/sub-pharmacological groups namely: fibrates (group 7.7.1); HMG-CoA reductase inhibitors (statins) (group 7.7.2); cholesterol absorption inhibitors (group 7.7.3); and "other" hipolipidaemic agents (group 7.7.4 including nicotinic acid) (Snyman, 2007:12a). Figure 4.1 is an illustration of how data for both study periods were analysed.

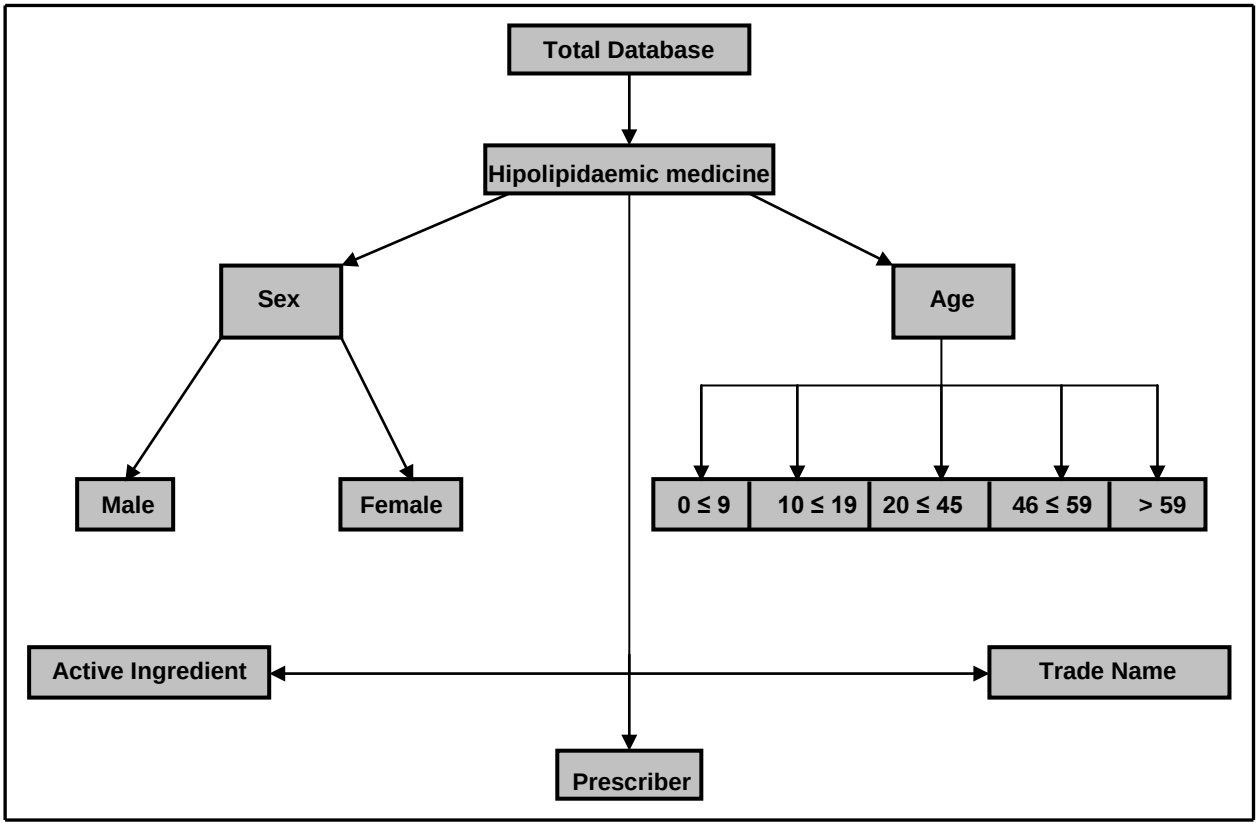

Figure 4.1: Schematic illustration of how data for both study periods were analysed

4.2 POINTS OF INTEREST APPLICABLE TO THE INTERPRETATION OF RESULTS

- It was assumed that all data obtained from the database were correct. Random data checks were performed and data were checked for outliers (refer to paragraph 3.3.5).
- The values of the data that were used were rounded to two decimals and may not add up to 100%.
- Both frequency and prevalence refer to the number of times that a trade name product was dispensed.
- Due to the extent of the use of trade name products and trade mark products throughout the study, the ™ and ® are not indicated.

4.3 OVERVIEW OF THE TOTAL DATABASE

In this section a general overview of the total database could be concluded. Table 4.1 provides a general description of the total database, based on respective study years (i.e., 1 January 2005 to 31 December 2005, and 1 January 2006 to 31 December 2006). Table 4.1 is a summarised table compiled from tables B1.1, B1.2, B1.3, B1.4, B1.5, B1.6, B1.7, B1.8, B1.9, B1.10, B1.11, B1.12, B1.19, B1.20, B1.21, B1.22, B1.23, B1.24, B1.25, B1.26, B1.27, B1.28 and B1.29 in appendix B, reflecting the data of the complete database. These tables refer to the complete data of both 2005 and 2006 and their indicidual periods.

Table 4.1: Basic characteristics of the total database; *n*

	AGE (YEARS)				
	0 ≤ 9	**10 ≤ 19**	**20 ≤ 49**	**46 ≤ 59**	**≥ 59**
Number of patients					
N_{2005} = 1 247 188	158 450	177 330	459 843	253 018	198 547
N_{2006} = 1 288 938	155 133	177 978	476 211	269 586	210 030
Number of prescriptions					
N_{2005} = 8 522 574	642 913	600 163	2 666 906	2 157 378	2 455 219
N_{2006} = 9 046 138	660 717	633 395	2 817 516	2 339 543	2 596 377
Average number of prescriptions per patient					
2005 (6.98 ± 7.83)	4.06 ± 3.93	3.38 ± 3.44	5.79 ± 7.83	8.51 ± 8.52	12.32 ± 10.47
2006 (7.17 ± 8.05)	4.26 ± 4.07	3.56 ± 3.61	5.91 ± 6.66	8.66 ± 8.73	12.31 ± 10.72
Number of medicine items					
N_{2005} = 19 860 593	1 600 919	1 390 573	5 933 729	4 901 485	6 033 952
N_{2006} = 21 473 062	1 668 287	1 499 217	6 377 057	5 447 080	6 481 394
Medicine items per prescription					
2005 (2.33 ± 1.55)	2.49 ± 1.35	2.32 ± 1.32	2.22 ± 1.35	2.27 ± 1.52	2.46 ± 1.87
2006 (2.37 ± 1.58)	2.52 ± 1.38	2.37 ± 1.35	2.26 ± 1.38	2.33 ± 1.55	2.50 ± 1.88
Total cost (based on medicine items) (R)					
N_{2005} = 1 893 376 921.00	89 329 200.00	97470392.52	478 014 067.00	497 543 992.00	731 018 016.00
N_{2006} = 2 046 944 383.00	92 540 896.32	104 158 833.00	506 572 755.00	549 795 116.00	793 875 296.00

Table 4.1: Basic characteristics of the total database; *n* (continued)

Average cost per prescription (R)					
2005 (R222.16 ± 463.13)	138.94±149.17	162.41±223.06	179.24±366.08	230.62±489.75	297.73±599.77
2006 (R226.25 ± 557.49)	140.06±183.25	164.45±252.81	179.79±390.95	235.00±630.71	305.76±723.08
Average cost per item (R)					
2005 (R95.33 ± 192.21)	55.80 ± 72.66	70.09 ± 113.40	80.56 ± 166.53	101.51 ± 208.21	121.15 ± 230.83
2006 (R95.33 ± 227.99)	55.47 ± 90.50	69.48 ± 124.47	79.44 ± 184.54	100.93 ± 248.34	122.49 ± 283.13
	SEX CATEGORIES				
	FEMALE		**MALE**		**UNKNOWN**
Number of patients					
N_{2005} = 1 218 368	675 824		540 874		1 670
N_{2006} = 1 259 099	698 477		559 535		1 087
Number of prescriptions					
N_{2005} = 8 522 574	5 112 329		3 403 193		7 192
N_{2006} = 9 046 138	5 421 150		3 621 060		4 875
Average number of prescriptions per patient					
2005 (6.98 ± 7.83)	7.55 ± 8.27		6.28 ± 7.18		4.30 ± 5.37
2006 (7.17 ± 8.05)	7.74 ± 8.51		6.46 ± 7.38		4.48 ± 5.93
Number of medicine items					
N_{2005} = 19 860 593	11 974 255		7 870 112		16 312
N_{2006} = 21 473 062	12 924 812		8 537 499		10 763
Number of items per prescription					
2005 (2.33 ± 1.55)	2.34 ± 1.59		2.31 ± 1.51		2.27 ± 1.39
2006 (2.37 ± 1.58)	2.38 ± 1.61		2.36 ± 1.53		2.21 ± 1.43
Total cost (based on medicine items) (R)					
N_{2005} = 1 893 376 921.00	1 128 652 112.00		763 226 111.00		1 498 697.05
N_{2006} = 2 046 944 383.00	1 213 068 356.00		832 725 542.00		1 150 484.20
Average cost per prescription (R)					
2005 (R222.16 ± 463.13)	220.77 ± 455.62		224.27 ± 473.73		208.38 ± 643.60
2006 (R226.25 ± 557.49)	223.77 ± 532.77		229.97 ± 592.88		236.00 ± 536.55
Average cost per item (R)					
2005 (R95.33 ± 192.21)	94.26 ± 185.03		96.98 ± 202.27		91.88 ± 331.55
2006 (R95.33 ± 227.99)	93.86 ± 219.20		97.54 ± 240.49		106.89 ± 338.51

* Data are *n*-values (means ± SD).

Due to missing data in the age categories, the totals of the number of prescriptions do not add up to the total number of prescriptions based on sex groups.

There was a total of 1 247 188 and 1 288 938 patients in the database of 2005 and 2006 respectively. A total number of 8 522 574 and 9 046 138 prescriptions were claimed during 2005 and 2006 respectively, with an average cost per prescription of R222.16 ± 463.13 and R226.28 ± R557.49 in 2005 and 2006 respectively. A *d*-value of no practical significance (Steyn, 1999:3) was calculated (d = 0.007) for the price difference between prescriptions during the two study periods. The average number of prescriptions per patient per year claimed was 6.98 ± 7.83 in 2005 and 7.17 ± 8.05 in 2006.

In 2005 a total number of 19 860 593 medicine items were claimed on the database and 21 473 062 medicine items were claimed in 2006. Medicine items claimed during 2005 on the total database had an average cost of R95.33 ± 192.21 and the average cost in 2006 was R95.33 ± 227.99. Medicine items in 2005 accounted for a total cost of R1 893 376 921.00 and for R2 046 944 383.00 in 2006. The total cost of medicine items represented, increased with 8.12% (n = 153 567 462) from 2005 to 2006. This increase might be explained by a rise in the number of medical scheme members and dependants administered by the PBM's database. There may also have been a rise in number of medicine items and prescriptions claimed during the study periods (refer to table 4.1).

Table 4.1 is subsequently discussed in detail for the different age and sex categories for the study periods of 2005 and 2006.

4.3.1 Analysis based on patients' age

The general analysis based on the different age group categories will now be discussed. The age groups' categories were as follows:

- Age group 1: Children between the ages of 0 and 9 years (0 ≤ 9 years).
- Age group 2: Adolescents between the ages of 10 and 19 years (10 ≤ 19 years).
- Age group 3: Young adults between the ages of 20 and 45 years (20 ≤ 45 years).
- Age group 4: Older patients between the ages of 46 and 59 years (46 ≤ 59 years).
- Age group 5: Patients older than 59 years of age (> 59 years).

4.3.1.1 Age group 1: Children between the ages of 0 and 9 years

According to table 4.1, the number of patients in age group 1 (patients aged 0 ≤ 9 years) represented 12.70% (N = 1 247 188) of the total number of patients in 2005, and 12.04% (N = 1 288 938) in 2006. The number of prescriptions represented 7.54% (N = 8 522 574) and 7.30% (N = 9 047 138) of the total number of prescriptions claimed in 2005 and 2006 respectively; whilst the total cost per prescription represented 8.06% (N = R1 893 376 921.00) and 8.52 % (N = R2 046 944 383.00) of the total cost in the respective study years. An average of 4.06 ± 3.93 and 4.26 ± 4.07 prescriptions per patient per year in this age group was claimed during 2005 and 2006 respectively; at an average cost per prescription of R138.94 ± 149.17 (2005) and R140.06 ± 183.25 (2006). A *d*-value was calculated for this price difference (*d* = 0.006), which was of no practical significance according to Steyn (1999:3).

An average of 2.49 ± 1.35 and 2.52 ± 1.38 medicine items was claimed per prescription for age group 1 in 2005 and 2006 correspondingly.

Medicine items for age group 1 represented 8.06% (N = 19 860 658) and 7.77% (N = 21 473 035) of the total number of medicine items claimed during 2005 and 2006. Corresponding costs incurred by this group accounted for 4.72% of total medicine item cost (N = R1 893 775 668.12) in 2005 and 4.52% (N = R2 046 942 896.32) in 2006. Table 4.1 furthermore shows that the average cost per medicine item for age group 1 was R55.80 ± 72.66 in 2005 compared to R55.47 ± 90.50 in 2006. A *d*-value of 0.004 was calculated, which is of no practical significance.

Cost prevalence indices were also calculated based on the cost percentage and prevalence percentage of medicine items claimed during both study periods. Values of 0.64 and 0.62 for 2005 and 2006 respectively were obtained, which indicates that treatment in this age group was relatively inexpensive.

4.3.1.2 Age group 2: Adolescents between the ages of 10 and 19 years

In 2005, the number of patients in age group 2 (patients 10 ≤ 19 years) represented 14.22% (N = 1 247 188) of the total number of patients, which decreased to 13.81% (N = 1 288 938) in 2006. The total number of prescriptions for this age group represented 7.05% (N = 8 506 735) in 2005 and 7.01% (N = 9 030 344) in 2006. The average number of prescriptions per patient per year in this age group was therefore 3.38 ± 3.44 in 2005 and 3.56 ± 3.61 in 2006. Total cost per prescription in this age group represented 7.00% (N = R1 893 376 921.00) in 2005 and 7.66% (N = R2 046 944 383.00) in 2006; average cost per prescriptions subsequently amounted to R162.41 ± 223.06 and R164.45 ± 252.81 respectively. A *d*-value was calculated (*d* = 0.008) which is of no practical significance according to Steyn (1999:3).

Medicine items for age group 2 represented 7.00% (N = 19 860 658) of the total number of medicine items in 2005 and 6.98% (N = 21 473 035) in 2006. In 2005, costs incurred by age group 2 accounted for 4.72% of the total medicine cost (N = R1 893 775 668.12) and 5.09% (N = R2 046 942 896.32) in 2006. The cost prevalence indices in 2005 and 2006 were 1.36 and 1.37 respectively, which indicates that treatment in this age group was relatively expensive.

An average of 2.32 ± 1.32 and 2.37 ± 1.35 medicine items per prescription for 2005 and 2006 respectively, was claimed at an average cost per item of R69.48 ± 124.47 (2005) compared to R70.09 ± 113.40 in 2006. A *d*-value of 0.005 was calculated, indicating that the price difference is of no practical significance according to Steyn (1999:3).

4.3.1.3 Age group 3: Young adults between the ages of 20 and 45 years

The number of patients in age group 3 represented 36.87% (N = 1 247 188) of the total number of patients in 2005, and 36.95% (N = 1 288 938) in 2006. The total number of prescriptions for age group 3 represented 31.32% (N = 8 506 735) and 31.18 % (N = 9 030 344) (refer to table 4.1). The average number of prescriptions per patient per year in this age group was 5.79 ± 7.83 in 2005 and 5.91 ± 6.66 in 2006.

The number of prescriptions in age group 3 (patients 20 ≤ 45 years) represented 31.29% (N =8 522 574) in 2005 and 31.14 % (N = 9 047 138) in 2006. The total cost per prescription represented 29.88% (N = R1 893 376 921.00) in 2005 and 32.56% (N = R2 046 944 383.00) in 2006. CPIs of 0.81 and 0.79 for 2005 and 2006 respectively were calculated, which indicates that treatment was relatively inexpensive in this age group. In age group 3, the average number of medicine items per prescription was 2.22 ± 1.35 in 2005 and 2.26 ± 1.38 in 2006. The average cost per prescription in 2005 and 2006 was R179.24 ± 366.08 and R179.79 ± 390.95 respectively. A *d*-value was calculated (*d* = 0.001) which is of no practical significance according to Steyn (1999:3).

Medicine items for age group 3 represented 29.88% (N = 19 860 658) of the total number of medicine items claimed in 2005 compared to 29.70% (N = 21 473 035) in 2006. In 2005, costs incurred by age group 3 accounted for 25.25% of the total medicine cost (N = R1 893 775 668.12) compared to 24.75% (N = R2 046 942 896.32) in 2006. The cost prevalence index was 1.18 in 2005 and 1.20 in 2006 respectively, which indicates that treatment in this age group was relatively expensive. The average cost per medicine item for age group 3 was R79.44 ± 184.54 in 2005 and R80.56 ± 166.53 in 2006. The *d*-value (*d* = 0.006) is of no practical significance according to Steyn (1999:3).

4.3.1.4 Age group 4: Older patients between the ages of 46 and 59 years

In 2005, the number of patients in age group 4 (patients 46 ≤ 59 years) represented 20.29% (N = 1 247 188) of the total number of patients, and 20.92 % (N = 1 288 938) in 2006. The total number of prescriptions for age group 4 represented 25.31% (N = 8 506 735) in 2005 and 25.86% (N = 9 030 344) in 2006. The average number of prescriptions per patient in this age group was therefore 8.51 ± 8.52 in 2005 and 8.66 ± 8.73 in 2006.

The total cost per prescription represented 24.68% (N = R1 893 376 921.00) in 2005, and increased to 27.82% of the total cost of all prescriptions (N = R2 046 944 383.00) during 2006. The average cost per prescription in 2005 and 2006 was R230.62 ± 489.75 and R235.00 ±

630.71 respectively. A *d*-value was calculated (*d* = 0.007), which indicates that the average price increase is of no practical significance (Steyn, 1999:3).

An average of 2.27 ± 1.52 (for 2005) and 2.33 ± 1.55 items per prescription for 2006 was claimed.

Medicine items for age group 4 represented 24.68% (N = 19 860 658) of the total number of medicine items in 2005 and 25.37% (N = 21 473 035) in 2006. Costs incurred in 2005 by this age group accounted for 26.28% of the total medicine cost (N = R1 893 775 668.12) and 26.86% (N = R2 046 942 896.32) in 2006. The average cost per medicine item was therefore R101.51 ± 208.21 in 2005 and R 100.93 ± 248.34 in 2006. A *d*-value of 0.002 was calculated which, according to Steyn (1999:3), is of no practical significance. The CPIs of respectively 0.94 and 0.94, indicate that treatment in this age group was relatively inexpensive.

4.3.1.5 Age group 5: Patients older than 59 years of age

The number of patients above the age of 59 represented 15.92% (N = 1 247 188) of the total number of patients on the database in 2005, which increased to 16.29% (N = 1 288 938) in 2006. The total number of prescriptions claimed for this age group represented 28.75% (N = 8 506 735) in 2005 and 28.63% (N = 9 030 344) in 2006 of all prescriptions claimed during the respective years. An average of 12.32 ± 10.47 prescriptions per patient per year was thus claimed in 2005 and 12.31 ± 10.72, in 2006. The reason for the higher average number of prescriptions claimed per patient in this age group might be since most of these patients are on chronic medication and therefore would need to renew their prescriptions each month, and thus would claim an average of 12 prescriptions during the year.

The total cost per prescription represented 30.38% (N = R1 893 376 921.00) in 2005 and decreased to 23.45 % (N = R2 046 944 383.00) in 2006. The average cost per prescription in 2005 and 2006 was R297.73 ± 599.77 and R305.76 ± 723.08 respectively. A *d*-value was calculated (*d* = 0.01) which indicate that the average price increase is of no practical significance (Steyn, 1999:3).

The average number of medicine items claimed per prescription for this age group was 2.46 ± 1.87 in 2005 and 2.50 ± 1.88 in 2006.

Medicine items represented 30.38% (N = 19 860 658) of the total number of medicine items claimed in 2005 and 30.18% (N = 21 473 035) in 2006. Costs incurred by patients above the age of 59 years accounted for 38.61% of the total medicine cost (N = R1 893 775 668.12) in

2005 and 38.78% (N = R2 046 942 896.32) in 2006. The cost prevalence indexes were 0.79 and 0.78 respectively in 2005 and 2006, which indicates that treatment in this age group was relatively inexpensive. The average cost per medicine item in for age group 5 was R121.15 ± 230.83 in 2005 compared to R122.49 ± 283.13 in 2006. A *d*-value of 0.004 was calculated, which according to Steyn (1999:3) is of no practical significance.

4.3.2 Analysis based on patients' sex

The general analysis on the different sex categories will now be discussed. The sex categories were as follows: females, males and "unknown". The latter category was used where the patient's sex had not been indicated.

4.3.2.1 Female patients

Female patients represented 55.47% (N = 1 218 368) of the total number of patients in the study population in 2005, and 55.47% (N = 1 259 099) in 2006. The total number of prescriptions claimed for the female sex represented 59.97% (N = 8 506 355) in 2005 and 59.91% (N = 9 029 912) in 2006. The average number of prescriptions per patient per year claimed in these females was 7.55 ± 8.27 in 2005 and 7.74 ± 8.51 in 2006; at an average of 2.34 ± 1.59 items per prescription for 2005 and 2.38 ± 1.61 items per prescription for 2006.

The total cost per prescription represented 60.29% (N = R1 893 376 921.00) in 2005 and 60.19% (N = R2 046 944 383.00) in 2006; at average costs per prescriptions of R220.77 ± 455.62 and R223.77 ± 532.77 respectively. A *d*-value was calculated (*d* = 0.006) for the differences in price, which is of no practical significance (Steyn, 1999:3).

Medicine items for the female sex represented 60.29% (N = 19 860 679) of the total number of medicine items in 2005 and 60.19% (N = 21 473 074) in 2006. In 2005, medicine item costs incurred by females accounted for 59.61% of total medicine cost (N = R1 893 776 920.05.12) *vs.* 59.26% (N = R2 046 944 382.20) in 2006. The CPIs were 1.01 in 2005 and 1.02 in 2006 respectively, which indicates that treatment in females was relatively expensive. The average cost per medicine item for the female sex was R94.26 ± 185.03 in 2005 and R93.86 ± 219.20 in 2006. A *d*-value of 0.004 was calculated, which is of no practical significance according to Steyn (1999:3).

4.3.2.2 Male patients

In 2005, males represented 44.39% (N = 1 218 368) of the total number of patients in the study population, and 44.44 % (N = 1 259 099) in 2006. A total of 39.94% (N = 8 506 355) and 40.04% (N = 9 029 912) was claimed in terms of prescriptions for these males. The average number of prescriptions per male patient was 6.28 ± 7.18 in 2005 and 6.46 ± 7.38 in 2006.

The total cost per prescription claimed represented 39.63% (N = R1 893 376 921.00) in 2005 and 39.76 % (N = R2 046 944 383.00) in 2006. Males received an average of 2.46 ± 1.87, and 2.50 ± 1.88 items per prescription in 2005 and 2006 respectively; at an average cost per prescription of R224.27 ± 473.73 and R229.97 ± 592.88 respectively. A *d*-value was calculated (*d* = 0.01) which is of no practical significance (Steyn, 1999:3).

Medicine items for the male sex represented 39.63% (N = 19 860 679) of the total number of medicine items claimed in 2005 and 39.76% (N = 21 473 074) in 2006. The costs incurred by the male sex accounted for 40.31% of the total medicine cost (N = R1 893 776 920.05.12) and 40.68% (N = R2 046 944 382.20) in 2006. The CPIs were 0.98 in 2005 and 0.98 in 2006. Treatment for males was thus relatively inexpensive.

The average cost per medicine item for males was R96.98 ± 202.27 in 2005 and R97.54 ± 240.49 in 2006. A *d*-value of 0.004 was calculated which is of no practical significance according to Steyn (1999:3).

4.3.2.3 Unknown sex category

This category represents such a small percentage of the total database that it barely has any effect and therefore will not be discussed in detail for the rest of this study after this point.

In 2005 the unknown sex category had a number of patients that represented 0.14% (N = 1 218 368) of total patients, which decreased in 2006 to 0.09% (N = 1 259 099). The average number of prescriptions per patient in this sex category was 4.30 ± 5.37 in 2005 and 4.48 ± 5.93 in 2006. The total number of prescriptions for the unknown sex category represented 0.08% (N = 8 506 355) in 2005 and decreased to 0.05% (N = 9 029 912) in 2006.

The number of prescriptions where the sex was unknown represented 0.08% (N = 8 522 574) in 2005 and 0.05% (N = 9 047 138) in 2006. The total cost per prescription represented 0.08% (N = R1 893 376 921.00) in 2005 and 0.05% (N = R2 046 944 383.00). In the unknown sex category the average number of items per prescription was 2.27 ± 1.39 in 2005 and 2.21 ± 1.43

in 2006. The average cost per medicine items in 2005 and 2006 was R208.38 ± 643.60 and R236.00 ± 536.55 respectively. A *d*-value was calculated (*d* = 0.04) which is of no practical significance (Steyn, 1999:3).

Medicine items in the category where the sex was unknown represented 0.08% (N = 19 860 679) of the total number of medicine items in 2005 and decreased to 0.05 % (N = 21 473 074) in 2006. Costs incurred by the unknown sex category accounted for 0.08% of the total medicine cost (N = R1 893 776 920.05.12) in 2005 and 0.06% (N = R2 046 944 382.20) in 2006. The average cost per medicine item for the unknown group was R91.88 ± 331.55 in 2005 and R106.89 ± 338.51 in 2006. A *d*-value of 0.004 was calculated.

The subsequent section will focus on the analysis of medicine items for the various age groups and sex categories and will be based on the type of generic indicator.

4.3.3 Analysis based on the type of generic indicator

There are four different types of generic indicators as indicated on the PBM's total database. These indicators include the following:

- **M** = Original patented drugs (placed in the market for further research).
- **N** = Non-substitutable drugs (there are currently no generic equivalents for the medicine items in this group).
- **O** = Original drugs (the original patented medicine was dispensed to the patient but the substance is, however, available as generic equivalent(s).
- **Y** = "Yes". (The generic equivalent was dispensed.)

4.3.3.1 Prevalence and cost analysis based on the type of generic indicator

In the following section, the cost analysis of medicine items of the total database for the time period of 2005 and 2006 will be discussed. Table 4.2 provides an overview on the average cost, final scheme amount and final levy of medicine items on the database, based on their type of generic indicator. Table 4.2 is a summarised table compiled from tables B1.13 and B1.14 in appendix B, reflecting the complete data on the database based on generic indicators.

Table 4.2: Breakdown of costs on the database, based on the type of generic indicator

Year	Generic indicator	Variable	Number of medicine items (N = 19 860 679)	Average cost (R)	Total cost (N = R1 893 376 922.00	CPI
2005	M	Total cost	137 965	86.99 ± 86.82	12 002 167.01	0.91
	N	Total cost	8 501 370	140.14 ± 267.20	1 191 350 141.00	1.47
	O	Total cost	2 728 603	100.22 ± 139.34	273 454 160.00	1.05
	Y	Total cost	8 492 741	49.05 ± 66.41	416 570 452.00	0.51
Year	**Generic indicator**	**Variable**	**Number of medicine items (N = 21 473 074)**	**Average cost (R)**	**Total cost (R) (N = R2 046 944 383.00)**	**CPI**
2006	M	Total cost	32 866	95.74 ± 38.57	3 146 633.19	1.00
	N	Total cost	8 133 997	145.55 ± 339.64	1 183 914 105.00	1.53
	O	Total cost	3 281 896	102.98 ± 164.66	337 960 440.00	1.08
	Y	Total cost	10 024 315	52.07 ± 70.13	521 923 204.00	0.55

Original patented drugs, placed in the market for further research (generic indictor M) represented 0.69% (N = 19 860 679) of total number of medicine items claimed in 2005, which decreased to 0.15% (N = 21 473 074) in 2006. The original patented items had a total cost representative of 0.63% (N = R1 893 376 922.00) of the total cost on the database in 2005, which also decreased to 0.15% (N = R2 046 944 383.00) in 2006. CPI-values of 0.91 and 1.00 were calculated respectively for 2005 and 2006, which indicate that this medicine category was relatively inexpensive.

The average cost per medicine item in the "M" generic category was R86.99 ± 86.82 in 2005 compared to R95.74 ± 38.57 in 2006. A *d*-value was calculated (*d* = 0.1), which indicates that the price difference was of no practical significance according to Steyn (1999:3).

Non-substitutable medicine items (N indicator) represented 42.81% (N = 19 860 679) of the total number of medicine items claimed in 2005 and decreased to 38.88% (N = 21 473 074) in 2006. In 2005, the medicine had a total cost that represented 62.92% (N = R1 893 376 922.00) of the total cost of all medicine items, which decreased to 57.84% (N = R2 046 944 383.00) in 2006. CPI-values were calculated for 2005 and 2006 as 1.47 and 1.53 respectively, indicating that treatment for this medicine category was relatively expensive in 2005 and 2006.

The average cost per non-substitutable medicine item was R140.14 ± 267.20 in 2005 and R145.55 ± 339.64 in 2006. The difference in the price between 2005 and 2006 is of no practical importance (Steyn, 1999:3) (*d* = 0.02).

Original patented medicine items (O indicator) represented 13.74% (N = 19 860 679) of the total number of medicine items claimed in 2005 and increased to 15.28% (N = 21 473 074) in 2006. In 2005 original patented medicine items had a total cost that represented 14.44% (N = R1 893 376 922.00) of the total cost on the database, which increased to 16.51% (N = R2 046 944

383.00) in 2006. CPIs were calculated for 2005 and 2006 as 1.05 and 1.08 respectively which is an indication that treatment for this medicine category was relatively expensive in 2005 and 2006. The average cost per medicine item in this category was R100.22 ± 139.34 in 2005 compared to R102.98 ± 164.66 in 2006. A *d*-value was calculated (*d* = 0.02) which is of no practical importance (Steyn, 1999:3).

Generic medicine items (Y indicator) represented 42.76% (N = 19 860 679) of the total number of medicine items in 2005 and increased to 46.68% (N = 21 473 074) in 2006. In 2005 these medicine items had a total cost that represented 22.00% (N = R1 893 376 922.00) of the total cost on the database, which increased to 25.50% (N = R2 046 944 383.00) in 2006. CPI-values of 0.51 and 0.55 were calculated for 2005 and 2006 respectively, which indicate that treatment for this medicine category was relatively inexpensive in 2005 and 2006. The average cost per medicine item was R49.05 ± 66.41 in 2005 compared to R52.07 ± 70.13 in 2006. A *d*-value was calculated (*d* = 0.04) which is of no practical importance (Steyn, 1999:3).

In the subsequent paragraphs the analysis of the generic indicators as it applies to the vaious age groups will be discussed.

4.3.3.2 Analysis of the different types of generic indicators based on age group

Table 4.3 provides an overview of the number of medicine items based on generic indicator and age group. Table 4.3 is a summarised table from tables B1.15 and B1.16 in appendix B, reflecting the complete data on the database based on generic indicators and age groups.

Table 4.3: Overview of medicine items based on generic indicators and age

Year	Generic indicator	Age category (years)	Number of medicine items	Average cost per item (R)	Total cost (R)	CPI
2005	M	0 ≤ 9	16 568	44.97 ± 14.12	745 045.63	0.47
		10 ≤ 19	13 740	57.47 ± 36.35	789 590.20	0.60
		20 ≤ 45	63 251	77.59 ± 67.19	4 907 916.42	0.81
		46 ≤ 59	26 794	101.43 ± 99.32	2 717 829.95	1.06
		> 59	17 612	161.36 ± 134.54	2 841 784.81	1.69
	N	0 ≤ 9	655 307	75.56 ± 92.02	49 515 773.91	0.79
		10 ≤ 19	536 056	102.88 ± 153.01	55 147 447.65	1.08
		20 ≤ 45	2 426 319	120.40 ± 234.10	292 126 228.00	1.26
		46 ≤ 59	2 156 233	150.56 ± 286.21	324 646 528.00	1.58
		> 59	2 727 440	172.29 ± 315.68	469913228.00	1.81
	O	0 ≤ 9	234 966	81.33 ± 71.62	19 109 497.73	0.85
		10 ≤ 19	192 224	89.78 ± 104.83	17 258 794.27	0.94
		20 ≤ 45	820 742	86.13 ± 129.64	70 694 191.40	0.90
		46 ≤ 59	652 906	100.91 ± 152.58	65 882 493.05	1.06
		> 59	827 765	121.42 ± 155.53	100 509 184.00	1.27
	Y	0 ≤ 9	694 078	28.76 ± 33.44	19 958 883.33	0.30
		10 ≤ 19	648 553	37.43 ± 53.50	24 274 560.40	0.39
		20 ≤ 45	2 623 417	42.04 ± 60.94	110 285 731.00	0.44
		46 ≤ 59	2 065 552	50.49 ± 68.95	104 297 141.00	0.53
		> 59	2 461 135	64.09 ± 75.96	157 753 819.00	0.67
Year	Generic indicator	Age category (years)	Number of medicine items	Average cost per item	Total cost (R)	CPI
2006	M	0 ≤ 9	44	72.03 ± 62.42	3 169.37	0.76
		10 ≤ 19	1 051	73.22 ± 25.98	76 958.83	0.77
		20 ≤ 45	13 332	72.95 ± 27.85	972 547.26	0.77
		46 ≤ 59	9 261	112.38 ± 39.09	1 040 766.53	1.18
		> 59	9 178	114.75 ± 33.27	1 053 191.20	1.20
	N	0 ≤ 9	632 705	78.11 ± 129.49	49 420 214.90	0.82
		10 ≤ 19	529 141	105.67 ± 182.78	55 913 320.95	1.11
		20 ≤ 45	2 389 910	120.43 ± 271.05	287 805 426.00	1.26
		46 ≤ 59	2 090 611	156.77 ± 368.83	327 754 218.00	1.64
		> 59	2 491 594	185.83 ± 420.48	463 019 510.00	1.95
	O	0 ≤ 9	271 793	72.33 ± 65.40	19 658 481.98	0.76
		10 ≤ 19	218 700	87.73 ± 95.08	19 187 178.08	0.92
		20 ≤ 45	902 605	89.97 ± 156.72	81 204 371.12	0.94
		46 ≤ 59	826 003	104.46 ± 170.77	86 284 674.37	1.10
		> 59	1 062 792	123.85 ± 190.72	131 625 664.00	1.30
	Y	0 ≤ 9	763 745	30.72 ± 36.60	23 459 030.07	0.32
		10 ≤ 19	750 325	38.63 ± 52.79	28 981 374.81	0.41
		20 ≤ 45	3 071 210	44.47 ± 61.30	136 590 411.00	0.47
		46 ≤ 59	2 521 205	53.43 ± 77.72	134 715 457.00	0.56
		> 59	2 917 830	67.92 ± 78.59	198 176 931.00	0.71

4.3.3.2.1 Age group 1: Children between the ages of 0 and 9 years

Original patented medicine items, placed in the market for further research (M indicator), represented 0.08% (N = 19 860 679) of the total number of medicine items claimed in 2005 and 0.0002% (N = 21 473 074) in 2006. These medicine items had a total cost that represented 0.04% (N = R1 893 376 922.00) of the total incurred cost during 2005, and 0.0002% (N = R2 046 944 383.00) in 2006. CPI-values were calculated for 2005 and 2006 as 0.47 and 0.76 respectively which indicated that treatment for this medicine category was relatively inexpensive in 2005 and 2006. The average cost per original patented medicine item in the "M" category in this age group was R44.97 ± 14.12 in 2005 compared to R72.03 ± 62.42 in 2006. A small to medium size-effect (*d* = 0.43) was calculated, but which is of no practical significance according to Steyn (1999:3).

Non-substitutable medicine items ("N" indicator) represented 3.30% (N = 19 860 679) of the total number of medicine items claimed in 2005 and 2.95% (N = 21 473 074) in 2006. Costs incurred by this category represented 2.62% (N = R1 893 376 922.00) in 2005 and 2.41% (N = R2 046 944 383.00) in 2006. CPIs calculated for 2005 and 2006 were 0.79 and 0.82 respectively, which indicated that treatment with non-substitutable medicine items was relatively inexpensive in 2005 and 2006 in this age group. The average cost per medicine item was R75.56 ± 92.02 in 2005 compared to R78.11 ± 129.49 in 2006. A *d*-value was calculated (*d* = 0.02) which is of no practical significance according to Steyn (1999:3).

Original patented medicine ("O" indicator) represented 1.18% (N = 19 860 679) of the total number of medicine items claimed in 2005 and 1.27% (N = 21 473 074) in 2006. The total costs of these items represented 1.01% (N = R1 893 376 922.00) in 2005 and 0.96% (N = R2 046 944 383.00) in 2006. CPI-values for 2005 and 2006 were calculated as 0.85 and 0.76 respectively which indicated that treatment with original, patented medicine was relatively inexpensive in 2005 and 2006. The average cost per medicine item was R81.33 ± 71.62 in 2005 compared to R72.33 ± 65.40 in 2006. A small *d*-value was calculated (*d* = 0.13) which is of no practical significance (Steyn, 1999:3).

Generic medicine items ("Y" indicator) represented 3.49% (N = 19 860 679) of the total medicine items claimed in 2005 and 3.56% (N = 21 473 074) in 2006. In 2005 generic medicine items had a total cost that representative of 1.05% (N = R1 893 376 922.00) and 1.15 % (N = R2 046 944 383.00) in 2006. CPIs were calculated for 2005 and 2006 as 0.30 and 0.32 respectively which indicated that treatment for this medicine category was relatively inexpensive in 2005 and 2006. The average cost per medicine item in the "Y" (generic) category was

R28.76 ± 33.44 in 2005 compared to R30.72 ± 36.60 in 2006. A *d*-value was calculated (*d* = 0.05) which is of no practical significance (Steyn, 1999:3).

4.3.3.2.2 Age group 2: Adolescents between the ages of 10 and 19 years

Original patented medicine items, placed in the market for further research represented 0.07% (N = 19 860 679) of the total number of medicine items claimed in 2005 and 0.005% (N = 21 473 074) in 2006. These medicine items had a total cost that represented 0.04% (N = R1 893 376 922.00) in 2005 and 0.003% (N = R2 046 944 383.00) in 2006. CPIs were calculated as 0.60 and 0.77 for 2005 and 2006 respectively which indicated that treatment for this medicine category was relatively inexpensive in 2005 and 2006 in age group 2. The average cost per medicine item in this medicine category was R57.47 ± 36.35 in 2005 compared to R73.22 ± 25.98 in 2006. A small to medium size-effect (*d* = 0.43) was calculated which is of no practical significance according to Steyn (1999:3).

Non-substitutable medicine items represented 2.70% (N = 19 860 679) of the total number of medicine items claimed in 2005 that decreased to 2.46% (N = 21 473 074) in 2006. Medicine items had a total cost that represented 2.91% (N = R1 893 376 922.00) in 2005 and 2.73% (N = R2 046 944 383.00) in 2006. Cost Prevalence Indices of 1.08 and 1.11 were calculated for 2005 and 2006 respectively which indicated that treatment for this medicine category was relatively expensive in 2005 and 2006. The average cost per medicine item in this category was R102.88 ± 153.01 in 2005 and R105.67 ± 182.78 in 2006. A small *d*-value was calculated (*d* = 0.02) indicating a price difference which is of no practical significance (Steyn, 1999:3).

Original patented medicine items 0.97% (N = 19 860 679) of the total number of medicine items claimed in 2005 and 1.02% (N = 21 473 074) in 2006. In 2005 medicine items that were categorised with an “O” indicator for age group 2 had a total cost that represented 0.91% (N = R1 893 376 922.00) of the total costs incurred which increased to 0.94 % (N = R2 046 944 383.00) in 2006. CPIs of 0.94 and 0.92 were calculated for 2005 and 2006 respectively which indicated that treatment for this medicine category was relatively inexpensive in 2005 and 2006. The average cost per medicine item in the “O” generic category was R89.78 ± 104.83 in 2005 and R87.73 ± 95.08 in 2006. A small *d*-value was calculated (*d* = 0.02) which indicated that the price difference is of no practical significance (Steyn, 1999:3).

Generic medicine items represented 3.27% (N = 19 860 679) of the total number of medicine items claimed in 2005 and 3.49% (N = 21 473 074) in 2006. Total costs incurred represented 1.28% (N = R1 893 376 922.00) in 2005 which increased to 1.42% (N = R2 046 944 383.00) in 2006. Subsequent CPIs were calculated for 2005 and 2006 as 0.39 and 0.41 respectively which

indicated that treatment for this medicine category was relatively inexpensive in 2005 and 2006. The average cost per medicine item in the "Y" category was R37.43 ± 53.50 in 2005 and R38.63 ± 52.79 in 2006. A small *d*-value was calculated (*d* = 0.02) which indicates that the price difference is of no practical significance (Steyn, 1999:3).

4.3.3.2.3 Age group 3: Young adults between the ages of 20 and 45 years

Original patented medicine items, placed in the market for further research represented 0.32% (N = 19 860 679) of the total number of medicine items claimed 2005, and decreased to 0.06% (N = 21 473 074) in 2006. The total costs incurred in 2005 represented 0.26% (N = R1 893 376 922.00) of the total cost of all medicine items claimed and decreased to 0.05% (N = R2 046 944 383.00) in 2006. CPI-values of 0.81 and 0.77 respectively were calculated for 2005 and 2006 which indicated that treatment for this medicine category was relatively inexpensive in 2005 and 2006. The average cost per medicine item in the "M" generic category for age group 3 was R77.59 ± 67.19 in 2005 and R72.95 ± 27.85 in 2006. A small *d*-value was calculated (*d* = 0.07) which indicates that the price difference is of no practical significance (Steyn, 1999:3).

Non-substitutable medicine items represented 12.22% (N = 19 860 679) of the total number of medicine items claimed in 2005 and 11.13% (N = 21 473 074) in 2006. The medicine items had a total cost that represented 15.54% (N = R1 893 376 922.00) of all medicine item costs on the database which decreased to 14.06% (N = R2 046 944 383.00) in 2006. CPIs of 1.26 were calculated for both 2005 and 2006 which indicated that treatment for this medicine category was relatively expensive in both years. The average cost per medicine item in the "N" category was R120.40 ± 234.10 in 2005 and R120.43 ± 271.05 in 2006.

Original patented medicine represented 4.13% (N = 19 860 679) of the total number of medicine items claimed in 2005 and 4.20% (N = 21 473 074) in 2006; at a total cost that represented 3.73% (N = R1 893 376 922.00) in 2005 and 3.97% (N = R2 046 944 383.00) in 2006. CPI-values were calculated for 2005 and 2006 as 0.90 and 0.94 respectively which indicated that treatment for this medicine category was relatively inexpensive in 2005 and 2006. The average cost per medicine item was R86.13 ± 129.64 in 2005 and R89.97 ± 156.72 in 2006. A small *d*-value was calculated (*d* = 0.02) which indicates that the price difference is of no practical importance (Steyn, 1999:3).

Generic medicine items represented 13.21% (N = 19 860 679) of the total number of medicine items claimed in 2005 and 14.20% (N = 21 473 074) in 2006; at a total cost that represented 5.82% (N = R1 893 376 922.00) of the total cost of all medicine items in 2005 which increased to 6.67% (N = R2 046 944 383.00) in 2006. CPIs were calculated for 2005 and 2006 as 0.44

and 0.47 respectively which indicated that treatment for this medicine category was relatively inexpensive in 2005 and 2006. The average cost per medicine item was R42.04 ± 60.94 in 2005 compared to R44.47 ± 61.30 in 2006. A small *d*-value was calculated (*d* = 0.04) which indicates that the price difference is of no practical importance (Steyn, 1999:3).

