

**Hypertension treatment in a section of the prescribed management benefit market
in South Africa**

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**Thesis submitted for the degree Doctor of Philosophy in Pharmacy Practice at the
Potchefstroom Campus of the North-West University**

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September 2012

ABSTRACT

Title: Hypertension treatment in a section of the prescribed benefit management market in South Africa.

The objective of this study was to develop certain cost thresholds for the purpose of decision-making in the private health-care sector of South Africa, with specific reference to the treatment of hypertensive patients.

This research was embedded in a drug utilisation review approach supported by various other measuring instruments, classification systems, arithmetical formulas and descriptive statistical methods. This study was done on a medicine claims database ranging over a four-year study period from 1 January 2005 to 31 December 2008. The total medicine claims database was divided into cardiovascular medicine items and then into antihypertensive medicine items. These were analysed according to treatment categories: treatment category 1 (TC1) consisted of medicine items listed in MIMS[®] group 7.3; treatment category 2 (TC2) consisted of medicine items listed in MIMS[®] group 16.1 and treatment category 3 (TC3) consisted of medicine items listed in both MIMS[®] group 7.3 and 16.1; age groups: age group 1 (patients ≤ 18 years), age group 2 (>18 and ≤ 45 years), age group 3 (>45 years), and gender. Analysis included general cost analysis, adherence to antihypertensive medicine items, combination treatment with antihypertensive medicine items, and the calculation of cost threshold ranges (with an upper and lower limit) and cost ratio thresholds. The refill-based adherence rate (RAR) was calculated per individual medicine item for all antihypertensive (AH) medicine items that had been prescribed more than once. A cost threshold range was developed from a fraction of the standard deviation (50% or 33%) that had been added or subtracted from the average cost per item to determine the upper and lower limits. To obtain a medicine cost ratio threshold, the estimated number of high-income households and total medication cost were used as applied in the private health-care sector of SA. This estimated total medication cost was used to calculate a net cost. This resulted in the cost ratio threshold as applied in this study.

The results showed that antihypertensive medicine items accounted for 7,68% to 9,69% of all medicine items on the database at an associated cost of 10,94% to 11,10% of the total cost during the four study years. Antihypertensive medicine items represented 7 695 151 (70,04% N = 10 986 407) of all the cardiovascular medicine items and 59,94% of the total cost of cardiovascular medicine items for all four study years collectively for these medicine items.

Between 16,6% and 19,7% of all prescriptions contained antihypertensive medicine items, at a cost of 11,5% to 11,7% of the total cost of all medicine items claimed during the four-year study period. An analysis of combination antihypertensive treatment revealed that most observations were made for prescriptions consisting of two and three-item antihypertensive medications respectively. Generic antihypertensive medicine items accounted for more than 50% of all the antihypertensive medicine items throughout the four-year study period. Cost savings to the amount of R22 685 689,65 and R50 412 643,73 could have been possible with generic substitution at levels of 45% and 100% respectively during the total study period. The usage of generic antihypertensive medicine items increased by 17,26% over the four year study period. Average refill-based adherence rates calculated across all treatment categories indicated that treatment category 1 and treatment category 3 had acceptable refill adherence rates at 86,20% and 85,50% respectively.

Cost threshold ranges of R68,50 – R142,00 and R80,90 – R129,50 were calculated for total antihypertensive medicine items for the year 2008. For male patients a higher cost threshold range was calculated than for their female counterparts (R72,14 – R147,66 and R84,98 – R134,82 vs. R67,01 – R137,75 and R78,24 – R125,56). On the basis of the cost threshold ratio method, a higher cost ratio threshold was calculated for female patients vs. male patients (R59,73 vs. R50,49).

In conclusion, this study described not only the prescribing patterns and costs of antihypertensive medicine items, but also the cost implications of over- and under-utilisation of these medicine items. Different cost threshold ranges and cost ratio thresholds were calculated for implementation in the private health-care sector of South Africa.

It is recommended that threshold development in the public health-care sector be investigated further.

Keywords: Hypertension, drug utilisation review, antihypertensive medicine items, cost analysis, generic substitution, compliance and adherence, cost threshold range, cost ratio threshold.

OPSOMMING

Titel: Hipertensiebehandeling in 'n deel van die voorgeskrewevoordele-bestuursmark in Suid-Afrika.

Die doel van hierdie studie was om spesifieke kostedrempelwaardes te bereken vir besluitnemingsprosesse in die private gesondheidsorgmark van Suid-Afrika, met spesifieke verwysing na die behandeling van hipertensiepasiënte.

Die navorsing het berus op 'n medisyneverbruikevaluering benadering ondersteun deur verskeie ander meetinstrumente, klassifikasiesisteme, wiskundige formules en beskrywende statistiese metodes. Die studie is uitgevoer op data van 'n medisyne-eise-databasis oor 'n vierjaar-studietydperk wat gestrek het van 1 Januarie 2005 tot 31 Desember 2008. Die totale medisyne-eise-databasis is verdeel in kardiovaskulêre medisyne-items en daarna antihipertensie-medisyne-items. Laasgenoemde is geanaliseer volgens behandelingskategorieë: behandelingskategorie 1, bestaande uit medisyne-items gelys in MIMS[®]-groep 7.3; behandelingskategorie 2, bestaande uit medisyne-items gelys in MIMS[®]-groep 16.1; en behandelingskategorie 3, bestaande uit medisyne-items gelys in beide MIMS[®]-groep 7.3 en 16.1; ouderdomsgroepe: ouderdomsgroep 1 (pasiënte ≤ 18 jaar); ouderdomsgroep 2 (>18 en ≤ 45 jaar); en ouderdomsgroep 3 (>45 jaar), en geslag. Data-analise het algemene koste, pasiëntmeewerking, kombinasie-antihipertensiebehandeling en die berekening van kostedrempelwaardestrekke (met 'n boonste en onderste limiet) en kosteverhoudingdrempelwaardes ingesluit. Die hervul-meewerkingskoers is bereken vir individuele hipertensiemedisyne-items wat meer as een maal voorgeskryf is. 'n Kostedrempelwaardestrek is ontwikkel deur 'n gedeelte van die standaardafwyking (50% of 33%) by die gemiddelde koste per item te tel of af te trek, wat dan die boonste en onderste limiete vorm. Die geskatte aantal hoë-inkomstehuishoudings en totale medisynekoste soos toegepas in die private gesondheidsorgsektor is gebruik om kosteverhoudingdrempelwaardes te bereken. Die geskatte totale medikasiekoste is daarna gebruik om 'n netto koste te bereken. Die resultaat hiervan was die kosteverhoudingdrempelwaarde.

Die resultate het getoon dat antihipertensiemedisyne-items 7,68% tot 9,69% van alle medisyne-items op die databasis beslaan het, met 'n geassosieerde koste van sowat 10,94% tot 11,10% van die totale koste gedurende die vierjaar-studietydperk. Antihipertensiemedisyne-items het sowat 7 695 151 (70,04% N = 10 986 407) van al die kardiovaskulêre medisyne-items en

59,94% van die totale koste van kardiovaskulêre medisyne-items vir al vier studiejare gesamentlik verteenwoordig. Tussen 16,6% en 19,7% van alle voorskrifte was vir antihipertensiemedisyne, met 'n geassosieerde koste van 11,5% tot 11,7% van die totale koste van alle medisyne-items waarvoor gedurende die vierjaar-studietydperkgeëis is. Analises van kombinasiehipertensiebehandeling het getoon dat die meeste observasies gemaak is vir voorskrifte wat twee of drie antihipertensiemiddels bevat. Generiese antihipertensie-items het meer as 50% van die totale hipertensiemiddels uitgemaak gedurende die vierjaar-studietydperk en kostebesparings ten bedrae van R22 685 689,65 en R50 412 643,73 kon behaal word met generiese vervanging op vlakke van 45% en 100% onderskeidelik. Die gebruik van generiese antihipertensiemiddels het deur die vierjaar-studietydperk met 17,26% toegeneem. Die gemiddelde hervul-meewerkingskoers wat bereken is vir behandelingskategorieë het getoon dat behandelingskategorie 1 en behandelingskategorie 3 aanvaarbare hervul-meewerkingskoerse van 86,20% en 85,50% onderskeidelik getoon het.