4.3.3.2.4 Age group 4: Older patients between the ages of 46 and 59 years

Original patented medicine items, placed in the market for further research represented 0.13% (N = 19 860 679) of the total number of medicine items claimed in 2005 and 0.04% (N = 21 473 074) in 2006; whilst the costs incurred by this age group in 2005 represented 0.14% (N = R1 893 376 922.00) in 2005 which decreased to 0.05% (N = R2 046 944 383.00) in 2006. CPI-values were calculated for 2005 and 2006 as 1.06 and 1.18 respectively which indicated that treatment for this medicine category was relatively expensive in 2005 and 2006. The average cost per medicine item in the "M" generic category was R101.43 ± 99.32 in 2005 compared to R112.38 ± 39.09 in 2006. A small *d*-value was calculated (*d* = 0.11) which indicated that the price difference was of no practical significance (Steyn, 1999:3).

Non-substitutable medicine items represented 10.86% (N = 19 860 679) of the total number of medicine items claimed in 2005 and decreased to 9.74% (N = 21 473 074) in 2006. In 2005, medicine items had a total cost that represented 17.15% (N = R1 893 376 922.00) which decreased to 16.01% (N = R2 046 944 383.00) in 2006. CPIs were calculated as 1.58 and 1.64 respectively for 2005 and 2006 which indicated that treatment for this medicine category was relatively expensive in 2005 and 2006. The average cost per medicine item in the "N" generic category was R150.56 ± 286.21 in 2005 compared to R156.77 ± 368.83 in 2006. A small *d*-value was calculated (*d* = 0.02) which indicates that the price difference is of no practical significance (Steyn, 1999:3).

Original patented medicine items represented 3.29% (N = 19 860 679) of the total number of medicine items claimed in 2005 and 3.85% (N = 21 473 074) in 2006; whilst the costs incurred by this age group in 2005 represented 3.48% (N = R1 893 376 922.00) which increased to 4.22% (N = R2 046 944 383.00) in 2006. CPI-values were calculated for 2005 and 2006 as 1.06 and 1.10 respectively which indicated that treatment for this medicine category was relatively expensive in 2005 and 2006. The average cost per medicine item in the "O" category for age group 4 was R100.91 ± 152.58 in 2005 compared to R104.46 ± 170.77 in 2006. A small *d*-value was calculated (*d* = 0.02) which indicates that the difference in price is of no practical significance (Steyn, 1999:3).

Generic medicine items represented 10.40% (N = 19 860 679) of the total number of medicine items claimed in 2005. This increased to 11.74% (N = 21 473 074) in 2006. Associated item costs represented 5.51% (N = R1 893 376 922.00) of the amount incurred in 2005 and 6.58% (N = R2 046 944 383.00) in 2006. CPI-values of 0.53 and 0.56 respectively were calculated for 2005 and 2006 which indicated that treatment for this medicine category was relatively inexpensive in 2005 and 2006. The average cost per medicine item in the "Y" generic category was R50.49 ± 68.95 in 2005 and R53.43 ± 77.72 in 2006. A small *d*-value was calculated (*d* = 0.04), indicating that the price difference is of no practical significance (Steyn, 1999:3).

4.3.3.2.5 Age group 5: Patients older than 59 years of age

Original patented medicine items, placed in the market for further research represented 0.09% (N = 19 860 679) of the total number of medicine items claimed in 2005 and 0.04% (N = 21 473 074) in 2006. Medicine items in patients older than 59 years had a total cost that represented 0.15% (N = R1 893 376 922.00) in 2005 and 0.05% (N = R2 046 944 383.00) in 2006. CPI-values were calculated for 2005 and 2006 as 1.69 and 1.20 respectively which indicated that treatment for this medicine category was relatively expensive in 2005 and 2006. The average cost per medicine item was R161.36 ± 134.54 in 2005 compared to R114.75 ± 33.27 in 2006. A small to medium size effect was calculated (*d* = 0.35), indicating that the price difference is of no practical significance (Steyn, 1999:3).

Non-substitutable medicine items represented 13.73% (N = 19 860 679) of the total number of medicine items claimed in 2005 and decreased to 11.60% (N = 21 473 074) in 2006. Costs associated with these medicine items represented 24.82% (N = R1 893 376 922.00) of the total cost of all medicine items claimed in 2005 which decreased to 22.62% (N = R2 046 944 383.000) in 2006. CPIs were calculated as 1.81 and 1.95 for 2005 and 2006 respectively which indicated that treatment with this medicine category was relatively expensive in 2005 and 2006. The average cost per medicine item in the "N" generic category was R172.29 ± 315.68 in 2005 compared to R185.83 ± 420.48 in 2006. A *d*-value was calculated (*d* = 0.03) which is of no practical significance according to Steyn (1999:3).

Original patented medicine items represented 4.17% (N = 19 860 679) of the total number of medicine items claimed in 2005 and 4.95% (N = 21 473 074) in 2006. The cost associated with these medicine items represented 5.31% (N = R1 893 376 922.00) in 2005 which increased to 6.43% (N = R2 046 944 383.00) in 2006. CPIs were calculated for 2005 and 2006 as 1.27 and 1.30 respectively which indicated that treatment for this medicine category was relatively expensive in 2005 and 2006. The average cost per medicine item in the "O" generic category for patients older than 59 years was R121.42 ± 155.53 in 2005 and R123.85 ± 190.72 in 2006.

A *d*-value was calculated (*d* = 0.01) which indicates that the price difference is of no practical importance (Steyn, 1999:3).

Generic medicine items represented 12.39% (N = 19 860 679) of the total number of medicine items claimed in 2005 and 13.59% (N = 21 473 074) in 2006. These items had a total cost that represented 8.33% (N = R1 893 376 922.00) of the total cost of medicine items on the database in 2005, which increased to 9.68% (N = R2 046 944 383.00) in 2006. CPI-values were calculated as 0.67 and 0.71 respectively for 2005 and 2006 which indicated that treatment for this medicine category was relatively inexpensive in 2005 and 2006. The average cost per medicine item in the "Y" generic category was R64.09 ± 75.96 in 2005 and R67.92 ± 78.59 in 2006. A *d*-value was calculated (*d* = 0.05) which indicates that the difference in price is of no practical importance (Steyn, 1999:3).

4.3.3.3 Analysis of the different types of generic indicators based on the sex of patients

The following section will provide a discussion on the analysis of the different types of generic indicators as it was conducted according to the sex of the patients. Table 4.4 provides an overview of medicine items based on generic indicators and sex. Table 4.4 is a summarised table from tables B1.17 and B1.18 in appendix B, reflecting the complete data on the database based on generic indicators and the sex of the patient.

4.3.3.3.1 Female patients

Original patented medicine items, placed in the market for further research claimed for females represented 0.42% (N = 19 860 679) of the total number of medicine items claimed in 2005 and decreased to 0.15% (N = 21 473 074) in 2006. The total costs associated with these medicine items represented 0.39% (N = R1 893 376 922.00) in 2005 which decreased to 0.15% (N = R2 046 944 383.00) in 2006. The average cost per medicine item in the "M" generic category for females was R87.59 ± 85.04 in 2005 compared to R97.09 ± 34.64 in 2006. A small *d*-value was calculated (*d* = 0.11) which indicates that the price difference is of no practical importance (Steyn, 1999:3).

Non-substitutable medicine items for females represented 26.43% (N = 19 860 679) of the total number of medicine items claimed in 2005 and decreased to 23.31% (N = 21 473 074) in 2006. The total cost of these items represented 37.69% (N = R1 893 376 922.00) in 2005 and decreased to 34.00% (N = R2 046 944 383.00) in 2006. CPI-values of 1.43 and 1.46 were respectively calculated for 2005 and 2006 which indicated that treatment with this medicine category was relatively expensive in 2005 and 2006 for the female sex. The average cost per

medicine item in the "N" generic category for the female sex was R135.93 ± 252.45 in 2005 compared to R139.06 ± 319.07 in 2006. A *d*-value was calculated (*d* = 0.01) which indicated that the price difference was of no practical importance (Steyn, 1999:3).

Table 4.4: Overview of medicine items based on generic indicators and sex

Year	Sex	Generic indicator	Number of medicine items	Mean ± Std Dev	Total cost (R)	CPI
2005	Female	M	83 787	87.59 ± 85.04	7 339 137.64	0.93
		N	5 249 767	135.93 ± 252.45	713 591 807.00	1.43
		O	1 613 565	101.29 ± 141.92	163 437 728.00	1.06
		Y	5 027 136	48.59 ± 67.04	244 283 439.76	0.51
	Male	M	54 069	86.13 ± 89.56	4 657 072.58	0.93
		N	3 245 727	146.89 ± 288.67	476 760 960.00	1.54
		O	1 113 027	98.68 ± 135.56	109 741 478.77	1.04
		Y	3 457 244	49.74 ± 65.51	171 966 600.57	0.52
	Unknown	M	109	54.65 ± 39.90	5 956.79	0.57
		N	5 876	169.74 ± 536.81	997 374.58	1.67
		O	1 966	88.99 ± 84.62	174 953.90	1.00
		Y	8 361	38.32 ± 55.74	320 411.78	0.50
Year	**Sex**	**Generic indicator**	**Number of medicine items**	**Mean ± Std Dev**	**Total cost (R)**	**CPI**
2006	Female	M	31 879	97.09 ± 34.64	3 095 085.64	1.02
		N	5 004 847	139.06 ± 319.07	695 969 262.00	1.46
		O	1 976 605	105.94 ± 175.63	209 395 823.05	1.11
		Y	5 911 481	51.53 ± 70.51	304 608 185.33	0.54
	Male	M	970	51.01 ± 94.31	49 479.63	0.54
		N	3 125 443	155.90 ± 369.65	487 260 210.00	1.64
		O	1 303 611	98.48 ± 146.41	128 381 254.31	1.03
		Y	4 107 475	52.84 ± 69.60	217 034 597.13	0.55
	Unknown	M	17	121.64 ± 10.74	2 067.92	1.28
		N	3 707	184.69 ± 560.18	684 632.63	1.94
		O	1 680	109.14 ± 94.47	183 362.92	1.14
		Y	5 359	52.33 ± 56.13	280 420.73	0.55

Original patented medicine items ("O" indicator) represented 8.12% (N = 19 860 679) of the total number of medicine items claimed in 2005 and 9.21 % (N = 21 473 074) in 2006. The total cost of these items represented 8.63% (N = R1 893 376 922.00) in 2005 which increased to 10.23% (N = R2 046 944 383.00) in 2006. CPIs of 1.06 and 1.11 were calculated for 2005 and 2006 respectively which indicated that treatment with this medicine category in females was relatively expensive in 2005 and 2006. The average cost per medicine item in the "O" generic category for the female sex was R101.29 ± 141.92 in 2005 and R105.94 ± 175.63 in 2006. A *d*-value was calculated (*d* = 0.03) for the difference in price, which is of no practical significance according to Steyn (1999:3).

Generic medicine items ("Y" indicator) for the females represented 25.31% (N = 19 860 679) of the total number of medicine items in 2005, which increased to 27.53% (N = 21 473 074) in 2006. The total costs of these medicine items represented 12.90% (N = R1 893 376 922.00) of

the total cost incurred in 2005, and 14.88 % (N = R2 046 944 383.00) in 2006. CPI-values were calculated as 0.51 and 0.54 for 2005 and 2006 respectively which indicated that treatment of females with this medicine category was relatively inexpensive in 2005 and 2006. The average cost per medicine item in the "Y" generic category for females were R48.59 ± 67.04 in 2005 compared to R51.53 ± 70.51 in 2006. A small *d*-value was calculated (*d* = 0.04), which indicates that the difference in price is of no practical importance (Steyn, 1999:3).

4.3.3.3.2 Male patients

Original patented medicine items, placed in the market for further research claimed for males represented 0.27% (N = 19 860 679) of the total number of medicine items claimed in 2005 and decreased to (0.00%) (N = 21 473 074; n = 970) in 2006. The total cost of these items represented 0.25% (N = R1 893 376 922.00) in 2005 and (0.00%) (N = R2 046 944 383.00; n = R49 479.63) in 2006. CPIs were calculated for 2005 and 2006 as 0.93 and 0.54 respectively which indicated that treatment with this medicine category was relatively inexpensive in 2005 and 2006. The average cost per medicine item in the "M" generic category for males was R86.13 ± 89.56 in 2005 compared to R51.01 ± 94.31 in 2006. A small to medium *d*-value was calculated (*d* = 0.4) to measure the difference in price – which, according to Steyn, (1999:3) is of no practical significance.

Non-substitutable medicine items claimed for males represented 16.34% (N = 19 860 679) of the total number of medicine items claimed in 2005 and decreased to 14.56% (N = 21 473 074) in 2006. The total cost associated with these items represented 25.18% (N = R1 893 376 922.00) in 2005, compared to 23.80% (N = R2 046 944 383.00) in 2006. CPI-values were calculated for 2005 and 2006 (*i.e*., 1.54 *vs.* 1.64) which indicated that treatment with this medicine category in males was relatively expensive in 2005 and 2006. The average cost per medicine item in the "N" generic category for the male sex was R146.89 ± 288.67 in 2005 compared to R155.90 ± 369.65 in 2006. A small *d*-value was calculated (*d* = 0.02) – indicating that the price difference is of no practical significance (Steyn, 1999:3).

Original patented medicine items claimed for males represented 5.60% (N = 19 860 679) of the total number of medicine items claimed in 2005 and 6.07% (N = 21 473 074) of those in 2006. The total cost of these items represented 5.80% (N = R1 893 376 922.00) of the total cost of claimed items in 2005 and 6.27% (N = R2 046 944 383.00) of those in 2006. CPIs were calculated for 2005 and 2006 as 1.04 and 1.03 respectively which indicated that treatment with this medicine category was relatively expensive in 2005 and 2006. The average cost per medicine item in the "O" generic category for males was similarly R98.68 ± 135.56 in 2005 and R98.48 ± 146.41 in 2006.

Generic medicine items claimed for males represented 17.41% (N = 19 860 679) of the total number of medicine items claimed in 2005 and 19.13% (N = 21 473 074) in 2006. Total cost associated with these items represented 9.08% (N = R1 893 376 922.00) of the total cost claimed in 2005, and 10.60% (N = R2 046 944 383.00) of that in 2006. CPI-values were calculated for 2005 and 2006 as 0.52 and 0.55 respectively which indicated that treatment with this medicine category in males was relatively inexpensive in 2005 and 2006. The average cost per medicine item in the "Y" generic category for males was R49.74 ± 65.51 in 2005 and R52.84 ± 69.60 in 2006. A small to medium size effect (*d*-value = 0.04) was calculated for the difference in price, which, is of no practical importance according to Steyn (1999:3).

4.3.3.3.3 Unknown sex category

Original patented medicine items, placed in the market for further research were claimed at a total number of 109 (N = 19 860 679) times in 2005, compared with 17 (N = 21 473 074) claims in 2006. The total cost associated with these items was (n = R5 956.79; N = R1 893 376 922.00) in 2005 and (n = R2 069.72; N = R2 046 944 383.00) in 2006. Calculated CPIs for 2005 and 2006 (*i.e*., 0.57 and 1.28 respectively), indicated that treatment for this medicine category was relatively inexpensive in 2005 versus relatively expensive in 2006. The average cost per medicine item in the "M" generic category was R54.65 ± 39.90 in 2005 compared to R121.64 ± 10.74 in 2006. A large *d*-value was calculated (*d* = 1.68) which is of practical significance (Steyn, 1999:3).

Non-substitutable medicine items represented 0.03% (N = 19 860 679) of the total number of medicine items claimed in 2005 and 0.02% (N = 21 473 074) of those in 2006. Total cost associated herewith represented 0.05% (N = R1 893 376 922.00) in 2005 and 0.03% (N = R2 046 944 383.00) in 2006. CPIs were calculated for 2005 and 2006 as 1.67 and 1.94 respectively which indicated that treatment with this medicine category was relatively expensive in 2005 and 2006. The average cost per medicine item in the "N" generic category was R169.74 ± 536.81 in 2005 compared to R184.69 ± 560.18 in 2006. A small *d*-value was calculated (*d* = 0.03) for the difference in price which is of no practical importance (Steyn, 1999:3).

Original, patented medicine items represented 0.01% (N = 19 860 679) of the total number of medicine items claimed in 2005 and 0.01% (N = 21 473 074) of those in 2006. The total cost of these items was 0.01% (N = R1 893 376 922.00) in 2005 and 0.01% (N = R2 046 944 383.00) in 2006. CPI-values were calculated for 2005 and 2006 as 1.00 and 1.14 respectively which indicated that treatment for this medicine category was relatively expensive in 2005 and 2006. The average cost per medicine item in the "O" generic category was R88.99 ± 84.62 in 2005

compared to R109.14 ± 94.47 in 2006. A small *d*-value was calculated (*d* = 0.21) which indicates that the difference in price is of no practical importance (Steyn, 1999:3).

Generic medicine items represented 0.04% (N = 19 860 679) of the total number of medicine items claimed in 2005 and 0.02% (N = 21 473 074) of those in 2006. The total cost of these items represented 0.02% (N = R1 893 376 922.00) of the total cost of claimed items in 2005, compared to 0.01% (N = R2 046 944 383.00) in 2006. CPIs were calculated for 2005 and 2006 (*i.e*., 0.50 and 0.55 respectively) which indicated that treatment for this medicine category was relatively inexpensive in 2005 and 2006. The average cost per medicine item in the "Y" generic category was R38.32 ± 55.74 in 2005 compared to R52.33 ± 56.13 in 2006. A small *d*-value was calculated for the price difference (*d* = 0.25), which is of no practical significance according to Steyn (1999:3).

4.3.4 Summary and discussion on the overview of the total database

In the subsequent paragraphs, the summaries based on the total database will be discussed.

4.3.4.1 Summary and discussion of the analysis based on the patient's age and sex

It can be concluded from the aforementioned results (paragraphs 4.4.1 – 4.4.2) that there was little to no change between the two consecutive study periods in terms of the number of medicine items per age group, the total cost incurred by the various age groups, the number of medicine items for each sex category and the total cost incurred by each sex category for the two study periods. There was subsequently also no difference in the average cost per prescription and the average cost per item between the two study periods.

Noteworthy findings from paragraphs 4.4.1 to 4.4.2 were the following:

- The number of medicine items claimed for patients in age groups 3, 4 and 5 (i.e. patients older than 20 years) were almost 5-6 times that of the number of claims for patients in age groups 1 and 2 (patients aged 0≤ 19 years of age). Older patients are more likely to use more prescriptions and over-the-counter (OTC) medicine than younger people. According to Medco Health Solutions (2008) an estimated 25 per cent of older adults take five or more medicine items on a regular basis. Older patients are furthermore more likely to have multiple prescribers (Boyd *et al*. 2005:716). According to the Centers for Disease Control and Prevention (CDC, 2001) older patients generally receive more prescriptions than younger patients; however, the increase in the rate of drug prescriptions is consistent across all age groups. Older patients are furthermore six times more likely than younger people to

receive new medications. Results of this study show that the average number of prescriptions per patient increased from 4.06 ± 3.93 and 4.26 ± 4.07 in children to 12.32 ± 10.47 and 12.31 ± 10.72 in patients older than 59 years of age during 2005 and 2006 respectively (see paragraphs 4.4.1.1 - 4.4.1.5).

- In both study periods more than half of the patients on the database were female. The relationship with regard to the total number of prescriptions, number of medicine items and total cost for females : males for the period of 2005 and 2006 were roughly 1.5 : 1. Studies in the USA and other countries show similar results (Svarstad *et al*., 1987:1089). According to Svarstad *et al*. (1987:1089) the reason for this may be the higher rate of physician utilisation among females, a tendency that increases the probability of obtaining a prescription. Subsequently, the yearly costs of prescriptions for females are greater than for males due to greater utilisation by females (Roe *et al*., 1999). Roe *et al*. (1999) also emphasised that females would also be more likely than males to fill at least one prescription during a year, however, at a lower average cost per prescription than for males. Similar results were found in this study (refer to paragraphs 4.4.2.1 and 4.4.2.2).
- Although of no practical significance according to Steyn (1999:3), the cost per medicine item for patients older that the age of 45 years (*i.e*., age groups 4 & 5) was almost double that of the age groups below 45 years of age (age groups 1, 2 & 3). Calculated CPIs, however, indicate that the medicine items claimed for the first three age categories were above 1; these items were therefore relatively expensive compared to the CPIs calculated for age categories 4 and 5, which were below 1 (indicating relative inexpensiveness).
- Based on cost prevalence indices (CPI), it was found that prescriptions of patients in age groups 1 to 3 were relatively cheaper than the treatment of age groups 4 and 5, with *d*-values calculated as follows: age group 1 (d = 0.006); age group 2 (d = 0.008); age group 3 (d = 0.001); age group 4 (d = 0.007) and age group 5 (d = 0.01). These *d*-values are of no practical significance according to Steyn (1999:3).

4.3.4.2 Summary and discussion of the analysis of the different types of generic indicators

Results of a recent study conducted by Steinman *et al*. (2007:646) to evaluate how frequently brand (trade) name products and generic name equivalents are used in clinical practice, show that physicians refer to medications by their brand names much more frequently than by their generic names. In the Steinman and coworker-study brand names were used almost exclusively for drugs without generic competition as well as for drugs with generic competition, although at lower rates and greater variability between drugs. Physicians may also prefer brand names for various reasons such as that brand names may be easier to remember and to pronounce, physicians may only be familiar with the brand name product and/or even unaware

of the correspondence between brand and generic names. In some cases physicians may also believe that the generic formulation is not as effective as the brand name product (Steinman *et al*., 2007:647). In the USA an estimated 10 to 11 per cent of prescriptions are dispensed using brand name medication when a molecularly identical generic formulation is available (Kwo *et al*., 2009:459). The use of brand name drugs when generic equivalents are available may reflect the skepticism of many physicians and patients toward generic drugs, physicians' lack of awareness of drug costs and patients' lack of awareness of their ability to request a generic version (Kwo *et al*., 2009:459).

Consumers' attitudes towards generic drugs also differ by age, education, race and ethnicity (Gaither *et al*., 2001:729). Kendall *et al*. (1991:182) reported that older patients are less willing to substitute generic drugs when offered the choice, whilst older patients are maybe more wary of the quality of generics. Perri *et al*. (1990:33) furthermore noted that consumers over the age of fifty were more concerned about the side-effects of generics than with brand name drugs.

Results of this study showed that only a small number of prescriptions for original items were claimed for older patients in the private health care sector of South Africa, in fact, the majority of items on the database and in all age and sex groups were the non-substitutable- ("N" indicator) and generic ("Y" indicator) medicine items. This discrepancy may be ascribed to the law, where in current form, the generic substitution provision in the Medicines and Related Substance Control Act 101 of 1965 of South Africa as amended in 1997 (implemented 2 May 2003) compels pharmacists to offer patients a generic equivalent/substitute for any medicine prescribed, unless the prescriber explicitly stated that the medicine should not be substituted, or in cases where the generic price is higher than that of the branded (original) product, but the final choice rests with the patient.

This section covered a general discussion of the total database. The subsequent discussions will be based on hipolipidaemic medicine items.

4.4 OVERVIEW OF HIPOLIPIDAEMIC MEDICINE

The basic characteristics of the study population are presented in table 4.5. This includes the total number of patients and prescriptions, as well as the medicine items and the direct medicine costs involved. Table 4.5 is a summarised table from tables B2.1, B2.2, B2.3, B2.4, B2.5, B2.6, B2.7, B2.8, B2.9, B2.10, B2.11, B2.12, B2.13, B2.14, B2.15, B2.16, B2.17, B2.18, B2.19, B2.20, B2.21, B2.22, B2.23 in appendix B, reflecting the hipolipidaemic data on the database of both 2005 and 2006 and their indicidual periods.

Table 4.5: Basic characteristics of hipolipidaemic medicine

	AGE CATEGORY (YEARS)				
	0 ≤ 9	10 ≤ 19	20 ≤ 49	46 ≤ 59	≥ 59
Number of patients					
N_{2005} = 87 214	631	306	10 960	28 862	46 455
N_{2006} = 91 528	473	263	10 606	30 001	50 185
Number of prescriptions					
N_{2005} = 604 824	707	994	54 017	188 910	360 190
N_{2006} = 678 297	561	809	56 703	209 554	410 658
Average number of prescriptions per patient per year					
2005 (7.11 ± 4.63)	1.12 ± 0.65	3.25 ± 3.48	4.93 ± 4.14	6.55 ± 4.48	7.75 ± 4.57
2006 (7.61 ± 4.50)	1.19 ± 1.02	3.08 ± 3.19	5.35 ± 4.18	6.98 ± 4.41	8.18 ± 4.38
Number of medicine items					
N_{2005} = 626 759	714	1 048	55 977	196 042	372 978
N_{2006} = 705 424	567	852	59 449	219 120	425 436
Number of items per prescription					
2005 (1.04 ± 0.22)	1.01 ± 0.11	1.05 ± 0.26	1.04 ± 0.21	1.04 ± 0.22	1.04 ± 0.22
2006 (1.04 ± 0.21)	1.01 ± 0.10	1.05 ± 0.23	1.05 ± 0.23	1.05 ± 0.23	1.04 ± 0.20
Total cost (based on medicine items) (R)					
N_{2005} = 106 943 348.53	42 014.53	186 962.39	10 196 222.52	34 619 455.14	61 898 693.95
N_{2006} = 117 862 631.87	34 947.98	154 194.71	10 602 379.49	38 177 425.29	68 893 684.40
Average cost per prescription (R)					
2005	59.43 ± 67.22	188.09 ± 110.07	188.76 ± 92.82	183.23 ± 89.83	171.85 ± 84.98
2006	62.30 ± 77.10	190.60 ± 120.02	186.98 ± 103.25	182.18 ± 97.66	167.76 ± 86.10
Average cost per item (R)					
2005 (170.63 ± 70.19)	58.84 ± 66.95	178.40 ± 77.11	182.15 ± 75.70	176.60 ± 71.67	165.96 ± 67.91
2006 (167.08 ± 71.93)	61.64 ± 71.65	180.98 ± 89.64	178.34 ± 77.84	174.23 ± 74.35	161.94 ± 69.10

	SEX CATEGORIES		
	FEMALE	MALE	UNKNOWN
Number of patients			
N_{2005} = 87 214	40 893	46 262	59
N_{2006} = 91 528	43 076	48 407	45
Number of prescriptions			
N_{2005} = 604 824	283 006	321 492	326
N_{2006} = 678 297	318 486	359 511	300
Average number of prescriptions per patient			
2005	7.08 ± 4.50	7.14 ± 4.40	5.52 ± 4.40
2006	7.56 ± 4.50	7.65 ± 4.49	6.98 ± 4.43
Number of medicine items			
N_{2005} = 626 759	292 495	333 933	331
N_{2006} = 705 424	329 695	375 416	313
Number of items per prescription			
2005	1.04 ± 0.21	1.04 ± 0.23	1.02 ± 0.12
2006	1.04 ± 0.20	1.04 ± 0.22	1.04 ± 0.20
Total cost (based on medicine items) (R)			
N_{2005} = 106 943 348.53	48 565 536.50	58 326 901.67	50 910.36
N_{2006} = 117 862 631.87	53 411 724.02	64 402 687.07	48 220.78

Table 4.5: Basic characteristics of hipolipidaemic medicine (continued)

Average cost per prescription (R)			
2005	171.61 ± 83.68	181.43 ± 90.66	156.17 ± 70.37
2006	167.71 ± 87.30	179.14 ± 95.20	160.74 ± 73.40
Average cost per item (R)			
2005	166.04 ± 68.22	174.67 ± 71.65	153.81 ± 65.25
2006	162.00 ± 69.72	171.55 ± 73.52	154.06 ± 63.28

* Data are *n*-values (means ± SD).

Due to missing data in the age categories, the totals of the number of prescriptions do not add up to the total number of prescriptions based on sex groups.

The hipolipidaemic study population consisted of 87 214 patients in 2005 and 91 528 patients in 2006, thus accounting for approximately 7.2% of the total number of patients on the database in both 2005 and 2006.

The total number of hipolipidaemic prescriptions accounted for between 7.1% and 7.5% of the total number of prescriptions on the database in 2005 and 2006 whilst hipolipidaemic medicine items accounted for 3.15% to 3.29% of the total number of medicine items on the database for both study years. The total hipolipidaemic medicine cost accounted for 5.65% of the total medicine cost on the database in 2005 and 5.76% in 2006.

Patients in the study population (*i.e*. who received hipolipidaemic medicine items) received on average 1 hipolipidaemic medicine item per prescription, compared with patients on the database who received on average between 2 and 3 items per prescription. Based on the NCEP guidelines (NIH, 2002:165), when the therapeutic lifestyle change (TLC) treatment plan fails to achieve the desired LDL cholesterol levels, patients must start with 1 hipolipidaemic medicine item together with TLC.

Results of the analyses based on the different age groups and the sex of patients as set out in table 4.5, are revealed in the subsequent paragraphs. A short summary and discussion will follow in paragraph 4.4.6.

4.4.1 Analysis of hipolipidaemic medicine based on patients' age group

The age groups' categories utilised in the analysis were as follows (refer also to table 3.1):

- Age group 1: Children between the ages of 0 and 9 years (0 ≤ 9 years).
- Age group 2: Adolescents between the ages of 10 and 19 years (10 ≤ 19 years).
- Age group 3: Young adults between the ages of 20 and 45 years (20 ≤ 45 years).

- Age group 4: Older patients between the ages of 46 and 59 years (46 ≤ 59 years).
- Age group 5: Patients older than 59 years of age (> 59 years).

4.4.1.1 Age group 1: Children between the ages of 0 and 9 years

Results of this study show that a number of children nine years and younger received prescriptions for hipolipidaemic medicine during the study period, representing 0.72% (N = 87 214) of the total number of hipolipidaemic receiving patients in 2005, and 0.51% (N = 91 528) in 2006 (In total 631 and 473 patients in 2005 and 2006 respectively). The number of hipolipidaemic prescriptions claimed represented 0.11% (N = 604 824) and 0.08% (N = 678 297) of all hipolipidaemic prescriptions in 2005 and 2006 respectively. Hipolipidaemic items claimed for this age group represented 0.11% (N = 626 759) and 0.08% (N = 705 424) of the total number of hipolipidaemic medicine items claimed during 2005 and 2006. An average of 1.12 ± 0.65 and 1.19 ± 1.02 prescriptions for hipolipidaemic medicines were thus claimed per child per year during 2005 and 2006 respectively; at an average of 1.01 ± 0.11 and 1.01 ± 0.10 medicine items per prescription for 2005 and 2006 respectively.

Corresponding costs incurred by claims for this group accounted for 0.04% of the total medicine item cost for hipolipidaemic medicine items (N = R106 943 348.50) in 2005 and 0.03% (N = R117 862 631.90) in 2006. Table 4.4 furthermore reveals that the average cost per medicine item for age group 1 was R58.84 ± 66.95 in 2005 compared to R61.64 ± 71.65 in 2006. A *d*-value of 0.04 was calculated, which is of no practical significance (Steyn, 1999:3). Cost prevalence indices were also calculated based on the cost and prevalence of medicine items claimed during both study periods. Values of 0.34 and 0.37 for 2005 and 2006 respectively were obtained, which indicated that treatment with hipolipidaemics in children nine years and younger was relatively inexpensive.

4.4.1.2 Age group 2: Adolescents between the ages of 10 and 19 years

In 2005, adolescents (patients 10 ≤ 19 years) represented 0.35% (N = 87 214) of the total number of patients in the study population, which decreased to 0.29% (N = 91 528) in 2006. The total number of prescriptions claimed for this age group represented 0.16% (N = 604 824) of the total number of hipolipidaemic items claimed in 2005 and 0.12% (N = 678 297) in 2006. The average number of prescriptions claimed per patient per year in this age group was therefore 3.25 ± 3.48 in 2005 and 3.08 ± 3.19 in 2006 at an average cost per prescription of R188.09 ± 110.07 and R190.60 ± 120.02 respectively. A *d*-value was calculated (*d* = 0.02) which indicates that this small difference in price is of no practical significance according to Steyn (1999:3).

Hipolipidaemic medicine claimed for adolescents represented 0.17% (N = 626 759) of the total number of hipolipidaemic medicine items claimed in 2005 and 0.12% (N = 705 424) in 2006. An average of 1.05 ± 0.26 and 1.05 ± 0.23 items per prescription for 2005 and 2006 respectively, was therefore claimed at an average cost per item of R178.40 ± 77.11 (2005) compared to R180.98 ± 89.64 in 2006. A *d*-value of 0.03 was calculated, indicating that the price difference is of no practical significance according to Steyn (1999:3).

In 2005, costs incurred by age group 2 accounted for 0.17% of the total hipolipidaemic medicine cost (N = R106 943 348.53) and 0.13% (N = R117 862 631.87) in 2006. The cost prevalence indices in 2005 and 2006 were 1.05 and 1.08 respectively, which indicated that treatment in this age group was relatively expensive.

4.4.1.3 Age group 3: Young adults between the ages of 20 and 45 years

Young adults receiving hipolipidaemic medicine items represented 12.27% (N = 87 214) of the total number of patients who received hipolipidaemic medicine items in 2005, and 11.59% (N = 91 528) of those in 2006. The total number of prescriptions claimed for these patients represented 8.9% (N = 604 824) in 2005 and 8.36% (N = 678 297) in 2006 (refer to table 4.4). The average number of prescriptions per patient in this age group was therefore 4.93 ± 4.14 in 2005 and 5.35 ± 4.18 in 2006.

Hipolipidaemic medicine items claimed for young adults represented 8.93% (N = 626 759) of the total number of hipolipidaemic medicine items in 2005 compared to 8.43% (N = 705 424) in 2006. According to calculations the average number of hipolipidaemic items per prescription was 1.04 ± 0.21 in 2005 and 1.05 ± 0.23 in 2006.

In 2005, costs of hipolipidaemic medicine items claimed by young adults accounted for 9.53% of the total hipolipidaemic medicine cost incurred by the study population (N = R106 943 348.50) compared to 9.00% (N = R117 862 631.90) in 2006. The average cost per medicine item was therefore R182.15 ± 75.70 in 2005 and R178.34 ± 77.84 in 2006. The *d*-value (*d* = 0.05) is of no practical significance according to Steyn (1999:3).

Cost prevalence indices of 1.07 and 1.07 in 2005 and 2006 respectively were determined, an indication that treatment in young adults was relatively expensive.

4.4.1.4 Age group 4: Older patients between the ages of 46 and 59 years

Older patients between the ages of 46 and 59 years, represented 33.09% (N = 87 214) of the total number of patients in 2005, and 32.78% (N = 91 528) of those in 2006. The total number of hipolipidaemic prescriptions for the group represented 31.23% (N = 604 824) in 2005 and 30.89% (N = 678 297) in 2006. The average number of hipolipidaemic prescriptions per patient per year in this age group was therefore 6.55 ± 4.48 in 2005 and 6.98 ± 4.41 in 2006.

Hipolipidaemic medicine items for age group 4 represented 31.28% (N = 626 759) of the total number of hipolipidaemic medicine items in 2005 and 31.06% (N = 705 424) in 2006. An average of 1.04 ± 0.22 (for 2005) and 1.05 ± 0.23 items per prescription for 2006 was claimed.

Costs incurred for hipolipidaemic items in 2005 by these patients accounted for 32.37% of total medicine cost (N = R106 943 348.50) and 32.39% (N = R117 862 631.90) in 2006. The average cost per hipolipidaemic medicine item was therefore R176.60 ± 71.67 in 2005 and R 174.23 ± 74.35 in 2006. A *d*-value of 0.03 was calculated for the difference in price which, according to Steyn (1999:3), is of no practical significance.

The CPIs of 2005 and 2006 were respectively 1.03 and 1.04. These index values serve as an indication that treatment in older patients between the ages of 46 and 59 with hipolipidaemic items was relatively expensive for both years.

4.4.1.5 Age group 5: Patients older than 59 years of age

The number of patients above the age of 59 represented 53.27% (N = 87 214) of the total number of patients on hipolipidaemic medication in 2005, which increased to 54.83% (N = 91 528) in 2006. The total number of hipolipidaemic prescriptions claimed for this age group represented 59.55% (N = 604 824) in 2005 and 60.54% (N = 678 297) in 2006 of the total number of claimed hipolipidaemic prescriptions. An average of 7.75 ± 4.57 hipolipidaemic prescriptions per patient per year was thus claimed in 2005 compared to 8.18 ± 4.38, in 2006.

The average cost per hipolipidaemic prescription in 2005 and 2006 was R171.85 ± 84.98 and R167.76 ± 86.10 respectively. A *d*-value was calculated (*d* = 0.05) which indicated that the price decrease was of no practical significance (Steyn, 1999:3).

Hipolipidaemic medicine items represented 59.51% (N = 626 759) of the total number of medicine items in 2005 and 60.31% (N = 705 424) in 2006. The average number of

hipolipidaemic items claimed per prescription for this age group was therefore 1.04 ± 0.22 in 2005 and 1.04 ± 0.20 in 2006.

Costs incurred by patients who received hipolipidaemic items above the age of 59 years accounted for 57.87% of the total medicine cost (N = R106 943 348.53) in 2005 and 58.45% (N = R117 862 631.87) in 2006. The average cost per hipolipidaemic item in these patients was R165.96 ± 67.91 in 2005 compared to R161.94 ± 69.10 in 2006. A *d*-value of 0.06 was calculated, which according to Steyn (1999:3) is of no practical significance. Cost prevalence indices of 0.97 and 0.97 were calculated for 2005 and 2006 respectively, which gave an indication that treatment in this age group was relatively inexpensive.

4.4.2 Analysis based on patients' sex

The sex categories employed in the analysis were as follows: females, males and "unknown". The latter category refers to missing data on the database.

4.4.2.1 Female patients

Females formed 46.89% (N = 87 214) of the total number of patients who received hipolipidaemic medicine in the study population in 2005, and 47.06% (N = 91 528) in 2006. The total number of hipolipidaemic prescriptions claimed for females represented 46.79% (N = 604 824) in 2005 and 46.95% (N = 678 297) in 2006 of all hipolipidaemic prescriptions claimed during the specific year. The average number of hipolipidaemic prescriptions claimed per female patient per year was therefore 7.08 ± 4.50 in 2005 and 7.56 ± 4.50 in 2006; at an average of 1.04 ± 0.21 hipolipidaemic items per prescription for 2005, and 1.04 ± 0.20 hipolipidaemic items per prescription in 2006.

The average cost per prescription was R171.61 ± 83.68 and R167.71 ± 87.30 respectively for 2005 and 2006. A *d*-value was calculated (*d* = 0.04) for the differences in price, which is of no practical significance (Steyn, 1999:3).

Hipolipidaemic medicine items claimed for females represented 46.67% (N = 626 759) of the total number of hipolipidaemic medicine items claimed in 2005 and 46.74% (N = 705 424) of those in 2006. In 2005, hipolipidaemic item costs incurred by these claims accounted for 45.41% of total hipolipidaemic medicine cost (N = R106 943 348.53) *vs.* 45.32% (N = R117 862 631.87) in 2006. The CPIs were 0.97 in 2005 and 0.97 in 2006 respectively, which indicated that hipolipidaemic treatment in females was relatively inexpensive.

The average cost per hipolipidaemic medicine item for females was R166.04 ± 68.22 in 2005 and R162.00 ± 69.72 in 2006. A *d*-value of 0.06 was calculated, which is of no practical significance according to Steyn (1999:3).

4.4.2.2 Male patients

In 2005, males represented 53.04% (N = 87 214) of the total number of patients who received hipolipidaemic medicine items in the study population, and 52.89% (N = 91 528) in 2006. A total of 53.15% (N = 604 824) and 53.00% (N = 678 297) was claimed in terms of hipolipidaemic prescriptions for these males. The average number of hipolipidaemic prescriptions per male patient per year was 7.14 ± 4.40 in 2005 and 7.65 ± 4.49 in 2006.

Males received an average of 1.04 ± 0.23, and 1.04 ± 0.22 hipolipidaemic medicine items per prescription in 2005 and 2006 respectively; at an average cost per prescription of R181.43 ± 90.66 and R179.14 ± 95.20 respectively. A *d*-value was calculated (*d* = 0.02) which indicates that the small price difference is also of no practical significance (Steyn, 1999:3).

Hipolipidaemic medicine items claimed for males represented 53.28% (N = 626 759) of the total number of hipolipidaemic medicine items claimed in 2005 and 53.22% (N = 705 424) in 2006. The costs incurred by these claims accounted for 54.54% of the total hipolipidaemic medicine cost (N = R107 943 348.53) and 54.64% (N = R117 862 631.87) in 2006. Calculated CPIs were 1.02 in 2005 and 1.03 in 2006. Hipolipidaemic treatment for males was thus relatively expensive. The average cost per medicine item for males was R174.67 ± 71.65 in 2005 and R171.55 ± 73.52 in 2006. A *d*-value of 0.04 was calculated which is of no practical significance according to Steyn (1999:3).

4.4.2.3 Unknown sex category

The gender was not specified for 59 patients in the study population (for 2005), and for a further 45 patients in 2006. Hipolipidaemic prescriptions claimed for these patients represented a mere 0.05% (N = 604 824) in 2005 compared to 0.04% (N = 678 297) in 2006. These items will not be included in the rest of the discussion.

4.4.3 Analysis of the hipolipidaemic active ingredients based on generic indicators

Table 4.6 provides an overview of the generic indicators that were related to the prescription of hipolipidaemic medicine items during both study periods. Table 4.6 is a summarised table from

tables B2.24 and B2.25, in appendix B, reflecting the hipolipidaemic data on the database of both 2005 and 2006 and their indicidual periods based on generic indicators.

Table 4.6: Overview of generic indicators as for prescribed hipolipidaemic medicine items

Year	Generic indicator	Number of medicine items (N = 626 759)	Mean ± Std Dev	Total cost (R) (N = R106 943 348.53)	CPI
2005	N	312320	217.73 ± 62.12	68000465.72	1.28
	O	30324	187.71 ± 65.23	5692061.52	1.10
	Y	284115	117.03 ± 28.86	33250821.29	0.69
Year	**Generic indicator**	**Number of medicine items (N = 705 424)**	**Mean ± Std Dev**	**Total cost (R) (N = R117 862 631.87)**	**CPI**
2006	N	324679	220.83 ± 65.23	71698603.37	1.32
	O	23758	196.02 ± 68.02	4657099.50	1.17
	Y	356987	116.27 ± 27.92	41506929.00	0.70

Table 4.6 shows that during 2005 non-substitutable hipolipidaemic medicine items represented 49.83% (N = 626 759) of the total number of hipolipidaemic medicine items claimed in that year and 46.03% (N = 705 424) in 2006. Non-substitutable medicine items had a total cost that represented 63.59% (N = R106 943 348.53) in 2005 and 60.83% (N = R117 862 631.87) in 2006. CPIs of 1.28 and 1.32 were calculated which indicated that treatment for this medicine category was relatively expensive in 2005 and 2006. The average cost per non-substitutable hipolipidaemic medicine item was R217.73 ± 62.12 in 2005 and R220.83 ± 65.23 in 2006. A small *d*-value was calculated (*d* = 0.05), indicating that this price difference was of no practical significance (Steyn, 1999:3).

Original patented hipolipidaemic medicine items represented 4.84% (N = 626 759) of the total number of hipolipidaemic medicine items in 2005 and 3.37% (N = 705 424) in 2006. These items had a total cost that represented 5.32% (N = R106 943 348.53) of the total costs incurred by all hipolipidaemic items in 2005, which decreased to 3.95% (N = R117 862 632.87) in 2006. CPIs of 1.10 and 1.17 were calculated for 2005 and 2006 respectively, indicating that treatment for this medicine category was relatively expensive in 2005 and 2006. The average cost per hipolipidaemic medicine item in the "O" category was R187.71 ± 65.23 in 2005 and R196.02 ± 68.02 in 2006. A *d*-value was calculated (*d* = 0.12) which indicated that the price difference was of no practical significance (Steyn, 1999:3).

Generic hipolipidaemic medicine items represented 45.33% (N = 626 759) of the total number of hipolipidaemic medicine items in 2005 and 50.61% (N = 705 424) in 2006. Total costs incurred by generic hipolipidaemic medicine items represented 31.09% (N = R106 943 348.53) in 2005 which increased to 35.22% (N = R117 862 631.87) in 2006. Subsequent CPIs were calculated for 2005 and 2006 as 0.69 and 0.70 respectively which indicated that treatment for this

medicine category was relatively inexpensive in both study periods. The average cost per hipolipidaemic medicine item in the "Y" category was R117.03 ± 28.86 in 2005 and R116.27 ± 27.92 in 2006. A small *d*-value was calculated (*d* = 0.03) which indicated that the price difference was of no practical significance (Steyn, 1999:3).

Results of the analysis based on the different age groups and the sex of patients as set out in table 4.6, are shown in the subsequent paragraphs. A short summary and discussion will follow in paragraph 4.4.6.1.

4.4.3.1 Analysis of the type of generic indicator for hipolipidaemic drugs based on age group

Table 4.7 provides an overview of the hipolipidaemic medicine items claimed by the study population, based on generic indicator by age group. A discussion on table 4.7 follows subsequently. The "M" category was not included for this part of the study since there were no available data on this category. Table 4.7 is a summarised table from tables B2.26 and B2.27, in appendix B, reflecting the hipolipidaemic data on the database of both 2005 and 2006 and their indicidual periods based on generic indicators and age groups.

Table 4.7: Number of medicine items based on generic indicator by age group

	Period	Generic indicator	Number of medicine items (N = 626 759)	Average cost per item (R)	Total cost (R) (N = R106 943 348.53)	CPI
Age 0 ≤ 9	2005	N	690	56.91 ± 66.96	39269.60	0.97
		O	2	138.49 ± 8.03	276.97	2.35
		Y	22	112.18 ± 36.99	2467.96	1.91
	Period	Generic indicator	Number of medicine items (N = 705 424)	Average cost per item (R)	Total cost (R) (N = R117 862 631.87)	CPI
	2006	N	517	57.42 ± 72.69	29677.50	0.93
		O	9	92.88 ± 49.27	835.96	1.51
		Y	41	107.92 ± 36.59	4424.52	1.75

	Period	Generic indicator	Number of medicine items (N = 626 759)	Average cost per item (R)	Total cost (R) (N = R106 943 348.53)	CPI
Age 10 ≤ 19	2005	N	745	200.97 ± 73.63	149724.10	1.13
		O	36	215.46 ± 99.33	7756.66	1.21
		Y	267	110.42 ± 26.28	29481.63	0.62
	Period	Generic indicator	Number of medicine items (N = 705 424)	Average cost per item (R)	Total cost (R) (N = R117 862 631.87)	CPI
	2006	N	605	208.08 ± 88.68	125890.07	1.15
		O	14	225.59 ± 70.15	3158.24	1.25
		Y	233	107.92 ± 36.41	25146.40	0.60

Table 4.7: Number of medicine items based on generic indicator by age group (continued)

Age 20 ≤ 45	Period	Generic indicator	Number of medicine items (N = 626 759)	Average cost per item (R)	Total cost (R) (N = R106 943 348.53)	CPI
	2005	N	31267	226.66 ± 66.17	7087010.04	1.24
		O	1731	205.99 ± 71.32	356564.30	1.13
		Y	22979	119.79 ± 31.45	2752648.18	0.66
	Period	Generic indicator	Number of medicine items (N = 705 424)	Average cost per item (R)	Total cost (R) (N = R117 862 631.87)	CPI
	2006	N	31035	228.72 ± 70.00	7098223.00	1.28
		O	1330	216.31 ± 72.04	287692.67	1.21
		Y	27084	118.76 ± 30.00	3216463.82	0.67
Age 46 ≤ 59	Period	Generic indicator	Number of medicine items (N = 626 759)	Average cost per item (R)	Total cost (R) (N = R106 943 348.53)	CPI
	2005	N	103045	222.80 ± 61.42	22958505.05	1.26
		O	8342	193.25 ± 66.35	1612054.49	1.09
		Y	84655	118.70 ± 29.87	10048895.60	0.67
	Period	Generic indicator	Number of medicine items (N = 705 424)	Average cost per item (R)	Total cost (R) (N = R117 862 631.87)	CPI
	2006	N	108537	226.15 ± 65.55	24545687.43	1.30
		O	6746	202.28 ± 71.29	1364596.95	1.16
		Y	103837	118.14 ± 28.79	12267141.21	0.68
Age > 59	Period	Generic indicator	Number of medicine items (N = 626 759)	Average cost per item (R)	Total cost (R) (N = R106 943 348.53)	CPI
	2005	N	176573	213.88 ± 60.51	37765956.93	1.29
		O	20213	183.81 ± 63.69	3715409.10	1.11
		Y	176192	115.88 ± 27.94	20417327.92	0.70
	Period	Generic indicator	Number of medicine items (N = 705 424)	Average cost per item (R)	Total cost (R) (N = R117 862 631.87)	CPI
	2006	N	183985	216.86 ± 63.16	39899115.37	1.34
		O	15659	191.64 ± 65.62	3000815.98	1.18
		Y	225792	115.12 ± 27.17	25993175.04	0.71

4.4.3.1.1 Age group 1: Children between the ages of 0 and 9 years

Non-substitutable hipolipidaemic medicine items ("N" indicator) represented 0.11% (N = 626 759) of the total number of hipolipidaemic items claimed in 2005 for children aged 0 ≤ 9 years and 0.07% (N = 705 424) in 2006. Costs incurred by this category represented 0.04% (N = R106 943 348.53) of all hipolipidaemic medicine items claimed in 2005 and 0.03% (N = R117 862 631.87) in 2006. CPIs calculated for 2005 and 2006 were 0.97 and 0.93 respectively, which indicated that treatment with non-substitutable hipolipidaemic items was relatively inexpensive in 2005 and 2006. The average cost per hipolipidaemic medicine item was R56.91 ± 66.96 in 2005 compared to R57.42 ± 72.69 in 2006. A *d*-value was calculated (*d* = 0.007) which was of no practical significance according to Steyn (1999:3).

Only two original, patented hipolipidaemic medicine items ("O" indicator) (0.0003%; N = 626 759) were claimed during 2005 for children under the age of 9 years, compared to 9 items

claimed during 2006 (0.001%; N = 705 424). The total costs of these items represented 0.0002% (N = R106 943 348.53) in 2005 and 0.0007% (N = R117 862 631.87) in 2006. CPI-values for 2005 and 2006 were therefore calculated as 2.35 and 1.51 respectively which indicated that these original, patented hipolipidaemic medicines were relatively expensive in 2005 and 2006. The average cost per hipolipidaemic medicine item was R138.49 ± 8.03 in 2005 compared to R92.88 ± 49.27 in 2006. A *d*-value was calculated (*d* = 0.93) which was assumed to have a practical significant importance according to Steyn (1999:3).

Generic hipolipidaemic medicine items ("Y" indicator) represented 0.004% (N = 626 759) of the total number of hipolipidaemic medicine items claimed for children aged 0 ≤ 9 years in 2005 and 0.006% (N = 705 424) of those in 2006. In 2005, these items had a total cost representative of 0.002% (N = R106 943 348.53) and 0.004% of all hipolipidaemic medicine items claimed (N = R117 862 631.87) in 2006. CPIs were calculated for 2005 and 2006 as 1.91 and 1.75 respectively; indicating that generic hipolipidaemics were relatively expensive in 2005 and 2006. The average cost per medicine item in the generic category was R112.18 ± 36.99 in 2005 compared to R107.92 ± 36.59 in 2006. A *d*-value was calculated (*d* = 0.12) which was of no practical significance (Steyn, 1999:3).

4.4.3.1.2 Age group 2: Adolescents between the ages of 10 and 19 years

Non-substitutable hipolipidaemic medicine items represented 0.12% (N = 626 759) of the total number of hipolipidaemic items claimed in 2005 that decreased to 0.09% (N = 705 424) in 2006. These medicine items had a total cost that represented 0.14% (N = R106 943 348.53) in 2005 and 0.11% (N = R117 862 631.87) in 2006 of the total cost of all hipolipidaemic medicine items. Cost prevalence indices of 1.13 and 1.15 were calculated for 2005 and 2006 respectively which indicated that treatment for this medicine category was relatively expensive in 2005 and 2006. The average cost per hipolipidaemic medicine item in this category was R200.97 ± 73.63 in 2005 compared to R208.08 ± 88.68 in 2006. A small *d*-value was calculated (*d* = 0.08) indicating a price difference which is of no practical significance (Steyn, 1999:3).

Original patented hipolipidaemic medicine items represented 0.005% (N = 626 759) of the total number of hipolipidaemic medicine items claimed in 2005 and 0.002% (N = 705 424) in 2006. In 2005 these items had a total cost that represented 0.007% (N = R106 943 348.53) of the total hipolipidaemic costs which decreased to 0.003% (N = R117 862 632.87) in 2006. CPIs of 1.21 and 1.25 were calculated for 2005 and 2006 respectively; indicating that these medicines were relatively expensive in both study periods. The average cost per hipolipidaemic medicine item in the "O" generic category was R215.46 ± 99.33 in 2005 and R225.59 ± 70.15 in 2006. A *d*-value

was calculated (*d* = 0.10) which indicated that the price difference is of no practical significance (Steyn, 1999:3).

Generic hipolipidaemic medicine items represented 0.04% (N = 626 759) of the total number of hipolipidaemic medicine items claimed in 2005 and 0.03% (N = 705 424) in 2006. Associated costs represented 0.03% (N = R106 943 348.53) of all hipolipidaemic medicine items claimed in 2005 which increased to 0.02% (N = R117 862 631.87) in 2006. Subsequent CPIs were calculated for 2005 and 2006 as 0.62 and 0.60 respectively which indicated that this medicine category was relatively inexpensive in both periods. The average cost per hipolipidaemic medicine item in the "Y" category was R110.42 ± 26.28 in 2005 and R107.92 ± 36.41 in 2006. A small *d*-value was calculated (*d* = 0.07) which indicates that the price difference is of no practical significance (Steyn, 1999:3).

4.4.3.1.3 Age group 3: Young adults between the ages of 20 and 45 years

Non-substitutable hipolipidaemic items represented 4.99% (N = 626 759) of the total number of hipolipidaemic medicine items claimed in 2005 and 4.40% (N = 705 424) in 2006. These medicine items had a total cost that represented 6.63% (N = R106 943 348.53) of all hiplipidaemic medicine item costs in 2005 and 6.02% (N = R117 862 631.87) in 2006. CPIs of 1.24 and 1.28 were calculated for both 2005 and 2006 respectively, which indicated that treatment for this medicine category was relatively expensive in both years. The average cost per hipolipidaemic medicine item in the "N" category was R226.66 ± 66.17 in 2005 and R228.72 ± 70.00 in 2006. A *d*-value was calculated (*d* = 0.03) which indicates that the price difference is of no practical significance (Steyn, 1999:3).

Original patented hipolipidaemic medicine represented 0.28% (N = 626 759) of the total number of hipolipidaemic medicine items claimed in 2005 and 0.19% (N = 705 424) in 2006; at a total cost that represented 0.33% (N = R106 943 348.53) of all hipolipidaemic medicine costs claimed in 2005 and 0.24% (N = R117 862 631.87) in 2006. CPI-values were calculated for 2005 and 2006 as 1.13 and 1.21 respectively which indicated that this medicine category was relatively expensive in 2005 and 2006. The average cost per hipolipidaemic medicine item in this category was R205.99 ± 71.32 in 2005 and R216.31 ± 72.04 in 2006. A small *d*-value was calculated (*d* = 0.14) which indicated that the price difference is of no practical importance (Steyn, 1999:3).

Generic hipolipidaemic medicine items represented 3.67% (N = 626 759) of the total number of hipolipidaemic medicine items claimed in 2005 and 3.84% (N = 705 424) in 2006; at a total cost that represented 2.57% (N = R106 943 348.53) in 2005 and 2.73% (N = R117 862 631.87) of

the total cost claimed for hipolipidaemics in 2006. CPIs were calculated for 2005 and 2006 as 0.66 and 0.67 respectively which indicated that treatment for this medicine category was relatively inexpensive in both study periods. The average cost per hipolipidaemic medicine item in the "Y" generic category was R119.79 ± 31.45 in 2005 compared to R118.76 ± 30.00 in 2006. A small *d*-value was calculated (*d* = 0.03) which indicated that the price difference is of no practical importance (Steyn, 1999:3).

4.4.3.1.4 Age group 4: Older patients between the ages of 46 and 59 years

Non-substitutable hipolipidaemic items represented 16.44% (N = 626 759) of the total number of hipolipidaemic medicine items claimed in 2005 and 15.39% (N = 705 424) in 2006. In 2005, non-substitutable hipolipidaemics had a total cost that represented 21.47% (N = R106 943 348.53) of all hipolipidaemic cost claimed and 20.83% (N = R117 862 631.87) in 2006. CPIs were calculated as 1.26 and 1.30 for 2005 and 2006 respectively, which indicated that treatment for this medicine category was relatively expensive. The average cost per hipolipidaemic medicine item in the "N" generic category was R222.80 ± 61.42 in 2005 compared to R226.15 ± 65.55 in 2006. A small *d*-value was calculated (*d* = 0.05) which indicates that the price difference is of no practical significance (Steyn, 1999:3).

Original patented hipolipidaemic items represented 1.33% (N = 626 759) of the total number of hipolipidaemic medicine items claimed in 2005 and 0.96% (N = 705 424) in 2006; whilst the costs incurred by this age group in 2005 represented 1.51% (N = R106 943 348.53) of all hipolipidaemic medicine cost claimed and 1.16% (N = R117 862 631.87) in 2006. CPI-values were calculated for 2005 and 2006 as 1.09 and 1.16 respectively which indicated that treatment for this medicine category was relatively expensive. The average cost per hipolipidaemic medicine item in the "O" category for age group 4 was R193.25 ± 66.35 in 2005 compared to R202.28 ± 71.29 in 2006. A small *d*-value was calculated (*d* = 0.13) which indicates that the difference in price is of no practical significance (Steyn, 1999:3).

Generic hipolipidaemic items represented 13.51% (N = 626 759) of the total number of hipolipidaemic medicine items claimed in 2005. This increased to 14.72% (N = 705 424) in 2006. Associated hipolipidaemic medicine item costs represented 9.40% (N = R106 943 348.53) of the amount incurred in 2005 and 10.41% (N = R117 862 631.87) in 2006. CPI-values of 0.67 and 0.68 respectively were calculated for 2005 and 2006 which indicated that treatment for this medicine category was relatively inexpensive in 2005 and 2006. The average cost per hipolipidaemic item in the "Y" generic category was R118.70 ± 29.87 in 2005 and R118.14 ± 28.79 in 2006. A small *d*-value was calculated (*d* = 0.02), indicating that the price difference

between generic hipolipidaemic medicine received by age group during 2005 and 2006 is of no practical significance (Steyn, 1999:3).

4.4.3.1.5 Age group 5: Patients older than 59 years of age

Non-substitutable hipolipidaemic items represented 28.17% (N = 626 759) of the total number of hipolipidaemic medicine items claimed in 2005 and decreased to 26.08% (N = 705 424) in 2006. Costs associated with these medicine items represented 35.31% (N = R106 943 348.53) of all hipolipidaemic medicine costs claimed in 2005 which decreased to 33.85% (N = R117 862 631.87) in 2006. CPIs were calculated as 1.29 and 1.34 for 2005 and 2006 respectively which indicated that this medicine category was relatively expensive in 2005 and 2006. The average cost per hipolipidaemic medicine item in the "N" generic category was R213.88 ± 60.51 in 2005 compared to R216.86 ± 63.16 in 2006. A *d*-value was calculated (*d* = 0.05) which is of no practical significance according to Steyn (1999:3).

Original patented hipolipidaemic items represented 3.23% (N = 626 759) of the total number of hipolipidaemic medicine items claimed in 2005 and 2.22% (N = 705 424) in 2006. The cost associated with these medicine items represented 3.47% (N = R106 943 348.53) of all hipolipidaemic medicine costs claimed in 2005 which decreased to 2.55% (N = R117 862 631.87) in 2006. CPIs were calculated for 2005 and 2006 as 1.11 and 1.18 respectively which indicated that this medicine category was relatively expensive in both study periods. The average cost per hipolipidaemic item in the "O" generic category for patients older than 59 years was R183.81 ± 63.69 in 2005 and R191.64 ± 65.62 in 2006. A *d*-value was calculated (*d* = 0.12) which indicated that the price difference is of no practical importance (Steyn, 1999:3).

Generic hipolipidaemic items represented 28.11% (N = 626 759) of the total number of hipolipidaemic items claimed in 2005, which increased to 32.01% (N = 705 424) in 2006. These items had a total cost that represented 19.09% (N = R106 943 348.53) of the total cost of hipolipidaemic medicine items in 2005, which increased to 22.05% (N = R117 862 631.87) in 2006. CPI-values were calculated as 0.70 and 0.71 respectively for 2005 and 2006 which indicated that treatment for this medicine category was relatively inexpensive in 2005 and 2006. The average cost per hipolipidaemic medicine item in the "Y" generic category was R115.88 ± 27.94 in 2005 and R115.12 ± 27.17 in 2006. A *d*-value was calculated (*d* = 0.03) which indicated that the difference in price is of no practical importance (Steyn, 1999:3).

4.4.4 Analysis of type of generic indicator for hipolipidaemic drugs based on sex

Table 4.8 provides an overview of claimed hipolipidaemic medicine items based on generic indicators and sex, which will be discussed in subsequent paragraphs. The "M" category was not included for this part of the study since there were no available data on this category. Table 4.8 is a summarised table from tables B2.28 and B2.29 in appendix B, reflecting the hipolipidaemic data on the database of both 2005 and 2006 and their indicidual periods based on generic indicators and the sex of the patient.

The data in table 4.8 will be discussed subsequently with regard to the sex of the patients in the study population (discussion follow the order of female, male and unknown sex categories).

Table 4.8: Breakdown of hipolipidaemic medicine items, prevalence based on generic indicator and sex

Gender	Period	Generic indicator	Number of medicine items N_{2005} = 626 759 N_{2006} = 705 424	Average cost per item (R)	Total cost (R) N_{2005} = R106 943 348.53 N_{2006} = R117 862 631.87	CPI
Female	2005	N	141 036	213.52 ± 61.28	30 114 845.39	1.25
		O	13 925	184.19 ± 62.27	2 564 883.21	1.08
		Y	137 534	115.50 ± 27.48	15 885 807.90	0.68
	2006	N	145 781	216.03 ± 64.41	31 492 801.61	1.29
		O	10 963	193.42 ± 65.24	2 120 501.55	1.16
		Y	172 951	114.47 ± 26.81	19 798 420.86	0.69
Male	2005	N	171 171	221.19 ± 62.59	37 861 064.46	1.30
		O	16 374	190.68 ± 67.53	3 122 269.36	1.12
		Y	146 388	118.48 ± 30.04	17 343 467.85	0.69
	2006	N	178 794	224.75 ± 65.64	40 183 145.86	1.35
		O	12 781	198.26 ± 70.26	2 533 932.21	1.19
		Y	183 841	117.96 ± 28.82	216 856.09	0.71
Unknown	2005	N	113	217.31 ± 56.54	24 555.87	1.27
		O	25	196.36 ± 46.77	4 908.95	1.15
		Y	193	111.12 ± 27.19	21 445.54	0.65
	2006	N	104	217.85 ± 53.38	22 655.90	1.30
		O	14	190.41 ± 36.40	2 665.74	1.14
		Y	195	117.43 ± 34.84	22 899.14	0.70

4.4.4.1 Female patients

Non-substitutable hipolipidaemic medicine items for females represented 22.50% (N =626 759) of the total number of hipolipidaemic medicine items claimed in 2005 and 20.67% (N = 705 424) in 2006. The total cost of these items represented 28.15% (N = R106 943 348.53) of the total hipolipidaemic medicine items claimed in 2005 and 26.72% (N = R117 862 631.87) in 2006. CPI-values of 1.25 and 1.29 respectively were calculated for 2005 and 2006 which indicated that this medicine category was relatively expensive in 2005 and 2006 for females. The

average cost per hipolipidaemic medicine item in the "N" generic category for females was R213.52 ± 61.28 in 2005 compared to R216.03 ± 64.41 in 2006. A *d*-value was calculated (*d* = 0.04) which indicated that the price difference is of no practical importance (Steyn, 1999:3).

Original patented hipolipidaemic medicine items ("O" indicator) claimed for females represented 2.22% (N = 626 759) of the total number of medicine items in 2005 and 1.55% (N = 705 424) in 2006. The total cost of these items represented 2.40% (N = R106 943 348.53) of the total hipolipidaemic medicine items claimed in 2005 and 1.80% (N = R117 862 631.87) in 2006. CPIs of 1.08 and 1.16 were calculated for 2005 and 2006 respectively which indicated that original hipolipidaemic patented medicine items was relatively expensive in 2005 and 2006 in females. The average cost per hipolipidaemic medicine item in the "O" generic category was R184.19 ± 62.27 in 2005 and R193.42 ± 65.24 in 2006. A *d*-value was calculated (*d* = 0.14) for the difference in price, which is of no practical significance according to Steyn (1999:3).

Generic hipolipidaemic medicine items ("Y" indicator) for the females represented 21.94% (N = 626 759) of the total number of medicine items claimed in 2005, and 24.52% (N = 705 424) in 2006. The total costs of these medicine items represented 12.90% (N = R106 943 348.53) of the total hipolipidaemic cost incurred in 2005, and 14.88% (N = R117 862 631.87) in 2006. CPI-values were calculated as 0.68 and 0.69 for 2005 and 2006 respectively which indicated that treatment with this medicine category in females was relatively inexpensive in 2005 and 2006. The average cost per medicine item in the "Y" generic category for females were R115.50 ± 27.48 in 2005 compared to R114.47 ± 26.81 in 2006. A small *d*-value was calculated (*d* = 0.04), which indicates that the difference in price is of no practical importance (Steyn, 1999:3).

4.4.4.2 Male patients

Non-substitutable hipolipidaemic medicine items claimed for males represented 27.31% (N = 626 759) of the total number of medicine items in 2005 and decreased to 25.35% (N = 705 424) in 2006. The total cost associated with these items represented 35.40% (N = R106 943 348.53) in 2005, compared to 34.09% (N = R117 862 631.87) of the total hipolipidaemic medicine items claimed in 2006. CPI-values were calculated for 2005 and 2006 (*i.e*., 1.30 *vs.* 1.35) which indicated that treatment with this medicine category in males was relatively expensive in 2005 and 2006. The average cost per hipolipidaemic medicine item in the "N" generic category for the male sex was R221.19 ± 62.59 in 2005 compared to R224.75 ± 65.64 in 2006. A small *d*-value was calculated (*d* = 0.05) – indicating that the price difference is of no practical significance (Steyn, 1999:3).

Original patented hipolipidaemic medicine items claimed for males represented 2.61% (N = 626 759) of the total number of hipolipidaemic medicine items in 2005 and 1.81% (N = 705 424) of that in 2006. The total cost of these items represented 2.92% (N = R106 943 348.53) of the total cost of claimed items in 2005 and 2.15% (N = R117 862 631.87) of those in 2006. CPIs were calculated for 2005 and 2006 as 1.12 and 1.19 respectively which indicated that treatment with this medicine category was relatively expensive in 2005 and 2006. The average cost per hipolipidaemic medicine item in the "O" generic category for males was similar in 2005 and 2006 (*i.e.*, R190.68 ± 67.53, and R198.26 ± 70.26). A *d*-value was calculated (*d* = 0.11), which indicated that the price difference is of no practical significance (Steyn, 1999:3).

Generic hipolipidaemic medicine items represented 23.36% (N = 626 759) of the total number of hipolipidaemic medicine items claimed in 2005 and 26.06% (N = 705 424) in 2006. Total cost associated with these hipolipidaemic items represented 16.22% (N = R106 943 348.53) of the total cost claimed in 2005, and 18.40% (N = R117 862 631.87) of that in 2006. CPI-values were calculated for 2005 and 2006 as 0.69 and 0.71 respectively which indicated that treatment with this medicine category in males was relatively inexpensive in 2005 and 2006. The average cost per hipolipidaemic medicine item in the "Y" generic category for males was R118.48 ± 30.04 in 2005 and R117.96 ± 28.82 in 2006. A small size effect (*d*-value = 0.02) was calculated for the difference in price, which is of no practical importance according to Steyn (1999:3).

4.4.4.3 Unknown sex category

Non-substitutable hipolipidaemic medicine items represented 0.02% (N = 626 759) of the total number of hipolipidaemic medicine items claimed in 2005 and 0.01% (N = 705 424) of those in 2006. Total cost associated herewith represented 0.02% (N = R106 943 348.53) of the total hipolipidaemic medicine items claimed in 2005 and 0.02% (N = R117 862 631.87) in 2006. CPIs were calculated for 2005 and 2006 as 1.27 and 1.30 respectively which indicated that treatment with this medicine category was relatively expensive in 2005 and 2006. The average cost per hipolipidaemic medicine item in the "N" generic category was R217.31 ± 56.54 in 2005 compared to R217.85 ± 53.38 in 2006. A small *d*-value was calculated (*d* = 0.009) for the difference in price which is of no practical importance (Steyn, 1999:3).

Original, patented hipolipidaemic medicine items represented 0.004% (N = 626 759) of the total number of hipolipidaemic medicine items in 2005 and 0.002% (N = 705 424) of those in 2006. The total cost of these items was 0.005% (N = R106 943 348.53) of the total hipolipidaemic medicine items claimed in 2005 and 0.002% (N = R117 862 631.87) in 2006. CPI-values were calculated for 2005 and 2006 as 1.15 and 1.14 respectively which indicated that treatment for this medicine category was relatively expensive in 2005 and 2006. The average cost per

hipolipidaemic medicine item in the "O" generic category was R196.36 ± 46.77 in 2005 compared to R190.41 ± 36.40 in 2006. A small *d*-value was calculated (*d* = 0.13) which is an indication that the difference in price is of no practical importance (Steyn, 1999:3).

Generic hipolipidaemic medicine items represented 0.03% (N = 626 759) of the total number of hipolipidaemic medicine items in 2005 and 0.03% (N = 705 424) of those in 2006. The total cost of these items represented 0.02% (N = R106 943 348.53) of the total cost of claimed items in 2005, compared to 0.02% (N = R117 862 631.87) in 2006. CPIs were calculated for 2005 and 2006 (*i.e.*, 0.65 and 0.70 respectively) which indicated that treatment for this medicine category was relatively inexpensive in 2005 and 2006. The average cost per medicine item in the "Y" generic category was R111.12 ± 27.19 in 2005 compared to R117.43 ± 34.84 in 2006. A small *d*-value was calculated for the price difference (*d* = 0.18), which is of no practical significance according to Steyn (1999:3).

4.4.5 Analysis of hipolipidaemic drugs based on prescribers

The following section is a general analysis of the various prescriber groups of hipolipidaemic medicines. The different prescribers in this study were cardiologists, general medical practitioners, other prescribers, pharmacotherapists, pharmacists and thoracic surgeons (refer to chapter 3, paragraph 3.5.5). Table 4.9 gives the general layout of hipolipidaemic medicine as prescribed by the various prescribers. Table 4.9 is a summarised table from tables B2.30, B2.31, B2.32, B2.33, B2.34, B2.35, B2.36, B2.37 in appendix B, reflecting the hipolipidaemic data on the database of both 2005 and 2006 and their indicidual periods based on generic indicators and age groups.

Table 4.9: General layout of hipolipidaemic drugs as prescribed

	Variable	Cardiologists	General Medicine Practitioner	Other	Pharmaco-therapists	Pharmacists	Thoracic Surgeons
2005	Number of prescriptions	49 657	448 894	104 667	1	391	1 491
	Average number of medicine items per prescription	1.06 ± 0.27	1.03 ± 0.20	1.05 ± 0.25	1.00 ± 0.00	1.01 ± 0.10	1.04 ± 0.23
	Total number of medicine items	52 425	462 890	109 482	1	395	1 557
	Average cost per medicine item (R)	188.39 ± 78.05	166.98 ± 67.45	177.45 ± 75.09	190.28 ± 00	129.23 ± 99.31	189.33 ± 91.63
	Total cost of medicine items / prescriptions(R)	9 876 518.51	77 292 156.85	19 427 191.02	190.28	51 044.35	294 790.97
	Number of patients	9 491	69 153	22 069	1	338	479
	Average number of prescriptions per patient	5.23 ± 4.06	6.49 ± 4.44	4.74 ± 3.97	1.00 ± 00	1.16 ± 0.56	3.11 ± 3.21
	Average cost per prescription (R)	198.89 ± 106.94	172.18 ± 81.08	185.61 ± 99.45	190.28 ± 00	130.55 ± 101.98	197.71 ± 105.09
	Variable	Cardiologists	General Medicine Practitioners	Other	Pharmaco-therapists	Pharmacists	Thoracic Surgeons
2006	Number of prescriptions	58 361	499 276	118 671	10	616	1 667
	Average number of medicine items per prescription	1.07 ± 0.28	1.03 ± 0.19	1.05 ± 0.24	1.10 ± 0.32	1.02 ± 0.13	1.06 ± 0.24
	Total number of medicine items	62 304	515 942	124 749	11	627	1 760
	Average cost per medicine item (R)	188.24 ± 81.66	162.83 ± 68.94	174.02 ± 76.00	26.76 ± 25.15	126.11 ± 97.08	188.50 ± 73.44
	Total cost of medicine items / prescriptions(R)	11 728 132.65	84 008 507.57	21 709 085.61	294.35	79 070.21	331 766.90
	Number of patients	10 616	72 512	24 009	5	550	487
	Average number of prescriptions per patient	5.50 ± 4.06	6.89 ± 4.34	4.94 ± 3.99	2.00 ± 2.24	1.12 ± 0.51	3.42 ± 3.38
	Average cost per prescription (R)	200.96 ± 117.95	168.26 ± 84.73	182.94 ± 100.36	29.44 ± 25.78	128.36 ± 104.55	199.02 99.63

* Data are *n*-values (means ± SD).

4.4.5.1 Analysis based on prescriber type: cardiologists

Based on table 4.9, cardiologists prescribed 8.21% (n = 49 657) of the hipolipidaemic prescriptions in 2005 and 8.64% (n = 58 361) in 2006. These prescriptions were prescribed with an average of 1.06 ± 0.27 medicine items per prescription in 2005 and 1.07 ± 0.28 in 2006. The average cost per prescription was R198.89 ± 106.94 in 2005 and R200.96 ± 117.95 in 2006. A small *d*-value (*d* = 0.02) was calculated that shows this price increase was of no practical significance (Steyn, 1999:3).

Cardiologists prescribed an average of 5.23 ± 4.06 hipolipidaemic prescriptions per patient in 2005 and 5.50 ± 4.06 prescriptions in 2006. The total number of hipolipidaemic medicine items represented 8.36% (n = 52 425) of the total number of hipolipidaemic medicine items in 2005 and increased to 8.83% (n = 62 304) in 2006. Hipolipidaemic medicine items prescribed by cardiologists had an average cost of R188.39 ± 78.05 and R188.24 ± 81.66 in 2005 and 2006 respectively (*d* = 0.001). Cardiologist contributed 9.24% (n = R9 876 518.51) in 2005 and 9.95% (n = R11 728 132.65) in 2006 to the total of hipolipidaemic medicine cost.

4.4.5.2 Analysis based on prescriber type: general medical practitioners

General medical practioners (laid out in table 4.9) prescribed 74.22% (n = 448 894) of the hipolipidaemic prescriptions in 2005 and 73.61% (n = 499 276) in 2006. These prescriptions were prescribed with an average of 1.03 ± 0.20 medicine items per prescription in 2005 and 1.03 ± 0.19 in 2006. The average cost per prescription was R172.18 ± 81.08 and R168.26 ± 84.73 in 2005 and 2006 respectively. A small *d*-value (0.05) was calculated that shows this price decrease was of no practical significance (Steyn, 1999:3).

General medical practioners prescribed an average of 6.49 ± 4.44 hipolipidaemic prescriptions in per patient in 2005 and 6.89 ± 4.34 prescriptions in 2006. The total number of hipolipidaemic medicine items prescribed by general medical practioners represented 73.85% (n = 462 890) of the total number of hipolipidaemic medicine items in 2005 and 73.14% (n = 515 942) in 2006. Hipolipidaemic medicine items were prescribed at an average cost of R166.97 ± 67.45 and R162.83 ± 68.94 in 2005 and 2006 respectively (*d* = 0.06). General medical practioners contributed 72.27% (n = R77 292 156.85) of the total cost of all hipolipidaemic items in 2005 and 71.28% (n = R84 008 507.57) in 2006 to the total of hipolipidaemic medicine cost.

4.4.5.3 Analysis based on prescriber type: other prescribers

Based on table 4.9, other prescribers prescribed 16.70% (n = 104 667) of the hipolipidaemic prescriptions in 2005 and 16.82% (n = 118 671) in 2006. These prescriptions were prescribed with an average of 1.05 ± 0.25 medicine items per prescription in 2005 and 1.05 ± 0.24 in 2006. The average cost per prescription was R185.61 ± 99.45 and R182.94 ± 100.36 in 2005 and 2006 respectively. A small *d*-value was calculated (*d* = 0.03) that shows this price increase was of no practical significance (Steyn, 1999:3).

Other prescribers prescribed an average of 4.74 ± 3.97 hipolipidaemic prescriptions per patient in 2005 and 4.94 ± 3.99 prescriptions in 2006. The total number of hipolipidaemic medicine items prescribed by other prescribers represented 17.47% (n = 109 482) of the total number of

hipolipidaemic medicine items in 2005 and increased to 17.68% (n = 124 749) in 2006. Hipolipidaemic medicine items were prescribed at an average cost of R177.45 ± 75.09 and R174.02 ± 76.00 in 2005 and 2006 respectively, which caused a *d*-value (*d* = 0.05) of no practical significance (Steyn, 1999:3). Other prescribers contributed 18.17% (n = R19 427 191.02) in 2005 and 18.42% (n = R21 709 085.61) in 2006 to the total of hipolipidaemic medicine cost.

4.4.5.4 Analysis based on prescriber type: pharmacotherapists

Pharmacotherapists prescribed only one hipolipidaemic medicine item in 2005. This item had a value of R190.28. In 2006, pharmacotherapists prescribed 10 hipolipidaemic medicine items, at an average of 1.10 ± 0.32 items per prescription. Prescriptions prescribed were R29.44 ± 25.78 in 2006.

4.4.5.5 Analysis based on prescriber type: pharmacists

Based on table 4.9, pharmacists prescribed 0.06% (n = 391) of the hipolipidaemic prescriptions in 2005 and 0.09% (n = 616) in 2006. These prescriptions were prescribed at an average of 1.01 ± 0.10 medicine items per prescription in 2005 and 1.02 ± 0.13 in 2006. The average cost per prescription was R130.55 ± 101.95 and R128.36 ± 104.55 in 2005 and 2006 respectively. A small *d*-value (0.02) was calculated that shows this price increase was of no practical significance (Steyn, 1999:3).

Pharmacists prescribed an average of 1.16 ± 0.56 hipolipidaemic prescriptions per patient in 2005 and 1.12 ± 0.51 prescriptions in 2006. The total number of hipolipidaemic medicine items prescribed by pharmacists represented 0.06% (n = 395) of the total number of hipolipidaemic medicine items in 2005 and increased to 0.09% (n = 627) in 2006. These items had an average cost of R129.33 ± 99.31 and R126.11 ± 97.08 in 2005 and 2006 respectively. A *d*-value of 0.03 indicated no practical significance (Steyn, 1999:3). Pharmacists contributed 0.05% (n = R51 044.35) in 2005 and 0.07% (n = R79 070.21) in 2006 to the total of hipolipidaemic medicine cost.

4.4.5.6 Analysis based on prescriber type: thoracic surgeons

Thoracic surgeons prescribed 0.25% (n = 1 491) of the hipolipidaemic prescriptions in 2005 and 0.25% (n = 1 667) in 2006. These prescriptions were prescribed with an average of 1.04 ± 0.23 medicine items per prescription in 2005 and 1.06 ± 0.24 in 2006. The average cost per prescription was R197.71 ± 105.09 and R199.02 ± 99.53 in 2005 and 2006 respectively. A

small *d*-value (*d* = 0.01) was calculated that showed this price increase was of no practical significance (Steyn, 1999:3).

Thoracic surgeons prescribed an average of 1.16 ± 0.56 hipolipidaemic prescriptions per patient in 2005 and 1.12 ± 0.51 prescriptions in 2006. The total number of hipolipidaemic medicine items prescribed by thoracic surgeons represented 0.25% (n = 1 557) of the total number of hipolipidaemic medicine items in 2005 and 0.25% (n = 1 760) in 2006. These items had an average cost of R189.33 ± 91.53 and R188.50 ± 73.44 in 2005 and 2006 respectively, and a small *d*-value of 0.009 was of no practical significance (Steyn, 1999:3). Thoracic surgeons contributed 0.28% (n = R294 790.97) in 2005 and 0.28% (n = R331 766.90) in 2006 to the total of hipolipidaemic medicine cost.

4.4.6 Summary and discussion on the overview of hipolipidaemic medicine

In the subsequent paragraphs summaries on the overview of hipolipidaemic medicine will be discussed.

4.4.6.1 Summary and discussion of the hipolipidaemic medicine analysis based on age groups and the patient's sex

It can be concluded that there was little to no change between the two consecutive study periods with regard to (1) the number of hipolipidaemic medicine items per age and gender groups, (2) the two consecutive study periods' total cost of hipolipidaemic medicine items incurred by the various age and gender groups, the average cost per item and/or prescriptions, the number of items per prescription and the average number of prescriptions per patient.

About 10 per cent of adolescents aged 12 to 19 years of age have cholesterol levels which exceed 200mg/dl (AHA, 2003), with triglyceride concentrations continuously increasing throughout puberty (11 – 14 years of age) (Bertrais *et al*., 2000:316). The mean total of cholesterol levels for males is 163mg/dl and 167mg/dl for females, *i.e.* among children and adolescents aged 4 to 19 years of age (AHA, 2003). Males thus have a lower cholesterol level than girls on average at the beginning of puberty. As both sexes age, LDL-cholesterol rises, with less severe levels experienced in males. At the age of 55, however, women's LDL-levels exceed those of men. Regardless of the sex group, males older than 45 years and females older than 55 years have increased levels of high cholesterol risk (Irons *et al*., 2002:1616; Yoffee, 2009).

Results of this study show that the relationship of female : male patients receiving hipolipidaemic medicine items was roughly 1 : 1.13, compared with the total database where the ratio was 1.25 : 1. It is thus clear that the males on average receive more hipolipdaemic medicine items than their female counterparts, compared with the total database where females receive more items. In accordance with the literature and the analysis of the total database, older patients (*i.e*. those older than 45 years of age) received more prescriptions than younger patients (refer to paragraph 4.4.1).

The cost per hipolipidaemic item for patients younger than the age of 10 years (*i.e*., age group 1) was about only a third of that of the age groups above the age of 10 years (*i.e.*, age groups 2, 3, 4 & 5). Hipolipidaemic medicine items claimed for this age group were mainly relatively non-expensive (CPIs are below 1), and are further discussed in paragraph 4.6.1.

Although calculated *d*-values showed no significance, it is clear that there was a difference of roughly R10.00 per prescription between males and females in both study periods. The CPIs in both study periods for females were <1 but for males they were >1. The cost of hipolipidaemic medicine items for treatment in females was thus relatively inexpensive compared to the cost to treat males in the study population. In general, the female population had lower cholesterol levels than males up until the age of 55. The 10-year Framingham risk score shows that males have a greater risk for cardiovascular disease up to 45 years of age and based on the treatment to target concept from the NCEP, higher drug dosages are used to lower cholesterol, and also to lower the patient's risk for cardiovascular disease (Appendix A; NIH, 2002:III-3) This might be the reason for males presenting with more prescriptions than females in the study period.

4.4.6.2 Summary and discussion on the analysis of hipolipidaemic drugs as based on generic indicators

Non-substitutable and generic hipolipidaemic medicine items carried the largest percentage of prevalence and cost in both study periods for both sex categories and all age groups. Original hipolipidaemic medicine items in both study periods accounted for a very small percentage of prevalence.

Non-substitutable and generic hipolipidaemic medicine items also accounted for the largest percentage of cost in both study periods. CPIs furthermore proved that generic hipolipidaemic medicine items were clearly the less expensive hipolipidaemic medicine of choice. In age group 1, however, treatment with a non-substitutable hipolipidaemic medicine item ("N") was relatively less expensive than treatment with "O" and "Y". Most of the items prescribed in this age group was the drug cholestyramine (refer to paragraph 4.6.1.1). This drug is a non-substitutable item,

with no generic item available. This is a schedule 2 medicine item and a calculated CPI (0.67) indicated that treatement with this medicine item was relatively inexpensive (refer to paragraph 4.6.1.1). The average cost per hipolipidaemic item in all the categories remained relatively stable during the two study periods and there were no *d*-values of practical significance.

Treatment with a non-substitutable hipolipidaemic medicine item ("N") in both males and females had the highest prevalence. The medicine item with the highest prevalence was Lipitor. Lipitor was commonly used and it had no generic equivalent available at the time of this study (refer to Appendix B2.40 and B2.41). The average cost per hipolipidaemic item in all the sex categories remained relatively stable during the two study periods and there were no *d*-values of practical significance.

4.4.6.3 Summary and discussion on the analysis of hipolipidaemic drugs based on prescriber type

During the two study periods of 2005 and 2006 very little change was noticed in the prescribing patterns for hipolipidaemic medicine items and prescriptions from the various prescribers.

In South Africa the Medicines Control Council (MCC) is a statutory body that was established in terms of the Medicines and Related Substances Control Act, 101 of 1965, to oversee the regulation of medicines (MCC, 2009). Hipolipidaemic medicine is scheduled as follows (Snyman, 2007:164):

- Fibrates (schedule 3).
- HMG CoA reductase inhibitors (schedule 4).
- Cholesterol absorption inhibitors (schedule 4).
- Others (schedule 2 & 3), including nicotinic acid (schedule 0).

Patients can thus only receive hipolipidaemic medicine items on a prescription prescribed by a legal prescriber (cardiologists, general medical practitioners, others, pharmacotherapists, pharmacists and thoracic surgeons) except for Questran Lite 4mg (cholestyramine) being a schedule 2 hipolipidaemic medicine item. For the purpose of this study nicotinic acid was classified as "others". The specific trade name items (active ingredients) prescribed are further discussed in paragraphs 4.6.3.

Based on table 4.9 general medical practitioners most frequently prescribed hipolipidaemic prescriptions, followed by other prescribers and then by cardiologists. Hipolipidaemic prescriptions mostly consisted of 1 hipolipidaemic medicine item per prescription and general

medical practitioners accounted for the majority of repeatable prescriptions (between 6 and 7 prescriptions per patient). The highest cost per prescription came from cardiologists and pharmacotherapists.

4.5 ANALYSIS OF THE PRESCRIBING PATTERNS OF HIPOLIPIDAEMICS BASED ON ACTIVE INGREDIENTS

Figure 4.2 contains (a) the prevalence percentages and (b) cost percentages of the different classes of hipolipidaemics prescribed in the two study periods. Figure 4.2 is drawn from tables B2.38, B2.39, B2.40 and B2.41 in appendix B, reflecting the hipolipidaemic data on the database of both 2005 and 2006 and their individual periods based on therapeutic classes.