Kostedrempelwaardestrekke van R68,50 – R142,00 en R80,90 – R129,50 is vir die totale getal antihipertensiemiddels vir 2008 bepaal. 'n Kostedrempelwaardestrek bereken per geslag het getoon dat manlike hipertensie pasiënte 'n hoër kostedrempelwaardestrek as vroulike pasiënte het (R72,14 – R147,66 en R84,98 – R134,82 vs. R67,01 – R137,75 en R78,24 – R125,56). 'n Drempelwaarde gebaseer op die kosteverhoudingdrempelwaarde toon dat vroulike pasiënte 'n hoër drempelwaarde as manlike hipertensie pasiënte (R59,73 vs, R50,49) het.

Om saam te vat, het hierdie studie nie net die voorskryfpatrone en koste van antihipertensiemedisyne-items uitgelig nie, maar ook die koste-implikasie van wangebruik van medisyne. Verskeie kostedrempelwaardestrekke en kosteverhoudingdrempelwaardes is bereken vir implementering in die private gesondheidsorgsektor van Suid-Afrika. Daar word aanbeveel dat drempelwaarde-ontwikkeling om te help met die besluitnemingsproses in die openbare gesondheidsorgsektor van Suid-Afrika verder ondersoek word .

Trefwoorde: Hipertensie, medisyneverbruiksevaluering, antihipertensiemedisyne-items, koste-analise, generiese vervanging, meewerking, kostedrempelwaardestrek, kosteverhoudingdrempelwaarde

ACKNOWLEDGEMENTS

Nothing is impossible through Him who gives us strength and guidance, and therefore I wish to express my sincere and humble appreciation to my Father in Heaven for granting me the ability, courage and strength to complete this study. Soli Deo Gloria.

I also want to express my sincere thankfulness and appreciation to the following people that has contributed to this dissertation:

- Professor J.H.P. Serfontein, in his capacity of supervisor of this dissertation, my appreciation for his expert supervision and all the time he invested in this study.
- Professor M.S. Lubbe, in her capacity as co-supervisor for all the advice and her assistance with regards to the analysis of the data.
- The subject group Pharmacy Practice for the technical support.
- Mediscor PBM for the provision of the data for this dissertation.
- Ms. A Bekker for her assistance with regards to the analysis of the data.
- All the personnel of the subject groups of Pharmacy Practice and Clinical Pharmacy for their continuous support and encouragement.
- Mrs W Liebenberg for editing this dissertation.
- Mrs H Hoffman for her assistance in the editing of the bibliography of this dissertation.
- Mrs P Gainsford for technical editing of the dissertation.
- My beloved husband André for his support, encouragement and unconditional love.
- My parents, brothers, sister, sisters-in-law and in-laws for their constant encouragement and faith in my abilities.
- My dearest friends Johanita and Lizelle for their friendship, support, and encouragement.

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LIST OF ABBREVIATIONS

ACE:	Angiotensin converting enzyme
AG:	Age group (AG1, AG2 and AG3)
ALLHAT:	Antihypertensive and Lipid-lowering Treatment to Prevent Heart Attack Trial
AR:	Adherence rate
ARB:	Angiotensin receptor blocker
ASHS;	South African Hypertension Society
BP:	Blood pressure
CBA:	Cost benefit analysis
CCD:	Clinical cardiovascular disease
CDL:	Chronic disease list
CEA:	Cost-effectiveness analysis
CET:	Cost-effectiveness threshold
CHD:	Coronary heart disease
CI:	Cost implication
CMA:	Cost-minimisation analysis
CMS:	Council for Medical Schemes
CNS:	Central nervous system
COI:	Cost-of-illness
CPI:	Cost prevalence index
CUA:	Cost utility analysis
CVD:	Cardiovascular disease
DUR:	Drug utilization review
ECG:	Electro-cardiogram
GBD:	Global burden of disease
GDP:	Gross domestic product
HOT study:	Hypertension Optimal Treatment study
ICER:	Incremental cost-effectiveness ratio
ISPOR:	International society of pharmacoeconomics and outcomes research
LVH:	Left ventricular hypertrophy
LYG:	Life years gained
MI:	Myocardial infarction
MIMS®:	Monthly index of medical specialties
MPR:	Medicine possession rate

MRC:	South African Medical Research Council
NAPPI:	National approved product pricing index (code)
NICE:	National Institute on Clinical Excellence
PBM:	Pharmacy benefit manager (company)
PDD:	Prescribed daily dosage
PPI:	Patient prevalence index
QALY:	Quality adjusted life-year
Rx:	Prescription
SA:	South Africa
SAHS:	South African Hypertension Society
SAMF®:	South African Medicines Formulary
SEP:	Single exit price
SHEP:	Systolic Hypertension in the Elderly Programme
SNS:	Sympathetic nervous system
TC:	Treatment category (TC1, TC2 and TC3)
TOD:	Target-organ diseases
UET:	Ultimate environmental threshold
USAID:	United States Agency for International Development
VAT	Value added tax
WHO:	World Health Organisation
WHO-CHOICE:	World Health Organisation Choosing Interventions that are Cost-effective
WTP:	Willingness to pay
YLS:	Years of life lost

CHAPTER 1: INTRODUCTION AND PROBLEM STATEMENT

1.1 INTRODUCTION

South Africa's health-care financing system consists of a public sector, financed mainly through general tax revenue, and a private sector dominated by medical schemes, covering approximately 14,4% of the population (Mid-year population estimates, StatsSA, 2006; Bletcher & Harrison, 2006:32). The Medicine Usage in South Africa (MUSA) research group estimated in 2008 that about 18% (or 2,1 million) of the households in South Africa (SA) belonged to a private medical aid. South Africa witnessed in the order of R135 billion or 8% of its GDP flowing through health-sector financing intermediaries in 2006. Of this, 44% went through the public sector intermediaries and the remaining R75 billion through private financing intermediaries. About 79% of the latter went through medical schemes (Bletcher & Harrison, 2006:32).

The inequities that result from the coexistence of the private and public health-care sectors in SA are a matter of policy concern, and the vision of the Department of Health is for all South Africans to have access to affordable and good quality health care. Traditionally the state has been responsible for providing health care to the poor, who have conventionally been excluded from the private medical aid system mainly for socio-economic reasons (Bletcher & Harrison, 2006:32; Luiz & Wessels. 2004:1). For this reason the South African national Department of Health announced the introduction of a national health insurance system for South Africa to be phased in over a period of 14 years, starting in 2012. One of the main objectives of the national health insurance system is to provide good health care for all the people of South Africa. This implies that more than basic health care will be available to all South Africans at limited direct cost to the patient (SA, 2010:2).

Although medical research is expected to continue to produce an ever-increasing number of alternatives for the detection, prevention and treatment of diseases (Devlin & Parkin, 2004:2), budgetary constraints will, however, not allow health-care systems to make all the available resources accessible to everyone. To overcome this, some health-care systems (for example in Australia, Canada, and the United Kingdom) have implemented an explicit or semi-explicit approach to guiding resource allocation decisions by formal health-economic

analysis, of which one of the most popular currently is the cost-effectiveness (CE) analysis (Eichler *et al.* 2004:518).