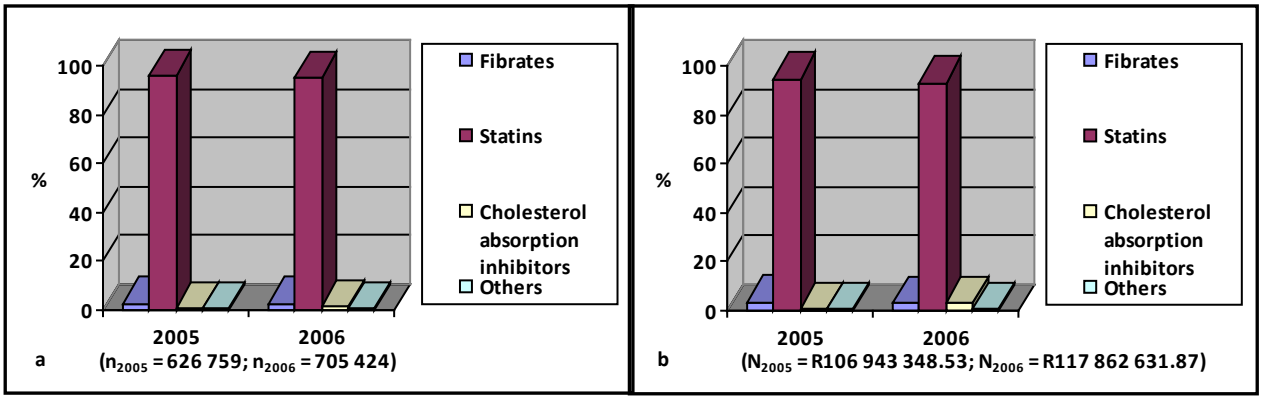

Figure 4.2: Prevalence percentages and cost percentages of the different hipolipidaemic classes in 2005 and 2006

Ranked first in both study periods based on prevalence was the therapeutic class of HMG-CoA reductase inhibitors (statins), accounting for 96.03% (N = 626 759) of all hipolipidaemic medicine items in 2005 and 95.23% (N = 705 424) in 2006. Statins ranked first regarding cost in both study periods accounting for 94.87% (N = R106 943 348.53) of the total hipolipidaemic cost in 2005 and 93.18% (N = R117 862 631.87) in 2006. The therapeutic class of fibrates ranked second in both study periods accounting for 2.83% (N = 626 759) and 2.68% (N = 705 424) of the total hipolipidaemic prevalence respectively. Fibrates also ranked second regarding total hipolipidaemic cost in 2005, accounting for 3.51% (N = R106 943 348.53) and ranked fourth in 2006, accounting for 3.04% (N = R117 862 631.87) of the total hipolipidaemic cost. The cholesterol absorption inhibitors ranked fourth for hipolipidaemic medicine items based on prevalence in 2005 accounting for 0.46% (N = 626 759); increasing to third place in 2006 accounting for 1.54% (N = 705 424). Cholesterol absorption inhibitors ranked third regarding total hipolipidaemic cost in 2005 with 0.95% (N = R106 943 348.53) of the total hipolipdiaemic cost, while it ranked second in 2006 with 3.27% (N = R117 862 631.87) of the total

hipolipidaemic cost. In both study periods the "others" therapeutic class accounted for less than 1% of hipolipidaemic medicine item prevalence and cost.

The prevalence, cost and average cost per item for each hipolipidaemic active ingredient that was prescribed during the study period of 2005 and 2006 will be discussed in the following section. Table 4.10 depicts the prescribing patterns of the active ingredients according to rank (based on prevalence and cost respectively) for 2005 and 2006.

Table 4.10: Prescribing patterns for hipolipidaemic active ingredients, ranked for prevalence and cost

Period	Description	Number of hipolipidaemic active ingredients (N = 626 759)	Average cost per active ingredient (R)	Total cost (R) (N = 106 943 348.53)	CPI
2005	**Acipimox**	261 **(13)**	181.36 ± 47.74	47 335.85 **(12)**	1.06
	Atorvastatin	260 090 **(2)**	218.34 ± 58.04	56 787 636.19 **(1)**	1.28
	Bezafibrate	14 683 **(5)**	187.13 ± 61.44	2 747 684.95 **(5)**	1.10
	Cholestyramine	3 659 **(6)**	179.08 ± 147.23	655 257.08 **(8)**	1.05
	Essential phospholipids	13 **(14)**	164.43 ± 201.02	2 137.54 **(14)**	0.96
	Ezetimibe	2 855 **(7)**	355.64 ± 28.08	1 015 359.60 **(6)**	2.08
	Fenofibrate	1 987 **(9)**	363.33 ± 88.16	721 930.12 **(7)**	2.13
	Fluvastatin	25 810 **(4)**	192.08 ± 32.93	4 957 629.23 **(4)**	1.13
	Gemfibrozil	1 057 **(11)**	270.73 ± 78.30	286 164.95 **(9)**	1.59
	Lovastatin	2 143 **(8)**	95.74 ± 16.30	205 177.74 **(10)**	0.56
	Nicotinic acid	393 **(12)**	13.80 ± 20.66	5 423.67 **(13)**	0.08
	Pravastatin	28 089 **(3)**	221.92 ± 54.06	6 233 557.76 **(3)**	1.30
	Simvastatin	284 232 **(1)**	116.52 ± 27.70	33 119 294.18 **(2)**	0.68
	Simvastatin/Vitamin C	1 487 **(10)**	106.77 ± 18.98	158 759.67 **(11)**	0.63
Period	**Description**	**Number of hipolipidaemic active ingredients (N = 705 424)**	**Average cost per active ingredient (R)**	**Total cost (R) (N = 117 862 631.87)**	**CPI**
2006	**Acipimox**	237 **(13)**	171.48 ± 41.78	40 640.85 **(13)**	1.03
	Atorvastatin	266 582 **(2)**	221.63 ± 58.05	59 082 942.42 **(1)**	1.33
	Bezafibrate	17 705 **(5)**	183.94 ± 57.17	3 256 680.48 **(6)**	1.10
	Cholestyramine	3 175 **(10)**	173.89 ± 148.49	552 101.07 **(10)**	1.04
	Ezetimibe	10 894 **(7)**	353.49 ± 39.85	3 850 942.22 **(5)**	2.12
	Fenofibrate	224 **(14)**	325.42 ± 69.03	72 894.72 **(12)**	1.95
	Fluvastatin	21 261 **(4)**	191.91 ± 31.10	4 080 275.00 **(4)**	1.15
	Gemfibrozil	989 **(11)**	261.44 ± 83.73	258 567.58 **(11)**	1.56
	Lovastatin	5 813 **(9)**	97.76 ± 15.62	568 297.45 **(9)**	0.59
	Nicotinic acid	444 **(12)**	14.26 ± 24.25	6 331.33 **(14)**	0.09
	Pravastatin	27 225 **(3)**	183.55 ± 55.08	4 997 137.02 **(3)**	1.10
	Rosuvastatin	14 346 **(6)**	208.15 ± 54.57	2 986 164.46 **(7)**	1.25
	Simvastatin	325 970 **(1)**	113.45 ± 24.47	36 983 938.41 **(2)**	0.68
	Simvastatin/Vitamin C	10 559 **(8)**	106.61 ± 20.67	1 125 718.86 **(8)**	0.64

The most common prescribed hipolipidaemic active ingredient for both study periods was simvastatin, accounting for 45.35% (N = 626 759) of all hipolipidaemic items in 2005 and 46.21% (N = 705 424) in 2006. The active ingredient, simvastatin, had an average cost of

R116.52 ± 27.70 per item in 2005 and R113.45 ± 24.47 in 2006. A d-value was calculated (*d* = 0.11) which according to Steyn (1999:3) is of no practical significance. The total cost of simvastatin, however, ranked second in both study periods with 30.97% (N = R106 943 348.53) of all hipolipidaemic medicine costs claimed in 2005 and 31.38% (R117 862 631.87) in 2006. CPIs calculated for simvastatin in both study periods were 0.68 which indicated that treatment therewith was relatively inexpensive.

Atorvastatin was the second most frequently prescribed hipolipidaemic active ingredient in both study periods following simvastatin representing 41.50% (N = 626 759) of all hipolipidaemic medicine items claimed in 2005 and 37.79% (N = 705 424). The average cost of atorvastatin in 2005 and 2006 was R218.34 ± 58.04 and R221.63 ± 58.05 respectively. A small *d*-value (*d* = 0.06) was calculated which is of no practical significance (Steyn, 1999:3). The total cost of atorvastatin ranked first in both study periods, accounting for 53.10% (N = R106 943 348.53) and 50.13% (N = R117 862 631.87) of the total cost of hipolipidaemic active ingredients in 2005 and 2006 respectively. CPIs for atorvastatin were 1.28 in 2005 and 1.31 in 2006, which indicated that treatment with atorvastatin was relatively expensive. The reason for this might be because atorvastatin was classified as a non-substitutable hipolipidaemic medicine item (active ingredient) on the database; no generic was available at a less expensive price at the time of the study (refer to Appendix B2.40 and B2.41).

Pravastatin was ranked third in both study periods for both the prevalence and cost. Pravastatin represented 4.48% (N = 626 759) during 2005 and 3.86% (N = 705 424) of active ingredients prescribed in 2006 respectively. The total cost of pravastatin accounted for 5.83% (N = R106 943 348.53) in 2005 and 4.24% (N = R117 862 631.87) in 2006 of the total cost for hipolipidaemic active ingredients. At an average cost of R221.92 ± 54.06 and R183.55 ± 55.08 for 2005 and 2006 respectively a *d*-value was calculated (*d* = 0.69) which may be significant (Steyn, 1999:3). CPIs were calculated respectively for 2005 and 2006 at 1.30 and 1.10 which indicated that treatment with pravastatin was relatively expensive.

In the therapeutic group HMG-CoA reductase inhibitors, CPIs for atorvastatin, fluvastatin and pravastatin in 2005 and 2006 were all above 1, giving an indication of relatively expensive treatment. Fluvastatin, like atorvastatin, was also classified as a non-substitutable medicine item on the database (refer to Appendix B2.40 and B2.41), which can be the reason for expensive treatment costs. Lovastatin, simvastatin and combinations of simvastatin with other ingredients (*i.e.*, simvastatin/Vitamin C) had CPIs less than 1 which indicated relative inexpensive treatment. Rosuvastatin was introduced to the market in 2006 (South Africa, 2006:10-12), and ranked sixth based on prevalence, with 2.03% (N = 705 424) of total hipolipidaemic active ingredients in 2006. Rosuvastatin had an average cost of R 208.15 ±

54.57 in 2006 and accounted for 2.53% (N = R117 862 631.87) of the total cost of hipolipidaemic active ingredients in 2006. The CPI for rosuvastatin in 2006 was 1.25 which indicated that treatment was relatively expensive.

In the therapeutic group of fibrates (bezafibrate, fenofibrate, and gemfibrozil) for both study periods CPIs were above 1 which indicated that treatment was relatively expensive. In 2005 fenofibrate had the highest CPI of all hipolipidaemic active ingredients *i.e.*, 2.19, and second highest in 2006 with 1.95. Fenofibrate (Lipsin 300mg and Lipanthyl 200mg) were classified as non-substitutable active ingredients on the database and no generic was available at a less expensive price at the time of the study. This could be a possible explanation for the relatively expensiveness of these products.

Cholestyramine is part of the cholesterol absorption inhibitor therapeutic group (Snyman, 2007:169). Based on prevalence, cholestyramine ranked sixth in 2005 and tenth in 2006; whilst ranking eighth and tenth in 2005 and 2006 respectively based on total cost. CPIs for both study periods were calculated at 1.08 and 1.04 respectively which indicated relatively expensive treatment. The reason for this might be that cholestyramine (Questran Lite 4mg) was also classified as a non-substitutable drug on the database, with no generic equivalent available at a less expensive price at the time of the study (refer to Appendix B2.40 and B2.41).

As part of the "others" therapeutic group, ezetimibe had very high CPIs in both study periods at 2.14 and 2.12 respectively. Ezetimibe represents the first compound of a new class of agents, the cholesterol absorption inhibitors (Snyman, 2007:170); and has as yet no available generic. Ezetimibe (Ezetrol 10mg) was therefore classified as a non-substitutable medicine item on the database, at an average cost of R355.64 ± 28.08 in 2005 and R353.49 ± 39.85 in 2006. Nicotinic acid[1] had the lowest CPI in both study periods at 0.08 and 0.09 respectively.

4.5.1 Analysis of the prescribing patterns of hipolipidaemic active ingredients based on age groups

The prescribing patterns of the various hipolipidaemics based on patients' age groups were recorded for both 2005 and 2006. Figure 4.3 contains the prevalence percentages of the different classes of hipolipidaemics prescribed to each age group in the two study periods. (Age groups in the figures are as follows: Figure a = 0≤ 9 years; b = 10 ≤ 19 years; c = 20 ≤ 45 years; d = 46 ≤ 59 years; e = > 59 years). Figure 4.3 is drawn from tables B2.42, B2.43, B2.44, B2.45, B2.46, B2.47, B2.48, B2.49, B2.50 and B2.51 in appendix B, reflecting the

[1] Nicotinic acid is not classified in the MIMS as part of the others therapeutic class, for the purpose of this study it was added to the others therapeutic class (refer to paragraph 2.5.6)

hipolipidaemic data on the database of both 2005 and 2006 and their indicidual periods based on active ingredients, trade names, generic indicators and age groups.

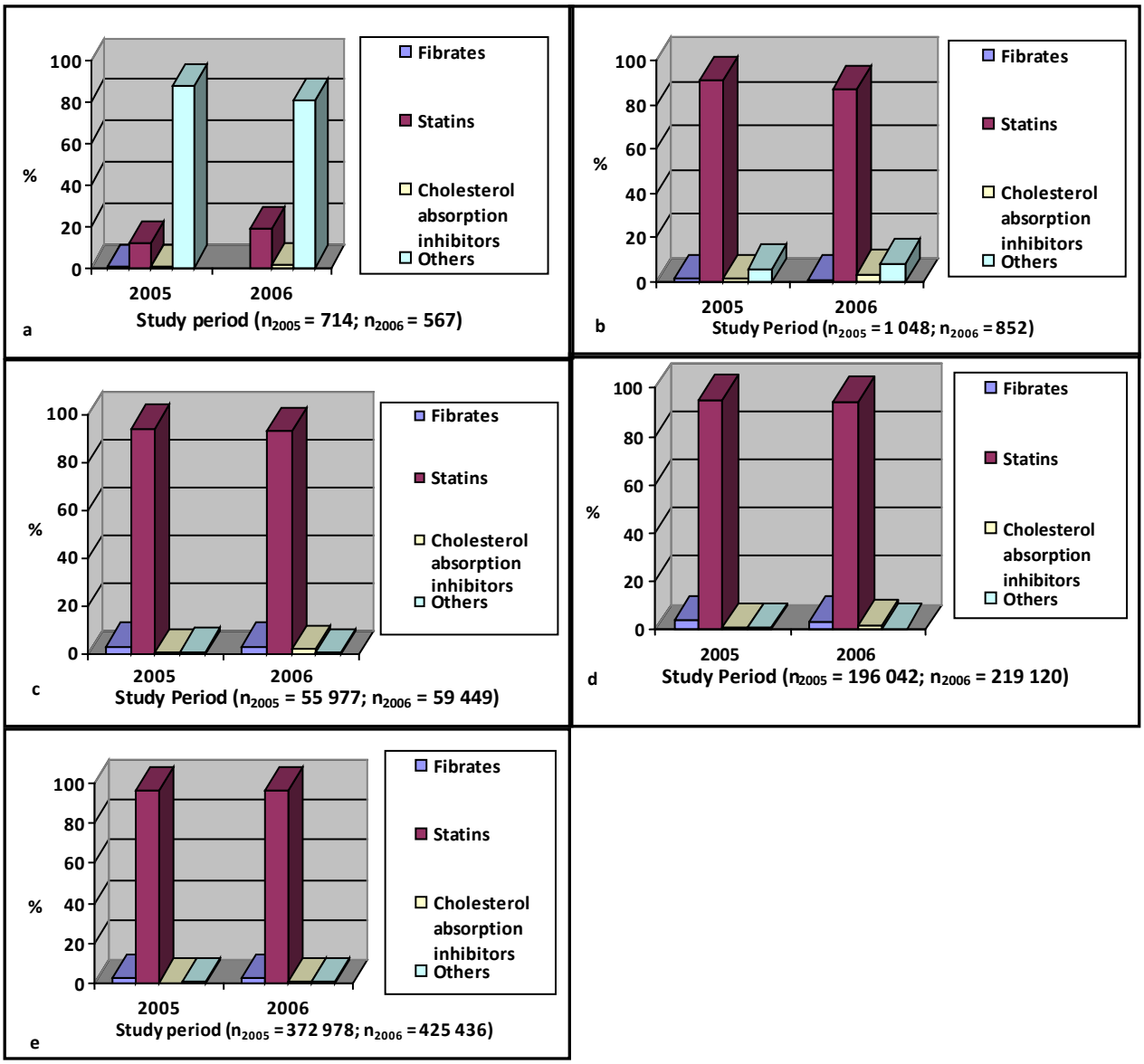

Figure 4.3: Prevalence percentages of the different classes of hipolipidaemics prescribed based on age group

4.5.1.1 Age group 1: Children between the ages of 0 and 9 years

In the age group of children 0≤ 9 years (Figure 4.3a), the most frequently prescribed hipolipidaemic was the “others” therapeutic group, in particular cholestyramine, accounting for 87.68% (n = 714) of active ingredients prescribed in this age group in 2005 and 80.25% (n = 567) in 2006.

The second most frequently prescribed hipolipidaemic class in this age group for both study periods was the HMG-CoA reductase inhibitors (statins). This included claims for atorvastatin

(8.54%; n = 61) and simvastatin (2.94%; n = 21) in 2005, and atorvastatin (9.35%; n = 53), simvastatin (8.11%; n = 46), pravastatin (0.71%; n = 4) and rosuvastatin (0.14%; n = 1) in 2006 (refer to Appendix B2.42 and B2.43).

The remaining two therapeutic classes, *i.e*. the fibrates and cholesterol absorption inhibitors, ranked very low in this age group accounting for approximately 1% of each class.

4.5.1.2 Age group 2: Adolescents between the ages of 10 and 19 years

Patients in the age group 10 ≤ 19 years (Figure 4.3b) received mostly hipolipidaemic medicine items from the HMG-CoA reductase inhibitors (statins) group, accounting for 91.03% (n = 1 048) of items prescribed in 2005 and 87.82% (n = 852) of those in 2006. The statin most often claimed in 2005 and 2006 was atorvastatin, accounting for 61.07% (n = 1 048) and 52.46% (n = 852) of active ingredients claimed respectively. The second most frequently claimed statin was simvastatin, accounting for 26.34% (n = 1 048) in 2005 and 24.88% (n = 852) in 2006 (refer to Appendix B2.44 and B2.45).

The “others” therapeutic class ranked second, accounting for 6.11% (n = 1 048) and 8.22% (n = 852) of all hipolipidaemic medicine costs claimed in 2005 and 2006 respectively, in particular the active ingredient cholestyramine (5.92% in 2005 and 7.39% in 2006) (refer to Appendix B2.44 and B2.45).

Fibrates, specifically bezafibrate, accounted for 1.53% (n = 1 048) of all hipolipidaemic medicine items claimed in 2005 and 1.06% (n = 852) in 2006. Ezetimibe accounted for 1.33% (n = 1 048) and 3.40% (n = 852) of active ingredients prescribed in 2005 and 2006 respectively (refer to Appendix B2.44 and B2.45).

4.5.1.3 Age group 3: Young adults between the ages of 20 and 45 years

Hipolipidaemic medicine items in age group 20 ≤ 45 years (Figure 4.3c) mostly consisted of the HMG-CoA reductase inhibitors (statins) group, accounting for 94.52% (n = 55 977) of all hipolipidaemic medicine items claimed in 2005 and 93.25% (n = 59 449) in 2006. Atorvastatin in particular accounted for 47.10% (n = 55 977) of active ingredients claimed in 2005 and 41.67% (n = 59 449) in 2006. The statin with the second highest number of claims in this age group was simvastatin, accounting for 39.53% (n = 55 977) and 41.48% (n = 59 449) of all hipolipidaemic medicine items claimed in 2005 and 2006 respectively (refer to Appendix B2.46 and B2.47).

Fibrates, as therapeutic class, ranked second highest for patients in age group 20 ≤ 45 years with 3.63% in 2005 and 3.67% in 2006, in particular bezafibrate, which accounted for 2.95% and 3.41% in 2005 and 2006 respectively. The cholesterol absorption inhibitors therapeutic class, *i.e*., ezetimibe, represented 0.77% (n = 55 977) and 2.23% (n = 59 449) in 2005 and 2006 respectively of all active ingredients (refer to Appendix B2.46 and B2.47).

Lastly the "others" therapeutic group represented 1.09% (n = 55 977) in 2005 and 0.85% (59 449) of medicine items claimed in 2006, particularly cholestyramine, with 0.94% (n = 55 977) in 2005 and 0.78% (n = 59 449) in 2006 (refer to Appendix B2.46 and B2.47).

4.5.1.4 Age group 4: Older adults between the ages of 46 and 59 years

Patients aged 46 ≤ 59 years (Figure 4.3d) received most claims for the HMG-CoA reductase inhibitors therapeutic group (statins) accounting for 95.37% (n = 196 042) of all hipolipidaemic medicine items claimed in 2005 and 94.62% (n = 219 120) of those in 2006. Atorvastatin, ranked first in 2005 with 44.65% (n = 196 042) of active ingredients claimed in this age group in 2005 and ranked second in 2006, accounting for 40.68% (n = 219 120). Simvastatin was the second most frequently claimed statin in this age group in 2005, accounting for 42.85% (n = 196 042) of all hipolipidaemic medicine items claimed. Simvastatin, however, ranked first in 2006 as the most frequently claimed statin in this specific age group, accounting for 44.19% (n = 219 120) (refer to Appendix B2.48 and B2.49).

The therapeutic class fibrates ranked second in both study periods in patients aged 46 ≤ 59 years, accounting for 3.65% (n = 196 042) and 3.13% (n = 219 120) of hipolipidaemic medicine items claimed in this age group in 2005 and 2006 respectively. Bezafibrate specifically accounted for 2.68% (n = 196 042) in 2005 and 2.95% (n = 219 120) in 2006 (refer to Appendix B2.48 and B2.49).

The therapeutic class which ranked third based on prevalence in patients aged 46 ≤ 59 years was the cholesterol absorption inhibitors (ezetimibe), accounting for 0.52 % (n = 196 042) and 1.90% (n = 219 120) of all hipolipidaemic medicine items claimed in 2005 and 2006 respectively. The "others" therapeutic group ranked fourth with 0.46% (n = 196 042)of all hipolipidaemic medicine items claimed in 2005 and 0.35% (n = 219 120) in 2006 (refer to Appendix B2.48 and B2.49).

4.5.1.5 Age group 5: Patients older than 59 years of age

Patients in the age group older the 59 years of age (Figure 4.3e), received mostly hipolipidaemic medicine items for the HMG-CoA reductase inhibitors (statins) group. Statins in this age group accounted for 96.33% (n = 372 978) of all hipolipidaemic medicine items claimed and 96.18% (n = 425 436) in 2005 and 2006 respectively. The statin that proved to be claimed most often in this age group was simvastatin, accounting for 48.11% (n = 372 978) of all active ingredients claimed in this age group in 2005 and 50.49% (n = 425 436) in 2006. Atorvastatin ranked second at 39.00% (n = 372 978) of all hipolipidaemic medicine items claimed in 2005 and 35.76% (n = 425 436) in 2006 (refer to Appendix B2.50 and B2.51).

Fibrates, as therapeutic class, ranked third, accounting for 2.53 % (n = 372 978) and 2.32% (n = 425 436) of claimed hipolipidaemic medicine items in this age group. Bezafibrate particularly made out 2.08% in 2005 and 2.16% in 2006. Cholesterol absorption inhibitors (ezetimibe) ranked fourth in claimed medicine items per therapeutic class in 2005 at 0.37 % (n = 372 978); these inhibitors, however, ranked third in 2006 with 1.26% (n = 425 436) (refer to Appendix B2.50 and B2.51).

The “others” therapeutic class ranked third in 2005 with 0.57% (n = 372 978) of hipolipidaemic medicine items, and cholestyramine specifically accounted for 0.47%. In 2006 the “others” therapeutic class ranked fourth, accounting for 0.24% (n = 425 436) (refer to Appendix B2.50 and B2.51).

4.5.2 Analysis of the cost of hipolipidaemics' active ingredients based on age groups

The costs of the various hipolipidaemics were recorded for both 2005 and 2006 based on patients' age groups. Figure 4.4 contains the percentages of the costs of the different classes of hipolipidaemics claimed for each age group in the two study periods. (Age groups in Figure 4.4 are as follows: Figure a = 0≤ 9 years, b = 10 ≤ 19 years, c = 20 ≤ 45 years, d = 46 ≤ 59 years, e = > 59 years). Figure 4.4 is drawn from the prevalence in tables B2.42, B2.43, B2.44, B2.45, B2.46, B2.47, B2.48, B2.49, B2.50 and B2.51 in appendix B, reflecting the hipolipidaemic data on the database of both 2005 and 2006 and their indicidual periods based on active ingredients, trade names and age groups.

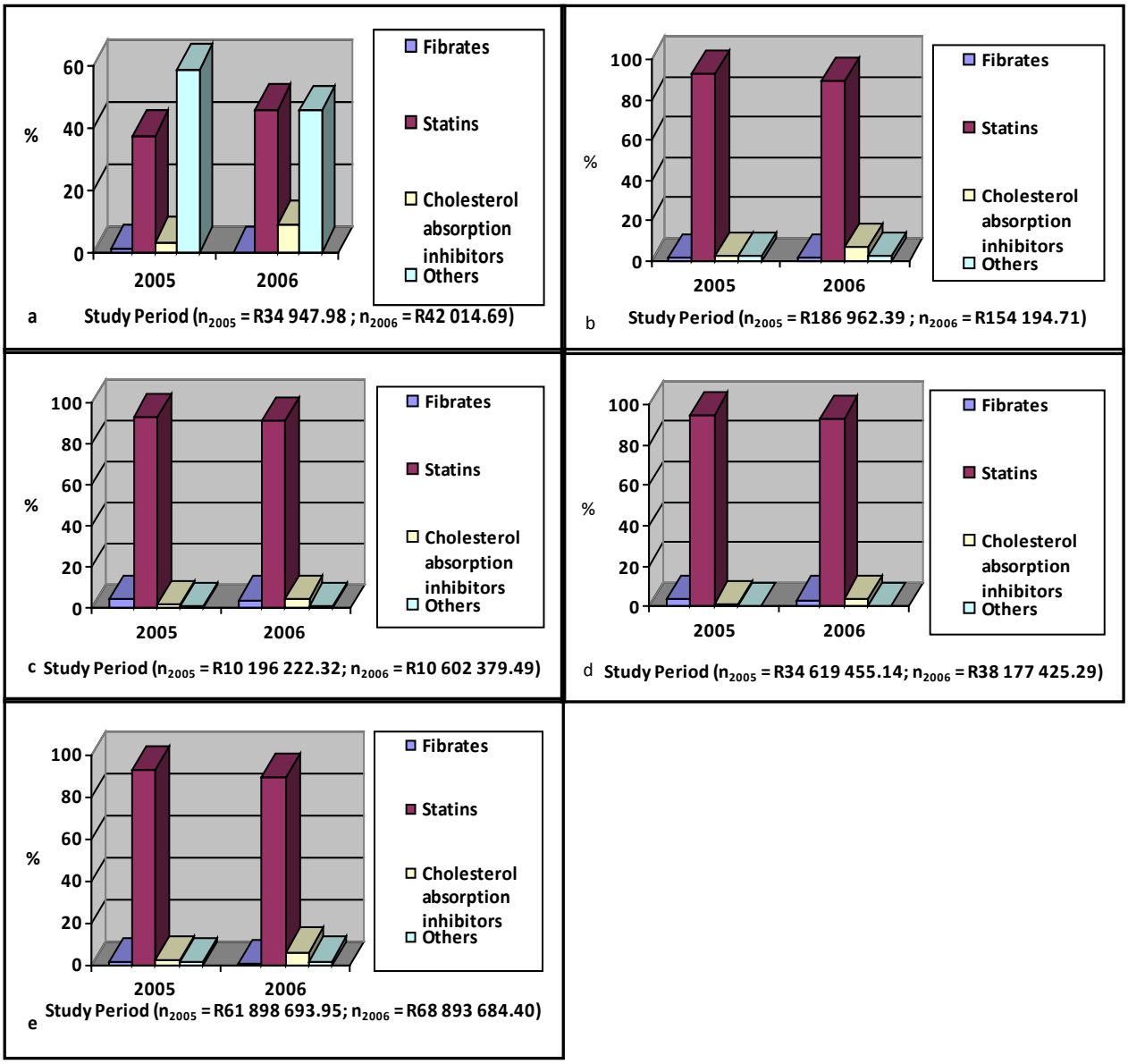

Figure 4.4: Cost percentages of the different classes of hipolipidaemic active ingredients based on age groups

4.5.2.1 Age group 1: Children between the ages of 0 and 9 years

In the age group of children 0 ≤ 9 years (Figure 4.4a), the "others" therapeutic group accounted for the highest cost percentage of hipolipidaemic medicine items with 58.91% (n = R42 014.69) in 2005. This group ranked second highest in cost in 2006, accounting for 45.54% (n = R34 947.98). The cost percentage of cholestyramine specifically accounted for 58.90% (n = 42 014.69) of all active ingredients in this age group in 2005, and 45.54% (n = R34 947.98) in 2006.

The HMG-CoA reductase inhibitor (statin) therapeutic class had the second highest cost in this age group in 2005, and ranked first in 2006, accounting for 37.32% (n = R 42 014.69) and 45.89% (n = R34 947.98) of all claimed hipolipidaemic medicine item costs respectively. During both study periods atorvastatin was the most frequently claimed statin, accounting for 31.64% (n = R 42 014.69) of all active ingredient costs in this age group in 2005 and 30.29% (n = R34 947.98) in 2006. Simvastatin was ranked second in 2005 and 2006, accounting for 5.68% (n = R42 014.69) and 13.83% (n = R34 947.98) respectively, followed by pravastatin and rosuvastatin (2006).

The cholesterol absorption inhibitors therapeutic group (ezetimibe) had the third highest cost of all hipolipidaemic medicine items claimed by children aged 0≤ 9 years in 2005 and 2006, accounting for 2.51% (n = R42 014.69) and 8.57% (n = R34 947.98) respectively. Specifically bezafibrate, from among the fibrates, was claimed in 2005 only, covering 0.84% (n = R42 014.69) of hipolipidaemic active ingredient cost in children aged 0 ≤ 9 years.

4.5.2.2 Age group 2: Adolescents between the ages of 10 and 19 years

The HMG-CoA reductase inhibitor (statin) therapeutic class accounted for the highest cost of hipolipidaemic medicine items in patients aged 10 ≤ 19 years (Figure 4.4b) in 2005 and 2006. Statins represented 92.93% (n = R186 962.39) of hipolipidaemic medicine item cost in this age group in 2005 and 89.40% (n = R154 194.71) in 2006. Atorvastatin was the statin that covered the largest percentage of cost of active ingredients in this age group, accounting for 72.74% (n = R186 962.39) in 2005 and 63.94% (n = R154 194.71) in 2006. Simvastatin ranked second highest with 16.85% (n= R186 962.39) and 15.05% (n = R154 194.71) in 2005 and 2006 respectively. In 2006, rosuvastatin ranked third highest in cost percentage of active ingredients in adolescents aged 10 ≤ 19 years, accounting for 7.42% (n = R154 194.71).

Cholesterol absorption inhibitors (ezetimibe) ranked second highest in the cost for hipolipidaemic medicine items in adolescents aged 10 ≤ 19 years, accounting for 2.63% (n =

R186 962.39) in 2005 and 6.71% (n = R154 194.71) in 2006. The "others" therapeutic class ranked third and fibrates fourth in both study periods. "Others" accounted for 2.24% (n = R186 962.39) of the total hipolipidaemic medicine cost in this age group in 2005 and 2.51% (n = R154 194.71) in 2006. Cholestyramine accounted for the highest percentage of total cost with 2.24% (n= R186 962.39) and 2.49% (n = R154 194.71) in 2005 and 2006 respectively. Fibrates (bezafibrate) accounted for 2.20% (n= R186 962.39) in 2005 and 1.38% (n = R154 194.71) in 2006.

4.5.2.3 Age group 3: Young adults between the ages of 20 and 45 years

In patients aged 20 ≤ 45 years (Figure 4.4c), the HMG-CoA reductase inhibitor (statins) therapeutic class accounted for the highest cost percentage of hipolipidaemic medicine items, at 93.36% (n = R10 196 222.52) in 2005 and 91.10% (n = R10 602 379.49) in 2006. In both study periods atorvastatin was the statin that accounted for the highest cost percentage of active ingredients in this age group, at 59.14% (n = R10 196 222.52) in 2005 and 54.02% (n = R10 602 379.49) in 2006. Simvastatin ranked second in 2005 and 2006, accounting for 25.43% (n = R10 196 222.52) and 26.53% (n = R10 602 379.49) respectively. In 2005 pravastatin ranked third, representing 4.21% (n = R10 196 222.52) of the total active ingredient cost in patients aged 19 ≤ 45, whilst in 2006, rosuvastatin filled this ranking position at 4.26% (n = R10 602 379.49).

Fibrates, as therapeutic class, ranked second in total cost of hipolipidaemic medicine cost in patients aged 20 ≤ 45 years for 2005, accounting for 4.41% (n = R10 196 222.52). Fibrates ranked third in 2006 based on total cost of hipolipidaemic medicine items for patients aged 20 ≤ 45 years with 3.92% (n = R10 602 379.49) of the total hipolipidaemic cost. In 2005, 3.19% (n = R10 196 222.52) of the hipolipidaemic cost in this age group was occupied by bezafibrate, where in 2006 it accounted for 3.56% (n = R10 602 379.49).

Ezetimibe (cholesterol absorption inhibitors) accounted for 1.48% (n = R10 196 222.52) of the hipolipidaemic cost in patients aged 20 ≤ 45 years in 2005, in 2006 it accounted for 4.39% (n = R10 602 379.49). The "others" therapeutic group ranked fourth for both study periods regarding cost percentage in this age group, with 0.75% in 2005 and 0.59% in 2006. Cholestyramine was the active ingredient in this therapeutic class which accounted for the highest cost percentage in 2005 and 2006, with 0.66% (n = R10 196 222.52) and 0.53% (n = R10 602 379.49) respectively.

4.5.2.4 Age group 4: Older adults between the ages of 46 and 59 years

In patients aged 46 ≤ 59 years (Figure 4.4d), the largest cost percentage in both 2005 and 2006 belonged to the HMG-CoA reductase inhibitors (statins) therapeutic class accounting for 94.63% (n = R34 619 455.14) and 92.39% (n = R38 177 425.29) respectively. Atorvastatin was the leading statin regarding cost in patients aged 46 ≤ 59 years. In 2005 it accounted for 56.41% (n = R34 619 455.14) of total active ingredient cost and for 52.95% (n = R38 177 425.29) in 2006. Simvastatin (from the HMG-CoA reductase inhibitors – statins class) accounted for the second highest cost percentage of active ingredients in patients aged 46 ≤ 59 years, at 28.45% (n = R34 619 455.14) and 28.99% (n = R38 177 425.29) in 2005 and 2006 respectively. Fluvastatin ranked third highest for percentage of active ingredient cost in patients aged 46 ≤ 59 years in 2005, at 4.59% (n = R34 619 455.14) of the total cost of all hipolipidaemic medicine costs claimed. In 2006, however, pravastatin ranked third highest in percentage of active ingredient cost in this age group, accounting for 3.69% (n = R38 177 425.29) of the total cost of all hipolipidaemic medicine costs claimed.

In 2005, fibrates ranked second in the percentage of total hipolipidaemic medicine cost in patients aged 46 ≤ 59 years, accounting for 3.84% (n = R34 619 455.14). In 2006 fibrates ranked third with 3.44% (n = R38 177 425.29) of the total hipolipidaemic medicine cost in patients 46 ≤ 59 years of age. Bezafibrate specifically accounted for 2.87% (n = R34 619 425.29) in 2005 and 3.14% (n = R38 177 425.29) in 2006. Fenofibrate and gemfibrozil both accounted for less than 1% in both study periods.

Cholesterol absorption inhibitors (ezetimibe) accounted for 1.05% (n = R34 619 455.14) of total hipolipidaemic medicine cost in this age group in 2005, ranking third. However, in 2006 cholesterol absorption inhibitors ranked second regarding total hipolipidaemic active ingredient cost in patients aged 46 ≤ 59 years, accounting for 3.85% (n = R38 177 425.14). The “others” therapeutic class accounted for the smallest percentage of hipolipidaemic medicine item cost in patients 46 ≤ 59 years of age in both 2005 and 2006, accounting for 0.48% (n = R34 619 455.14) of all hipolipidaemic medicine costs claimed and 0.32% (n = R38 177 425.29) respectively. Cholestyramine accounted for 0.44% (n = R34 619 455.14) of all hipolipidaemic medicine costs claimed in 2005 and 0.28% (n = R38 177 425.29) in 2006.

4.5.2.5 Age group 5: Patients older than 59 years of age

In 2005 and 2006, the HMG-CoA reductase inhibitor (statins) therapeutic class accounted for the largest cost percentage of hipolipidaemic medicine in patients aged > 59 years (Figure 4.4e), at 95.31% (n = R61 898 693.95) in 2005 and 93.96% (n = R68 893 684.40) in 2006.

Amongst the statins, atorvastatin accounted for the highest percentage of active ingredient cost in this age group in both study periods at 50.21% (n = R61 898 693.95) in 2005 and 47.94% (n = R68 893 684.40) in 2006. Ranked second highest, following atorvastatin for total cost percentage of active ingredients in patients aged > 59 years, was simvastatin, accounting for 33.62% (n = R61 898 693.95) in 2005 and 35.12% (n = R68 893 684.40) in 2006. Pravastatin succeeded simvastatin in cost percentage of total active ingredient cost in this age group in both study periods, accounting for 6.57% (n = R61 898 693.95) and 4.71% (n = R68 893 684.40) in 2005 and 2006 respectively.

In 2005, fibrates ranked second in the percentage of total hipolipidaemic medicine cost in patients aged > 59 years, accounting for 3.18% (n = R61 898 693.95). Fibrates ranked third in 2006 with 2.71% (n = R68 893 684.40) of the total hipolipidaemic medicine cost in patients > 59 years of age. Bezafibrate specifically accounted for 2.30% (n = R61 898 693.95) in 2005 and 2.45% (n = R68 893 684.40) in 2006. Both fenofibrate and gemfibrozil presented with less than 1% in both study periods.

Cholesterol absorption inhibitors (ezetimibe) accounted for 0.80% (n = R61 898 693.95) of total hipolipidaemic medicine cost in this age group in 2005, ranking third. In 2006, however, cholesterol absorption inhibitors ranked second regarding total hipolipidaemic medicine cost in patients aged > 59 years, accounting for 2.76% (n = R68 893 684.40). The “others” therapeutic class presented with the lowest cost percentage of hipolipidaemic medicine item in patients > 59 years of age in both 2005 and 2006, accounting for 0.71% (n = R61 898 693.95) and 0.57% (n = R68 893 684.40) respectively. Cholestyramine represented 0.66% (n = R61 898 693.95) of all hipolipidaemic medicine costs claimed in 2005 and 0.54% (n = R68 893 684.40) in 2006.

4.5.3 Analysis of the prescribing patterns of hipolipidaemic active ingredients based on patients’ sex

Figure 4.5 contains the prevalence percentages of the different classes of hipolipidaemics prescribed based on the patient’s sex in the two study periods. Patients’ sex is indicated in figure 4.5 as follows: Figure a = female; b = male. Figure 4.5 is drawn from the prevalence in tables B2.52 and B2.53 in appendix B, reflecting the hipolipidaemic data on the database of both 2005 and 2006 and their indicidual periods based on active ingredients, trade names and the sex of the patient.

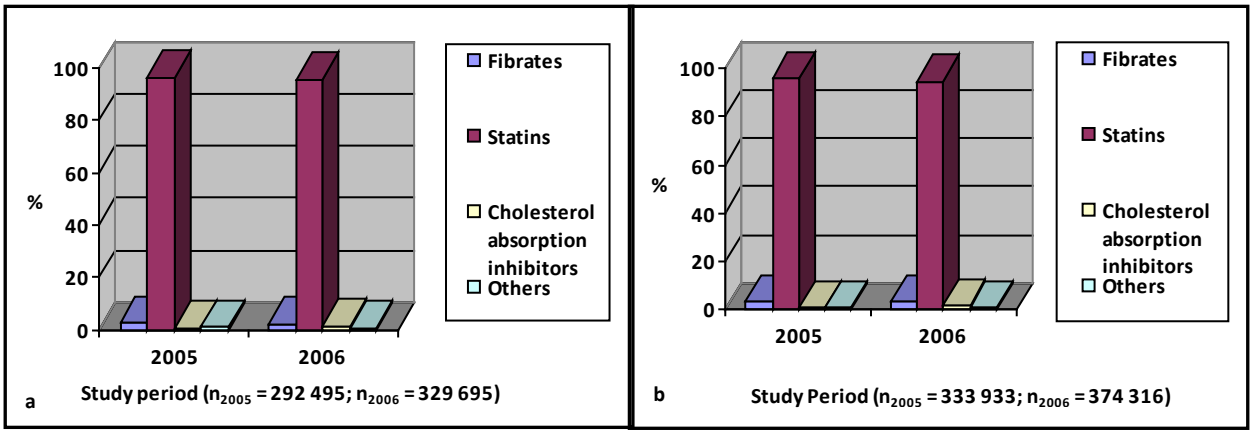

Figure 4.5: Prevalence percentages of the different classes of hipolipidaemics based on patients' sex

4.5.3.1 Female patients

Female patients (Figure 4.5a) mostly received hipolipidaemic medicine items from the statins therapeutic class. Statins accounted for 96.40% (n = 292 495) of all prescribed hipolipidaemic medicine items in the female sex in 2005 and 95.77% (n = 329 695) in 2006. The statin that was prescribed mostly in females in 2005 and 2006 was simvastatin, accounting for 47.41% (n = 292 495) and 49.69% (n = 329 695) respectively for all active ingredients prescribed to the female sex. The second most frequently prescribed statin was atorvastatin, accounting for 39.41% (n = 292 495) of all active ingredients prescribed to females in 2005, and 35.86% (n = 329 695) in 2006. In 2005 and 2006, pravastatin ranked third following simvastatin and atorvastatin, accounting for 4.75% (n = 292 495) and 4.16% (n = 329 695) respectively.

Fibrates as therapeutic class ranked second among the most frequently prescribed hipolipidaemic medicine in females, accounting for 2.38% (n = 292 495) in 2005 and 2.14% (n = 329 695) in 2006. Bezafibrate in particular accounted respectively for 2.01% (n = 292 495) and 2.03% (n = 329 695) of all active ingredients prescribed to females in 2005 and 2006.

Ranked fourth in 2005 and third in 2006 for prescribed hipolipidaemic medicine items was the therapeutic class cholesterol absorption inhibitors (ezetimibe), accounting for 0.43% (n = 292 495) in 2005 and 1.47% (n = 329 695) in 2006. The "others" therapeutic class represented 0.79% (n = 292 495) of all hipolipidaemic medicine items prescribed to the female sex in 2005, and 0.67% (n = 329 695) in 2006. Cholestyramine specifically accounted for 0.68% (n = 292 495) in 2005 and 0.56% (n = 329 695) in 2006.