As medical science has developed, treatments have become available for increasingly complex conditions, costs of medical care have risen (Diderichsen, 2004:3), and there has been an increasing awareness that resource allocation must be addressed in a systematic rather than intuitive manner. Several countries have introduced guidelines or legislation to mandate CE assessment of some aspects of health care, most often for the reimbursement of pharmaceuticals. It is therefore reasonable to expect that decisions about resource allocation will increasingly rely on CE and related analyses. This will, inevitably, call for more transparency and consistency in the decision-making process and, in turn, for the definition of what policymakers regard as an 'acceptable threshold' of cost-effectiveness below which they will make available a technology and above which they will ration access. For this reason the inclusion of an economic perspective in the evaluation of health and health care has progressively become a more accepted component of health policy and planning (Eichler *et al.* 2004:525).

In a health-care system as diverse as the South African one there can and will be different approaches or perspectives for implementing a threshold. Most probably a 'reasonable threshold' will be more applicable in the South African market. After the 1994 election the South African government introduced eight Batho Pele principles, which are 'People first' principles in which the government strives to improve service delivery. In terms of these principles a 'reasonable threshold' in terms of qualitative and quantitative service delivery should be established, focussing on treatment affordability (value for money) and resource availability. While this approach is followed in the non-private medical market, it is just as applicable in the private health-care sector of SA.

Since there are two sectors in the South African health-care system, there is likely to be at least two sets of thresholds – one for decision-making in the private health-care sector and a second threshold for the public domain. Using the available medication for hypertension treatment as example: since the public health-care sector is administered by the national Department of Health, the implementation of thresholds for decision-making would possibly be easier to administer due to the regulation of the availability of medicine and other primary health-care interventions. . The private health-care sector is, however, characterised by a number of medical schemes, with their own rules and regulations, and pharmaceutical benefit management companies, and therefore it would be more difficult to set a single cost-effectiveness threshold for decision-making. It is more likely that within each medical

scheme there will be a range of threshold benefits that will be used. These regulations are governed by the South African Council for Medical Schemes.

In the development of thresholds as management tool for the treatment of hypertension, at least two sides to the design of such a threshold can be defined. The first will include the 'human side', which includes individual patient needs, the prevalence of the disease in a population, certain risk factors (including age, gender, geographical distribution of the patients, etc.) as well as patient adherence and compliance. The second will include the 'business side' of hypertension treatment. These include, inter alia, treatment cost, availability and accessibility of hypertension treatment and providers, affordability of hypertension treatment and medical aid plans. For the purposes of this study and the development of a threshold, the study mainly focuses on the 'business side' of hypertension treatment. However, the two approaches (human side vs. business side) are not independent, but depend on each other. In business terms it can be presented by a 'balance sheet' as a method of counterbalancing the medication treatment inputs (treatment costs) and outputs (treatment outcomes). However in practice the number of alternative choices (clinical and cost) can be bewildering and intimidating to many health-care providers, with the result that rules and regulations are introduced to limit choices and benefits. The results of these limitations may not lead to optimum efficiency in health-care delivery, thus a complex Batho Pele situation arises.

In the business world, including health care, a variety of measurements are applied to evaluate the 'health of the business' by analysing financial statements. Loth (2012) identified six major categories presenting 30 measurements for the investing process. While not necessarily the same, similar measurements are needed to evaluate the medicine usage and cost processes. Of the six categories Loth (2012) listed, two are directly applicable to this study, namely profitability indicator ratios or savings (in this study the focus will be on savings, for example substitution of generic medicine) and operating performance ratios (which can also be seen as stock turnover ratios, for example the calculation of adherence rates).

In 1998 the World Health Organisation (WHO) developed a programme, the *CHOICE* (*CHOosing Interventions that are Cost-Effective*) project, with the aim of providing policymakers with the support for deciding on the interventions and programmes that maximise health with the available resources. In terms of thresholds for considering an intervention to be cost-effective, WHO-CHOICE has been using criteria suggested by the Commission on Macroeconomics and Health, namely the gross domestic product (GDP), as

a readily available indicator to derive three categories of cost-effectiveness. For an intervention to be cost-effective, the cost per quality-adjusted life year (QALY) must be less than GDP per capita, to be cost-effective it must be between one and three times GDP per capita, and if the cost per QALY value is more than three times GDP per capita (the threshold), the intervention would be regarded as not cost-effective (WHO, 2006a; WHO, 2006b). The choice of a cost-effectiveness threshold depends on who is making the decision; what the purpose of the analysis is; how the decision-maker values health, money and risk; and what the available resources are (Owen, 1998:717).

In this study two major types of cost thresholds will be proposed as measuring instruments. The first threshold is a cost-range threshold that will be calculated by using the average cost per medicine item, the corresponding standard deviation and the median, and it will have an upper and lower limit. The second threshold is a cost-ratio threshold. To calculate this cost-ratio threshold a medical aid market will be estimated and this cost-ratio threshold will be expressed as treatment cost per household, as the household for this study purpose is regarded as the finance unit. This treatment cost per household or threshold will exclude value added tax (VAT) (income resource for the state) and a logistics fee or gross profit as a resource of income for the provider.

The cost of cardiovascular and related diseases to a country is twofold. Initially, there is the direct cost of the increased health care attributable to a person having heart disease, and secondly, there are indirect costs due to the fact that these patients cannot be optimally productive at work or are absent from work as a result of the illness or premature death (Steyn, 2007:27).

In the United States hypertension is accountable for nearly 500 000 hospital admissions per year, and is also the primary reason for visits to a physician (Dalzell, 2003:10). The economic and public health-care outcomes of both hypertension and the failure to manage it are massive (Dalzell, 2003:6). The economic, medical and human toll and impact of inadequately controlled hypertension are enormous, not only in the United States, but also in South Africa. According to the World Health Organisation (WHO), approximately 17 million people die of cardiovascular diseases (CVDs) every year. In 2002 as many as 7,2 million people died from coronary heart diseases, 5,5 million died from strokes and approximately 900 000 people died from hypertensive heart disease (WHO, 2006).

According to the South African Medical Research Council's (MRC) Burden of Disease research unit, approximately 92 000 people died from cardiovascular diseases in South

Africa in 2000. Ischemic heart diseases and hypertensive heart diseases accounted for 35,7% and 15,4% of all cardiovascular-related deaths respectively (MRC, 2007). It has been estimated that in 2000, in South Africa, 9% of all deaths of persons 30 years and older were caused by a high BP (Norman *et al.* 2007:695). According to the South African Council for Medical Schemes' annual reports, in 2005 hypertension affected 69 cases per 1 000 people (SA, 2006), and by 2008 hypertension had affected 105,6 cases per 1 000 people (SA, 2009).

One of the Pharmacy Benefit Managers (PBMs) in South Africa stated that antihypertensives accounted for 11,6% and 8,8% respectively of the total cost and total items of the top 25 therapeutic groups for 2005. According to Serfontein (1989:180), with a cost-prevalence index (CPI) of more than 1, antihypertensive medicine can be classified as relatively expensive treatment (see Chapter 3, section 3.7.3.2 for the calculation of the CPI). Antihypertensives also accounted for 37,5% of the total chronic disease list (CDL) items paid for during the last quarter of 2005 (Bester *et al.* 2005:15). Since hypertension is a chronic disease, compliance with antihypertensive medicine is recognised as essential to the successful management of hypertension (Christensen *et al.* 1997:1164). A very important fact to remember is that hypertension treatment will probably be part of the patient's life for the rest of his life.

This thesis will focus on the development of possible cost-related thresholds for decision-making purposes in South Africa by evaluating the literature and by developing certain cost models that may be used. As was stated earlier, it is a complex situation since it contains emotional as well as rational cost implications, and therefore (Eichler *et al.* 2004:518) it needs a responsible approach.