4.5.3.2 Male patients

Patients of the male sex (Figure 4.5b) mostly received hipolipidaemic medicine items from the statins therapeutic group. Statins accounted for 95.70% (n = 333 933) of all prescribed hipolipidaemic medicine items in males in 2005 and 94.73% (n = 374 316) in 2006. The statin that was prescribed most frequently in males in 2005 and 2006 was simvastatin, accounting for 43.97% (n = 333 933) and 45.79% (n = 374 316) respectively for all active ingredients prescribed; followed by atorvastatin, accounting for 43.34% (n = 333 933) in 2005, and 39.61% (n = 374 316) in 2006. In 2005 and 2006, pravastatin ranked third after simvastatin and atorvastatin, accounting for 4.25% (n = 333 933) and 3.61% (n = 374 316) respectively.

Fibrates as therapeutic class ranked second for the most frequently prescribed hipolipidaemic medicine in males, accounting for 3.22% (n = 333 933) in 2005 and 3.17% (n = 374 316) in 2006. Bezafibrate in particular accounted respectively for 2.63% (n = 333 933) and 2.94% (n = 374 316) of all active ingredients prescribed to males in 2005 and 2006.

Ranked fourth in 2005 and third in 2006 for prescribed hipolipidaemic medicine items was the therapeutic class cholesterol absorption inhibitors (ezetimibe), accounting for 0.48% (n = 333 933) in 2005 and 1.66% (n = 374 316) in 2006. The “others” therapeutic class represented 0.60% (n = 333 933) of all hipolipidaemic medicine items prescribed to the male sex in 2005, and 0.44% (n = 374 316) in 2006. Cholestyramine specifically accounted for 0.49% (n = 333 933) in 2005 and 0.35% (n = 374 316) in 2006.

4.5.4 Analysis of the cost of hipolipidaemics active ingredients based on patient’s sex

Figure 4.6 contains the percentages of the costs of the different classes of hipolipidaemics prescribed to each sex in the two study periods. Patients’ sex in the figure is indicated as follows: Figure a = female and b = male. Figure 4.6 is drawn from the total cost in tables B2.52 and B2.53 in appendix B, reflecting the hipolipidaemic data on the database of both 2005 and 2006 and their indicidual periods based on active ingredients, trade names and the sex of the patient.

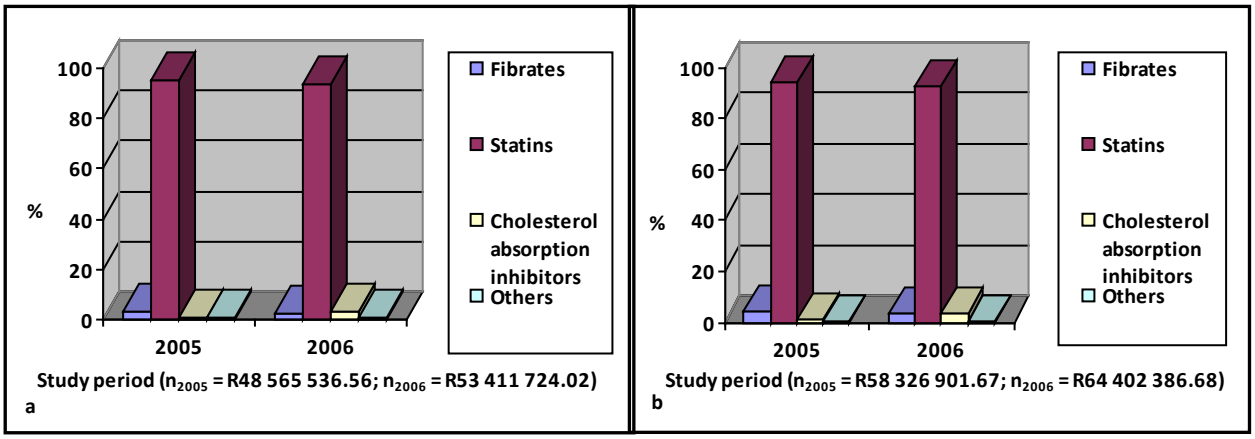

Figure 4.6: Cost percentages of the different classes of hipolipidaemic active ingredients based on sex

4.5.4.1 Female patients

In female patients (Figure 4.6a), the largest percentage of cost in both 2005 and 2006 was taken up by the HMG-CoA reductase inhibitors (statins) therapeutic class. Statins accounted for 95.34% (n = R48 565 536.56) and 93.79% (n = R53 411 724.02) of all hipolipidaemic medicine costs claimed for 2005 and 2006 respectively Atorvastatin was the leading statin regarding cost in female patients. In 2005 it accounted for 50.93% (n = R48 565 536.56) of total active ingredient cost and for 48.13% (n = R53 565 536.56) in 2006. Simvastatin accounted for the second highest cost percentage of active ingredients in female patients, with 32.86% (n = R48 565 536.56) in 2005 and 34.29% (n = R53 411 724.02) in 2006. Pravastatin ranked third highest for cost percentage of active ingredients in female patients in 2005 and 2006, representing 6.23% (n = R48 565 536.56) of the total cost in 2005 and 4.63% (n = R53 411 724.02) in 2006.

In 2005, the fibrates ranked second in the percentage of total hipolipidaemic medicine cost in female patients, accounting for 2.96% (n = R48 565 536.56). However, in 2006 fibrates ranked third with 2.47% (n = R53 411 724.02) of the total hipolipidaemic medicine cost in female patients. Bezafibrate specifically accounted for 2.23% (n = R48 565 536.56) in 2005 and 1.28% (n = R53 411 724.02) in 2006. Fenofibrate and gemfibrozil both accounted for less than 1% in both study periods.

Cholesterol absorption inhibitors (ezetimibe) made up 0.91% (n = R48 565 536.56) of the total hipolipidaemic medicine cost in this age group in 2005, ranking third, and shifting up to second place in 2006 at 3.08% (n = R53 411 724.02). The “others” therapeutic class accounted for the lowest percentage of hipolipidaemic medicine item cost in female patients in both 2005 and 2006, accounting for 0.79% (n = R48 565 536.56) and 0.66% (n = R53 411 724.02)

respectively. Cholestyramine accounted for 0.74% (n = R48 565 536.56) in 2005 and 0.62% (n = R53 411 724.02) in 2006.

4.5.4.2 Male patients

In male patients (Figure 4.6b), the largest percentage of cost in both 2005 and 2006 was taken up by the statins therapeutic class, accounting for 94.49% (n = R58 326 901.67) and 92.68% (n = R64 402 386.68) respectively. Atorvastatin was the leading statin regarding cost in male patients, accounting for 54.93% (n = R58 326 901.67) of the total active ingredient cost in 2005 and for 51.80% (n = R64 402 386.68) in 2006. Simvastatin ranked second highest in cost percentage of active ingredients in male patients, at 29.64% (n = R58 326 901.67) in 2005 and 30.66% (n = R64 402 386.68) in 2006. Simvastatin was followed by pravastatin accounting for 5.50% (n = R58 326 901.67) in 2005 and 3.92% (n = R64 402 386.68) in 2006.

Fibrates ranked second in the percentage of total hipolipidaemic medicine cost in male patients in 2005, accounting for 3.97% (n = R58 326 901.67). The ranking position of fibrates however, moved to third place in 2006 with 3.51% (n = R64 402 386.68) of the total hipolipidaemic medicine cost in male patients. Bezafibrate specifically accounted for 2.85% (n = R58 326 901.67) in 2005 and 3.17% (n = R64 402 386.68) in 2006. Fenofibrate and gemfibrozil both accounted for less than 1% in both study periods.

Cholesterol absorption inhibitors (ezetimibe) represented 0.98% (n = R58 326 901.67) of the total active ingredient cost in this age group in 2005, ranking third. However, in 2006 cholesterol absorption inhibitors ranked second regarding total hipolipidaemic medicine cost in male patients, accounting for 3.42% (n = R64 402 386.68). The “others” therapeutic class accounted for the lowest percentage of hipolipidaemic medicine item cost in male patients in both 2005 and 2006, accounting for 0.56% (n = R58 326 901.67) and 0.39% (n = R64 402 386.68) respectively. Cholestyramine accounted for 0.51% (n = R58 326 901.67) in 2005 and 0.35% (n = R64 402 386.68) in 2006.

4.5.5 Analysis of hipolipidaemic active ingredients based on generic indicator and age groups

This section will focus on the generic indicators related to hipolipidaemic active ingredients as prescribed to the different age groups in 2005 and 2006. Figure 4.7 through to figure 4.11 represent (a) the prevalence and (b) cost percentages of generic indicators related to specific age groups. The percentages of active ingredients per age group resemble the percentages

that were made up by that specific active ingredient (refer to paragraph 4.6.1 and Appendix B2.42, B2.43, B2.44, B2.45, B2.46, B2.47, B2.48, B2.49, B2.50, B2.51).

4.5.5.1 Age group 1: Children between the ages of 0 and 9 years

Figure 4.7 contains (a) the prevalence and (b) cost percentages for generic indicators of active ingredients as recorded for children aged 0 ≤ 9 years of age during 2005 and 2006. Figure 4.7 is drawn from the prevalence and cost in tables B2.42 and B2.43 in appendix B, reflecting the hipolipidaemic data on the database of both 2005 and 2006 and their indicidual periods based on active ingredients, generic indicators and age group 1.

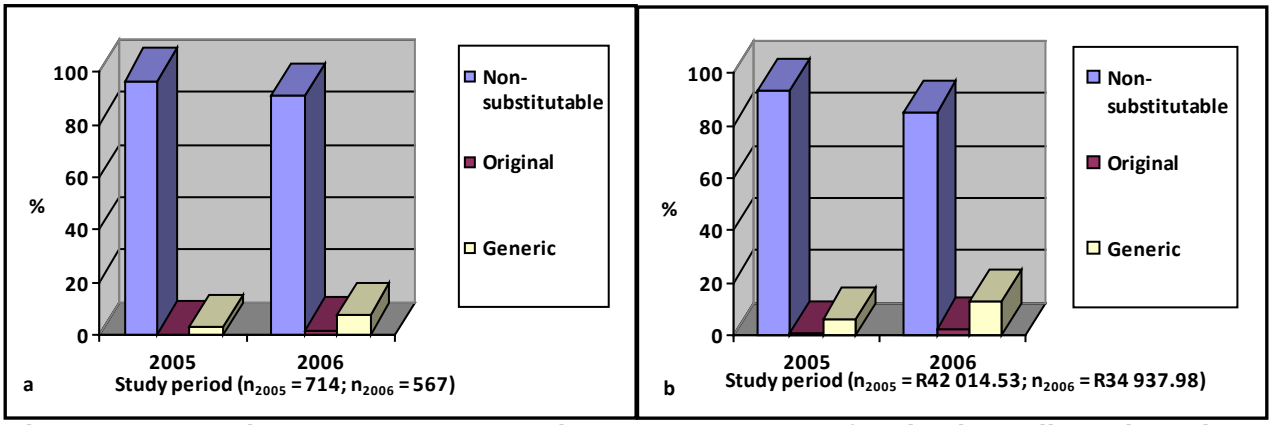

Figure 4.7: Prevalence percentages and cost percentages of active ingredients based on generic indicators in children between the ages of 0 ≤ 9 years

Non-substitutable hipolipidaemic medicine items accounted for 96.64% (n = 714) of all hipolipidaemic medicine items in children aged 0 ≤ 9 years of age in 2005 and 91.18% (n = 567) in 2006 (Figure 4.7a). In both study periods, cholestyramine was the leading active ingredient in this group based on prevalence, accounting for 87.54% (n = 714) in 2005 and 80.25% (n = 567) in 2006. Atorvastatin ranked second in 2005 and 2006, accounting for 8.54% (n = 714) and 9.36% (n = 567) of all active ingredients in this age group respectively. Non-substitutable hipolipidaemic medicine items accounted for 93.47% (n = R42 014.53) of the total hipolipidaemic medicine cost in this age group (Figure 4.7b) in 2005 and 84.94% (n = R34 937.98) in 2006. Cholestyramine specifically represented 58.90% (n = R42 014.53) of the total active ingredient cost in this age group in 2005, and also accounted for 45.54% (n = R34 937.98) in 2006. Atorvastatin accounted for 30.29% (n = R42 014.53) and 31.64% (n = R34 937.98) of the total active ingredient cost in children aged 0≤ 9 years in 2005 and 2006 respectively.

Original hipolipidaemic medicine items in children aged 0 ≤ 9 years of age (Figure 4.7a) accounted for 0.28% (n = 714) in 2005 and 1.59% (n = 567) in 2006. Simvastatin was the only

original claimed active ingredient in 2005, thus carrying the total 0.28% (n = 714) of all active ingredients in this age group, whilst in 2006, pravastatin accounted for 0.71% (n = 567) of the total active ingredients in this age group and simvastatin 0.88% (n = 567). Original hipolipidaemic medicine items respectively presented 0.66% (n = R42 014.53) and 2.39% (n = R34 937.98) of the total cost of hipolipidaemic medicine items in children aged ≤ 9 years in 2005 and 2006 (Figure 4.7b). The active ingredient, simvastatin accounted for 0.66% (n = R42 014.53) of the total hipolipidaemic cost in this age group in 2005 and 1.17% (n = R34 937.98) in 2006. Pravastatin accounted for 1.22% (n = R34 937.98) of active ingredient cost in children 0 ≤ 9 years of age in 2006.

Generic hipolipidaemic medicine items respectively accounted for 3.08% (n = 714) and 7.23% (n = 567) of hipolipidaemic medicine items in this age group in 2005 and 2006 (Figure 4.7a). Generic simvastatin had the highest prevalence percentage in this age group in both study periods with 2.66% (n = 714) in 2005 and 7.24% (n = 567) in 2006 at a cost percentage of 5.02% (n = R42 014.53) of the total hipolipidaemic cost in 2005 and 12.66% (n = R34 937.98) in 2006 (Figure 4.7b). Overall, generic hipolipidaemic active ingredients represented 5.87% (n = R42 014.53) of the total hipolipidaemic cost in children aged 0 ≤ 9 years in 2005 and 12.66% (n = R34 937.98) in 2006. Simvastatin was the only generic hipolipidaemic active ingredient claimed for children aged 0 ≤ 9 years in 2006.

4.5.5.2 Age group 2: Adolescents between the ages of 10 and 19 years

Figure 4.8 contains (a) the prevalence percentages and (b) cost percentages for generic indicators of hipolipidaemic medicine items as recorded for adolescents aged 10 ≤ 19 years of age during 2005 and 2006. Figure 4.8 is drawn from the prevalence and cost in tables B2.44 and B2.45 in appendix B, reflecting the hipolipidaemic data on the database of both 2005 and 2006 and their indicidual periods based on active ingredients, generic indicators and age group 2.

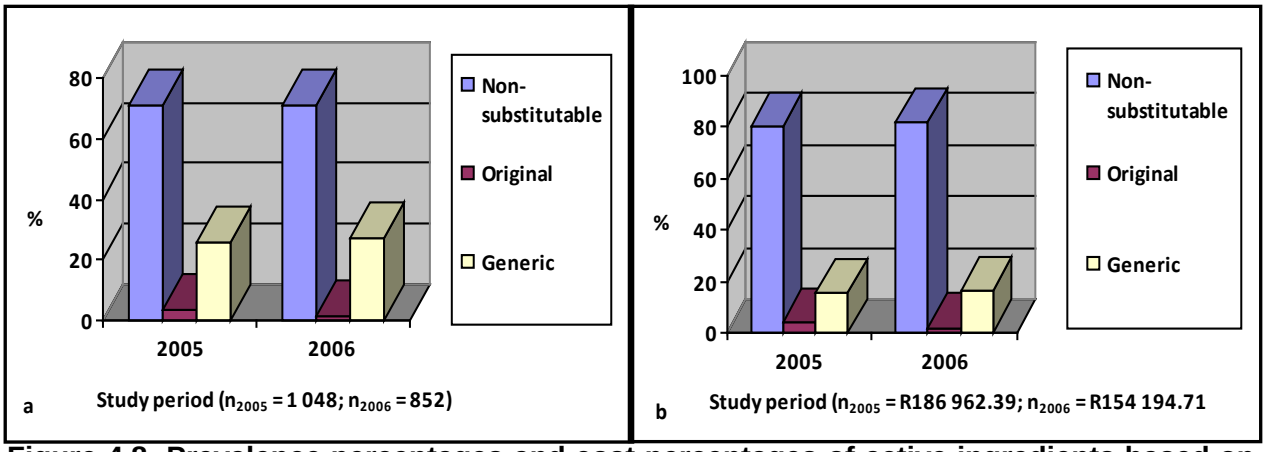

Figure 4.8: Prevalence percentages and cost percentages of active ingredients based on generic indicators in adolescents between the ages of 10 and 19 years

Non-substitutable hipolipidaemic medicine items accounted for 71.09% (n = 1 048) of all hipolipidaemic medicine items in adolescents aged 10 ≤ 19 years of age in 2005 and 71.01% (n = 852) in 2006 (Figure 4.8a). In both study periods atorvastatin was the leading non-substitutable active ingredient based on prevalence, accounting for 61.07% (n = 1 048) in 2005 and 52.46% (n = 852) in 2006. Atorvastatin was followed by cholestyramine in second ranking position in 2005 and 2006 representing 5.92% (n = 1 048) and 7.39% (n = 852) of all active ingredients in this age group respectively. Non-substitutable medicine items accounted for 80.08% (n = R186 962.39) of the total hipolipidaemic medicine cost in this age group (Figure 4.8b) in 2005 and 81.64% (n = R154 194.71) in 2006. Atorvastatin specifically accounted for 72.74% (n = R186 962.39) of the total active ingredient cost in this age group in 2005, and also accounted for 63.94% (n = R154 194.71) in 2006. Ezetimibe followed atorvastatin at the second highest cost percentage for active ingredients in adolescents aged 10 ≤ 19 years of age accounting for 2.63% (n = R186 962.39) and 6.71% (n = R154 194.71) in 2005 and 2006 respectively.

Original hipolipidaemic medicine items in adolescents aged 10 ≤ 19 years of age (Figure 4.8a) accounted for 3.44% (n = 1 048) of all hipolipidaemic medicine items in 2005 and 1.64% (n = 852) in 2006. Original simvastatin claimed the first ranking position of active ingredients in 2005 at 1.71% (n = 1 048); whilst in 2006 this ranking position was occupied by pravastatin at 0.71% (n = 852). In 2006, simvastatin accounted for 0.58% (n = 852) of the total number of hipolipidaemic active ingredients. In 2005 and 2006 original hipolipidaemic medicine items respectively accounted for 4.15% (n = R186 962.39) and 2.05% (n = R154 194.71) of the total cost percentage of hipolipidaemic medicine items in this age group (Figure 4.8b). Bezafibrate accounted for 1.47% (n = R186 962.39) of the total active ingredient cost in this age group in 2005. However, it accounted for only 0.66% (n = R154 194.71) in 2006. Simvastatin represented 1.63% (n = R186 962.39) of the total cost in 2005 and 0.57% (n = R154 194.71) in

2006. Pravastatin accounted for 1.05% (n = R186 962.39) of active ingredient cost in adolescents 10 ≤ 19 years of age in 2005 and 0.82% (n = R154 194.71) in 2006.

Generic hipolipidaemic medicine items respectively accounted for 25.48% (n = 1 048) and 27.35% (n = 852) of hipolipidaemic medicine items in adolescents aged 10 ≤ 19 years of age in 2005 and 2006 (Figure 4.8a). Generic simvastatin had the highest prevalence percentage in both study periods with 24.62% (n = 1 048) in 2005 and 24.28% (n = 852) in 2006; followed by generic bezafibrate with a prevalence percentage of 0.38% (n = 1048) in 2005 and generic pravastatin in 2006 with 1.64% (n = 852). Generic hipolipidaemic medicine items made up 15.77% (n = R186 962.39) of the total hipolipidaemic cost in this age group in 2005 and 16.31% (n = R154 194.71) in 2006 (Figure 4.8b). Simvastatin accounted for 15.22% (n = R42 014.53) of the total hipolipidaemic cost in 2005 and 14.48% (n = R34 937.98) in 2006.

4.5.5.3 Age group 3: Young adults between the ages of 20 and 45 years

Figure 4.9 shows (a) the prevalence percentages and (b) cost percentages for generic indicators of hipolipidaemic medicine items as recorded for adults aged 20 ≤ 45 years of age during 2005 and 2006. Figure 4.9 is drawn from the prevalence and cost in tables B2.46 and B2.47 in appendix B, reflecting the hipolipidaemic data on the database of both 2005 and 2006 and their indicidual periods based on active ingredients, generic indicators and age group 3.

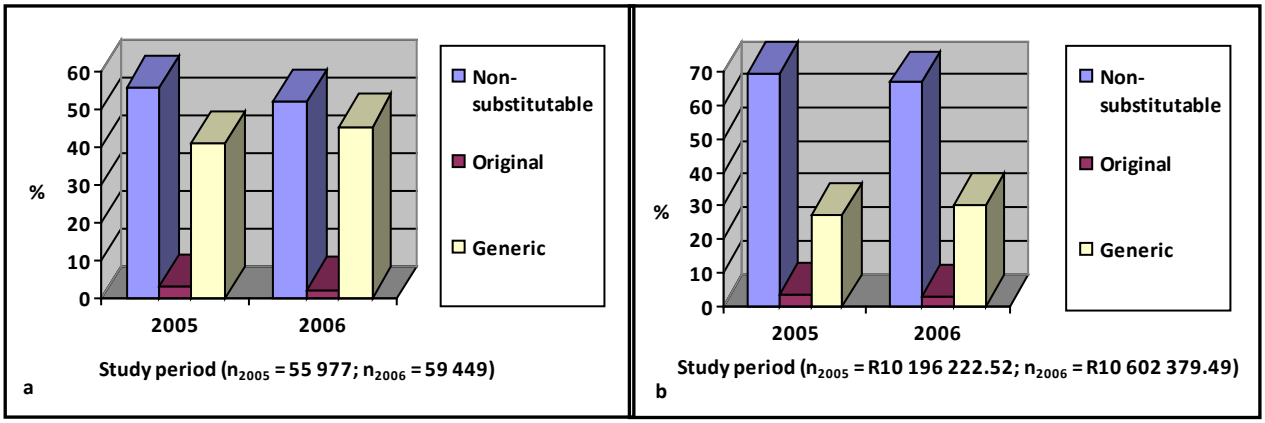

Figure 4.9: Prevalence percentages and cost percentages of active ingredients based on generic indicators in young adults between the ages of 20 and 45 years

Non-substitutable medicine items accounted for 55.86% (n = 55 977) of all hipolipidaemic medicine items in patients aged 20 ≤ 45 years of age in 2005 and 52.20% (n = 59 449) in 2006 (Figure 4.9a). In both study periods, based on prevalence, atorvastatin was the leading non-substitutable active ingredient accounting for 47.09% (n = 55 977) in 2005 and 41.67% (n = 59 449) in 2006. Fluvastatin ranked second in 2005 for patients aged 20 ≤ 45 years, representing 3.92% (n = 55 977) and in 2006 rosuvastatin accounted for 3.68% (n = 59 449) of all active

ingredients in this age group. Non-substitutable hipolipidaemic medicine items accounted for 69.51% (n = R10 196 222.52) of the total hipolipidaemic medicine cost in this age group in 2005 and 66.95% (n = R10 602 379.49) in 2006 (Figure 4.9b). Atorvastatin specifically accounted for 59.14% (n = R10 196 222.52) of the total active ingredient cost in this age group in 2005, and also accounted for 54.02% (n = R10 602 379.49) in 2006' followed by fluvastatin in the second highest cost percentage ranking position for 2005 for active ingredients in this age group accounting for 4.26% (n = R10 196 222.52). In 2006, ezetimibe was the active ingredient with the second highest cost percentage for active ingredients in this age group with 4.39% (n = R10 602 379.49) of the total hipolipidaemic cost in this age group and was followed by rosuvastatin at 4.26% (n = R10 602 379.49).

Original hipolipidaemic medicine items in patients aged 20 ≤ 45 years of age (Figure 4.9a) accounted for 3.09% (n = 55 977) in 2005 and 2.24% (n = 59 449) in 2006. Original simvastatin, ranking highest in prevalence percentage, accounted for 1.59% (n = 55 977) of the total active ingredients in this age group in 2005; whereas in 2006, this ranking position was filled by pravastatin accounting for 1.12% (n = 59 449) of the total active ingredients in this age group. In 2005 and 2006 original hipolipidaemic medicine items respectively represented 3.50% (n = R10 196 222.52) and 2.71% (n = R10 602 379.49) of the total cost of hipolipidaemic medicine items in patients aged 20 ≤ 45 years (Figure 4.9b). Original pravastatin represented 1.52% (n = R10 196 222.52) of the total active ingredient cost in this age group in 2005 and 1.34% (n = R10 602 379.49) in 2006. Original simvastatin ranked second in cost percentage after pravastatin at 1.34% (n = R10 196 222.52) in 2005 and 0.74% (n = R10 602 379.49) in 2006. Original bezafibrate accounted for 0.64% (n = R10 196 222.52) of active ingredient cost in patients 20 ≤ 45 years of age in 2005 and 0.49% (n = R10 602 379.49) in 2006.

Generic hipolipidaemic medicine items accounted for 41.05% (n = 55 977) and 45.56% (n = 59 449) of hipolipidaemic medicine items in this age group respectively in 2005 and 2006 (Figure 4.9a). Generic simvastatin had the highest prevalence percentage in both study periods in this age group with 37.94% (n = 55 977) in 2005 and 40.60% (n = 59 449) in 2006. Generic hipolipidaemic medicine items represented 27.00% (n = R10 196 222.52) of the total hipolipidaemic medicine cost for patients aged 20 ≤ 45 years in 2005 and 30.34% (n = R10 602 379.49) in 2006 (Figure 4.9b). Generic simvastatin accounted for 24.09% (n = R10 196 222.52) of the total active ingredient cost in 2005 and 25.77% (n = R10 602 379.49) in 2006. Generic bezafibrate had the second highest ranking based on cost percentage of active ingredients in this age group in both study periods, accounting for 2.38% (n = R10 196 222.52) in 2005 and 2.90% (n = R10 602 379.49) in 2006.

4.5.5.4 Age group 4: Older adults between the ages of 46 and 59 years

Figure 4.10 contains (a) the prevalence percentages and (b) cost percentages for generic indicators of hipolipidaemic medicine items as recorded for adults aged 46 ≤ 59 years of age during 2005 and 2006. Figure 4.10 is drawn from the prevalence and cost in tables B2.48 and B2.49 in appendix B, reflecting the hipolipidaemic data on the database of both 2005 and 2006 and their indicidual periods based on active ingredients, generic indicators and age group 4.

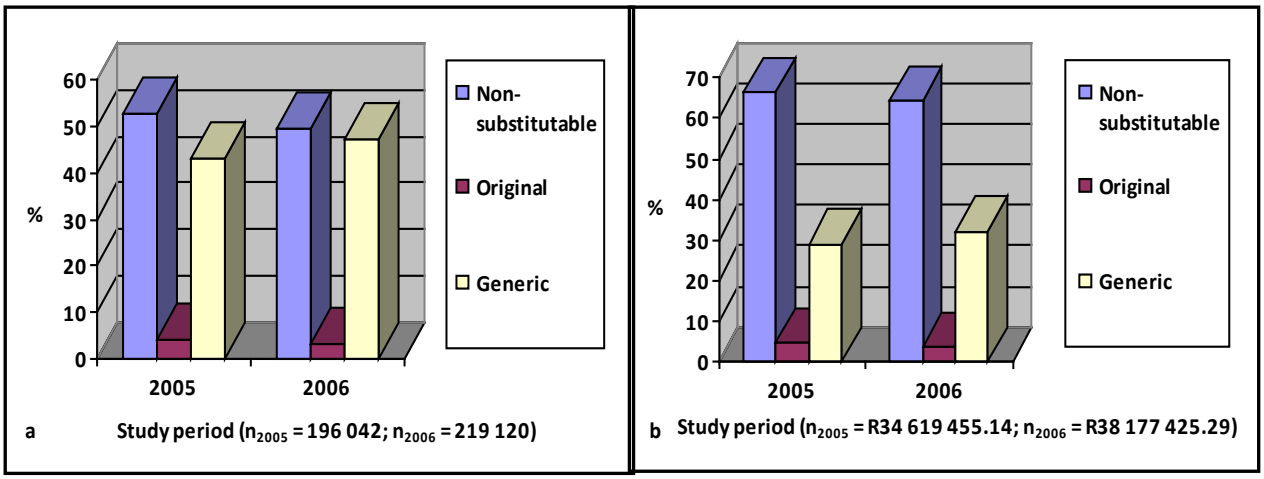

Figure 4.10: Prevalence and cost percentages of active ingredients based on generic indicators in older adults between the ages of 46 and 59 years

Non-substitutable hipolipidaemic medicine items accounted for 52.56% (n = 196 042) of all hipolipidaemic medicine items in patients aged 46 ≤ 59 years of age in 2005 and 49.53% (n = 219 120) in 2006 (Figure 4.10a). In both study periods atorvastatin was the leading non-substitutable active ingredient based on prevalence, accounting for 44.64% (n = 196 042) in 2005 and 40.68% (n = 219 120) in 2006. Fluvastatin ranked second in 2005 for non-substitutable active ingredients for patients aged 46 ≤ 59 years, accounting for 4.14% (n = 196 042) and 2.84% (n = 219 120) in 2006. Rosuvastatin ranked third based on prevalence of active ingredients in this age group in 2006, accounting for 2.49% (n = 219 120). Non-substitutable hipolipidaemic medicine items accounted for 66.32% (n = R34 619 455.14) of the total hipolipidaemic medicine cost in this age group in 2005 and 64.29% (n = R34 619 455.14) (Figure 4.10b). Atorvastatin specifically accounted for 56.41% (n = R34 619 455.14) of the total active ingredient cost in this age group in 2005, also accounting for 52.95% (n = R38 177 425.29) in 2006. Fluvastatin, had the second highest cost percentage for active ingredients in this age group accounting for 4.59% (n = R34 619 455.14) in 2005; whilst ezetimibe filled this ranking position in 2006 at 3.85% (n = R38 177 425.29), followed by rosuvastatin, at 2.99% (n = R38 177 425.29).

Figure 4.10a shows that original hipolipidaemic medicine items in patients aged 46 ≤ 59 years of age accounted for 4.26% (n = 196 042) in 2005 and 3.08% (n = 219 120) in 2006. Original simvastatin accounted for 2.53% (n = 196 042) in 2005, and 1.50% (n = 219 120) in 2006. Original pravastatin ranked second based on prevalence percentage for total active ingredients in this age group, accounting for 1.52% (n = 196 042) in 2005 and 1.39% (n = 219 120) in 2006. In 2005 and 2006 original hipolipidaemic medicine items respectively accounted for 4.66% (n = R34 619 455.14) and 3.57% (n = R38 177 425.29) of the total cost of hipolipidaemic medicine items in this age group (Figure 4.10b). In 2005, original simvastatin ranked first regarding cost percentage for active ingredients in this age group representing 2.21% (n = R34 619 455.14) of the total active ingredient cost in this age group; followed by pravastatin at 2.03% (n = R34 619 455.14). An invert utilisation pattern followed in 2006, with pravastatin as the highest ranking ingredient accounting for 1.88% (n = R38 177 425.29) of the total active ingredient cost followed by original simvastatin at 1.30% (n = R38 177 425.29). Original bezafibrate accounted for less than 0.50% of the total cost of active ingredients in both study periods in patients aged 46 ≤ 59 years.

Generic hipolipidaemic medicine items accounted for 43.18% (n = 196 042) and 47.39% (n = 219 120) respectively of hipolipidaemic medicine items in patients aged 46 ≤ 59 years in 2005 and 2006 (Figure 4.10a). Generic simvastatin had the highest prevalence percentage in both study periods at 40.22% (n = 196 042) in 2005 and 42.65% (n = 219 120) in 2006, followed by generic bezafibrate accounting for 2.34% (n = 196 042) in 2005 and 2.63% (n = 219 120) in 2006. Figure 4.10b shows that generic hipolipidaemic medicine items accounted for 29.03% (n = R34 619 455.14) of the total hipolipidaemic cost in this age group in 2005 and 32.13% (n = R38 177 425.29) in 2006. Generic simvastatin, ranking also first for cost percentage in patients aged 46 ≤ 59 years, accounted for 26.22% (n = R34 619 455.14) of the total active ingredient cost in 2005 and 27.66% (n = R38 177 425.29) in 2006. Bezafibrate had the second highest ranking again in both study periods, accounting for 2.29% (n = R34 619 455.14) in 2005 and 2.61% (n = R38 177 425.29) in 2006. Generic pravastatin accounted for 0.48% (n = R34 619 455.14) and 1.81% (n = R38 177 425.29) respectively for 2005 and 2006.

4.5.5.5 Age group 5: Patients older than 59 years of age

Figure 4.11 contains (a) the prevalence percentages and (b) cost percentages for generic indicators of hipolipidaemic medicine items as recorded for adults aged > 59 years of age during 2005 and 2006. Figure 4.11 is drawn from the prevalence and cost in tables B2.50 and B2.51 in appendix B, reflecting the hipolipidaemic data on the database of both 2005 and 2006 and their indicidual periods based on active ingredients, generic indicators and age group 5.

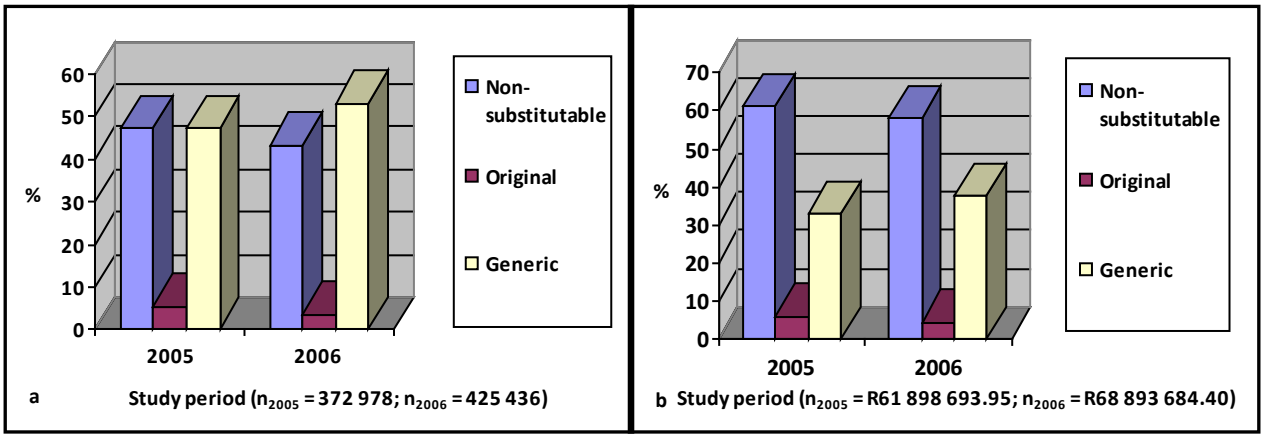

Figure 4.11: Prevalence percentages and cost percentages of active ingredients based on generic indicators in patients older than 59 years of age

Non-substitutable hipolipidaemic medicine items accounted for 47.34% (n = 372 978) of all hipolipidaemic medicine items in patients aged > 59 years of age in 2005 and 43.25% (n = 425 436) in 2006 (Figure 4.11a). In both study periods atorvastatin was the leading non-substitutable active ingredient based on prevalence, accounting for 39.00% (n = 372 978) in 2005 and 35.76% (n = 425 436) in 2006. Fluvastatin ranked second in 2005 at 4.15% (n = 372 978) and 3.21% (n = 425 436) in 2006, followed by rosuvastatin accounting for 1.56% (n = 425 436) of all active ingredients prescribed for patients aged > 59 years of age in 2006. According to Figure 4.11b, non-substitutable medicine items accounted for 61.01% (n = R61 898 693.95) of the total hipolipidaemic medicine cost in this age group in 2005 and 57.91% (n = R68 893 684.40) in 2006. Atorvastatin specifically accounted for 50.21% (n = R61 898 693.95) of the total active ingredient cost in 2005, and also accounted for 47.94% (n = R68 893 684.40) in 2006. Fluvastatin, ranking second highest in 2005 in this age group accounted for 4.75% (n = R61 898 693.95); and was followed by pravastatin at 3.31% (n = R61 898 693.95). In 2006, ezetimibe had the second highest cost percentage for active ingredients in this age group at 2.76% (n = R68 893 684.40) of the total cost, followed by fluvastatin at 3.76% (n = R68 893 684.40).

Original hipolipidaemic medicine items in patients aged > 59 years of age accounted for 5.42% (n = 372 978) in 2005 and 3.68% (n = 425 436) in 2006 (Figure 4.11a). Original pravastatin ranked first based on prevalence percentage for total active ingredients in this age group, accounting for 1.94% (n = 372 978) of total hipolipidaemic medicine items in 2005, and 1.55% (n = 425 436) in 2006. Original simvastatin ranked second, accounting for 3.30% (n = 372 978) in 2005 and 1.96% (n = 425 436) in 2006. In 2005 and 2006 original hipolipidaemic medicine items respectively represented 6.00% (n = R61 898 693.95) and 4.36% (n = R68 893 684.40) of the total cost of hipolipidaemic medicine items in this age group (Figure 4.11b). Original simvastatin ranked first in 2005 regarding cost percentage of active ingredients in this age

group accounting for 2.96% (n = R61 898 693.95), and was succeeded by original pravastatin at 2.69% (n = R61 898 693.95). In 2006 an inverse ranking order between original pravastatin and original simvastatin occurred, with pravastatin ranking first, accounting for 2.22% (n = R68 893 684.40) and simvastatin accounting for 1.81% (n = R68 893 684.40). Bezafibrate accounted for less than 0.40% of the total cost of active ingredients in both study periods in patients aged > 59 years.

Generic hipolipidaemic medicine items respectively accounted for 47.24% (n = 372 978) and 53.07% (n = 425 436) of hipolipidaemic medicine items claimed in patients aged > 59 years of age in 2005 and 2006 (Figure 4.11a). Generic simvastatin had the highest prevalence percentage in both study periods with 44.82% (n = 372 978) in 2005 and 48.50% (n = 425 436) in 2006. Generic bezafibrate ranked second at 1.73% (n = 372 978) in 2005; and third in 2006 at 1.86% (n = 425 436) of the total active ingredients in this age group. Generic pravastatin had the second highest ranking position in patients > 59 years of age in 2006, accounting for 2.65% (n = 425 436). According to Figure 4.11b, generic hipolipidaemic medicine items made up 32.99% (n = R61 898 693.95) of the total hipolipidaemic medicine item cost in this age group in 2005 and 37.73% (n = R68 893 684.40) in 2006. Generic simvastatin, ranking first for active ingredients in patients aged > 59 years in both study periods, accounted for 30.66% (n = R61 898 693.95) of the total active ingredient cost in 2005 and 33.29% (n = R68 893 684.40) in 2006. Generic bezafibrate had the second highest ranking based on cost percentage of active ingredients in this age group in 2005, accounting for 1.75% (n = R61 898 455.14), followed by generic pravastatin in the third position at 0.57% (n = R61 898 693.95). An inverse utilisation pattern was observed in 2006 by the latter two active ingredients, with generic pravastatin in the second position accounting for 2.49% (n = R68 893 684.40) of total hipolipidaemic medicine cost in patients aged > 59 and bezafibrate in the third position at 1.95% (n = R68 893 684.40).

4.5.6 Analysis of hipolipidaemic active ingredients based on generic indicator and sex categories

This section will focus on the generic indicators related to hipolipidaemic active ingredients as prescribed based on the patient's sex in 2005 and 2006. Figure 4.12 and figure 4.13 represent (a) the prevalence percentages and (b) cost percentages of generic indicators related to the specific sex of the patient. The percentages of active ingredients per sex group resemble the percentages that were made up by that specific active ingredient (paragraph 4.6.2 and Appendix B2.52 and B2.53).

4.5.6.1 Female patients

Figure 4.12 contains (a) the prevalence percentages and (b) cost percentages for generic indicators of hipolipidaemic medicine items as recorded for female patients during 2005 and 2006. Figure 4.12 is drawn from the prevalence and cost in tables B2.52 and B2.53 in appendix B, reflecting the hipolipidaemic data on the database of both 2005 and 2006 and their indicidual periods based on active ingredients, generic indicators and the female sex.

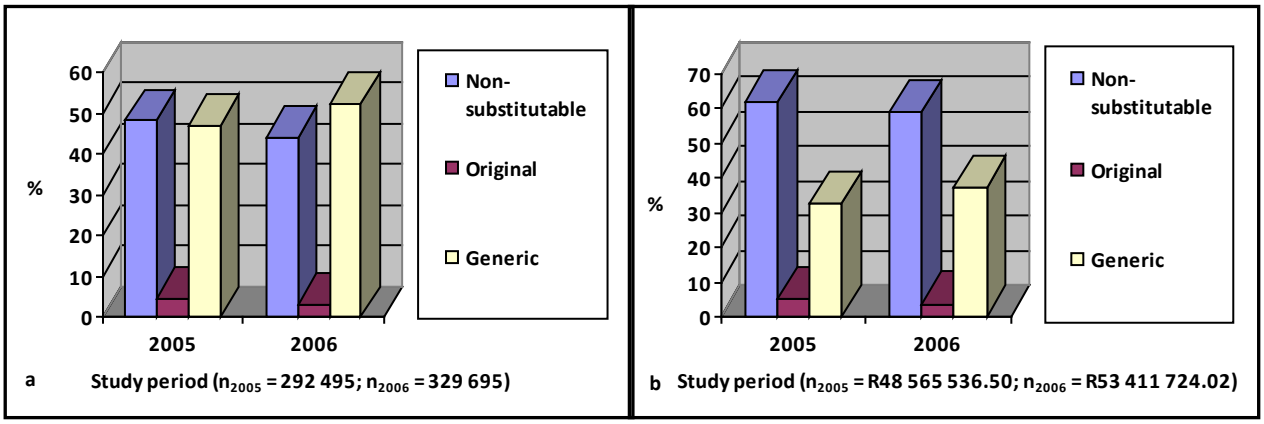

Figure 4.12: Prevalence percentages and cost percentages based on generic indicators in female patients

Non-substitutable hipolipidaemic medicine items accounted for 48.22% (n = 292 495) of all hipolipidaemic medicine items in female patients in 2005 and 44.22% (n = 329 695) in 2006 (Figure 4.12a). In both study periods, based on prevalence, atorvastatin was the leading non-substitutable hipolipidaemic medicine item, accounting for 39.42% (n = 292 495) of all hipolipidaemic medicine items claimed in 2005 and 35.86% (n = 329 695) in 2006. Fluvastatin ranked second in 2005 for non-substitutable hipolipidaemic medicine items for female patients, accounting for 4.44% (n = 292 695) and 3.22% (n = 329 695) in 2006. Rosuvastatin succeeded fluvastatin in 2006, at 1.89% (n = 329 695). Figure 4.12b shows that non-substitutable hipolipidaemic medicine items accounted for 62.01% (n = R48 565 536.50) of the total hipolipidaemic medicine cost in females in 2005 and 58.96% (n = R53 411 724.02) in 2006. Atorvastatin specifically accounted for 50.93% (n = R48 565 536.50) of the total active ingredient cost in females in 2005, and also accounted for 48.13% (n = R53 411 724.02) in 2006. Fluvastatin ranked the second highest in cost percentage for active ingredients prescribed to females at 5.08% (n = R48 565 536.50) in 2005 and 3.76% (n = R53 411 724.02) in 2006. Pravastatin accounted for 3.17% (n = R48 565 536.50) of the total active ingredient cost in female patients, ranking third for non-substitutable medicine items in 2005. Ezetimibe had the third highest cost percentage for active ingredients in the female sex with 3.08% (n = R53 411 724.02) in 2006. Rosuvastatin accounted for 1.89% (n = R53 411 724.02) of the total cost in 2006.