1.2 OBJECTIVES OF THIS STUDY

1.2.1 General objective

The general objective of this study was to develop certain cost thresholds for the purpose of decision-making in the private health-care sector of South Africa, with specific reference to the treatment of hypertensive patients.

1.2.2 Specific objectives

The specific objectives of the empirical study were as follows:

- To review original pharmacoeconomic related studies with reference to the application of hypertension treatment;
- To determine the prevalence and cost implications of hypertension medicine treatment in a section of the private health-care sector of South Africa by means of demographical factors and geographical distribution;
- To analyse the prescription patterns for different types of antihypertensive drugs according to a medicine claims database in the pharmacy benefit-management environment;
- To conduct applicable pharmacoeconomic studies on the data in order to make some evaluations on the usage and cost of antihypertensive treatment;
- To investigate patient compliance/adherence with reference to antihypertensive treatment;
- To develop and propose threshold value/values for the treatment cost of hypertension in South Africa.

1.3 RESEARCH QUESTIONS

The following research questions were formulated:

- Why is economic evaluation important?
- What are the different techniques used in economic evaluations?
- What is a threshold?
- On what is medical decision-making in South Africa currently based?
- What is the prevalence of hypertension in a segment of the private health-care sector of South Africa according to age, gender and geographical distribution?
- What is the current most common treatment regimen of hypertension treatment in South Africa and how does the cost of treatments differ?
- What does patient compliance/adherence entail?
- What are the adherence or compliance rates for antihypertensive treatment in a section of the private health-care sector of South Africa and what are the cost implications of over or underutilisation of antihypertensive medicine items?

What is the perspective of the different role-players on the treatment of hypertension?

1.4 METHODOLOGY

A retrospective drug utilisation study was done on medicine and claims data provided by a South African pharmacy benefit manager (PBM). Comparisons and analyses were done by

using the Statistical Analysis System (SAS for Windows 9.1, 2005). An ethical application was submitted to the Ethics Committee of the North-West University.

The study consisted of two phases, namely a literature review on pharmacoeconomics and hypertension, and the empirical and statistical analysis of the medicine data by means of pharmacoeconomic methods. The data consisted of membership data and claims data of a private South African PBM.

1.5 RATIONALE OF THE STUDY

In today's challenging world resources are scarce. However, choices must be made concerning the deployment of resources. Methods such as 'educated guesses' are not always better than the organised consideration of factors involved in a decision to commit resources to one use instead of to another. This statement is true for three reasons, namely that without systematic analysis it is difficult to identify clearly the relevant alternatives; a viewpoint assumed in an analysis is important; and thirdly that without some attempt at measurement, the uncertainty surrounding orders of magnitude can be critical (Drummond *et al.* 1999:7).

Hypertension is an especially important area of concern for pharmacoeconomics because of the broad range of the problem as well as the high cost of treatment for complications. Patients' risk factors are critical in the field of pharmacoeconomics because the costs of alternative interventions and their effects on patients vary across patient risk groups (McCombs, 1998:113S).

This study mainly focused on a section of the private health-care sector in SA regarding the usage and cost of antihypertensive medicine treatment. One of the aims was to aid decision-makers in identifying, measuring and comparing input costs with consequences, or health outcomes, of the treatment regime for a specific disease (hypertension).

1.6 DIVISION OF CHAPTERS

Chapter 1: Introduction and problem statement

Chapter 2: The thresholds of hypertension medicine treatment in the South African context

Chapter 3: Empirical investigation

Chapter 4: Results and discussion

1.7 CHAPTER SUMMARY

In this first chapter an overview was given of the rationale for and background of this study. Some general and specific objectives were stated and a few research questions were asked.

In Chapter 2 an overview of the concepts of a threshold, threshold as management tool, hypertension and hypertension management and treatment will be presented.

CHAPTER 2:

THE THRESHOLDS OF HYPERTENSION MEDICINE TREATMENT IN THE SOUTH AFRICAN CONTEXT

2.1 ENTER THE THRESHOLD

The term threshold has been used to describe many benchmark settings and can be applied to many fields, for example economic, engineering, environmental, scientific and medical. The Oxford English Dictionary (2011) defines a threshold as ‘the piece of timber or stone which lies below the bottom of a door, and has to be crossed in entering a house; the sill of a doorway; hence, the entrance to a house or building’. It is also defined as the border or a limit of a region, or, in technical language, a lower limit. From a **physiological** perspective a threshold can be seen as the limit below which a stimulus is not perceptible, or the magnitude or intensity of a stimulus that has to be exceeded for it to produce a certain response. When thresholds are looked at in the contexts of wages and taxation, it is a limit where wage or tax increases become due or obligatory when some predetermined conditions are fulfilled (Oxford English Dictionary Online, 2011).

WordNet®, a large lexical database of English, developed under the direction of George A Miller, defines a threshold as ‘the starting point for a new state or experience’, or as ‘the smallest detectable sensation’, or ‘a region marking a boundary’ (WordNet®, 2011).

In **science**, the term ‘threshold’ (originally meaning the point of entry) has a similar meaning to the term ‘critical level’, which is the point where a stimulus leads to a significant response. When studying climate or environmental affairs, there are basically four main types of thresholds, namely: absolute thresholds (if exceeded can lead to immediate and significant stress, e.g. the wind speed at which major structural damage occurs on buildings), preconditioned thresholds (where the values depend on the previous condition of the exposure unit, e.g. the temperature damage on the growth of plants), cumulative thresholds (where significant effects are observed on the exposure unit only after a given time has elapsed, due to the accumulated effect of previous climatic events, for example the onset and progression of drought), and coincidental thresholds (where significant effects are felt on the exposure unit due to a combination of climatic conditions occurring either simultaneously or consecutively) (Parry *et al.* 1996:2).

In the **tourism industry** problems that result from tourism development in attractive and fragile natural environments occur often and therefore ecologically sound planning techniques are required to minimise the effect of humans on the environment. In line with this, the Ultimate Environmental Threshold (UET) originated. The UET can be seen as: 'The stress limit beyond which a given ecosystem becomes incapable of returning to its original condition and balance. Where these limits are exceeded as a result of the functioning or development of particular activities a chain reaction is generated leading towards irreversible environmental damage of the whole ecosystem or of its essential parts' (Kozlowski, *et al.* 1988:329).

In **health care and medicine** the word 'threshold' is used in many different contexts. The Quality Assurance Project, with the aim of strengthening the quality of health care in developing and middle income countries, in support of the Bureau for Global Health and country Missions of the United States Agency for International Development (USAID) defines a threshold as a level of achievement that determines the difference between what is deemed to be acceptable quality or not. For example, the minimum acceptable level of coverage for the immunisation programme is 50 per cent, which means that every coverage figure lower than that is an indication of a possible quality problem (Quality Assurance Project, 2008).

Since measles is one of the most contagious diseases in humans, the global effort to reduce measles mortality aims to achieve routine measles vaccination coverage of at least 90 per cent in every district throughout the world. The high vaccination coverage has changed the epidemic pattern drastically, but a proper understanding of the size and timing of the outbreaks is a prerequisite for adequate monitoring of a vaccination programme, and essential for assessing the risk of future measles outbreaks. The size of an outbreak depends on both the fraction of susceptible individuals in the population and on chance events in the transmission process. Therefore, a critical threshold level should exist for the fraction of susceptible individuals below which the introduction of infection can lead only to minor outbreaks. This so-called threshold underlies the concept of herd immunity, and explains why it is possible to eradicate an infectious agent event without achieving complete vaccine coverage (Wallinga *et al.* 2005:1153).

Another use of the term 'threshold' is an allergy threshold. The allergy threshold is the amount of an allergen a person can be exposed to before he begins to react to it (Anisman-Reiner, 2008).

In medicine, the smallest amount of a drug required to bring out a response is called its threshold dose (Hanson *et al.* 2005:149).

In South Africa, some of the medical schemes have a so-called 'above threshold benefit' that provides extra cover once the patient's expenses have reached a fixed rand amount, called the 'annual threshold' (Anon, 2008a). This is an indication that thresholds also have an 'exit' value and not only an input acceptable value. This view could also be applied to maximum and minimum medication dosage volumes.

Another use for the word threshold is in **economics**, where the word 'poverty threshold' is used to describe a country's poverty line. The poverty line should be constructed as a measure of the money income required to attain a basic minimal standard of living. There is, however, no exact definition of a poverty line, and the approaches to the construction of such a threshold differ between countries (StatsSA, 2007).

As indicated, the term threshold can be used almost in every possible discipline, from environmental affairs, through science, technology, health care, medicine and even physiology and education. However, for the purpose of this study a threshold can be defined as follows:

A threshold analysis determines the monetary value with regard to the medicine usage and cost of antihypertension treatment.

Medical research is expected to continue to produce an ever-increasing number of alternatives for the detection, prevention, and treatment of diseases (Devlin & Parkin, 2004). Budgetary constraints will, however, not allow health-care systems to make all of these accessible to everyone. To overcome this, some health-care systems (for example Australia, Canada, and the United Kingdom) have implemented an explicit or semi-explicit approach to guiding resource allocation decisions by formal health-economic analysis, of which the most popular currently is the cost-effectiveness (CE) analysis (Eichler *et al.* 2004:518).

As medical science has developed, treatments have become available for increasingly complex conditions, the costs of medical care have risen (Diderichsen, 2004:3), and there has been an increasing awareness that resource allocation must be addressed in a systematic rather than intuitive manner. Several countries have recently introduced guidelines or legislation to mandate CE assessment of some aspects of health care, most often for the reimbursement of pharmaceuticals. It is therefore reasonable to expect that decisions about resource allocation will increasingly rely on CE analysis. This will, inevitably, call for more transparency and

consistency in the decision-making process and, in turn, for the definition of what policymakers regard as an 'acceptable threshold' of cost-effectiveness below which they will make available a technology and above which they will ration access. For this reason the inclusion of an economic perspective in the evaluation of health and health care has progressively become a more accepted component of health policy and planning (Eichler *et al.* 2004:525).

Cost-effectiveness analysis (CEA) has been used as a tool for addressing issues of efficiency in the allocation of scarce health resources, providing as it does a method for comparing the relative costs as well as health gains of different (and often challenging) health interventions (Hutubessy *et al.* 2003). The cost-effectiveness plane is a useful geometric framework for presenting data on incremental cost-effectiveness and permits a graphical representation of an accept-reject decision rule based upon incremental cost (ΔC), incremental effectiveness (ΔE) and the ratio of the two being the incremental cost-effectiveness ratio (ICER) (O'Brien *et al.* 2002).

In order to curb financial expenditure, thresholds for cost-effectiveness ratios may be established for the acceptance of reimbursement or formulary listing (Eichler *et al.* 2004:518).

The theory of the usage of thresholds in the health environment was originally proposed by Weinstein and Zeckhauser in 1973. They provided the theoretical foundation for the use of a threshold ICER, also known as λ (lambda), as a decision rule. They showed that the 'critical ratio', λ , represents the opportunity cost of the resources at the margin under conditions of perfect divisibility and constant returns to scale of all programmes (Gafni, 2005; Torrance, Siegel & Luce, 1996). Furthermore, Weinstein and Zeckhauser (1973) showed that health benefits maximised from available resources will occur under one of two processes, namely one where all projects are ranked from the lowest to the highest ICER and selected in descending order until all the resources are exhausted (i.e. the league table approach), or the specification of the 'critical ratio' (λ) directly and the implementation of all projects with an ICER below or equal to λ (i.e. the threshold ICER approach) (Gafni, 2005).

Cost-effectiveness thresholds (CET) have primarily two major characteristics, namely that they can be explicit or implicit, and that thresholds have a certain degree of flexibility that distinguishes between 'hard' and 'soft' thresholds (Eichler *et al.* 2004:519). An explicit threshold means that decision-makers formally approve and make public any threshold in advance, whilst implicit thresholds are not official. If a 'hard' threshold approach is used it indicates that results from cost-effectiveness analysis are taken *prima facie* and become the sole decision measure for resource allocation.

The rigid approach of a 'hard' threshold offers the theoretical advantages of transparency, consistency, and predictability, and denies the likelihood of incorporating into the decision other non-cost-effectiveness-based societal preferences. A 'soft' threshold, in contrast, would make room for the consideration of other preferences. With the latter approach, the cost-effectiveness acceptability criterion does not lead to automatic acceptance or rejection but rather to notifying decision-makers. This implies that instead of a single figure, there is a threshold range with lower and upper boundaries. Interventions that fall below the lower boundary will as a rule be accepted and made available, while interventions that lie above the upper level will typically be rejected. An intervention that falls between the lower and upper boundaries will be judged predominantly upon additional criteria (see Figure 2-1) (Eichler *et al.* 2004:519, 520).

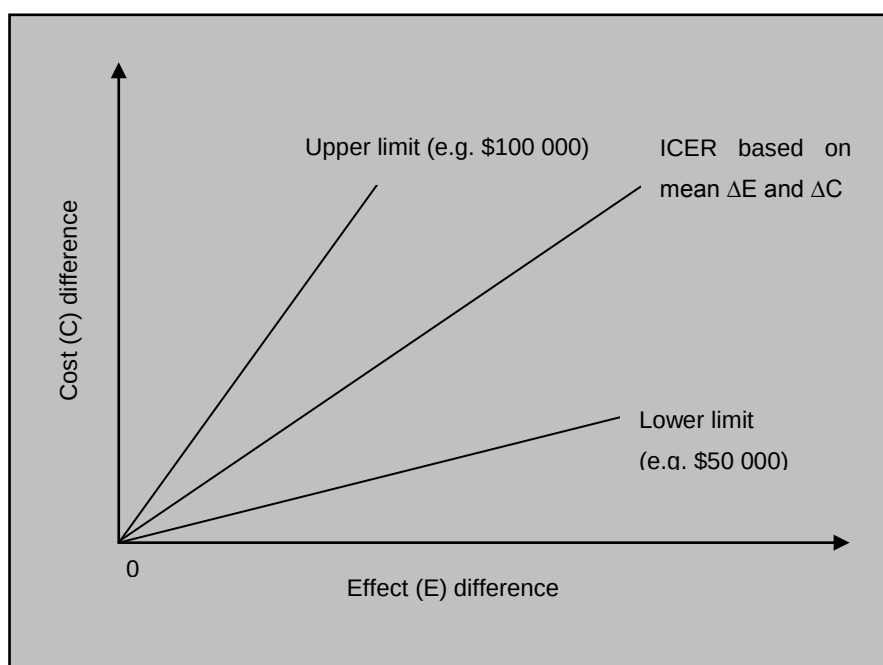


Figure 2-1: The cost-effectiveness threshold for decision making (adapted from Drummond *et al.* 2005:262).

Owen (1998:716) stated that the choice of a cost-effectiveness threshold is a value judgement that depends on a number of factors. Firstly, the choice depends on who the decision-maker is and what the purpose of the CEA is, since this will determine the perspective from which the study is performed. The perspective will determine whose costs and benefits are included, and since different entities may have different CETs, the perspective is important. The way in which a decision-maker values health outcomes and money and how they are willing to substitute one for the other, and their attitude towards risk can be seen as the second factor in the choice of a CET. Since people vary substantially in their willingness to pay to improve health, people who are more averse to the risk of serious illness and death will have a higher CET than a person

who is less concerned about such risks. The third factor is the resources available. A decision-maker's cost-effectiveness threshold may change as resources change (Owen, 1998:716).