Original hipolipidaemic medicine items in female patients (Figure 4.12a) accounted for 4.76% (n = 292 495) in 2005 and 3.33% (n = 329 695) in 2006. Original simvastatin ranked first based on prevalence percentage of active ingredients in female patients, accounting for 2.80% (n = 292 495) in 2005 and 1.62% (n = 329 695) in 2006. Original pravastatin ranked second based on prevalence percentage for active ingredients in females in 2005, accounting for 1.81% (n = 292 495), and 1.57% (n = 329 695) in 2006. In 2005 and 2006 original hipolipidaemic medicine items respectively represented 5.28% (n = R48 565 536.50) and 3.97% (n = R53 411 724.02) of the total cost of hipolipidaemic medicine items in the female sex (Figure 4.12b). Original simvastatin ranked first regarding cost percentage for active ingredients in this age group accounting for 2.49% (n = R48 565 536.50) in 2005, followed by original pravastatin at 2.48% (n = R48 565 536.50). The latter two active ingredients followed an inverse ranking order in 2006, with pravastatin ranking at 2.21% (n = R53 411 724.02), and simvastatin second at 1.47% (n = R53 411 724.02). Original bezafibrate accounted for less than 0.15% of the total cost of active ingredients in female patients for both study periods.

Generic hipolipidaemic medicine items respectively accounted for 47.02% (n = 292 495) and 52.46% (n = 329 695) in 2005 and 2006 in the female sex (Figure 4.12a). Generic simvastatin had the highest prevalence percentage in both study periods at 44.60% (n = 292 495) in 2005 and 48.08% (n = 329 695) in 2006. Generic bezafibrate ranked second based on prevalence percentage in 2005, accounting for 1.72% (n = 292 495), followed by generic pravastatin at 0.64% (n = 292 495). Generic pravastatin ranked second in 2006 with 2.60% (n = 329 695), preceding generic bezafibrate in the third place at 1.75% (n = 329 695). Generic hipolipidaemic medicine items represented 32.71% (n = R48 565 536.50) of the total hipolipidaemic cost in females in 2005 and 37.07% (n = R53 411 724.02) in 2006 (Figure 4.12b). Generic simvastatin, ranked first in female patients, accounted for 30.37% (n = R48 565 536.50) of the generic ingredient cost in 2005 and was followed by generic bezafibrate at 1.75% (n = R48 565 536.50), and generic pravastatin at 0.58% (n = R48 565 536.50). Generic simvastatin again ranked first in female patients in 2006, at 32.80% (n = R53 411 724.02), and was followed by generic pravastatin in the second place at 2.42% (n = R53 411 724.02) and thirdly, generic bezafibrate at 1.83% (n = R53 411 724.02).

4.5.6.2 Male patients

Figure 4.13 contains (a) the prevalence percentages and (b) cost percentages for generic indicators of hipolipidaemic medicine items as recorded for male patients during 2005 and 2006. Figure 4.13 is drawn from the prevalence and cost in tables B2.52 and B2.53 in appendix B, reflecting the hipolipidaemic data on the database of both 2005 and 2006 and their indicidual periods based on active ingredients, generic indicators and the male sex.

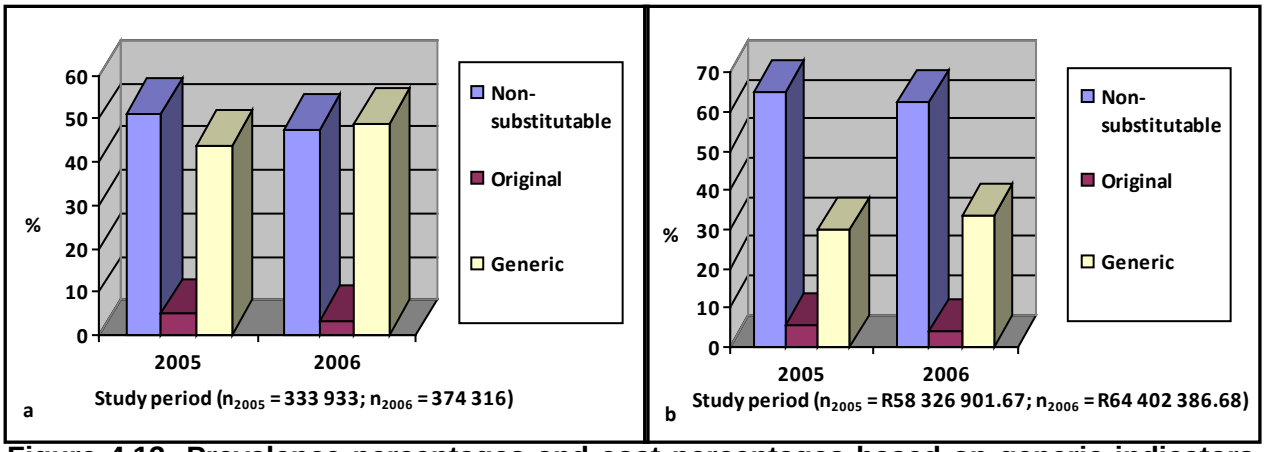

Figure 4.13: Prevalence percentages and cost percentages based on generic indicators in male patients

Non-substitutable items accounted for 51.26% (n = 333 933) of all hipolipidaemic medicine items in male patients in 2005 and 47.63% (n = 374 316) in 2006 (Figure 4.13a). In both study periods atorvastatin was the leading non-substitutable hipolipidaemic medicine item based on prevalence, accounting for 43.34% (n = 333 933) in 2005 and 39.62% (n = 374 316) in 2006. Fluvastatin ranked second in 2005 accounting for 3.82% (n = 333 933) and 2.84% (n = 374 316) in 2006. Rosuvastatin ranked third based on prevalence of active ingredients in males in 2006, accounting for 2.17% (n = 374 316). Non-substitutable hipolipidaemic medicine items accounted for 64.91% (n = R58 326 901.67) of the total hipolipidaemic medicine cost in the male sex in 2005 and 62.39% (n = R64 402 386.68) in 2006 (Figure 4.13b). Atorvastatin specifically represented 54.93% (n = R58 326 901.67) of the active ingredient cost in males in 2005, and also accounted for 51.80% (n = R64 402 386.68) in 2006. Fluvastatin had the second highest cost percentage for active ingredients claimed in 2005 accounting for 4.25% (n = R58 326 901.67), followed by pravastatin in the third place at 2.73% (n = R58 326 901.67). Ezetimibe ranked second for male patients regarding total cost in 2006, accounting for 3.42% (n = R64 402 386.68). Fluvastatin ranked third in 2006 with 3.21% (n = R64 402 386.68) of total active ingredient cost in male patients. Rosuvastatin accounted for 2.17% (n = R64 402 386.68) of the total cost of active ingredients in male patients in 2006.

Original hipolipidaemic medicine items in male patients (Figure 4.13a) accounted for 4.90% (n = 333 933) in 2005 and 3.40% (n = 374 316) in 2006. Original simvastatin ranked first based on prevalence percentage of active ingredients in male patients in 2005, accounting for 2.99% (n = 333 933), followed by original pravastatin at 1.66% (n = 333 933). A similar utilisation pattern followed in 2006, with original simvastatin ranking first at 1.83% (n = 374 316) and original pravastatin second based on prevalence percentage for total active ingredients in males in 2006, accounting for 1.36% (n = 374 316) in 2006. Original hipolipidaemic medicine items respectively accounted for 5.35% (n = R58 326 901.67) and 3.93% (n = R64 402 386.68) of the

total cost of hipolipidaemic medicine items in the male sex in 2005 and 2006 (Figure 4.13b). In accordance with the prevalence percentage original active ingredients in males in 2005, original simvastatin ranked first in 2005 regarding cost percentage of active ingredients accounting for 2.60% (n = R58 326 901.67) in males, followed by original pravastatin at 2.27% (n = R58 326 901.67). In 2006, however, original simvastatin ranked second at 2.27% (n = R64 402 386.68), preceded by original pravastatin at 1.90% (n = R64 402 386.68) of the total active ingredient cost in 2006. Original bezafibrate accounted for less than 0.50% of the total cost of active ingredients in male patients in both study periods.

Generic hipolipidaemic medicine items respectively accounted for 43.84% (n = 333 933) and 48.97% (n = 374 316) of hipolipidaemic medicine items in male patients in 2005 and 2006 (Figure 4.13a). Generic simvastatin had the highest prevalence percentage in both study periods in males at 40.98% (n = 333 933) in 2005 and 43.93% (n = 374 316) in 2006. Generic bezafibrate ranked second in 2005, accounting for 2.22% (n = 333 933). Bezafibrate also ranked second in 2006 at 2.59% (n = 374 316) of the total number of active ingredients in males. Generic pravastatin ranked third as in 2005, accounting for 0.55% (n = 333 933) and 2.24% (n = 329 695) in 2006. Figure 4.13b shows that generic hipolipidaemic medicine items made up 29.74% (n = R58 326 901.67) of the total hipolipidaemic cost in the male sex in 2005 and 33.67% (n = R64 402 386.68) in 2006. Simvastatin, ranking first for generic active ingredients in male patients, accounted for 27.04% (n = R58 326 901.67) of the total cost in 2005 and 29.04% (n = R64 402 386.68) in 2006. Bezafibrate had the second highest ranking based on cost percentage of active ingredients in the male sex in 2005 and 2006, accounting for 2.18% (n = R58 326 901.67) and 2.59% (n = R64 402 386.68). Generic pravastatin accounted for 0.50% (n = R58 326 901.67) in 2005, and for 2.02% (n = R64 402 386.68) in 2006, thus ranking third in both study periods.

4.5.7 Summary and discussion on the prescribing patterns of hipolipidaemics based on active ingredients

In the subsequent sections summaries on the prescribing patterns of hipolipidaemics based on active ingredients will be discussed.

4.5.7.1 Summary and discussion on the analysis of the prevalence and cost of hipolipidaemic active ingredients

In conclusion to the previous paragraphs, it is clear that the HMG-CoA reductase inhibitor therapeutic class (statins) contributed to the largest percentage of hipolipidaemic medicine items in both study periods; specifically the active ingredients simvastatin and atorvastatin. An

equal number of statins had CPIs-values above- and below 1, indicating expensive and inexpensive treatment products on the market. Fibrates in both study periods had CPIs above one, indicating that that fibrates in general can be considered as expensive treatment. Ezetimibe (cholesterol absorption inhibitors) was also relatively high-priced, with CPIs in both study periods of above 2. Simvastatin, which was the largest contributor to the total number of active ingredients on the database, was relatively inexpensive in both study periods.

Raymond and co-workers (2007:2107) conducted a study of statin utilisation in British Columbia and found that the use of statins in an entire population increased dramatically, especially the use of simvastatin, atorvastatin and rosuvastatin.

HMG-CoA reductase inhibitors (in particular, atorvastatin and simvastatin) formed the leading therapeutic class in hipolipidaemic medicine items in all age groups on the database, except for children aged 0 ≤ 9 years of age, where the "others" group, cholestyramine (e.g., Questran Lite 4mg) was claimed more frequently. Cholestyramine is advocated by the WHO as adjunct therapy after adequate rehydration in infants with acute diarrhoea (Isolauri & Vesikari, 1985:366) and may be used for the treatment of persistent diarrhoea in infants and children in South Africa (Hill *et al*., 1986:477). Cholestyramine is furthermore regarded as effective in the reduction of LDL-cholesterol levels in children with inherited hyperlipidaemia (Liacouras *et al*., 1993:477).

In the other four age groups, atorvastatin and simvastatin were most frequently claimed. Limited data are, however, available concerning the efficacy of fibrates in the treatment of hyperlipidaemia in children, and use should be restricted to the rare patients with severe hypertriglyceridaemia or type III hyperlipidaemia (Goldenberg *et al.,* 2008:134; Illingworth, 1991:126). In a retrospective study conducted by Clauss *et al*. (2009:869), it was found that the use of ezetimibe in children and adolescents with hypercholesterolaemia was safe and effective in lowering LDL cholesterol levels.

4.5.7.2 Summary and discussion of the analysis of the prescribing patterns and cost of hipolipidaemic active ingredients based on the patients' sex

It is clear that the HMG-CoA reductase inhibitors (statins) formed the leading therapeutic class in both study periods in both female and male patients on the database, followed by the fibrates, cholesterol absorption inhibitors and "others". In the statin group, simvastatin and atorvastatin accounted for most of the hipolipidaemic active ingredients claimed, followed by pravastatin. In the fibrates therapeutic class bezafibrate was the leading active ingredient being claimed in both

study periods, followed by fenofibrate and gemfibrozil. Cholestyramine was the most frequently prescribed active ingredient in the "others" therapeutic class.

Similar patterns as for the various age categories were noticed for female and male patients during the two study periods. In accordance with the prevalence of hipolipidaemics in patients, the cost of the statins dominated in both sex categories (in particular, simvastatin and atorvastatin), followed by the fibrate, bezafibrate in 2005.

According to Eisenberg and Wells (2008) there is no direct evidence of specific hipolipidaemic drug benefits for females. Heterogeneity also suggests that extrapolation from men to women is statistically inappropriate.

4.5.7.3 Summary and discussion of the analysis of hipolipidaemic active ingredients based on generic indicators and age and sex categories

In children and adolescents, non-substitutable hipolipidaemic medicine items (mostly atorvastatin and cholestyramine) were claimed, otherwise generic medicine items were claimed. Adults and older (older than 20 years of age) followed the same pattern concerning non-substitutable hipolipidaemic medicine items, except that the most popular active ingredients were atorvastatin and fluvastatin, where simvastatin was the most frequently claimed in the generic category.

In the sex categories, both females and males most frequently claimed hipolipidaemic medicine items from the generic category except in cases where medicine items were non-substitutable.

Further discussions on the specific products claimed will follow (refer to paragraph 4.6).

4.6 ANALYSIS OF THE TOP TEN TRADE NAME PRODUCTS PRESCRIBED

The analysis of the top ten trade name products prescribed based on the various age and sex categories will be discussed in the subsequent paragraphs.

4.6.1 The top ten trade name products based on age groups

In the following section the top ten trade name products, identified by prevalence and total cost in 2005 and 2006, will be investigated based on the different age groups, with the exception of age group 1 (children 0 ≤ 9 years), where only a "top five" list was compiled.

4.6.1.1 The top five trade name products for children between the ages of 0 and 9 years (age group 1)

In this section the top five trade name products based on prevalence and total cost will be investigated for age group 1 (refer to Table 4.11). Age group 1 did not have many hipolipidaemic medicine items, therefore only a top five list was recorded. The ranking order is indicated in the table in brackets next to each applicable value. Table 4.11 is compiled from the tables B2.42 and B2.43 in appendix B, reflecting the hipolipidaemic data on the database of both 2005 and 2006 and their indicidual periods based on trade names and age group 1.

The top five trade name products accounted for 97.20% (n = 714) and 94.00% (n = 567) of the overall hipolipidaemic medicine prevalence for age group 1 in 2005 and 2006. The top five trade name products in age group 1 also accounted for 91.70% (n = R42 014.29) of the total hipolipidaemic cost of this age group in 2005 and 83.04% (n = R34 947.98) in 2006.

Table 4.11: The top five trade name products for age group 1 based on prevalence and cost

Year	Trade name product	Number of medicine items (n = 714)	Average cost (R)	Total cost (R) (n = R42 014.29)	CPI
2005	**Questran Lite 4mg**	625 **(1)**	39.60 ± 37.03	24 746.97 **(1)**	0.67
	Lipitor 10mg	30 **(2)**	175.41 ± 29.70	5 262.32 **(3)**	2.98
	Lipitor 20mg	27 **(3)**	267.60 ± 34.88	7 225.28 **(2)**	4.55
	Adco-Simvastatin 10mg	6 **(4)**	100.90 ± 3.68	605.48 **(5)**	1.71
	Adco-Simvastatin 20mg	6 **(5)**	114.69 ± 1.69	688.14 **(4)**	1.95
Total		**694**		**38 528.19**	
Year	**Trade name product**	**Number of medicine items (n = 567)**	**Average cost (R)**	**Total cost (R) (n = R34 947.98)**	**CPI**
2006	**Questran Lite 4mg**	455 **(1)**	34.98 ± 28.61	15 915.23 **(1)**	0.57
	Lipitor 10mg	34 **(2)**	170.26 ± 37.71	5 788.80 **(2)**	2.76
	Adco-Simvastatin 10mg	20 **(3)**	100.72 ± 3.17	2 014.49 **(4)**	1.63
	Lipitor 20mg	17 **(4)**	254.24 ± 73.73	4 322.05 **(3)**	4.12
	Adco-Simvastatin 20mg	7 **(5)**	139.79 ± 84.46	978.56 **(5)**	2.27
Total		**533**		**29 019.13**	

Questran Lite 4mg ranked first in prevalence in children aged 0 ≤ 9 years in both study periods with 87.54% (n = 714) in 2005 and 80.25% (n = 567) in 2006. Positions 2 to 4 on the

prevalence list were occupied by products from the pharmacological class of statins, starting with Lipitor 10mg in the second place in both 2005 and 2006, accounting for 4.20% (n = 714) and 6.00% (n = 567) respectively. Lipitor 20mg accounted for 3.78% (n = 714) and 3.00% (n = 567) of the overall hipolipidaemic medicine prevalence for age group 1 in 2005 and 2006, ranking third and fourth respectively. Adco-simvastatin 10mg and 20mg accounted for 0.84% (n = 714) of the total number of hipolipidaemic medicine items in children aged 0 ≤ 9 years in 2005, where Adco-simvastatin 10mg ranked third in 2006, accounting for 3.52% (n = 567).

The total cost of the top five trade name products for age group 1 stayed relatively the same in both study periods, and relatively in accordance with the prevalence of the hipolipidaemic medicine items for age group 1. The cost of the top five trade name products represented 91.70% (n = R42 014.29) and 83.04% (n = R34 947.98) of the total hipolipidaemic medicine item cost in age group 1. The following deductions can also be made for patients in age group 1 according to table 4.11:

- Questran Lite 4mg ranked first in both years and represented 58.90% (n = R42 014.29) and 45.54% (n = R34 947.98) of the total hipolipidaemic medicine cost for age group 1 in 2005 and 2006 respectively. The average cost per Questran Lite 4mg per item was R39.60 ± 37.03 in 2006 and R34.98 ± 28.61 in 2006. A small *d*-value (*d* = 0.12) was calculated for this price difference but is of no practical significance (Steyn, 1999:3). CPIs of 0.67 and 0.57 in 2005 and 2006 respectively indicated that treatment with Questran Lite 4mg was relatively inexpensive.
- Lipitor 20mg ranked second in 2005 and third in 2006, respectively accounting for 17.20% (n = R42 014.29) and 12.37% (n = R34 947.98) of the total hipolipidaemic medicine cost for age group 1. Lipitor 20mg had an average price of R267.60 ± 34.88 in 2005 and R254.24 ± 73.73 in 2006. A small *d*-value (*d* = 0.18) notes no practical significance (Steyn, 1999:3) in the price difference. Calculated CPIs of 4.55 and 4.12, however, indicated that Lipitor 20mg was a relatively high-priced item.
- In 2005 Lipitor 10mg accounted for 12.53% (n = R42 014.29) of the total hipolipidaemic cost in age group 1. In 2006, Lipitor 10mg ranked second, accounting for 16.56% (n = R34 947.98) of the total cost for age group 1. In both study periods Lipitor 10mg had an average cost of R175.41 ± 29.70 and R170.26 ± 37.71 respectively. A small *d*-value of 0.13 indicates no significance in the price difference. CPIs of 2.98 in 2005 and 2.76 in 2006 indicated that Lipitor 10mg was relatively expensive in this age group.
- Adco-Simvastatin 10mg ranked fourth in both study periods, accounting for 1.44% (n = R42 014.29) in 2005 and 5.76% (n = R34 947.98) in 2006. Calculated CPIs for Adco-Simvastatin 10mg of 1.71 and 1.63 respectively indicated that it was a relatively expensive hipolipidaemic medicine item in this age group.

4.6.1.2 The top ten trade name products for adolescents between the ages of 10 and 19 years (age group 2)

In this section the top ten trade name products based on prevalence and total cost will be investigated for age group 2 (depicted in table 4.12). The ranking order is indicated in the table in brackets next to each applicable value. Table 4.12 is compiled from the tables B2.44 and B2.45 in appendix B, reflecting the hipolipidaemic data on the database of both 2005 and 2006 and their indicidual periods based on trade names and age group 2.

Table 4.12: The top ten trade name products for age group 2 based on prevalence and cost

Year	Trade name product	Number of medicine items (n = 1 048)	Average cost (R)	Total cost (R) (n = R186 962.39)	CPI
2005	**Lipitor 10mg**	392 **(1)**	186.11 ± 22.44	72 955.23 **(1)**	1.04
	Lipitor 20mg	197 **(2)**	246.75 ± 73.06	48 610.38 **(2)**	1.38
	Adco-Simvastatin 10mg	88 **(3)**	97.64 ± 5.29	8 592.73 **(5)**	0.55
	Adco-Simvastatin 20mg	81 **(4)**	114.25 ± 8.61	9 254.02 **(4)**	0.64
	Questran Lite 4mg	62 **(5)**	67.47 ± 59.02	4 182.94 **(7)**	0.38
	Lipitor 40mg	51 **(6)**	283.04 ± 64.15	14 434.80 **(3)**	1.59
	Simvotin 10mg	24 **(7)**	96.13 ± 15.64	2 307.15 **(8)**	0.54
	Simvotin 20mg	17 **(8)**	106.48 ± 16.51	1 810.19 **(10)**	0.60
	Simvotin 40mg	15 **(9)**	146.51 ± 20.83	2 197.71 **(9)**	0.82
	Ezetrol 10mg	14 **(10)**	351.70 ± 00	4 923.80 **(6)**	1.97
Total		**941**		**169 268.95**	
Year	**Trade name product**	**Number of medicine items (n = 852)**	**Average cost (R)**	**Total cost (R) (n = R154 194.71)**	**CPI**
2006	**Lipitor 10mg**	239 **(1)**	175.33 ± 41.72	41 904.32 **(1)**	0.97
	Lipitor 20mg	141 **(2)**	264.04 ± 46.38	37 229.92 **(2)**	1.46
	Adco-Simvastatin 20mg	86 **(3)**	106.74 ± 26.35	9 179.33 **(5)**	0.59
	Adco-Simvastatin 10mg	68 **(4)**	101.40 ± 8.88	6 894.87 **(6)**	0.56
	Questran Lite 4mg	63 **(5)**	60.88 ± 69.87	3 835.30 **(10)**	0.34
	Lipitor 40mg	52 **(6)**	303.64 ± 50.35	15 789.50 **(3)**	1.68
	Crestor 10mg	33 **(7)**	170.44 ± 37.41	5 624.36 **(7)**	0.94
	Ezetrol 10mg	29 **(8)**	356.68 ± 13.34	10 343.66 **(4)**	1.97
	Crestor 20mg	21 **(9)**	267.73 ± 50.74	5 622.41 **(8)**	1.48
	Lipitor 80mg	15 **(10)**	244.22 ± 82.20	3 663.25 **(9)**	1.35
	Simvacor 20mg	15 **(10)**	114.00 ± 5.41	1 710.02 **(12)**	0.63
Total		**762**		**141 796.94**	

The top ten trade name products accounted for 89.79% (n = 1 048) and 89.44% (n = 852) of the total prevalence of hipolipidaemic medicine items in age group 2 in 2005 and 2006. Trade name products from the therapeutic class of HMG-CoA reductase inhibitors (statins), accounted for 91.92% (n = 1 048) and 87.93% (n = 852) of the total prevalence for hipolipidaemic medicine items in age group 2 for 2005 and 2006 respectively. The top ten trade name products

accounted for 90.54% (n = R186 962.39) of the total hipolipidaemic medicine cost in age group 2 in 2005 and 91.96% (n = R154 194.71) in 2006.

Other notations from table 4.12 regarding prevalence and cost of hipolipidaemic medicine items in patients from age group 2 include the following:

- Lipitor 10mg ranked first in both study periods regarding prevalence and cost of hipolipidaemic medicine items for adolescents (age group 2). The prevalence of Lipitor 10mg accounted for 37.40% (n = 1 048) and 28.05% (n = 852) of the total hipolipidaemic medicine prevalence for age group 2 in 2005 and 2006 respectively. Focusing on total hipolipidaemic medicine cost for age group 2, Lipitor 10mg accounted for 39.02% (n = 186 962.39) in 2005 and 27.18% (n = 154 194.71) in 2006 and had an average cost of R186.11 ± 22.44 and R175.33 ± 41.72 respectively. A *d*-value of 0.25 is of no practical significance (Steyn, 1999:3). A CPI of 1.04 in 2005 indicates that this treatment was relatively expensive in this age group whereas in the CPI in 2006, *i.e.*, 0.97, indicates relatively inexpensive treatment.
- Lipitor 20mg ranked second for total prevalence and total cost of hipolipidaemic medicine items in age group 2 for 2005 and 2006, representing 18.80% (1 048) and 16.55% (n = 852) of the total prevalence, and 26.00% (n = R186 962.39) in 2005 and 24.14% (n = R154 194.71) in 2006 of the total hipolipidaemic medicine cost for this age group. Lipitor 20mg had an average cost of R246.75 ± 73.06 in 2005 and R264.04 ± 46.38 in 2006. A small *d*-value of 0.24 was calculated and is of no practical significance (Steyn, 1999:3). Lipitor 20mg had a CPI of 1.38 in 2005 and 1.46 in 2006 and both of these CPIs support the conclusion that treatment with Lipitor 20mg was relatively expensive.
- Though ranking sixth regarding prevalence in both study periods, Lipitor 40mg claimed the third highest ranking for both years regarding total hipolipidaemic cost in adolescents (age group 2). Cost of Lipitor 40mg accounted for 7.72% (n = R186 962.39) and 10.24% (n = R154 194.71) in 2005 and 2006 respectively. Lipitor 40mg had CPIs of 1.59 and 1.68 in 2005 and 2006 respectively, indicating a relatively expensive choice of treatment. The average cost was R283.04 ± 64.15 in 2005 and R303.64 ± 50.35 in 2006 (*d*= 0.32).
- Questran Lite 4mg ranked fifth in total hipolipidaemic prevalence for items claimed for adolescents (age group2) in 2005 and 2006, accounting for 5.92% (n = 1048) and 7.39% (n = 852) respectively, but ranked tenth for total hipolipidaemic cost in this age group in 2005 and seventh in 2006, at 2.24% (n = R186 962.39) and 2.49% (n = R154 194.71) of costs respectively. Questran Lite had an average cost of R67.47 ± 59.02 in 2005 and R60.88 ± 69.87 in 2006, being relatively inexpensive and associated with respective CPIs of 0.38 and 0.34.

- Crestor 10mg ranked seventh regarding prevalence for age group 2 in 2006, the year it was placed on the market (South Africa, 2006:10), accounting for 3.87% (n = 852). Crestor 10mg had an average cost of R267.73 ± 50.74 and a CPI of 1.48, indicating that this was a relatively high-priced treatment item in age group 2.
- Adco-Simvastatin 10mg and 20mg, a generic equivalent for Zocor 10mg and 20mg, had very low CPIs (both beneath 1), in 2005 and 2006, indicating that these generic medicine items were relatively inexpensive in this age group.
- Ezetrol 10mg ranked tenth in prevalence in age group 2 in 2005 with 1.34% (n = 1 048), but ranked sixth in medicine cost, accounting for 2.63% (n = 186 962.39). In 2006, though ranking eighth in prevalence, Ezetrol 10mg ranked fourth regarding total cost, accounting for 6.71% (154 194.74). Ezetrol 10mg had an average price of R 351.70 ± 00 in 2005 and R 356.68 ± 13.34 in 2006 (*d* = 0.37); with CPIs of 1.97 in both study periods.

4.6.1.3 The top ten trade name products for young adults between the ages of 20 and 45 years (age group 3)

In this section the top ten trade name products based on prevalence and total cost will be investigated for age group 3 (depicted in table 4.13). The ranking order is indicated in the table in brackets next to each applicable value. Table 4.13 is compiled from the tables B2.46 and B2.47 in appendix B, reflecting the hipolipidaemic data on the database of both 2005 and 2006 and their indicidual periods based on trade names and age group 3.

The top ten trade name products accounted for 85.73% (n = 55 977) and 81.59% (n = 59 449) of the total prevalence of hipolipidaemic medicine items in age group 3 in 2005 and 2006. Trade name products from the therapeutic class HMG-CoA reductase inhibitors (statins) accounted for nine products of the top ten in 2005, and eight out of ten in 2006. The top ten trade name products accounted for 85.36% (n = R10 196 222.52) of the total hipolipidaemic medicine cost in age group 3 in 2005 and 83.38% (n = R10 602 379.49) in 2006.

Table 4.13: The top ten trade name products for age group 3 based on prevalence and cost

Year	Trade name product	Number of medicine items (n = 55 977)	Average cost (R)	Total cost (R) (n = R10 196 222.52)	CPI
2005	**Lipitor 10mg**	14 931 **(1)**	190.38 ± 24.43	2 842 575.75 **(1)**	1.15
	Adco-Simvastatin 20mg	8 738 **(2)**	113.19 ± 14.60	989 082.76 **(3)**	0.62
	Lipitor 20mg	8 104 **(3)**	272.90 ± 40.83	2 211 610.55 **(2)**	1.50
	Adco-Simvastatin 10mg	4 134 **(4)**	101.95 ± 10.03	421 464.63 **(6)**	0.56
	Adco-Simvastatin 40mg	3 056 **(5)**	145.76 ± 39.98	445 452.51 **(5)**	0.80
	Lipitor 40mg	2 973 **(6)**	294.32 ± 92.48	875 017.60 **(4)**	1.62
	Simvotin 20mg	1 929 **(7)**	112.49 ± 12.46	216 997.89 **(9)**	0.62
	Lescol XL 80mg	1 655 **(8)**	208.82 ± 18.46	345 596.39 **(7)**	1.15
	Sandoz Bezafibrate 400mg	1 371 **(9)**	176.90 ± 45.94	242 530.28 **(8)**	0.97
	Simvotin 10mg	1 100 **(10)**	102.78 ± 7.31	113 052.84 **(10)**	0.56
Total		**47 991**		**8 703 381.20**	
Year	**Trade name product**	**Number of medicine items (n = 59 449)**	**Average cost (R)**	**Total cost (R) (n = R10 602 379.49)**	**CPI**
2006	**Lipitor 10mg**	12 933 **(1)**	190.74 ± 25.23	2 466 878.01 **(1)**	1.07
	Adco-Simvastatin 20mg	9 757 **(2)**	111.26 ± 17.41	1 085 563.82 **(3)**	0.62
	Lipitor 20mg	7 854 **(3)**	274.87 ± 49.00	2 158 864.11 **(2)**	1.54
	Adco-Simvastatin 10mg	4 406 **(4)**	100.21 ± 15.42	441 543.72 **(7)**	0.56
	Adco-Simvastatin 40mg	3 642 **(5)**	138.20 ± 33.32	503 311.15 **(5)**	0.77
	Lipitor 40mg	3 113 **(6)**	280.71 ± 77.31	873 856.79 **(4)**	1.57
	Simvotin 20mg	1 981 **(7)**	111.74 ± 11.56	221 358.23 **(10)**	0.63
	Sandoz Bezafibrate 400mg	1 783 **(8)**	172.38 ± 31.77	307 357.82 **(9)**	0.97
	Crestor 10mg	1 707 **(9)**	185.31 ± 42.35	316 331.75 **(8)**	1.04
	Ezetrol 10mg	1 327 **(10)**	350.53 ± 41.21	465 151.31 **(6)**	1.97
Total		**48 503**		**8 840 216.71**	

Other deductions that can be made from table 4.13 for patients in age group 3 include the following:

- Lipitor 10mg ranked first in age group 3 for both 2005 and 2006, accounting for 26.67% (n = 55 977) and 21.76% (n = 59 449) respectively for the total hipolipidaemic prevalence. Lipitor 10mg had an average cost of R190.38 ± 24.43 in 2005 and R190.74 ± 25.23 in 2006. Lipitor 10mg accounted for 27.88% (n = R10 196 222.52) of the total hipolipidaemic cost for this age group in 2005, and 23.27% (n = R10 602 379.49) in 2006, ranking first regarding total hipolipidaemic medicine cost in this age group. CPIs of 1.15 and 1.07 were calculated, indicating relative expensiveness.
- Adco-Simvastatin 20mg had the second highest prevalence, accounting for 15.61% (n = 55 997) and 16.41% (n = 59 447) of the total hipolipidaemic medicine items claimed in this age group for 2005 and 2006 respectively. Adco-Simvastatin 20mg also ranked third for total hipolipidaemic medicine cost in 2005 and 2006 in patients aged 20 to 45 years of age, accounting for 9.70% (n = R10 196 222.52) and 10.24% (n = R10 602 379.49) respectively, at an average cost of R113.19 ± 14.60 in 2005 and R111.26 ± 17.41 in 2006. Calculated

CPIs of 0.62 for Adco-Simvastatin 20mg in both study years indicate relative inexpensiveness of this hipolipidaemic treatment item in young adults (age group 3).

- Lipitor 20mg ranked third in prevalence for both 2005 and 2006 accounting for 14.48% (n = 55 977) and 13.21% (n = 59 449) of the total hipolipidaemic medicine items claimed for this age group respectively. Lipitor 20mg had an average cost of R272.90 ± 40.83 in 2005 and R274.87 ± 49.00 in 2006. Lipitor 20mg accounted for 21.69% (n = R10 196 222.52) of the total hipolipidaemic cost for young adults in 2005, and 20.36% (n = R10 602 379.49) in 2006, ranking second regarding total hipolipidaemic medicine cost in young adults in both study years. CPIs of 1.50 and 1.54 indicate that this product was relatively expensive in patients belonging to age group 3.
- Lipitor 40mg ranked sixth in prevalence for both 2005 and 2006, accounting for 5.31% (n = 55 977) and 5.24% (n = 59 449) of the total hipolipidaemic medicine prevalence in this age group respectively. Costs for Lipitor 40mg accounted for 8.58% (n = R10 196 222.52) of the total hipolipidaemic cost in age group 3 in 2005, and 8.24% (n = R10 602 379.49) in 2006, ranking fourth regarding total hipolipidaemic medicine cost. CPIs of 1.62 and 1.57 indicate that Lipitor 40mg was a relatively expensive item during the study period.
- Lescol XL 80mg (ranking 8th) and Sandoz Bezafibrate 400mg (ranking 9th) are two trade name products occurring in age group 3 in 2005 without having appeared in age group 2. Sandoz Bezafibrate 400mg ranked 8th in 2006.
- Ezetrol 10mg ranked tenth in prevalence in 2006, accounting for 2.23% (n = 59 449), but at an average cost of R350.53 ± 41.21. Ezetrol 10mg ranked sixth for total hipolipidaemic cost in young adults, accounting for 4.39% (n = R10 602 379.49). Ezetrol 10mg had a CPI in 2006 of 1.97, thus indicating the product to be relatively expensive in age group 3.
- Crestor 10mg, only introduced to the market in 2006 (South Africa, 2006:10; Snyman, 2007:166), again ranked among the top ten trade name products, ranking ninth (2.87%; n = 59 449) and accounting for 2.98% (n = R10 602 379.49) of the total hipolipidaemic cost in young adults. Crestor 10mg had an average cost of R185.31 ± 42.35 and a CPI of 1.04, thus being relatively expensive in age group 3.

4.6.1.4 The top ten trade name products for older adults between the ages of 46 and 59 years (age group 4)

In this section the top ten trade name products based on prevalence and total cost will be investigated for age group 4 (depicted in table 4.14). The ranking order is indicated in the table in brackets next to each applicable value. Table 4.14 is compiled from the tables B2.48 and B2.49 in appendix B, reflecting the hipolipidaemic data on the database of both 2005 and 2006 and their indicidual periods based on trade names and age group 4.

Table 4.14: The top ten trade name products for age group 4 based on prevalence and cost

Year	Trade name product	Number of medicine items (n = 196 042)	Average cost (R)	Total cost (R) (n = R34 619 455.14)	CPI
2005	**Lipitor 10mg**	53 408 **(1)**	190.49 ± 24.15	10 173 730.85 **(1)**	1.08
	Adco-Simvastatin 20mg	32 973 **(2)**	112.59 ± 16.16	3 712 471.28 **(3)**	0.64
	Lipitor 20mg	25 573 **(3)**	272.07 ± 43.87	6 957 664.00 **(2)**	1.54
	Adco-Simvastatin 10mg	15 437 **(4)**	101.85 ± 9.50	1 572 295.42 **(6)**	0.58
	Adco-Simvastatin 40mg	11 929 **(5)**	142.54 ± 42.48	1 700 301.95 **(5)**	0.81
	Lipitor 40mg	7 898 **(6)**	281.10 ± 92.17	2 220 139.54 **(4)**	1.59
	Simvotin 20mg	6 435 **(7)**	111.88 ± 14.72	719 942.57 **(9)**	0.63
	Lescol XL 80mg	5 826 **(8)**	207.38 ± 26.37	1 208 189.67 **(7)**	1.17
	Sandoz Bezafibrate 400mg	4 597 **(9)**	172.34 ± 28.69	792 257.34 **(8)**	0.98
	Simvacor 20mg	3 691 **(10)**	113.02 ± 21.55	417 146.47 **(10)**	0.64
Total		**167 767**		**29 474 139.09**	
Year	**Trade name product**	**Number of medicine items (n = 219 120)**	**Average cost (R)**	**Total cost (R) (n = R38 177 425.29)**	**CPI**
2006	**Lipitor 10mg**	50 711 **(1)**	191.22 ± 26.14	9 697 182.40 **(1)**	1.10
	Adco-Simvastatin 20mg	37 863 **(2)**	111.06 ± 17.71	4 204 893.27 **(3)**	0.64
	Lipitor 20mg	26 929 **(3)**	273.46 ± 44.92	7 364 058.99 **(2)**	1.57
	Adco-Simvastatin 10mg	15 924 **(4)**	100.21 ± 12.67	1 595 702.69 **(6)**	0.58
	Adco-Simvastatin 40mg	15 082 **(5)**	133.43 ± 33.13	2 012 387.84 **(5)**	0.77
	Lipitor 40mg	9 394 **(6)**	278.09 ± 75.09	2 612 382.08 **(4)**	1.60
	Simvotin 20mg	7 212 **(7)**	111.51 ± 11.11	804 181.65 **(9)**	0.64
	Sandoz Bezafibrate 400mg	5 773 **(8)**	172.31 ± 28.18	994 740.69 **(7)**	0.99
	Lescol XL 80mg	4 633 **(9)**	206.22 ± 25.34	955 402.78 **(8)**	1.18
	Crestor 10mg	4 236 **(10)**	188.60 ± 36.47	798 911.94 **(10)**	1.08
Total		**177 757**		**31 039 844.33**	

The top ten trade name products accounted for 85.58% (n = 196 042) and 81.12% (n = 219 120) of the total prevalence of hipolipidaemic medicine items in age group 4 in 2005 and 2006. Trade name products from the therapeutic class HMG-CoA reductase inhibitors (statins) accounted for nine of the top ten products in 2005 and 2006. The top ten trade name products accounted for 85.13% (n = R34 619 455.14) of the total hipolipidaemic medicine cost in age group 4 in 2005 and 81.30% (n = R38 177 425.29) in 2006.

The following deductions can be made from table 4.14 for patients in age group 4:

- Lipitor 10mg ranked first in prevalence for both 2005 and 2006, accounting for 27.64% (n = 196 042) and 23.14% (n = 219 120) of the total hipolipidaemic prevalence in this age group respectively. Lipitor 10mg also ranked first in total hipolipidaemic medicine cost in this age group, accounting for 29.39% (n = R34 619 455.14) in 2005, and 25.40% (n = R38 177 425.29) in 2006. Lipitor 10mg had an average cost of R190.49 ± 24.15 in 2005 and R191.22 ± 26.14 in 2006. CPIs of 1.08 and 1.10 indicate that the product was relatively expensive in this age group.

- Adco-Simvastatin 20mg had the second highest prevalence for 2005 and 2006, accounting for 16.82% (n = 196 042) and 17.28% (n = 219 120). Adco-Simvastatin 20mg ranked third for total hipolipidaemic medicine cost in age group 4 in 2005 and 2006, accounting for 10.72% (n = R34 619 455.14) and 11.01% (n = R38 177 425.29) respectively. At an average cost of R112.59 ± 16.16 in 2005 and R111.06 ± 17.71 in 2006 Adco-Simvastatin 20mg had calculated CPIs of 0.64 in both study years, thus being a relatively inexpensive hipolipidaemic medicine item.
- Lipitor 20mg ranked third in prevalence for both 2005 and 2006 accounting for 13.04% (n = 196 042) and 12.29% (n = 219 120) of the total hipolipidaemic prevalence in this age group respectively. Lipitor 20mg accounted for 20.10% (n = R34 619 455.14) of the total hipolipidaemic cost in age group 4 in 2005, and 19.29% (n = R38 177 425.29) in 2006, ranking second regarding total hipolipidaemic medicine cost. CPIs of 1.54 and 1.57 indicate that Lipitor 20mg was relatively expensive in age group 4.
- Ranking sixth regarding prevalence in both study periods, Lipitor 40mg claimed the third highest ranking for both years regarding total hipolipidaemic cost in age group 4. Lipitor 40mg made out 4.03% (n = R34 619 455.14) of the total hipolipidaemic cost in age group 4 and 4.29% (n = R38 177 425.29) in 2005 and 2006 respectively. Lipitor 40mg had CPIs of 1.59 and 1.60 in 2005 and 2006 respectively, indicating that it was relatively expensive for age group 4. The average cost was R281.10 ± 92.17 in 2005 and R278.09 ± 75.09 in 2006.
- Crestor 10mg again ranked among the top ten trade name products in 2006, ranking tenth for prevalence and cost, accounting for 2.87% (n = 59 449) of the total hipolipidaemic prevalence in age group 4 and accounting for 2.98% (n = R10 602 379.49) of the total hipolipidaemic cost in this age group. Crestor 10mg had an average cost of R188.60 ± 36.47 and a CPI of 1.08, thus being relatively expensive for age group 4.
- Except for nine trade name products being statins, Sandoz Bezafibrate 400mg was the only other therapeutic class listed among the top ten.

4.6.1.5 The top ten trade name products for patients older than 59 years of age (age group 5)

In this section the top ten trade name products based on prevalence and total cost will be investigated for age group 5 (depicted in table 4.15). The ranking order is indicated in the table in brackets next to each applicable value. Table 4.15 is compiled from the tables B2.50 and B2.51 in appendix B, reflecting the hipolipidaemic data on the database of both 2005 and 2006 and their indicidual periods based on trade names and age group 5.