The idea of using thresholds in decision-making has met some criticism. The application of the critical threshold approach is only legitimate under a number of assumptions, including perfect divisibility of health-care programmes, constant returns to scale, and constant marginal opportunity costs. It has been argued that the use of CE thresholds may lead to uncontrolled growth in health-care expenditure (Gafni & Birch, 1993:913). The application of CE thresholds alone ignores the fact that health-care systems are resource constrained and decision-makers need to balance their budgets. However, in real-life situations considerations of CE alone are inadequate to inform decision-makers. Decision-makers can either maximise health gain for a given budget, which gives an implicit CE ratio at the margin, or determine the budget based on an acceptable CE ratio (Eichler *et al.* 2004:528). For societal decision-makers the CET decision rule gives the impression that it is more appropriate, as opposed to the so-called health-care budget approach (Eichler *et al.* 2004:528).

In a health-care system as diverse as the South African health-care system there can and will be different approaches or perspectives for implementing a threshold. Since there are two sectors in the South African health-care system, there is likely to be at least two sets of thresholds – one for decision-making in the private health-care sector and a second threshold for the public domain. Since the public health-care sector is administered by the national Department of Health the implementation of thresholds for decision-making would possibly be easier to administer due to the regulation of the availability of medicine and other primary health-care interventions, e.g. the available medication for hypertension treatment. However, the private health-care sector is characterised by a number of medical schemes with their own rules and regulations, and pharmaceutical benefit management companies, and therefore it would be more difficult to set a single cost-effectiveness threshold for decisionmaking. It is more likely that within each medical scheme there will be a range of thresholds that will be used. These regulations will, however, be governed by the South African Council for Medical Schemes.

2.2 PHARMACOECONOMIC METHODOLOGIES

Economic evaluation is formally defined as the comparison of the costs and consequences of two or more alternative courses of action (Larson, 2001:4).

Drummond and colleagues (1999:7) stated that economic evaluations are important, because without systematic analysis it is difficult to clearly identify the relevant alternatives, as the viewpoint assumed in an analysis is important. Without some attempt at measurement, the uncertainty surrounding orders of magnitude can therefore be critical. Drummond *et al.* (1999:8) also stated that because of the two characteristics of economic evaluations, namely that they deal with inputs and outputs, and that they are concerned with choices, economic evaluation can be defined as the comparative threshold analysis of alternative courses of action in terms of both their costs and consequences.

Pharmacoeconomics is not related to a particular science, but has rather evolved through a collection of sciences. The research methods used by scientists in this discipline are drawn from several areas, including economics, epidemiology, pharmacy, medicine and the social sciences (Wilson, 1999:56). Pharmacoeconomics can thus be defined as a comparison of costs associated with competing drug therapies (e.g. acquisition costs, physician visits, laboratory tests and adverse reactions to therapies) and the adverse or beneficial effect of each therapy to determine the preferred or most desirable intervention (Wertheimer & Navarro, 1999:377).

In easier terms, pharmacoeconomics research recognises, measures, and compares the costs (resources consumed) and consequences/outcomes (benefits, effectiveness, quality of life, utility, efficacy, safety, morbidity, mortality) of pharmaceutical products (Struwig, 2001:3).

The discipline of economic evaluation and pharmacoeconomics relies on a number of tools. These tools include cost-effectiveness analysis (CEA), cost-benefit analysis (CBA), cost-minimisation analysis (CMA), cost-utility analysis (CUA), cost-of-illness (COI) and sensitivity-analysis (McCombs, 1998:114S). Since only medicine cost was available for this study, the focus will be only on CEA and CMA, but the differences between these studies will be illustrated in Table 2-1.

In this section the relevant pharmacoeconomic methodologies will be discussed briefly. A summary of all the pharmacoeconomic methodologies will, however, be given in Table 2-1.

2.2.1 Cost-effectiveness analysis (CEA)

Cost-effectiveness analysis (CEA) is a research method designed to help determine which health interventions provide the most effective medical care that can be afforded. It is also a method for comparing the health outcomes (effectiveness) and the net costs of a programme or an intervention with other alternatives with similar health outcomes (net cost includes the costs

for providing the treatment and for committing the resources after the subtraction of non-health benefits, illustrated in monetary or rand value) (Carriere & Huang, 2001:23; Muennig, 2002:3). In easier terms, CEA is used to evaluate health interventions that have a comparable outcome, but in natural units, for example life-years saved, or healthy years of life added, etc. The main purpose of cost-effectiveness analysis is to inform the decision-makers in the health-care industry about the value of a health-care programme (Torrance *et al.* 1996:55).

In order to perform a CEA, the researcher needs to gather certain information, such as the way a health intervention will change the health state of a group of people (Muennig, 2002:3). Only when the capability of a CEA as the framework for the analysis has been established and an appropriate outcome measure has been decided upon, the benefits are combined with the costs in a cost-effectiveness ratio. A CEA would estimate the incremental cost per unit of effectiveness gained for a medicine, relative to the standard. This will provide clinicians with guidance concerning how much it costs to achieve an additional case free of the condition. This estimate is called the incremental cost-effectiveness ratio (ICER), which indicates how much it costs to save one year of healthy life relative to other interventions aimed at treating or preventing the same disease (Hughes *et al.* 2004:11; Muennig, 2002:14).

$\begin{aligned} \text{Incremental cost effectiveness} &= \frac{(\text{cost of drug A} - \text{cost of drug B})}{(\text{benefits of drug A} - \text{benefits of drug B})} \\ &= \frac{\text{difference in costs (A - B)}}{\text{difference in benefits (A - B)}} \end{aligned}$

Figure 2-2 : The incremental cost-effectiveness ratio

The ICER reveals the cost per unit of benefit of switching from one treatment option to an alternative treatment option, i.e. the extra cost per unit of extra outcome obtained with the alternative (Hughes *et al.* 2004:111).

The incremental cost and incremental effect can be represented visually using the incremental cost-effectiveness plane (see figure 2-3).

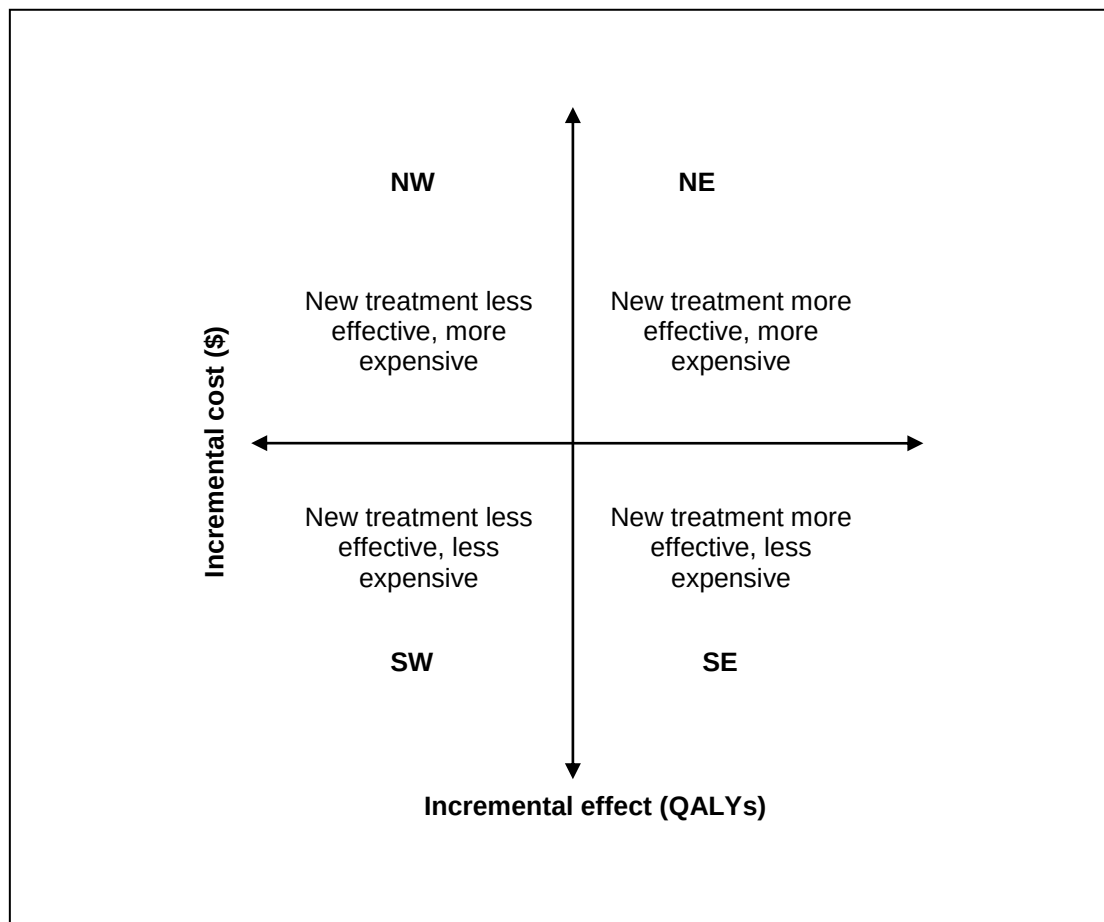


Figure 2-3: The incremental cost-effectiveness plane.

NE = northeast quadrant; NW = northwest quadrant; SE = southeast quadrant; SW = southwest quadrant; QALYs = quality adjusted life year (Fenwick, *et al.* 2006:54 & Walley, 2004:73).

According to Hughes *et al.* (2004:111) and as illustrated in Figure 1, there are four possible qualitative results that arise after a CEA has been done.

- If costs are lower and health benefits higher for one drug relative to another, the former is said to dominate and would be the preferred treatment (SE quadrant).
- The opposite also applies, i.e. if the new drug is more expensive and less effective, it will be considered inferior and not recommended for introduction into the health-care market (NW quadrant).
- Where the new drug is both more effective and more expensive than the standard, then the ICER's judgement must be about whether the additional benefits are worth the extra costs of the new drug, and therefore whether it is cost-effective. A threshold ICER value may then be used to define cost-effectiveness (NE quadrant).
- The same as in the previous step, but with the roles of the new and the standard therapies reversed. Here the question arises whether the extra benefits provided by the standard

therapy justify the additional costs of retaining it as preferred treatment when the option of a new, cheaper but less effective drug exists (SW quadrant).

From the above it can be concluded that decision-making shifting from one quadrant to another will involve the threshold value.

2.2.2 Cost-minimisation analysis (CMA)

Cost-minimisation analysis can be used when treatments being evaluated have similar health outcomes, thus the comparison is limited to analysing the costs. Generic prescribing is commonly accepted as a means of optimising cost-effectiveness, and can therefore be regarded as a different form of CMA (National Medicines Information Centre, 2002). It is important to remember that CMA can be rightfully used only if there is certainty that two therapies have the same outcome (Hughes *et al.* 2004:102).

When two treatments are compared, there are a few conditions that are obligatory for a CMA to be suitable. Firstly, the question concerning the efficacy of the treatments compared must be raised. No future economic evaluation starts out as a CMA. Only after the clinical health outcomes that were generated have demonstrated that two treatments are 'identical' or 'similar' can CMA be adopted as methodology of choice. 'Identical' or 'similar' health outcomes imply that the efficacy and the effectiveness of the treatments should be identical, and therefore a common measure of efficacy needs to be available. To verify the similarity in efficacy of the compared treatment, the evidence of clinical trial studies is used. If these results are similar, the question of relevancy needs to be answered, namely whether these trial results are relevant in a real-life situation. The results obtained in a real-life situation could vary from those obtained in clinical trials, and it is even possible for two treatments with similar efficacy to achieve different levels of effectiveness (Laurier, *et al.* 1992:1; Haycox, 2009:92). It is important to remember that, if there is no proof that one treatment is clinically superior to its comparator, it does not mean that the two treatment outcomes are equivalent. A CMA then becomes unsuitable and a more sophisticated approach is necessary (Haycox, 2010:92).

Secondly, one must also investigate the side effects and adverse drug reactions. If both treatments have the same side effects and adverse reactions, or if there is no clinical difference in the safety of the two treatments under investigation, a CMA is an appropriate method to use. If there is a considerable difference in the side-effect profile of the two treatments, it may lead to a difference in patient compliance, and that may lead to a difference in health outcomes. In this case a CMA will not be the most appropriate model to use (Laurier *et al.* 1992:1).

The literature contains several examples where CMA was used as a method of economic evaluation of antihypertensive treatment. These include studies done by Laurier *et al.* (1992), Pearce *et al.* (1998) Fretheim *et al.* (2003), Fujikawa *et al.* (2003) and Chen *et al.* (2005).

Laurier *et al.* in 1992 performed a CMA comparing Fosinopril to other ACE-I (captopril, enalapril and lisinopril). Since Fosinopril shares the same side-effect and efficacy profile as the other ACE-I in the class, a CMA was the appropriate study to perform. In the Laurier study it was found that Fosinopril can lower the treatment cost for hypertension (Laurier *et al.* 1992:iii).

In a study done by Pearce *et al.* in 1998, they carried out a CMA based on number-needed-to-treat derived from the meta analysis of 15 important clinical trials of hypertension treatment. In their study, Pearce *et al.* (1998:618) compared diuretics, beta blockers, ACE-inhibitors, alpha blockers and calcium channel blockers with each other in terms of cost. Their estimates of effectiveness were directly calculated from clinical trials. They combined data from trials evaluating treatment for uncomplicated mild to moderate hypertension. Furthermore they used only studies with myocardial infarction (MI), stroke or death as endpoint. They used only one drug per pharmacological group, which was based on the most commonly prescribed antihypertensive items in the United States or the least expensive antihypertensive medicine items, based on the lowest average wholesale price. Pearce *et al.* (1998:623) found that the generic diuretics and beta-receptor blockers were likely to prevent major cardiovascular disease (CVD) events at a much lower cost than ACE-inhibitors, calcium channel blockers or alpha-receptor blockers among patients with uncomplicated mild to moderate hypertension. This result implies that threshold values may be calculated by using CMA.

In a study done by Fretheim *et al.* in 2003 they performed a CMA where the drug costs associated with thiazide and non-thiazide treatment were compared. In the study they performed, they assumed, after thorough study of randomised control trials, that no class of antihypertensive medicine is superior to any other class. Therefore, they found that there is a considerable probability for savings if thiazides are used as first-choice medicine in the treatment of hypertension (Fretheim *et al.* 2003:e216).

In a study done by Fujikawa *et al.* in 2003, they conducted a cost-minimisation analysis by estimating the medicine cost associated with hypertension treatment from the perspective of the insurer. In their study they included the direct medicine cost, and if any concomitant medicine items were prescribed, the representative drug for each class was chosen either by prescribing frequency or least expensive. They compared Nifedipine extended release products with ACE-

inhibitors. Fujikawa *et al.* (2003:591) concluded that Nifedipine extended release treatment was more cost-effective and cost saving when compared to ACE-inhibitors. This result was an indication that a possible changes in therapy may attribute to cost savings.