Table 4.15: The top ten trade name products for age group 5 based on prevalence and cost

Year	Trade name product	Number of medicine items (n = 372 978)	Average cost (R)	Total cost (R) (n = R61 898 693.95)	CPI
2005	**Lipitor 10mg**	97 775 **(1)**	187.74 ± 30.23	18 356 531.20 **(1)**	1.13
	Adco-Simvastatin 20mg	70 441 **(2)**	111.91 ± 16.59	7 883 224.10 **(3)**	0.67
	Adco-Simvastatin 10mg	37 838 **(3)**	101.44 ± 10.88	3 838 203.90 **(4)**	0.61
	Lipitor 20mg	37 086 **(4)**	267.00 ± 51.96	9 901 874.47 **(2)**	1.61
	Adco-Simvastatin 40mg	25 278 **(5)**	139.52 ± 41.20	3 526 856.73 **(5)**	0.84
	Simvotin 20mg	11 101 **(6)**	111.25 ± 11.80	1 235 034.68 **(8)**	0.67
	Lipitor 40mg	9 968 **(7)**	266.07 ± 86.54	2 652 178.58 **(6)**	1.60
	Lescol XL 80mg	9 309 **(8)**	205.82 ± 25.25	1 915 949.46 **(7)**	1.24
	Simvotin 10mg	6 908 **(9)**	100.37 ± 12.54	693 377.31 **(10)**	0.60
	Simvacor 20mg	6 709 **(10)**	114.39 ± 24.29	767 426.10 **(9)**	0.69
Total		**312 413**		**50 770 656.53**	
Year	**Trade name product**	**Number of medicine items (n = 425 436)**	**Average cost (R)**	**Total cost (R) (n = R68 893 684.40)**	**CPI**
2006	**Lipitor 10mg**	96 583 **(1)**	188.73 ± 30.11	18 228 432.11 **(1)**	1.17
	Adco-Simvastatin 20mg	82 330 **(2)**	110.33 ± 16.49	9 083 840.14 **(3)**	0.68
	Adco-Simvastatin 10mg	41 282 **(3)**	99.53 ± 12.81	4 108 646.75 **(4)**	0.61
	Lipitor 20mg	40 601 **(4)**	267.79 ± 48.50	10 872 422.76 **(2)**	1.65
	Adco-Simvastatin 40mg	31 421 **(5)**	129.42 ± 34.59	4 066 349.18 **(5)**	0.80
	Simvotin 20mg	13 751 **(6)**	110.87 ± 11.27	1 524 552.53 **(8)**	0.68
	Lipitor 40mg	12 605 **(7)**	265.80 ± 78.84	3 350 456.31 **(6)**	1.64
	Lescol XL 80mg	8 725 **(8)**	205.44 ± 20.87	1 792 468.34 **(7)**	1.27
	Simvacor 20mg	8 180 **(9)**	115.15 ± 21.41	941 955.54 **(10)**	0.71
	Sandoz Bezafibrate 400mg	7 930 **(10)**	169.06 ± 27.67	1 340 637.25 **(9)**	1.04
Total		**343 408**		**55 309 760.91**	

The top ten trade name products in age group 5 for 2005 and 2006 accounted for 83.76% (n = 372 978) and 80.72% (n = 425 436) of the total prevalence of hipolipidaemic medicine items in age group 5. Trade name products from the therapeutic class HMG-CoA reductase inhibitors (statins) accounted for all of the top ten products in 2005 and nine out of ten in 2006. The top ten trade name products accounted for 82.02% (n = R61 898 693.95) of the total hipolipidaemic medicine cost in age group 5 in 2005 and 80.28% (n = R68 893 684.40) in 2006.

The following deductions can be made for patients in age group 5 (from Table 4.15):

- Lipitor 10mg ranked first in prevalence for both 2005 and 2006, accounting for 26.21% (n = 372 978) and 22.70% (n = 425 436) respectively of the total hipolipidaemic prevalence in this age group. Lipitor 10mg accounted for 29.66% (n = R61 898 693.95) in 2005, and 26.46% (n = R68 893 684.40) in 2006, ranking first regarding total hipolipidaemic medicine cost in age group 5. CPIs of 1.13 and 1.17 indicate that the product was relatively expensive. Lipitor 10mg had an average cost in 2005 of R187.74 ± 30.23 and R188.73 ± 30.11 in 2006.

- Adco-Simvastatin 20mg had the second highest prevalence for 2005 and 2006, accounting for 18.89% (n = 372 978) and 19.35% (n = 425 436) of the total hipolipidaemic prevalence in this age group. In terms of cost, Adco-Simvastatin 20mg ranked third in 2005 as well as in 2006, accounting for 12.74% (n = R61 898 693.95) and 13.19% (n = R68 893 684.40) of the total hipolipidaemic cost in this age group. CPIs were calculated as 0.67 in 2005 and 0.68 in 2006, thus indicating the product to be relatively inexpensive.
- In both 2005 and 2006, Adco-Simvastatin 10mg ranked third in prevalence, respectively accounting for 10.14% (n = 372 978) and 9.70% (n = 425 436) of the total hipolipdiaemic prevalence in this age group. Having an average cost of R101.44 ± 10.88 in 2005 and R99.53 ± 12.81 in 2006, Adco-Simvastatin 10mg accounted for 6.20% (n = R61 898 693.95) of the total hipolipidaemic medicine cost in age group 5 in 2005 and 5.96% (n = R68 893 684.40) in 2006, ranking fourth in both study years regarding total hipolipidaemic medicine cost in age group 5. In 2005 and 2006, Adco-Simvastatin 10mg had a CPI of 0.61 in both study periods, indicating relative inexpensiveness for patients aged older than 59 years of age.
- Lipitor 20mg ranked fourth in both 2005 and 2006 for the total hipolipidaemic medicine prevalence in age group 5, accounting for 9.94% (n = 372 978) and 9.54% (n = 425 436) of the total hipolipidaemic prevalence in this age group for each the two years mentioned. Lipitor 20mg had an average cost in 2005 of R267.00 ± 51.96 and R267.79 ± 48.50 in 2006. CPIs of 1.61 and 1.65 indicate that it was a relative expensive product for patients aged older than 59 years of age. Lipitor 20mg ranked second in both 2005 and 2006 for total hipolipidaemic cost in age group 5, accounting for 16.00% (n = R61 898 693.95) in 2005, and 15.78% (n = R68 893 684.40) in 2006.
- Crestor 10mg did not appear among the top ten trade name products as was the case iin the previous three age groups (age groups 2, 3 and 4). Instead Simvacor 20mg, containing simvastatin as active ingredient (Snyman, 2007:169), ranked tenth in 2005 and ninth in 2006 for total hipolipidaemic medicine prevalence in age group 5, accounting for 1.80% (n = 372 978) in 2005 and 1.92% (n = 425 436) in 2006. Simvacor 20mg ranked ninth in 2005 for the total hipolipidaemic medicine cost in age group 5, accounting for 1.24% (n = R61 898 693.95) and ranked tenth in 2006 with 1.37% (n = R68 893 684.40) of the total hipolipidaemic medicine cost in age group 5.

4.6.2 The top ten trade name products based on patients' sex (male/female)

In the following section the top ten trade name products will be investigated based on the different categories of sex (male/female) for 2005 and 2006. The top ten trade name product will be identified by prevalence and total cost in that specific study period.

4.6.2.1 The top ten trade name product based on the female sex

In this section the top ten trade name products based on prevalence and total cost will be investigated for the female sex (depicted in table 4.16). The ranking order is indicated in the table in brackets next to each applicable value. Table 4.16 is compiled from the tables B2.52 and B2.53 in appendix B, reflecting the hipolipidaemic data on the database of both 2005 and 2006 and their indicidual periods based on trade names and the female sex.

Table 4.16: The top ten trade name products for females based on prevalence and cost

Year	Trade name product	Number of medicine items (n = 292 495)	Average cost (R)	Total cost (R) (n = R48 565 536.56)	CPI
2005	**Lipitor 10mg**	77 623 **(1)**	187.91 ± 28.12	14 585 759.67 **(1)**	1.13
	Adco-Simvastatin 20mg	55 435 **(2)**	112.05 ± 16.54	6 211 598.68 **(3)**	0.67
	Adco-Simvastatin 10mg	30 918 **(3)**	101.34 ± 10.49	3 133 184.52 **(4)**	0.61
	Lipitor 20mg	29 266 **(4)**	267.39 ± 51.44	7 825 335.82 **(2)**	1.61
	Adco-Simvastatin 40mg	17 981 **(5)**	139.05 ± 41.19	2 500 253.37 **(5)**	0.84
	Simvotin 20mg	8 601 **(6)**	111.53 ± 14.48	959 308.01 **(8)**	0.67
	Lescol XL 80mg	8 022 **(7)**	206.04 ± 29.89	1 652 857.88 **(7)**	1.24
	Lipitor 40mg	7 869 **(8)**	277.03 ± 89.33	2 179 978.46 **(6)**	1.67
	Simvotin 10mg	5 419 **(9)**	100.64 ± 11.14	545 365.19 **(10)**	0.61
	Simvacor 20mg	5 290 **(10)**	114.20 ± 25.25	604 103.94 **(9)**	0.69
Total		**246 424**		**40 197 745.54**	
Year	**Trade name product**	**Number of medicine items (n = 329 695)**	**Average cost (R)**	**Total cost (R) (n = R53 411 724.02)**	**CPI**
2006	**Lipitor 10mg**	75 676 **(1)**	188.67 ± 28.38	14 277 564.89 **(1)**	1.16
	Adco-Simvastatin 20mg	65 061 **(2)**	110.22 ± 16.85	7 171 172.31 **(3)**	0.68
	Adco-Simvastatin 10mg	33 118 **(3)**	99.44 ± 13.30	3 293 332.40 **(4)**	0.61
	Lipitor 20mg	31 169 **(4)**	268.49 ± 49.71	8 368 495.73 **(2)**	1.66
	Adco-Simvastatin 40mg	21 925 **(5)**	128.88 ± 34.69	2 825 802.13 **(5)**	0.80
	Simvotin 20mg	10 198 **(6)**	110.97 ± 11.25	1 131 722.25 **(8)**	0.69
	Lipitor 40mg	9 648 **(7)**	271.69 ± 73.33	2 621 268.47 **(6)**	1.68
	Lescol XL 80mg	6 747 **(8)**	205.00 ± 23.99	1 383 147.59 **(7)**	1.27
	Simvacor 20mg	6 021 **(9)**	114.43 ± 20.53	688 966.51 **(10)**	0.71
	Sandoz Bezafibrate 400mg	5 778 **(10)**	169.03 ± 25.08	976 664.99 **(9)**	1.04
Total		**265 341**		**42 738 137.27**	

The top ten trade name products accounted for 84.25% (n = 292 495) and 80.48% (n = 329 695) of the total prevalence of hipolipidaemic medicine items in females in 2005 and 2006. Trade name products from the therapeutic class HMG-CoA reductase inhibitors (statins) accounted for all of the top ten products in females in 2005 and nine out of ten in 2006. The top ten trade name products accounted for 82.77% (n = R48 565 536.56) of the total hipolipidaemic medicine cost in females and 80.02% (n = R53 411 724.02) in 2006.

The following deductions for female patients can be made from table 4.16:

- Lipitor 10mg ranked first in both 2005 and 2006 for the total hipolipidaemic medicine prevalence in females, accounting for 26.54% (n = 292 495) and 22.70% (n = 329 695) respectively. Lipitor 10mg had an average cost in 2005 of R187.91 ± 28.12 and R188.76 ± 28.38 in 2006. Lipitor 10mg accounted for 30.03% (n = R48 565 536.56) of the total hipolipidaemic cost in females in 2005, and 26.73% (n = R53 411 724.02) in 2006, ranking first regarding the total hipolipidaemic medicine cost for the female sex. CPIs of 1.13 and 1.16 indicate that the product was relatively expensive in females.
- Adco-Simvastatin 20mg had the second highest prevalence for 2005 and 2006, respectively accounting for 18.95% (n = 292 495) and 19.73% (n = 329 695) of the total hipolipidaemic prevalence in females. Adco-Simvastatin 20mg ranked third for the total hipolipidaemic medicine cost in females in 2005 and 2006, accounting for 12.79% (n = R48 565 536.56) and 13.43% (n = R53 411 724.02) respectively. CPIs of 0.67 in 2005 and 0.68 in 2006 were calculated, thus indicating Adco-Simvastatin 20mg to be a relatively inexpensive treatment item in females.
- In both study years, 2005 and 2006, Adco-Simvastatin 10mg ranked third for the total hipolipidaemic medicine prevalence in females, respectively accounting for 18.95% (n = 292 495) and 19.73% (n = 329 695). Having an average cost of R101.34 ± 10.49 in 2005 and R99.44 ± 13.30 in 2006, Adco-Simvastatin 10mg accounted for 12.79% (n = R48 565 536.56) of the total hipolipidaemic medicine cost in females in 2005 and 13.43% (n = R53 411 724.02) in 2006, ranking fourth in both study years regarding total hipolipidaemic medicine cost for female patients. Calculated CPIs of 0.61 in both 2005 and 2006 prove that Adco-Simvastatin 10mg was relatively inexpensive in the treatment of female patients.
- Lipitor 20mg ranked fourth in both 2005 and 2006 for the total hipolipidaemic medicine prevalence in female patients, accounting for 10.01% (n = 292 495) and 9.45% (n = 329 695) respectively of the total hipolipidaemic prevalence. Lipitor 20mg had an average cost in 2005 of R267.39 ± 51.44 and R268.49 ± 49.71 in 2006. CPIs of 1.61 and 1.66 indicate that the product was a relatively expensive treatment item in females. Lipitor 20mg ranked second in both 2005 and 2006 for total hipolipidaemic cost in females, accounting for 16.11% (n = R48 565 536.56) in 2005, and 15.67% (n = R53 411 724.02) in 2006.
- In 2006, Sandoz Bezafibrate 400mg broke into the top ten trade name products in females, ranking tenth and being the only product not from the HMG-CoA therapeutic class. Sandoz Bezafibrate 400mg ranked tenth in female patients regarding total hipolipidaemic medicine prevalence, accounting for 1.75% (n = 329 695). Ranking ninth it accounted for 1.83% (n = R48 565 536.56) of the total hipolipidaemic medicine cost in females in 2006. Sandoz Bezafibrate 400mg had an average cost of R169.03 ± 25.08 in 2006 and a CPI of 1.04, thus being relatively expensive.

4.6.2.2 The top ten trade name products based on the male sex

In this section the top ten trade name products based on prevalence and total cost will be investigated for the male sex (depicted in table 4.17). The ranking order is indicated in the table in brackets next to each applicable value. Table 4.17 is compiled from the tables B2.52 and B2.53 in appendix B, reflecting the hipolipidaemic data on the database of both 2005 and 2006 and their indicidual periods based on trade names and the male sex.

Table 4.17: The top ten trade name products for males based on prevalence and cost

Year	Trade name product	Number of medicine items (n = 333 933)	Average cost (R)	Total cost (R) (n = R58 326 901.67)	CPI
2005	**Lipitor 10mg**	88 863 **(1)**	189.68 ± 27.72	16 855 208.20 **(1)**	1.09
	Adco-Simvastatin 20mg	56 746 **(2)**	112.37 ± 16.09	6 376 696.26 **(3)**	0.64
	Lipitor 20mg	41 699 **(3)**	270.88 ± 45.64	11 295 518.88 **(2)**	1.55
	Adco-Simvastatin 10mg	26 535 **(4)**	101.87 ± 16.46	2 703 119.71 **(6)**	0.58
	Adco-Simvastatin 40mg	22 269 **(5)**	142.70 ± 41.77	3 170 998.59 **(5)**	0.82
	Lipitor 40mg	13 023 **(6)**	275.07 ± 90.54	3 582 255.22 **(4)**	1.57
	Simvotin 20mg	10 881 **(7)**	111.61 ± 13.60	1 214 477.32 **(9)**	0.64
	Lescol XL 80mg	8 761 **(8)**	207.23 ± 19.69	1 815 526.04 **(7)**	1.19
	Sandoz Bezafibrate 400 mg	7 420 **(9)**	171.18 ± 31.91	1 270 162.27 **(8)**	0.98
	Simvacor 20mg	6 095 **(10)**	113.80 ± 21.89	693 587.99 **(10)**	0.65
Total		**282 292**		**48 977 550.48**	
Year	**Trade name product**	**Number of medicine items (n = 374 316)**	**Average cost (R)**	**Total cost (R) (n = R64 402 386.68)**	**CPI**
2006	**Lipitor 10mg**	84 779 **(1)**	190.54 ± 28.75	16 154 064.45 **(1)**	1.11
	Adco-Simvastatin 20mg	64 935 **(2)**	111.01 ± 17.04	7 208 438.15 **(3)**	0.65
	Lipitor 20mg	44 351 **(3)**	271.98 ± 45.66	12 062 518.39 **(2)**	1.58
	Adco-Simvastatin 10mg	28 501 **(4)**	100.10 ± 12.57	2 853 001.34 **(6)**	0.58
	Adco-Simvastatin 40mg	28 207 **(5)**	133.12 ± 33.68	3 755 001.01 **(5)**	0.77
	Lipitor 40mg	15 517 **(6)**	272.70 ± 79.99	4 231 532.08 **(4)**	1.58
	Simvotin 20mg	12 752 **(7)**	111.28 ± 11.24	1 419 036.47 **(9)**	0.65
	Sandoz Bezafibrate 400mg	9 705 **(8)**	171.62 ± 30.18	1 665 571.48 **(7)**	1.00
	Lescol XL 80mg	7 600 **(9)**	206.88 ± 20.61	1 572 275.66 **(8)**	1.20
	Simvacor 20mg	7 200 **(10)**	114.65 ± 20.47	825 481.01 **(10)**	0.67
Total		**303 547**		**51 746 920.04**	

The top ten trade name products accounted for 84.54% (n = 333 933) and 81.09% (n = 374 316) of the total prevalence of hipolipidaemic medicine items in males in 2005 and 2006. Trade name products from the therapeutic class HMG-CoA reductase inhibitors (statins) accounted for nine out of the top ten products for males in 2005 and 2006. The top ten trade name products accounted for 83.97% (n = R58 326 901.67) in 2005 and 80.35% (n = R64 402 386.68) in 2006, *i.e.* of the total hipolipidaemic medicine cost in males.

The following deductions for males can be made from table 4.17:

- Lipitor 10mg ranked first in both 2005 and 2006 for the total hipolipidaemic medicine prevalence in males, accounting for 26.61% (n = 333 933) and 22.65% (n = 374 316) respectively of the total hipolipidaemic prevalence. Lipitor 10mg had an average cost in 2005 of R189.68 ± 27.72 and R190.54 ± 28.75 in 2006. CPIs of 1.09 and 1.11 indicate that it was a relatively expensive treatment in males. Lipitor 10mg accounted for 28.90% (n = R58 326 901.67) of the total hipolipidaemic cost in males in 2005, and 25.08% (n = R64 402 386.68) in 2006, ranking first.
- Adco-Simvastatin 20mg had the second highest prevalence in males for 2005 and 2006, accounting for 16.99% (n = 333 933) and 17.35% (n = 374 316). Adco-Simvastatin 20mg ranked third for total hipolipidaemic medicine cost in males in 2005 and 2006, accounting for 10.93% (n = R58 326 901.67) and 11.19% (n = R64 402 386.68) respectively. Average costs for Adco-Simvastatin 20mg were R112.37 ± 16.09 in 2005 and R111.01 ± 17.04 in 2006. CPIs of 0.64 in 2005 and 0.65 in 2006 were calculated, thus indicating the product to be relatively inexpensive in this group.
- Lipitor 20mg ranked third in both 2005 and 2006 for the total hipolipidaemic medicine prevalence in male patients, resulting in 12.49% (n = 333 933) in 2005 and 11.85% (n = 374 316) 2006 of the total hipolipidaemic prevalence. Lipitor 20mg had an average cost in 2005 of R270.88 ± 45.64 and R271.98 ± 45.66 in 2006. CPIs of 1.55 and 1.58 indicate that it was a relatively expensive item in males. Lipitor 20mg ranked second in both 2005 and 2006 for total hipolipidaemic cost in males, accounting for 19.37% (n = R58 326 901.67) in 2005, and 18.73% (n = R64 402 386.68) in 2006.
- Adco-Simvastatin 10mg had the fourth highest prevalence in males for 2005 and 2006, accounting for 7.95% (n = 333 933) and 7.61% (n = 374 316). Adco-Simvastatin 10mg ranked sixth for total hipolipidaemic medicine cost in males in 2005 and 2006, accounting for 4.64% (n = R58 326 901.67) and 4.43% (n = R64 402 386.68) respectively. It presented with an average cost of R101.87 ± 16.46 in 2005 and R100.10 ± 12.57 in 2006. CPIs of 0.58 were calculated for 2005 and 2006, giving an indication that the product was a relatively inexpensive item in males.
- Lipitor 40mg ranked sixth in both 2005 and 2006 for the total hipolipidaemic medicine prevalence in males, accounting for 3.90% (n = 333 933) and 4.15% (n = 374 316) respectively for the total hipolipidaemic prevalence. Lipitor 40mg had an average cost in 2005 of R275.07 ± 90.54 and R272.70 ± 79.99 in 2006. CPIs of 1.57 and 1.58 indicate that it was a relatively expensive item in males. Lipitor 40mg accounted for 6.14% (n = R58 326 901.67) of the total hipolipidaemic cost in males in 2005, and 6.57% (n = R64 402 386.68) in 2006, ranking fourth regarding the total hipolipidaemic medicine cost for the male sex.

- Sandoz Bezafibrate 400mg ranked ninth in 2005 and eighth in 2006 for total hipolipidaemic medicine prevalence in males, accounting for 2.22% (n = 333 933) and 2.59% (n = 374 316). Having an average price of R171.18 ± 31.91 in 2005 and R171.62 ± 30.18 in 2006 Sandoz Bezafibrate 400mg accounted for 2.18% (n = R58 326 901.67) of the total hipolipidaemic medicine price in 2005 and 2.59% (n = R64 402 386.68) in 2006. Calculated CPIs of 0.98 in 2005 and 1.00 in 2006 prove that Sandoz Bezafibrate 400mg was relatively inexpensive in males in 2005 and relatively expensive in 2006.

4.6.3 Analysis of the top ten trade name products based on prescriber type

The following section will be based on the top ten trade name products prescribed by the different prescribers during the study periods of 2005 and 2006. The prescriber types for this specific study were divided into six major categories namely; cardiologists, general medical practitioners, other medical prescribers, pharmacotherapists, pharmacists and thoracic surgeons (refer to paragraph 3.2.2).

4.6.3.1 Analysis of the top ten trade name products prescribed by cardiologists

The following section presents the top ten trade name products prescribed by cardiologists analysed according to prevalence and cost (depicted in table 4.18). The ranking order is indicated in the table in brackets next to each applicable value. Table 4.18 is compiled from the tables B2.56 and B2.57 in appendix B, reflecting the hipolipidaemic data on the database of both 2005 and 2006 and their indicidual periods based on trade names and prescriber type.

Table 4.18: The top ten trade name products prescribed by cardiologists based on prevalence and cost

Year	Trade name product	Number of medicine items (n = 52 425)	Average cost (R)	Total cost (R) (n = R9 876 518.51)	CPI
2005	**Lipitor 10mg**	11 882 **(1)**	189.90 ± 25.42	2 256 383.05 **(1)**	1.11
	Adco-Simvastatin 20mg	7 961 **(2)**	113.67 ± 15.44	904 944.66 **(4)**	0.67
	Lipitor 20mg	7 599 **(3)**	273.38 ± 48.80	2 077 382.80 **(2)**	1.60
	Adco-Simvastatin 40mg	4 307 **(4)**	144.32 ± 37.89	621 565.25 **(5)**	0.85
	Lipitor 40mg	3 734 **(5)**	278.06 ± 93.50	1 038 258.70 **(3)**	1.63
	Adco-Simvastatin 10mg	2 913 **(6)**	102.28 ± 8.49	297 952.73 **(7)**	0.60
	Lescol XL 80mg	1 569 **(7)**	208.28 ± 27.35	326 786.25 **(6)**	1.22
	Simvotin 20mg	1 331 **(8)**	112.07 ± 11.88	149 164.76 **(9)**	0.66
	Zocor 20mg	1 014 **(9)**	148.88 ± 15.34	150 968.93 **(8)**	0.87
	Simvacor 20mg	907 **(10)**	117.48 ± 22.34	106 554.16 **(10)**	0.69
Total		**43 217**		**7 929 961.29**	

Table 4.18: The top ten trade name products prescribed by cardiologists based on prevalence and cost (continued)

Year	Trade name product	Number of medicine items (n = 62 304)	Average cost (R)	Total cost (R) (n = R11 728 132.65)	CPI
2006	**Lipitor 10mg**	11 302 **(1)**	189.29 ± 26.48	2 139 305.80 **(2)**	1.13
	Adco-Simvastatin 20mg	9 279 **(2)**	112.07 ± 19.30	1 039 864.16 **(4)**	0.67
	Lipitor 20mg	8 617 **(3)**	273.05 ± 45.80	2 352 867.44 **(1)**	1.63
	Adco-Simvastatin 40mg	5 375 **(4)**	137.22 ± 29.76	737 551.93 **(6)**	0.82
	Lipitor 40mg	4 453 **(5)**	280.77 ± 74.30	1 250 274.76 **(3)**	1.68
	Adco-Simvastatin 10mg	3 121 **(6)**	99.91 ± 12.01	311 503.50 **(8)**	0.60
	Ezetrol 10mg	2 363 **(7)**	352.56 ± 38.43	833 104.63 **(5)**	2.11
	Lipitor 80mg	1 770 **(8)**	253.81 ± 79.16	449 238.07 **(7)**	1.52
	Simvotin 20mg	1 708 **(9)**	111.94 ± 9.43	191 190.84 **(10)**	0.67
	Crestor 10mg	1 391 **(10)**	188.32 ± 37.78	261 947.83 **(9)**	1.13
Total		**49 379**		**9 566 848.96**	

Table 4.18 portrays that the top ten trade name products prescribed by cardiologists contributed 82.44% (n = 52 425) in 2005 and 79.25% (n = 62 304) in 2006 of the total hipolipidaemic medicine items prescribed by cardiologists. In 2005, all of the top ten trade name products prescribed by cardiologists were from the HMG-CoA reductase inhibitors (statins), and nine out of the top ten trade name products in 2006 were statins. The top ten trade name products prescribed by cardiologists in 2005 accounted for 80.29% (n = R9 876 518.51) of the total hipolipidaemic medicine cost contributed by cardiologists and for 81.57% (n = R11 728 132.65) in 2006. The top ten trade name products prescribed during the two study periods only changed slightly.

Lipitor 10mg was positioned first in both study periods and represented 22.66% (n = 52 425) and 18.14% (n = 62 304) of the overall hipolipidaemic medicine prevalence by cardiologists in 2005 and 2006 respectively. The total hipolipidaemic medicine cost by cardiologists for Lipitor 10mg also ranked first in 2005 and second in 2006, accounting for 22.85% (n = R9 876 518.51) in 2005 and 18.24% (n = R11 728 132.65) in 2006. The average cost of Lipitor 10mg was R189.90 ± 25.42 in 2005 and R189.29 ± 26.48 in 2006.

Adco-Simvastatin 20mg had the second highest prevalence for prescribed hipolipidaemic medicine items by cardiologists 2005 and 2006, accounting for 15.19% (n = 52 425) and 14.89% (n = 62 304). Adco-Simvastatin 20mg ranked fourth for total hipolipidaemic medicine cost by cardiologists in 2005 and 2006, accounting for 9.16% (n = R9 876 518.51) and 8.87% (n = R11 728 132.65) respectively, at an average cost of R113.67 ± 15.44 in 2005 and R112.07 ± 19.30 in 2006.

Lipitor 20mg ranked third in both 2005 and 2006 for the total hipolipidaemic medicine prevalence prescribed by cardiologists, accounting for 14.49% (n = 52 425) and 13.83% (n = 62

304) respectively. Lipitor 20mg, as prescribed by cardiologists had an average cost in 2005 of R273.38 ± 48.80 and R273.05 ± 45.80 in 2006. Lipitor 20mg ranked second in 2005 and first in 2006 for total hipolipidaemic cost by cardiologists, accounting for 21.03% (n = R9 876 518.51) in 2005, and 20.06% (n = R11 728 132.65) in 2006.

Adco-Simvastatin 40mg had the fourth highest prevalence for hipolipidaemic medicine items prescribed by cardiologists in 2005 and 2006, accounting for 8.22% (n = 52 425) and 8.63% (n = 62 304). Adco-Simvastatin 40mg ranked fifth and sixth for total hipolipidaemic medicine cost prescribed by cardiologists in 2005 and 2006 respectively, accounting for 6.29% (n = R9 876 518.51) in 2005 and 6.29% (n = R11 728 132.65) in 2006. The average cost was of R144.32 ± 37.89 in 2005 and R137.22 ± 29.76 in 2006.

Lipitor 40mg ranked fifth in both 2005 and 2006 for the total hipolipidaemic medicine prevalence by cardiologists, accounting for 7.12% (n = 52 425) and 7.15% (n = 62 304) respectively. The average cost in 2005 was R278.06 ± 93.50 and R280.77 ± 74.30 in 2006. Lipitor 40mg accounted for 10.51% (n = R9 876 518.51) of the total hipolipidaemic cost of products prescribed by cardiologists in 2005, and 10.66% (n = R11 728 132.65) in 2006, ranking third.

Ezetrol 10mg was the only non-statin among the top ten trade name products prescribed by cardiologists in 2006. Ezetrol 10mg ranked seventh regarding the total hipolipidaemic prevalence in 2006 at 3.79% (n = 62 304) and ranked fifth for the total hipolipidaemic medicine cost by cardiologists in 2006 with 7.10% (n = R11 728 132.65). Ezetrol 10mg had an average cost of R352.56 ± 38.43.

Crestor 10mg, registered in April 2006 and introduced to the South African market in 2006 (South Africa, 2006:10), made the top ten trade name list for hipolipidaemic medicine items prescribed by cardiologists in 2006, ranking tenth regarding prevalence and ninth regarding cost.

4.6.3.2 Analysis of the top ten trade name products as prescribed by general medical practioners

The following section presents an analysis of the top ten trade name products prescribed by general medical practioners based on prevalence and cost (depicted in table 4.19). The ranking order is indicated in the table in brackets next to each applicable value. Table 4.19 is compiled from the tables B2.56 and B2.57 in appendix B, reflecting the hipolipidaemic data on the database of both 2005 and 2006 and their indicidual periods based on trade names and prescriber type.

Table 4.19: The top ten trade name products prescribed by general medical practioners based on prevalence and cost

Year	Trade name product	Number of medicine items (n = 462 890)	Average cost (R)	Total cost (R) (n = R77 292 156.85)	CPI
2005	**Lipitor 10mg**	124 728 **(1)**	189.50 ± 27.41	23 511 150.01 **(1)**	1.10
	Adco-Simvastatin 20mg	85 664 **(2)**	112.05 ± 16.28	9 598 415.00 **(3)**	0.66
	Lipitor 20mg	50 325 **(3)**	267.57 ± 48.62	13 465 381.45 **(2)**	1.57
	Adco-Simvastatin 10mg	44 923 **(4)**	101.41 ± 10.76	4 555 482.48 **(4)**	0.59
	Adco-Simvastatin 40mg	28 829 **(5)**	139.54 ± 41.79	4 022 707.60 **(5)**	0.82
	Simvotin 20mg	15 492 **(6)**	111.49 ± 14.37	1 727 200.43 **(8)**	0.65
	Lipitor 40mg	12 717 **(7)**	271.56 ± 84.73	3 453 384.90 **(6)**	1.59
	Lescol XL 80mg	12 351 **(8)**	206.39 ± 25.95	2 549 110.19 **(7)**	1.21
	Simvotin 10mg	9 428 **(9)**	100.65 ± 11.56	9 48 928.98 **(10)**	0.59
	Sandoz Bezafibrate 400mg	9 221 **(10)**	169.45 ± 28.66	1 562 521.53 **(9)**	0.99
Total		**393 678**		**65 394 282.57**	
Year	**Trade name product**	**Number of medicine items (n = 515 942)**	**Average cost (R)**	**Total cost (R) (n = R84 008 507.57)**	**CPI**
2006	**Lipitor 10mg**	119 878 **(1)**	189.61 ± 28.14	22 729 968.76 **(1)**	1.13
	Adco-Simvastatin 20mg	98 884 **(2)**	110.48 ± 16.72	10 925 034.92 **(3)**	0.66
	Lipitor 20mg	52 586 **(3)**	269.39 ± 48.10	14 166 103.67 **(2)**	1.61
	Adco-Simvastatin 10mg	47 968 **(4)**	99.69 ± 12.86	4 781 831.20 **(4)**	0.60
	Adco-Simvastatin 40mg	36 001 **(5)**	129.65 ± 35.09	4 667 001.05 **(5)**	0.78
	Simvotin 20mg	18 345 **(6)**	111.12 ± 11.28	2 038 541.00 **(8)**	0.67
	Lipitor 40mg	15 622 **(7)**	267.53 ± 76.76	4 179 429.83 **(6)**	1.60
	Sandoz Bezafibrate 400mg	11 326 **(8)**	170.46 ± 26.96	1 930 665.95 **(9)**	1.02
	Lescol XL 80mg	10 437 **(9)**	205.90 ± 22.53	2 148 964.73 **(7)**	1.23
	Simvacor 20mg	9 767 **(10)**	115.25 ± 22.11	1 125 687.44 **(10)**	0.69
Total		**420 814**		**68 693 228.55**	

Table 4.19 shows that the top ten trade name products prescribed by general medical practioners contributed 85.05% (n = 462 890) in 2005 and 81.56% (n = 515 942) in 2006. In both study periods, nine of the top ten trade name products prescribed by general medical practioners were from the HMG-CoA reductase inhibitors (statins). The top ten trade name products prescribed by general medical practioners in 2005 accounted for 84.61% (n = R77 292 156.85) of the total hipolipidaemic medicine cost contributed by general medical practioners and for 81.77% (n = R84 008 507.57) in 2006. During the two study periods the top ten trade name products changed slightly with only Simvacor 20mg in 2006 replacing the Simvotin10mg of 2005.

Lipitor 10mg was positioned first in both study periods and represented 26.95% (n = 462 890) and 23.23% (n = 515 942) of the overall hipolipidaemic medicine prevalence prescribed by general medical practioners in 2005 and 2006 respectively. The total hipolipidaemic medicine cost by general medical practioners for Lipitor 10mg also ranked first in both 2005 and 2006, accounting for 30.42% (n = R77 292 156.85) in 2005 and 27.06% (n = R84 008 507.57) in 2006.

Adco-Simvastatin 20mg had the second highest prevalence for prescribed hipolipidaemic medicine items by general medical practitioners in 2005 and 2006, accounting for 18.50% (n = 462 890) and 19.17% (n = 515 942). Adco-Simvastatin 20mg ranked third for total hipolipidaemic medicine cost prescribed by general medical practitioners in 2005 and 2006, accounting for 12.42% (n = R77 292 156.85) and 13.00% (n = R84 008 507.57) respectively.

Lipitor 20mg ranked third in both 2005 and 2006 for the total hipolipidaemic medicine prevalence prescribed by general medical practioners, accounting for 10.87% (n = 462 890) and 10.19% (n = 515 942) respectively. Lipitor 20mg had an average cost in 2005 of R267.57 ± 48.62 and R269.39 ± 48.10 in 2006. CPIs of 1.57 and 1.61 indicate that it was a relatively expensive hipolipidaemic item prescribed by general medical practioners. Lipitor 20mg ranked second in 2005 and 2006 for total hipolipidaemic cost by general medical practitioners, accounting for 17.42% (n = R77 292 156.85) in 2005, and 16.86% (n = R84 008 507.57) in 2006.

Adco-Simvastatin 10mg had the fourth highest prevalence for hipolipidaemic medicine items prescribed by general medical practioners in 2005 and 2006, accounting for 9.70% (n = 462 890) and 9.30% (n = 515 942). Adco-Simvastatin 10mg also ranked fourth for total hipolipidaemic medicine cost by general medical practioners in 2005 and 2006 respectively, accounting for 5.89% (n = R77 292 156.85) in 2005 and 5.69% (n = R84 008 507.57) in 2006.

Adco-Simvastatin 40mg ranked fifth in both 2005 and 2006 for the total hipolipidaemic medicine prevalence prescribed by general medical practioners, accounting for 6.23% (n = 462 890) and 6.98% (n = 515 942) respectively. The average cost in 2005 was R139.54 ± 41.79 and R129.65 ± 35.09 in 2006. CPIs of 0.82 and 0.78 indicate that it was a relatively inexpensive hipolipidaemic item prescribed by general medical practioners. Adco-Simvastatin 40mg accounted for 5.20% (n = R77 292 156.85) of the total hipolipidaemic cost by general medical practioners in 2005, and 5.56% (n = R84 008 507.57) in 2006, ranking fifth.

Sandoz Bezafibrate 400mg was the only medicine item from another therapeutic class than the HMG-CoA reductase inhibitors that appeared in the top ten trade name list as prescribed by general medical practioners. Ranking tenth in 2005 with 1.99% (n = 462 890) of the total hipolipidaemic medicine prevalence by general medical practioners, and eighth in 2006, accounting for 2.20% (n = 515 942). Regarding total hipolipidaemic cost from general medical practioners, Sandoz Bezafibrate 400mg ranked ninth in both 2005 and 2006, accounting for 2.02% (n = R77 292 156.85) and 2.30% (n = R84 008 507.57) respectively. Calculated CPIs were 0.99 in 2005 and 1.02 in 2006, thus changing from being a relatively inexpensive

hipolipidaemic medicine item prescribed by general medical practioners in 2005 to being a relatively expensive hipolipidaemic medicine item in 2006.

Lescol XL 80mg ranked eighth and ninth respectively in 2005 and 2006 regarding total hipolipidaemic prevalence from general medical practioners, and ranked seventh in both study periods regarding total hipolipidaemic cost. Simvacor 20mg came into the top ten in 2006 regarding total prevalence and cost for hipolipidaemic medicine items prescribed by general medical practitioners.

4.6.3.3 Other prescribers

The following section presents the top ten trade name products prescribed by other prescribers based on prevalence and cost (depicted in table 4.20). The ranking order is indicated in the table in brackets next to each applicable value. Table 4.20 is compiled from the tables B2.56 and B2.57 in appendix B, reflecting the hipolipidaemic data on the database of both 2005 and 2006 and their indicidual periods based on trade names and prescriber type.

Table 4.20: The top ten trade name products prescribed by other prescribers based on prevalence and cost

Year	Trade name product	Number of medicine items (n = 109 482)	Average cost (R)	Total cost (R) (n = R19 427 191.02)	CPI
2005	**Lipitor 10mg**	29 395 **(1)**	189.88 ± 29.20	5 581 544.42 **(1)**	1.11
	Adco-Simvastatin 20mg	18 308 **(2)**	112.36 ± 16.87	2 057 131.60 **(3)**	0.66
	Lipitor 20mg	12 784 **(3)**	274.47 ± 45.46	3 508 828.67 **(2)**	1.61
	Adco-Simvastatin 10mg	9 573 **(4)**	102.16 ± 9.65	978 021.59 **(6)**	0.60
	Adco-Simvastatin 40mg	6 990 **(5)**	144.51 ± 42.42	1 010 142.53 **(5)**	0.85
	Lipitor 40mg	4 363 **(6)**	285.53 ± 100.51	1 245 782.47 **(4)**	1.67
	Lescol XL 80mg	2 853 **(7)**	207.00 ± 19.11	590 580.75 **(7)**	1.21
	Simvotin 20mg	2 623 **(8)**	111.85 ± 12.73	293 376.01 **(9)**	0.66
	Sandoz Bezafibrate 400mg	2 358 **(9)**	173.84 ± 34.82	409 922.46 **(8)**	1.02
	Simvacor 20mg	1 804 **(10)**	117.92 ± 22.06	212 729.25 **(10)**	0.69
Total		**91 051**		**15 888 059.75**	
Year	**Trade name product**	**Number of medicine items (124 749)**	**Average cost (R)**	**Total cost (R) (n = 21 709 085.61)**	**CPI**
2006	**Lipitor 10mg**	28 845 **(1)**	190.02 ± 31.13	5 481 208.11 **(1)**	1.14
	Adco-Simvastatin 20mg	21 545 **(2)**	110.56 ± 16.93	2 381 990.38 **(3)**	0.66
	Lipitor 20mg	14 027 **(3)**	273.26 ± 45.67	3 833 029.16 **(2)**	1.64
	Adco-Simvastatin 10mg	10 526 **(4)**	100.04 ± 13.77	1 053 032.10 **(6)**	0.60
	Adco-Simvastatin 40mg	8 566 **(5)**	134.34 ± 32.41	1 150 735.43 **(5)**	0.80
	Lipitor 40mg	4 986 **(6)**	279.88 ± 81.24	1 395 506.21 **(4)**	1.68
	Sandoz Bezafibrate 400mg	2 967 **(7)**	169.86 ± 26.75	503 984.32 **(9)**	1.02
	Simvotin 20mg	2 844 **(8)**	110.74 ± 12.04	314 947.33 **(10)**	0.66
	Ezetrol 10mg	2 748 **(9)**	354.68 ± 43.70	974 656.47 **(7)**	2.12
	Lescol XL 80mg	2 645 **(10)**	206.56 ± 20.09	546 357.06 **(8)**	1.24
Total		**99 699**		**17 635 446.57**	

Table 4.20 shows that the top ten trade name products prescribed by other prescribers contributed 83.16% (n = 109 482) in 2005 and 79.92% (n = 124 749) in 2006 of the total hipolipidaemic medicine items prescribed by other prescribers. In 2005, nine out of the top ten trade name products prescribed by other prescribers were from the HMG-CoA reductase inhibitors (statins), and eight out of ten in 2006. The top ten trade name products prescribed by other prescribers in 2005 accounted for 81.78% (n = R19 427 191.02) of the total hipolipidaemic medicine cost contributed by other prescribers and for 81.24% (n = R21 709 085.61) in 2006. During the two study periods the top ten trade name products prescribed by other prescribers only had minor changes, with nine of the top ten remaining the same in both study years.

Lipitor 10mg was positioned first in both study periods and represented 26.86% (n = 109 482) and 23.12% (n = 124 749) of the overall hipolipidaemic medicine prevalence prescribed by other prescribers in 2005 and 2006 respectively. The total hipolipidaemic medicine cost by other prescribers for Lipitor 10mg also ranked first in both 2005 and 2006, accounting for 28.73% (n = R19 427 191.02) in 2005 and 25.25% (n = R21 709 085.61) in 2006. The average cost was R189.88 ± 29.20 in 2005 and R190.02 ± 31.13 in 2006. Lipitor 10mg presented with respective CPIs of 1.11 and 1.14 which indicated that it was a relatively expensive hipolipidaemic medicine item prescribed by other prescribers in both study periods.

Adco-Simvastatin 20mg had the second highest prevalence for prescribed hipolipidaemic medicine items by other prescribers in 2005 and 2006, accounting for 16.72% (n = 109 482) and 17.27% (n = 124 749). Adco-Simvastatin 20mg ranked third for total hipolipidaemic medicine cost by other prescribers in 2005 and 2006, accounting for 10.59% (n = R19 427 191.02) and 10.97% (n = R21 709 085.61) respectively. The average cost was R112.36 ± 16.87 in 2005 and R110.56 ± 16.93 in 2006. Adco-Simvastatin 20mg provided calculated CPIs of 0.66 in 2005 and 2006, thus being a relatively inexpensive hipolipidaemic treatment item prescribed by other prescribers.

Lipitor 20mg ranked third in both 2005 and 2006 for the total hipolipidaemic medicine prevalence prescribed by other prescribers, accounting for 11.68% (n = 109 482) and 11.24% (n = 124 749) respectively. Lipitor 20mg ranked second in 2005 and 2006 for total hipolipidaemic cost by other prescribers, accounting for 18.06% (n = R19 427 191.02) in 2005, and 17.66% (n = R21 709 085.61) in 2006. Lipitor 20mg had an average cost in 2005 of R274.47 ± 45.46 and R273.26 ± 45.67 in 2006. CPIs of 1.61 and 1.64 indicate that it was a relatively expensive hipolipidaemic item prescribed by other prescribers.

Adco-Simvastatin 10mg had the fourth highest prevalence for hipolipidaemic medicine items prescribed by other prescribers in 2005 and 2006, accounting for 8.74% (n = 109 482) and

8.44% (n = 124 749). Adco-Simvastatin 10mg ranked sixth for total hipolipidaemic medicine cost by other prescribers in 2005 and 2006 respectively, and had calculated CPIs of 0.60 in 2005 and 2006, thus showing to be a relatively inexpensive hipolipidaemic item prescribed by other prescribers.

Adco-Simvastatin 40mg ranked fifth in both 2005 and 2006 for the total hipolipidaemic medicine prevalence by other prescribers, accounting for 6.38% (n = 109 482) and 6.87% (n = 124 749) respectively. Adco-Simvastatin 40mg accounted for 5.20% (n = R19 427 191.02) of the total hipolipidaemic cost by other prescribers in 2005, and 5.30% (n = R21 709 085.61) in 2006, ranking fifth. Adco-Simvastatin 40mg, as prescribed by other prescribers had an average cost of R144.51 ± 42.42 in 2005 and R134.34 ± 32.41 in 2006. CPIs of 0.85 and 0.80 indicated that it was a relatively inexpensive hipolipidaemic item prescribed by other prescribers.

Lipitor 40mg ranked fourth regarding total hipolipidaemic medicine cost as prescribed by other prescribers in both 2005 and 2006, accounting for 6.41% (n = R19 427 191.02) and 6.43% (n = R21 709 085.61) respectively. Lipitor 40mg had an average cost of R285.53 ± 100.51 in 2005 and R279.88 ± 81.24 in 2006. CPIs of 1.67 and 1.68 were calculated, indicating that it was a relatively expensive hipolipidaemic medicine item prescribed by other prescribers.

Ezetrol 10mg was among the top ten trade name products prescribed by other prescribers in 2006. Ezetrol 10mg ranked ninth regarding the total hipolipidaemic prevalence in 2006 when it accounted for 2.20% (n = 124 749) and ranked seventh for the total hipolipidaemic medicine cost by other prescribers in 2006 with 4.49% (n = R21 709 085.61). Ezetrol 10mg, had an average cost of R354.68 ± 43.70 and provided a CPI of 2.12 which indicates that it was a relatively expensive prescribed hipolipidaemic medicine item.

4.6.3.4 Pharmacotherapists

In 2005 there was only one hipolipidaemic medicine item on the database prescribed by a pharmacotherapist, which was Lipitor 10mg. In 2006 eleven hipolipidaemic medicine items were prescribed by pharmacotherapist/s, these items being Liponil Forte (1 item), Questran Lite 4mg (2 items), Be-Tabs Nicotinic acid 10mg (7 items) and 100mg (1 item).

4.6.3.5 Pharmacists

The following section presents a discussion on the top ten trade name products prescribed by pharmacists analysed according to prevalence and cost (depicted in table 4.21). The ranking order is indicated in the table in brackets next to each applicable value. Table 4.21 is compiled

from the tables B2.56 and B2.57 in appendix B, reflecting the hipolipidaemic data on the database of both 2005 and 2006 and their indicidual periods based on trade names and prescriber type.

Table 4.21: The top ten trade name products prescribed by pharmacists based on prevalence and cost

Year	Trade name product	Number of medicine items (n = 395)	Average cost (R)	Total cost (R) (n = R51 044.35)	CPI
2005	**Questran Lite 4mg**	135 **(1)**	90.79 ± 85.14	12 256.53 **(1)**	0.53
	Lipitor 10mg	64 **(2)**	182.40 ± 36.21	11 673.51 **(2)**	1.07
	Be-Tabs Nicotinic acid 100mg	52 **(3)**	14.44 ± 27.39	750.69 **(10)**	0.08
	Adco-Simvastatin 20mg	30 **(4)**	104.65 ± 22.84	3 139.42 **(4)**	0.61
	Lipitor 20mg	29 **(5)**	266.40 ± 45.87	7 725.73 **(3)**	1.56
	Adco-Simvastatin 10mg	17 **(6)**	104.89 ± 22.48	1 783.10 **(7)**	0.61
	Lescol XL 80mg	12 **(7)**	188.85 ± 51.39	2 266.25 **(5)**	1.11
	Adco-Simvastatin 40mg	12 **(7)**	122.95 ± 40.44	1 475.34 **(8)**	0.72
	Lipitor 40mg	8 **(9)**	254.76 ± 69.29	2 038.10 **(6)**	1.49
	Sandoz Bezafibrate 400mg	5 **(10)**	167.73 ± 1.18	838.63 **(9)**	0.98
Total		**364**		**43 947.30**	
Year	**Trade name product**	**Number of medicine items (n = 627)**	**Average cost (R)**	**Total cost (R) (n = R79 070.21)**	**CPI**
2006	**Questran Lite 4mg**	161 **(1)**	103.75 ± 120.79	16 703.79 **(1)**	0.62
	Lipitor 10mg	93 **(2)**	179.34 ± 38.31	16 678.49 **(2)**	1.07
	Liponil Forte	75 **(3)**	80.51 ± 25.07	6 038.35 **(4)**	0.48
	Be-Tabs Nicotinic acid 100mg	60 **(4)**	24.53 ± 39.50	1 471.91 **(9)**	0.15
	Adco-Simvastatin 20mg	58 **(5)**	101.89 ± 23.52	5 909.63 **(5)**	0.61
	Lipitor 20mg	30 **(6)**	260.68 ± 62.36	7 820.48 **(3)**	1.56
	Adco-Simvastatin 10mg	30 **(6)**	95.89 ± 14.41	2 876.69 **(7)**	0.57
	Adco-Simvastatin 40mg	27 **(8)**	126.88 ± 31.40	3 425.81 **(6)**	0.76
	Be-Tabs Nicotinic acid 10mg	10 **(9)**	13.73 ± 8.92	137.32 **(10)**	0.08
	Ezetrol 10mg	7 **(10)**	354.24 ± 2.38	2 479.70 **(8)**	2.12
Total		**551**		**61 062.47**	

In 2005, Questran Lite 4mg accounted for 34.17% (n = 395) of the total hipolipidaemic medicine prevalence prescibed by pharmacists, and for 25.68% (n = 627) in 2006. In both study years it also accounted for the highest cost percentage regarding total hipolipidaemic cost from pharmacists, accounting for 24.01% (n = R51 044.35) and 21.12% (n = R79 070.21) in 2005 and 2006 respectively. Questran Lite 4mg showed CPIs of 0.53 in 2005 and 0.62 in 2006, thus being relatively inexpensive.

Be-Tabs Nicotinic acid 100mg was also a very common prescribed item by pharmacists and seemed very inexpensive in both study periods with CPIs of 0.08 in 2005 and 0.15 in 2006.

4.6.3.6 Thoracic surgeons

The following section presents an analysis of the top ten trade name products prescribed by thoracic surgeons based on prevalence and cost (depicted in table 4.22). The ranking order is indicated in the table in brackets next to each applicable value. Table 4.22 is compiled from the tables B2.56 and B2.57 in appendix B, reflecting the hipolipidaemic data on the database of both 2005 and 2006 and their indicidual periods based on trade names and prescriber type.

Table 4.22: The top ten trade name products prescribed by thoracic surgeons based on prevalence and cost

Year	Trade name product	Number of medicine items (n = 1 557)	Average cost (R)	Total cost (R) (n = 294 790.97)	CPI
2005	**Lipitor 10mg**	466 **(1)**	193.38 ± 84.92	90 114.08 **(1)**	1.13
	Adco-Simvastatin 20mg	276 **(2)**	112.64 ± 13.41	31 089.62 **(3)**	0.66
	Lipitor 20mg	249 **(3)**	270.42 ± 37.21	67 333.70 **(2)**	1.58
	Adco-Simvastatin 40mg	140 **(4)**	136.52 ± 34.94	19 112.93 **(5)**	0.80
	Adco-Simvastatin 10mg	77 **(5)**	102.89 ± 3.23	7 922.26 **(6)**	0.60
	Lipitor 40mg	70 **(6)**	325.28 ± 101.24	22 769.51 **(4)**	1.91
	Prava 20mg	31 **(7)**	224.76 ± 48.93	6 967.52 **(7)**	1.32
	Simvotin 20mg	30 **(8)**	111.87 ± 14.62	3 355.96 **(9)**	0.66
	Prava 20mg	25 **(9)**	239.86 ± 14.48	5 996.38 **(8)**	1.41
	Simvacor 20mg	22 **(10)**	114.26 ± 3.20	2 513.65 **(10)**	0.67
Total		**1 386**		**257 175.61**	
Year	**Trade name product**	**Number of medicine items (n = 1 760)**	**Average cost (R)**	**Total cost (R) (n = R331 766.90)**	**CPI**
2006	**Lipitor 10mg**	382 **(1)**	191.16 ± 22.91	73 024.48 **(2)**	1.14
	Lipitor 20mg	282 **(2)**	273.32 ± 39.35	77 077.08 **(1)**	0.68
	Adco-Simvastatin 20mg	273 **(3)**	113.37 ± 7.93	30 950.47 **(3)**	1.64
	Adco-Simvastatin 40mg	189 **(4)**	134.48 ± 28.37	25 416.26 **(4)**	0.80
	Crestor 10mg	97 **(5)**	186.26 ± 34.81	18 066.87 **(7)**	1.11
	Lipitor 40mg	87 **(6)**	266.99 ± 81.54	23 228.28 **(5)**	1.60
	Ezetrol 10mg	65 **(7)**	343.37 ± 45.00	22 319.11 **(6)**	2.06
	Adco-Simvastatin 10mg	55 **(8)**	101.07 ± 3.14	5 559.03 **(9)**	0.60
	Pranalip 20mg	42 **(9)**	161.96 ± 8.11	6 802.36 **(8)**	0.97
	Simvotin 20mg	38 **(10)**	114.81 ± 4.17	4 362.77 **(10)**	0.69
Total		**1 510**		**286 806.71**	

Table 4.22 portrays that the top ten trade name products in this category contributed 89.02% (n = 1 557) in 2005 and 85.80% (n = 1 760) in 2006 of the total hipolipidaemic medicine items prescribed by thoracic surgeons. In 2005 all of the top ten trade name products which were prescribed by thoracic surgeons were from the HMG-CoA reductase inhibitors (statins), and nine out of the top ten trade name products in 2006 were statins. The top ten trade name products prescribed in 2005 accounted for 87.24% (n = R294 790.97) of the total hipolipidaemic medicine cost contributed by thoracic surgeons and for 86.45% (n = R331 766.90) in 2006.

During the two study periods the top ten trade name products only changed slightly with Ezetrol 10mg being the only non-statin among the top ten in 2006.

Lipitor 10mg was positioned first in both study periods and represented 29.93% (n = 1 557) and 21.70% (n = 1 760) of the overall hipolipidaemic medicine prevalence prescribed by thoracic surgeons in 2005 and 2006 respectively. The total hipolipidaemic medicine cost by thoracic surgeons for Lipitor 10mg also ranked first in 2005 and second in 2006, accounting for 30.57% (n = R294 790.97) in 2005 and 22.01% (n = R331 766.90) in 2006. The average cost was R193.38 ± 84.92 in 2005 and R191.16 ± 22.91 in 2006. Lipitor 10mg presented respective CPIs of 1.13 and 1.14 which indicated that it was a relatively expensive hipolipidaemic medicine item as prescribed by thoracic surgeons in both study periods.

Adco-Simvastatin 20mg had the second highest prevalence for prescribed hipolipidaemic medicine items by thoracic surgeons in 2005 and third highest in 2006, accounting for 17.73% (n = 1 557) and 21.70% (n = 1 760). Adco-Simvastatin 20mg ranked third for total hipolipidaemic medicine cost prescribed by thoracic surgeons in 2005 and 2006, accounting for 10.55% (n = R294 790.97) and 9.33% (n = R331 766.90) respectively. The average cost was R112.64 ± 13.41 in 2005 and R113.37 ± 7.93 in 2006.

Lipitor 20mg ranked third in 2005 and second in 2006 for the total hipolipidaemic medicine prevalence prescribed by thoracic surgeons, representing 15.99% (n = 1 557) and 16.02% (n = 1 760) respectively. Lipitor 20mg ranked second in 2005 and first in 2006 for total hipolipidaemic cost by thoracic surgeons, accounting for 22.84% (n = R294 790.97) in 2005, and 23.23% (n = R331 766.90) in 2006. Lipitor 20mg, as prescribed by thoracic surgeons had an average cost of R270.42 ± 37.21 in 2005 and R273.32 ± 39.35 in 2006. CPIs of 1.58 and 1.64 indicate that it was a relatively expensive hipolipidaemic item prescribed by thoracic surgeons.

Adco-Simvastatin 40mg had the fourth highest prevalence for hipolipidaemic medicine items prescribed by thoracic surgeons in 2005 and 2006, accounting for 8.99% (n = 1 557) and 10.74% (n = 1 760). Adco-Simvastatin 40mg ranked fifth and fourth for total hipolipidaemic medicine cost by thoracic surgeons in 2005 and 2006 respectively, accounting for 6.48% (n = R294 790.97) in 2005 and 7.66% (n = R331 766.90) in 2006. An average cost of R136.52 ± 34.94 in 2005 and R134.48 ± 28.38 in 2006 was calculated.

Adco-Simvastatin 10mg, that ranked fifth in 2005 for total hipolipidaemic medicine prevalence for thoracic surgeons, ranked eighth in 2006, accounting for 4.95% (n = 1 557) and 3.13% (n = 1 760) in 2005 and 2006 respectively. Regarding the total hipolipidaemic medicine cost for

items prescribed by thoracic surgeons, Adco-Simvastatin 10mg ranked sixth in 2005 and ninth in 2006. CPIs of 0.60 in both study periods still prove that it was a relatively inexpensive hipolipidaemic medicine item prescribed by thoracic surgeons.

Crestor 10mg appeared among the top ten trade name products prescribed by thoracic surgeons in 2006 only. Crestor 10mg ranked fifth regarding the total hipolipidaemic prevalence when it accounted for 5.51% (n = 1 760) and ranked seventh for the total hipolipidaemic medicine cost by thoracic surgeons at 5.45% (n = R331 766.90). Crestor 10mg had an average cost of R186.26 ± 34.81 and a CPI of 1.11 which indicated that it was a relatively expensive hipolipidaemic medicine item prescribed in 2006.

Prava 20mg ranked seventh regarding total hipolipidaemic prevalence for items prescribed by thoracic surgeons in 2005 as a non-substitutable product. The status of the product changed thereafter to original (refer to Appendix B2.40) in the middle of 2005. Original Prava 20mg then ranked ninth regarding total prevalence. The generic products Pranalip, Aspen Pravastatin and Sandoz Pravastatin first appeared on the market in 2006 (refer to Appendix B2.56).

4.6.4 Summary and discussion of the top ten trade name products prescribed

In the subsequent sections the summaries of the top ten trade name products will be discussed.

4.6.4.1 Summary and discussion of the top ten trade name products based on the age and sex categories of patients

Hipolipidaemic trade name products followed relatively the same claims pattern in each age group except for age group 1, where Questran Lite 4mg was by far the leading hipolipidaemic medicine item. Lipitor 10mg, Lipitor 20mg, Adco-Simvastatin 10mg and Adco-Simvastatin 20mg were the leading trade name products in age group 2 through to 5. Adco-Simvastatin 10mg, 20mg and 40mg were present among the top ten trade name products in age groups 3 to 5.

From the aforementioned results it is evident that statins were the drugs of choice in all age groups, with the exception of cholestyramine in children. Statins were also the drugs of choice in both sex categories.

Questran Lite 4mg is commonly used in primary hypercholesterolaemia or in obstructive diarrhoea (Snyman, 2007:170) and a reason for this might be because Questran Lite 4mg can also be used in pruritus associated with bile acid retention and bile salt diarrhoea (Gibbon, 2008:168) which could be one of the reasons for the high prevalence in this age group. de

Jonge *et al*. (2002:2232) conducted a study on the efficacy and safety of statin therapy in children with familial hypercholesterolaemia and came to the conclusion that simvastatin significantly reduced LDL cholesterol, total cholesterol, triglyceride, VLDL cholesterol and apolipoprotein B levels and was well tolerated in children. No evidence of adverse effects of simvastatin on growth and pubertal development were detected and therefore simvastatin doses up to 40 mg proved to be well tolerated and effective in therapy for children with familial hypercholesterolaemia (de Jonge *et al*., 2002:2232). Simvastatin at doses of 40 mg also proved to be a well-tolerated and effective therapy for heterozygous familial hypercholesterolaemia (de Jonge *et al*., 2002:2232).

Products of local generic pharmaceutical companies (Adcock Ingram, Sandoz, Ranbaxy & Pharma Dynamics) featured on the top 10 lists for nearly all the age and sex groups. Adcock Ingram is the longest standing pharmaceutical company and was founded 116 years ago. The company has an extensive range of prescription, generic and OTC products and is the largest over-the-counter pharmaceutical company in the country (Shevel, 2009). It also provides life-saving hospital equipment, diagnostic products and services (Anon., 2009). The manufacturer of Adco-products, *i.e.*, Adcock Ingram pharmaceutical company, was relisted on the Johannesburg Stock Exchange (JSE) in 2008 after being absent for eight years (Shevel, 2009; Still, 2009:287). Sandoz is a global company and a global generic supplier that specialises in manufacturing, marketing and selling of generic medicines. Sandoz medicines are available to 90% of people worldwide (Anon., 2009).

4.6.4.2 Summary and discussion of the top ten trade name products based on prescriber type

From paragraphs 4.6.1 – 4.6.3 it can be concluded that the majority of claims for hipolipidaemic medicine items were prescribed by general medical practitioners, followed by “other prescribers” and then by cardiologists. Only a small number of prescriptions claimed were prescribed by thoracic surgeons and even fewer by pharmacotherapists and pharmacists. Trade name products that were mostly prescribed were Lipitor and Simvastatin (Adco-Simvastatin).

Pharmacotherapists hardly prescribed any hipolipidaemic medicine items in both 2005 and 2006, with only 12 items covering both study periods. As described by Fed-Health (2008), a pharmacotherapist is a qualified pharmacist with an extra qualification which allows him/her to provide primary health services, e.g. pregnancy tests, blood pressure monitoring, care of wounds and a few other similar services. According to the Medicines and Related Substances Control Act 101 of 1965 (South Africa, 2007a) after amendment by the Medicines and Related Substances Control Amendment Act (Act 90 of 1997), “The Director-General may, after

consultation with the Interim Pharmacy Council of South Africa, issue a permit to any person or organisation performing a health service, authorising such a person or organisation to acquire, possess, use or supply any specified Schedule 1, Schedule 2, Schedule 3, Schedule 4 or Schedule 5 substance, and such permit shall be subject to such conditions as the Director-General may determine" (South Africa, 2007b:MAE-27).

Pharmacists mostly prescribed Questran Lite 4 mg which is a Schedule 2 medicine item (Snyman, 2007:170). In terms of the Pharmacy Act, 1974 (Act No. 53 of 1974), pharmacists are not registered to prescribe hipolipidaemic medicine items as they are usually classified as schedule 3 or 4 medication. A possible reason for some of the following items, e.g. Lipitor 10 mg, 20 mg, 40 mg, Adco-Simvastatin 10 mg, 20 mg, 40 mg and Lescol XL 80mg being on the database might be since there can be mistakes made by the pharmacist while dispensing. These findings should be further investigated. The reason for this might be that Questran Lite 4 mg is classified as a schedule 2 medication and is commonly used for diarrhoea in infants and children (Snyman, 2007:170).

4.7 POTENTIAL COST SAVINGS ATTRIBUTABLE TO GENERIC SUBSTITUTION

Since generic medicine items are usually considered to be less expensive than original branded medicine items, the utilisation of generic medicine items can be expected to lead to substantial cost savings (Anderson *et al*., 2004:341). In this section possible cost savings will be investigated as related to generic substitution of hipolipidaemic medicine items. Cost savings will be calculated using the average medicine treatment cost with the formula: *Cost saving* = $(Average\ cost_O - Average\ cost_G)n_O$; where average $cost_O$ = the average cost of the original branded product; average $cost_G$ = average cost of the generic equivalent(s) and n_O = number of original branded products available (refer to paragraph 3.3.4).

For the purpose of this section, in cases where the original branded product is less expensive than the available generic equivalent(s) or in cases where there is no generic equivalent available, the specific item will be excluded from the analysis. Table 4.23 contains the possible cost savings for 2005 and 2006 and will be discussed subsequently.

Table 4.23: Potential cost savings due to generic substitution for 2005 and 2006

Substance (strength)	2005			2006		
	Original n; (x ± SD)	Generic n; (x ± SD)	Potential saving (R)	Original n; (x ± SD)	Generic n; (x ± SD)	Potential saving (R)
Bezafibrate (200mg)	977 (196.84 ± 83.68)	–	–	953 (193.20 ± 88.22)	–	–
Bezafibrate (400mg)	1 265 (344.21 ± 48.23)	12 441 (170.40 ± 29.55)	219 869.65	1 261 (340.20 ± 58.74)	15 491 (170.65 ± 28.40)	213 802.55
Fenofibrate (200mg)	1987 (363.33 ± 88.16)	–	–	38 (259.25 ± 15.28)	–	–
Fenofibrate (300mg)	–	–	–	186 (338.94 ± 67.93)	–	–
Gemfibrozil (600mg)	1 057 (270.73 ± 78.30)	–	–	989 (261.44 ± 83.73)	–	–
Total Fibrates			**219 869.65**			**213 802.55**
Atorvastatin (10mg)	166 536 (188.85 ± 27.93)	–	–	160 500 (189.66 ± 28.59)	–	–
Atorvastatin (20mg)	70 987 (269.44 ± 48.14)	–	–	75 542 (270.54 ± 47.41)	–	–
Atorvastatin (40mg)	20 892 (275.81 ± 90.09)	–	–	25 165 (272.31 ± 77.50)	–	–
Atorvastatin (80mg)	1 675 (267.08 ± 72.73)	–	–	5 375 (251.73 ± 77.04)	–	–
Fluvastatin (20mg)	4 392 (145.12 ± 14.03)	–	–	3 632 (144.36 ± 17.07)	–	–
Fluvastatin (40mg)	4 624 (183.76 ± 21.20)	–	–	3 270 (182.92 ± 17.91)	–	–
Fluvastatin (80mg)	16 794 (206.65 ± 25.08)	–	–	14 359 (205.99 ± 22.27)	–	–
Lovastatin (20mg)	1 285 (91.71 ± 12.36)	–	–	3 272 (92.72 ± 13.75)	–	–
Lovastatin (40mg)	858 (101.79 ± 19.35)	–	–	2 541 (104.26 ± 15.48)	–	–
Pravastatin (10mg)	2 848 (198.38 ± 23.88)	850 (129.16 ± 15.40)	197 138.56	2 718 (197.12 ± 28.57)	3 810 (128.76 ± 14.33)	185 802.48
Pravastatin (20mg)	4 479 (238.99 ± 34.62)	1 653 (157.34 ± 15.06)	365 710.35	4 294 (236.88 ± 38.38)	7 554 (157.19 ± 21.28)	342 188.86
Pravastatin (40mg)	3 544 (251.61 ± 64.73)	1 248 (165.94 ± 34.99)	303 614.48	3 308 (257.39 ± 61.49)	5 541 (165.08 ± 38.03)	305 361.48
Simvastatin (10mg)	6 605 (135.22 ± 19.45)	76 620 (101.14 ± 11.24)	225 098.40	4 380 (134.25 ± 20.44)	84 014 (99.55 ± 12.64)	151 986.00
Simvastatin (20mg)	8 049 (147.59 ± 27.89)	143 961 (112.24 ± 16.72)	284 532.15	5 645 (147.48 ± 22.30)	176 669 (110.66 ± 16.57)	207 848.90
Simvastatin (40mg)	3 534 (183.48 ± 43.58)	46 949 (141.46 ± 40.63)	148 498.68	2 152 (187.34 ± 42.36)	63 464 (131.58 ± 33.36)	119 995.52
Total Statins			**1 524 592.62**			**1 313 183.24**
Ezetimibe (10mg)	2 855 (355.64 ± 28.08)	–	–	10 894 (353.49 ± 39.85)	–	–
Total cholesterol absorptions inhibitors			**–**			**–**
Acipimox (250mg)	261 (181.36 ± 47.75)	–	–	237 (171.48 ± 41.78)	–	–
Cholestyramine (4mg)	3 659 (179.08 ± 147.23)	–	–	3 175 (173.89 ± 148.49)	–	–
Essential phospholipids (5ml)	13 (164.43 ± 201.02)	–	–	–	–	–

Table 4.23: Potential cost savings due to generic substitution for 2005 and 2006 (continued)

Nicotinic acid (10mg)	–	–	–	–	89 (10.82 ± 8.91)	–
Nicotinic acid (100mg)	–	393 (13.80 ± 20.66)	–	–	355 (15.12 ± 26.69)	–
Total "others"			**–**			**–**
Total cost saving			**1 744 462.27**			**1 526 985.79**

(-) Denotes cases where no generic equivalent was available or the generic equivalent available was more expensive than the original item.

From table 4.23 it is clear that there were not many generic equivalents available for hipolipidaemic medicine items during the study periods of 2005 and 2006. From the four therapeutic classes, only two classes, *i.e.* the statins and fibrates, and the active substance, nicotinic acid, were included in the cost-savings analysis. There were no generic equivalent(s) available for the cholesterol absorption inhibitor therapeutic class or the "others" therapeutic class. During 2005, a potential total cost saving for the fibrates therapeutic class to the value of R219 869.65 was obtained and a saving of R1 524 592.62 for the HMG-CoA reductase inhibitors (statins) therapeutic class. Fibrates were able to produce a cost saving of R213 803.55 and R1 526 985.79 for statins in 2006 (from Table 4.23).

A maximum potential cost saving would occur if 100% of the original hipolipidaemic medicine items were to be substituted for available, less expensive generic equivalents. With total substitution (100%) of original hipolipidaemic medicine items with the average price of all available generic hipolipidaemic medicine items on the database and where the generic items were less expensive than the original (innovator) products, a cost saving of R1 744 462.27 or 1.63% (N = R106 943 348.53) would have been possible in 2005. In 2006, a total cost saving of R1 526 985.79 or 1.30% (N = R117 862 631.87) of the total cost incurred could be calculated.

These cost savings are, however, difficult to achieve in practice as there will always be those patients and prescribers who would prefer the original product (Banahan & Kolassa, 1997:2080; Geither *et al*., 2001:729; Mott & Cline, 2002:662). Based on a scenario where 80% of the original (innovator) hipolipidaemic medicine items on the database with available generic equivalent(s) were substituted, an amount of R1 395 569.82 or 1.30% (N = R106 943 348.53) could have been saved in 2005, and in 2006, R1 221 588.63 or 1.04% (N = R117 862 631.87) could have been saved. With a scenario of 60% substitution during 2005 and 2006, a total cost saving of R1 046 677.36 or 0.98% (N = R106 943 348.53) could have been made in 2005, and a total cost saving of R916 191.47 or 0.78% (N = R117 862 631.87) could have been made in 2006. With a 45% substitution rate, cost savings could have been made to the value of R785 008.02 or 0.73% and R687 143.37 or 0.58% in 2005 and 2006 respectively.

4.8 POTENTIAL COST SAVINGS ATTRIBUTABLE TO THERAPEUTIC SUBSTITUTION: THE CASE OF LIPITOR (ATORVASTATIN)

During the study periods of 2005 and 2006, no generic equivalent was available for Lipitor. The generic equivalent Aspavor was only available on the market in 2007 (registered in December 2006) (South Africa, 2006:6), thus at the time of this study there were no available data on Aspavor. Gumbs *et al*. (2007:680) conclude that from an economic point of view, substantial costs can be saved by means of therapeutic substitution.

Table 4.24 portrays a summary of therapeutic equivalents to Lipitor (Atorvastatin), based on LDL-cholesterol lowering effects (compiled from Jones *et al*., 1998:585; Radar, 2006:2)

Table 4.24: Therapeutic equivalents of Lipitor (atorvastatin)

Treatment group	Change in LDL-cholesterol (mean percentage change)
• Atorvastatin 10mg	-38
• Atorvastatin 20mg	-46
• Simvastatin 20mg	-35
• Simvastatin 40mg	-41
• Rosuvastatin 10mg	-45
• Lovastatin 40mg	-31
• Pravastatin 40mg	-34

Drugs were only selected if LDL-cholesterol lowering were in the same category as atorvastatin, and available at a less expensive price.

4.8.1 Simvastatin as therapeutic equivalent for atorvastatin

According to a study in the United Kingdom, the substitution for atorvastatin 10mg for simvastatin 20 mg or 40 mg can lead to a saving of up to £2 billion (~ R 25 billion)[2] over a five year period (Moon & Bogle, 2006:1344). Table 4.25 illustrates the possible cost savings if Lipitor 10 mg items were to be completely (100%) substituted for simvastatin 20 mg (the average cost of simvastatin 20 mg generic equivalents will be used, refer to Appendix B2.58). Table 4.25 reveals that a staggering R12 758 322.96 or 11.93% (N = R106 943 348.53) of the total hipolipidaemic cost could have been saved with the therapeutic substitution of Lipitor 10 mg for Simvastatin 20 mg in 2005. Calculations for 2006 indicate that R12 679 500.00 or 10.76% (N = R117 862 631.87) of the total hipolipidaemic cost could have been saved.

[2] 1 British Pound = R12.32 (2005-2006) (OANDA, 2009).

Table 4.25: The potential cost saving for Lipitor 10 mg with therapeutic substitution for Simvastatin 20 mg

Year	Hipolipidaemic product	Number of medicine items	Average cost (R)	Total cost (R)	Potential cost saving (R)
2005	Lipitor 10mg	166 536	188.85 ± 27.93	31 451 055.35	12 758 322.96
	Simvastatin 20mg	143 961	112.24 ± 16.72	16 157 795.58	
2006	Lipitor 10mg	160 500	189.66 ± 28.59	30 440 185.64	12 679 500.00
	Simvastatin 20mg	176 669	110.66 ± 16.57	19 549 767.94	

- Based on a scenario where 80% of the therapeutic equivalent had been substituted, R10 206 658.37 or 9.54% (N = R106 943 348.53) on the total hipolipidaemic cost could have been saved in 2005 and R10 143 600.00 or 8.61% (N = R117 862 631.87) in 2006.
- With a 60% therapeutic substitution, a total cost saving of R7 654 993.78 or 7.16% (N = R106 943 348.53) and R7 607 700.00 or 6.45% (N = R117 862 631.87) on the total hipolipidaemic cost could have occurred in 2005 and 2006 respectively.
- Based on a 45% therapeutic substitution scenario, a total of R5 741 245.33 or 5.36% (N = R106 943 348.53) on the total hipolipidaemic cost could still have been saved in 2005, and a total cost saving of R5 705 775.00 or 4.84% (N = R117 862 631.87) could have occurred in 2006.

Therapeutic substitution of Lipitor 10 mg can also be made possible with Simvastatin 40 mg. Table 4.26 illustrates the possible cost savings if Lipitor 10 mg were completely substituted for Simvastatin 40 mg (the average cost of Simvastatin 40 mg generic equivalents will be used, refer to Appendix B2.58). Table 4.26 reveals that R7 892 141.04 or 7.38% (N = R106 943 348.53) could have been saved with the therapeutic substitution of Lipitor 10 mg for Simvastatin 40 mg in 2005, compared to R9 321 840.00 or 7.91% (N = R117 862 631.87) in 2006. These results (table 4.26) were based on the possibility of a 100% substitution rate of therapeutic equivalents.

Table 4.26: The potential cost saving for Lipitor 10 mg with therapeutic substitution for Simvastatin 40 mg

Year	Hipolipidaemic product	Number of medicine items	Average cost (R)	Total cost (R)	Potential cost saving (R)
2005	Lipitor 10mg	166 536	188.85 ± 27.93	31 451 055.35	7 892 141.04
	Simvastatin 40mg	46 949	141.46 ± 40.63	6 641 422.40	
2006	Lipitor 10mg	160 500	189.66 ± 28.59	30 440 185.64	9 321 840.00
	Simvastatin 40mg	63 464	131.58 ± 33.36	8 350 814.20	

- Based on a scenario where 80% of the therapeutic equivalent had been substituted, R6 313 712.83 or 5.90% (N = R106 943 348.53) on the total hipolipidaemic cost could have been

saved in 2005 and R7 457 472.00 or 6.33% (N = R117 862 631.87) could have been saved in 2006.

- With a 60% therapeutic substitution, a total cost saving of R4 735 284.62 or 4.43% (N = R106 943 348.53) and R5 593 104.00 or 4.75% (N = R117 862 631.87) on the total hipolipidaemic cost could have occurred in 2005 and 2006 respectively.
- Based on 45% therapeutic substitution scenario, a total of R3 551 463.47 or 3.32% (N = R106 943 348.53) could have been saved in 2005, and a total cost saving of R4 194 828.00 or 3.56% (N = R117 862 631.87) could have occurred in 2006.

Therapeutic substitution of Lipitor 20 mg can also be made possible by means of simvastatin 40 mg. Table 4.27 illustrates the possible cost-savings if Lipitor 20 mg were completely substituted for Simvastatin 40 mg (the average cost of Simvastatin 40 mg generic equivalents will be used - refer to Appendix B2.57).

Table 4.27: The potential cost saving for Lipitor 20mg with therapeutic substitution for Simvastatin 40 mg

Year	Hipolipidaemic product	Number of medicine items	Average cost (R)	Total cost (R)	Potential cost saving (R)
2005	Lipitor 20mg	70 987	269.44 ± 48.14	19 126 984.68	9 084 916.26
	Simvastatin 40mg	46 949	141.46 ± 40.63	6 641 422.40	
2006	Lipitor 20mg	75 542	270.54 ± 47.41	20 436 897.83	10 497 316.32
	Simvastatin 40mg	63 464	131.58 ± 33.36	8 350 814.20	

Based on the results obtained from table 4.27 (100% therapeutic substitution), it is shown that a total cost saving of R9 084 916.26 or 8.50% (N = R106 943 348.53) on the total hipolipidaemic cost could have occurred in 2005, compared to R10 497 316.32 or 8.91% (N = R117 862 631.87) in 2006.

- With an 80% therapeutic substitution scenario, R7 267 933.01 or 6.80% (N = R106 943 348.53) of the total hipolipidaemic cost could have been saved in 2005 and R8 397 853.06 or 7.13% (N = R117 862 631.87) in 2006.
- R5 450 949.76 or 5.10% (R106 943 348.53) and R6 298 389.79 or 5.34% (N = R117 862 631.87) could have been the total cost saved on the total hipolipidaemic cost in 2005 and 2006 respectively if a 60% therapeutic substitution had taken place.
- In a scenario where 45% of the therapeutic equivalent were to be substituted, R4 088 212.32 or 3.82% (N = R106 943 348.53) could have been saved on the total hipolipidaemic cost in 2005 and, R4 723 792.34 or 4.01% (N = R117 862 631.87) could have been the total cost saved in 2006.

4.8.2 Rosuvastatin as therapeutic equivalent for atorvastatin

According to a study conducted by Farahani (2009:e212), 10 mg atorvastatin could be therapeutically substituted for 5 mg Rosuvastatin, and as for 20 mg atorvastatin for 10 mg Rosuvastatin. Rosuvastatin is not available in 5 mg tablets, thus the cost savings will be calculated for 10mg (Rosuvastatin 20 mg and 40 mg were more expensive than Lipitor and were therefore excluded from the analysis). Table 4.28 illustrates the possible cost savings if Lipitor 20 mg were completely (100%) substituted for 10mg Rosuvastatin. Rosuvastatin was available on the market in 2006 for the first time (South Africa, 2006:10-12), thus cost saving will be calculated for that year only (the average cost of Rosuvastatin 10mg generic equivalents will be used, refer to Appendix B2.41).

Table 4.28: The potential cost saving for Lipitor 20 mg with therapeutic substitution for Rosuvastatin 10 mg

Year	Hipolipidaemic product	Number of medicine items	Average cost (R)	Total cost (R)	Potential cost saving (R)
2006	**Lipitor 20mg**	75 542	270.54 ± 47.41	20 436 897.83	6 217 106.60
	Rosuvastatin 10mg	11 214	188.24 ± 35.42	2 110 917.94	

Table 4.28 portrays that a staggering R6 217 106.60 or 5.27% (N = R117 862 631.87) could have been saved with the therapeutic substation of Lipitor 20 mg for Rosuvastatin 10 mg in 2006. The results from table 4.28 were based on 100% substitution of the therapeutic equivalent.

- Based on a scenario where 80% of the therapeutic equivalent had been substituted, R4 973 685.28 or 4.22% (N = R117 862 631.87) on the total hipolipidaemic cost could have been saved in 2006.
- With a 60% therapeutic substitution, a total cost saving of R3 730 263.96 or 3.16% (N = R117 862 631.87) on the total hipolipidaemic cost could have occurred in 2006.
- Based on a 45% therapeutic substitution scenario, a total cost saving of R2 797 697.97 or 2.37% (N = R117 862 631.87) on the total hipolipidaemic cost could have occurred in 2006.

4.8.3 Lovastatin as therapeutic equivalent for atorvastatin

According to a study conducted by Jones *et al*. (1998:585), 10 mg atorvastatin could be therapeutically substituted for Lovastatin 40 mg. Table 4.29 illustrates the possible cost savings if Lipitor 10 mg (atorvastatin) were completely (100%) substituted for 40 mg Lovavastatin, (the average cost of Lovavastatin 40 mg generic equivalents will be used, refer to Appendix B2.41).

Table 4.29: The potential cost saving for Lipitor 10 mg with therapeutic substitution for Lovastatin 40 mg

Year	Hipolipidaemic product	Number of medicine items	Average cost (R)	Total cost (R)	Potential cost saving (R)
2005	Lipitor 10mg	166 536	188.85 ± 27.93	31 451 055.35	14 498 624.16
	Lovastatin 40mg	858	101.79 ± 19.35	87 334.45	
2006	Lipitor 10mg	160 500	189.66 ± 28.59	30 440 185.64	13 785 345.00
	Lovastatin 40mg	691	103.77 ± 18.42	71 704.40	

Table 4.29 portrays that R14 498 624.16 or 13.55% (N = R106 943 348.53) on the total hipolipidaemic cost could have been saved with the therapeutic substitution of Lipitor 10 mg for Lovavastatin 40 mg in 2005 and 2006 indicates that R13 785 345.00 or 11.70% (N = R117 862 631.87) could have been saved. These results (table 4.29) were based on 100% substitution of the therapeutic equivalent.

- Based on a scenario where 80% of the therapeutic equivalent had been substituted, R11 598 899.33 or 10.85% (N = R106 943 348.53) could have been saved on the total hipolipidaemic cost in 2005 and R11 028 276.00 or 9.36% (N = R117 862 631.87) could have been saved in 2006.
- With a 60% therapeutic substitution, a total cost saving of R8 699 174.50 or 8.13% (N = R106 943 348.53) and R8 271 207.00 or 7.02% (N = R117 862 631.87) could have occurred on the total hipolipidaemic cost in 2005 and 2006 respectively.
- Based on a 45% therapeutic substitution scenario, a total of R6 524 380.86 or 6.10% (N = R106 943 348.53) could have been saved on the total hipolipidaemic cost in 2005, and a total cost saving of R6 203 405.25 or 5.26% (N = R117 862 631.87) could have occurred in 2006.

4.8.4 Pravastatin as therapeutic equivalent for atorvastatin

According to a study conducted by Jones *et al*. (1998:585), 10 mg atorvastatin could be therapeutically substituted for Pravastatin 40 mg. Table 4.30 illustrates the possible cost savings if Lipitor 10 mg (atorvastatin) were completely (100%) substituted for 40 mg Pravastatin, (the average cost of Pravastatin 40 mg generic equivalents will be used, refer to Appendix B2.58). Table 4.30 portrays, that based on a 100% substitution rate, R3 815 339.76 or 3.57% (N = R106 943 348.53) could have been saved on the total hipolipidaemic cost with the therapeutic substitution of Lipitor 10 mg (atorvastatin) for Lovavastatin 40 mg in 2005, compared to a R3 945 090.00 or 3.35% (N = R117 862 631.87) saving in 2006.

Table 4.30: The potential cost-saving for Lipitor 10 mg with therapeutic substitution with Pravastatin 40 mg

Year	Hipolipidaemic product	Number of medicine items	Average cost (R)	Total cost (R)	Potential cost saving (R)
2005	Lipitor 10mg	166 536	188.85 ± 27.93	31 451 055.35	3 815 339.76
	Pravastatin 40mg	1 248	165.94 ± 34.99	207 088.84	
2006	Lipitor 10mg	160 500	189.66 ± 28.59	30 440 185.64	3 945 090.00
	Pravastatin 40mg	5 541	165.08 ± 38.03	914 725.99	

- Based on a scenario where 80% of the therapeutic equivalent had been substituted, R3 052 271.81 or 2.85% (N = R106 943 348.53) could have been saved in 2005 and R3 156 072.00 or 2.68% (N = R117 862 631.87) could have been saved in 2006.
- With a 60% therapeutic substitution, a total cost saving of R2 289 203.86 or 2.14% (N = R106 943 348.53) and R2 367 054.00 or 2.01% (N = R117 862 631.87) could have occurred in 2005 and 2006 respectively.
- Based on 45% therapeutic substitution scenario, a total of R1 716 902.89 or 1.61% (N = R106 943 348.53) could have been saved in 2005, and a total cost saving of R1 775 290.50 or 1.51% (N = R117 862 631.87) could have occurred in 2006.

4.8.5 Summary and discussion on generic and therapeutic substitution

Based on the before discussions directly above (paragraphs 4.7 – 4.8), it is evident that significant cost savings are possible with generic and therapeutic substitution. Roughly from a minimum (45%) to a maximum (100%) *via* generic substitution, cost savings of R785 008.02 (minimum) and R1 744 462.27 (maximum) could have occurred in 2005, and R687 143.37 (minimum) and R1 526 985.79 (maximum) cost saving could have occurred in 2006.

Generic substitution could thus, compared to the total database, have provided a minimum cost-saving percentage of 0.04% (N = R1 893 376 921.00) in 2005 and 0.09% (N = R1 893 376 921.00) maximum in 2005, compared to a minimum cost-saving percentage of 0.03% (N = R2 046 944 383.00) in 2006 and 0.07% (N = R2 046 944 383.00) maximum in 2006.

Therapeutic substitution provided a maximum cost saving with 100% substitution of R14 498 624.16 in 2005 and a minimum cost saving with 100% substitution in 2005 of R3 815 339.76, in 2006 a maximum cost saving with 100% substitution of R13 785 345.00 and a minimum cost saving with 100% of R3 945 090.00.

Although smaller, minimum substitution ratios of 45% would still have recorded a minimum cost saving of R1 716 902.89 in 2005, and R1 775 290.50 in 2006. With 45% substitution ratios, a

maximum cost saving in 2005 could have amounted to R5 741 245.33, and R5 705 775.00 in 2006.

In comparison to the total database, therapeutic substitution could thus have, on a 100% substitution rate, provided a minimum cost-saving percentage of 0.20% (N = R1 893 376 921.00) in 2005 and a maximum of 0.77% (N = R1 893 376 921.00). A minimum cost-saving percentage on the total database of 0.19% (N = R2 064 944 383.00) could have a occurred in 2006, compared to a maximum-saving of 0.67% (N = R2 064 944 383.00). Based on 45% therapeutic substitution rates, a minimum cost-saving percentage on the total database of 0.09% (N = R1 893 376 921.00) could have occurred in 2005 and 0.08% (N = R2 064 944 383.00) in 2006. A maximum cost-saving percentage on the total database, based on 45% therapeutic substitution rates of 0.30% (N = R1 893 376 921.00) could have occurred in 2005 and 0.28% (N = R2 064 944 383.00) in 2006.

4.9 CHAPTER SUMMARY

In this chapter the results of the empirical investigation were outlined, with focus on the prescribing patterns of hipolipidaemics in various age groups and sex categories, also on the various prescribers for hipolipidaemics, generic indicators for hipolipidaemics and the top ten trade name products.

Chapter 5 will be based on the conclusions and recommendations for this study which will also include some suggestions regarding future studies.