Chen *et al.* (2005) used the Systolic Hypertension in the Elderly Program (SHEP) and other data to perform a CMA. They presented the cost as the cost of number-needed-to-treat of patients over a five-year period to prevent one adverse CVD event. They found that diuretic-based antihypertensive therapy, which includes either a low-dose Reserpine or Atenolol, is an effective and relatively inexpensive strategy for the prevention of CVD events in older patients with isolated systolic hypertension, and that diuretic-based therapy was the most cost-effective treatment in patients at high risk of developing CVD. This study emphasised the fact that demographic factors may have a significant influence on the determination of threshold values.

2.3 SUMMARY

Table 2-1 summarises the different pharmacoeconomic methodologies and their distinguishing features.

Table 2-1: Categories of pharmacoeconomic techniques (Smith 2003:226; Bootman *et al.* 2005:7-9)

Technique	Distinguishing features
Cost-benefit	Identifying all the benefits that result from a program or intervention, measuring it in monetary or rand value.
Cost-effectiveness	Measures, defines and compare the inputs and outcomes of two interventions, with inputs measured in physical units and valued in monetary terms, and outcomes measured in natural units (e.g. lowering in blood pressure, etc.)
Cost-minimisation	If two treatments are proven to have equivalent outcomes, the costs of the two treatments can be evaluated and compared.
Cost-utility	Measures the cost of treating an illness, but measuring intervention results in terms of quality and quantity of life.
Cost-of-illness	Identifies and measures the costs of the medical resources, nonmedical resources and lost of productivity in monetary or rand value, but <i>does not</i> measure treatment outcomes.
Sensitivity analysis	Allows researchers to test and analyse the impact of uncertainty in economic evaluations.

The use of cost-benefit analysis falls outside the scope of this study since no monetary benefits gained were measurable. Furthermore, no effectiveness data were available therefore cost-effectiveness and cost-utility analyses were also not possible. For both cost-effectiveness and

cost-utility analyses the willingness-to-pay of the patient also plays an important role. Since all hypertensive medication is supposed to have the same outcome, namely to lower blood pressure, cost-minimisation analyses were used to determine a cost threshold. Cost-of-illness studies can partly be used due to the availability of medication cost.

2.4 EVALUATION OF COSTS

Economic evaluation is essential for modern health care and the identification of insufficient resources should be determined without bias and scientifically, and should not be politically or emotionally influenced (Alcocer & Cueto, 2008:152).

Economic evaluation is a process by which the costs and consequences of an intervention are assessed. This can include a new medicine item, pharmaceutical service or medical device, etc. The result of any economic evaluation is to determine the influence that such a new intervention has on health care resource utilisation, the patient, and the society (Ortmeier, 1996:386).

It is important to specify the viewpoint because an item may be a cost from one point of view, but not a cost from another. For example, travel costs is a cost incurred by the patient, and therefore a cost from the patients' and society's perspective, but not from the Department of Health's viewpoint. Workers compensation, on the other side, is a cost to the paying government, a gain to the patient (or recipient), and neither a cost nor a gain to society. If the evaluation is being commissioned by a given body, this may give a clue to the relevant perspectives. When in doubt, however, the analyst should always adopt the societal point of view, which is the broadest one and is always applicable (Drummond, *et al.* 2005:55).

2.5 THE PHARMACOECONOMIC EVALUATION PROCESS

When designing a pharmacoeconomic study, Drummond *et al.* (2006:458) identified nine steps that need to be addressed. These steps will now be discussed shortly.

Firstly it is important to make sure that a clear hypothesis or research question is provided, and that it is relevant and appropriate to the real world. It should also be possible to test the stated hypothesis within the results (Drummond *et al.* 2006:458; Haycox, 2004:156).

Secondly, it must be clearly indicated whose perspective is considered in the study. Is it from a society perspective, healthcare payer, patient, or healthcare provider's perspective (Abarca, 2005: 364; Haycox, 2004:156)?

The third step or question that needs to be looked at is whether the choice of methodology is appropriate to the comparison that needs to be undertaken. The type of methodology is also dependent on the nature of the comparison (Haycox, 2004:157). The methodology should also include the study design, for example was it a decision analysis, retrospective, prospective or randomised control trial, etc. The time-line or time horizon for the study should also be included or stipulated in the methodology as well as the subjects or patient population (Abarca, 2005:364).

Step 4 should include the question of comparators or alternatives. Is there a comparator or alternative included in the study, and is it appropriate and realistic for the setting in which the study is undertaken? Reasons for including or excluding certain alternatives should also be indicated and justified (Abarca, 2005:365; Haycox, 2004:157).

Next, the researcher needs to determine whether the evaluation is based on good clinical evidence and if this evidence is accessible and precise (Haycox, 2004:157).

In step 6, it is important to clarify if all the relevant costs and consequences are included in the evaluation, and whether these costs and consequences is in line with the perspective and time horizon stated. It should also be stated if future costs were discounted and what the discount rate were (Abarca, 2005:365; Haycox, 2004:158).

It is also important to remember that any pharmacoeconomic study needs to identify the extra costs and benefits that occur as a result of a new or alternative treatment (Haycox, 2004:158). This may have a direct influence on the determination of a threshold value.

In step 8 the researcher control whether a sensitivity analysis was undertaken for variables that may not be measured with certainty (Abarca, 2005:365). It is very important that key parameters underlying health economic analyses are subject to a sensitivity analysis (Haycox, 2004:159).

Finally it is important to ensure that local costs and methods or clinical management is included in the overall structure (Haycox, 2004:160). Furthermore the results of the study should also be discussed within the context of the research question or hypothesis, the limitations and

shortcomings must be stipulated and the results must be compared to other published studies (Abarca, 2005:366).

It is thus clear that various factors must be taken into account for threshold values to be used as management tool in health care and especially medication usage.

2.6 THRESHOLDS AS A MANAGEMENT TOOL

According to the Oxford English Dictionary Online (2012), management can be defined as the process of dealing with or controlling people or things. In the context of this study, management will entail the process of dealing with or controlling healthcare and or hypertension treatment. Traditionally the management process consists of four activities, namely planning, organizing, leading and controlling strategic efforts (Venter, 2009:404; Hellriegel *et al.* 2010:10).

In the development of thresholds as management tool for the treatment of hypertension there can be two sides to the design of such a threshold. The first will include the “human side”, which will include individual patient needs, the prevalence of the disease in a population, certain risk factors (including age, gender, geographical distribution of the patients, etc.) as well as patient adherence and compliance. The second will include the “business side” of hypertension treatment. This may include treatment cost, availability and accessibility of hypertension treatment and providers, affordability of hypertension treatment, medical aid plans, etc. For the purpose of this study and the development of a threshold, the researcher will focus on the “business side” of hypertension treatment.

Literature prominently mentions a threshold by which cost-effectiveness experts can judge the affordability of health care services namely, those interventions that produce a quality adjusted life year (QALY) for \$50 000 or less are a bargain, whereas those that require \$100 000 or more are considered unaffordable. The \$50 000 to \$100 000 QALY cut-off goes back to the early 1980s, and is based on the cost-effectiveness ratio calculated for the use of dialysis for patients with chronic renal failure, which is a federal entitlement to all US citizens (Ubel, 2003:1637). In the Netherlands the cost-effectiveness threshold value is set at €20 000 per life year gained (LYG), whilst the National Institute on Clinical Excellence (NICE) uses a value of £30 000 per LYG for the United Kingdom (Devlin & Parkin, 2004:2; Zwart-van Rijkom *et al.* 2000:150).

In 1998 the World Health Organization (WHO) developed a programme, namely the *CHOICE* (*CHO*osing Interventions that are *Cost-Effective*) project, with the objective of providing policy makers with the support for deciding on the interventions and programmes which maximize

health for the available resources. In terms of thresholds for considering an intervention to be cost-effective, WHO-CHOICE has been using criteria suggested by the Commission on Macroeconomics and Health, namely the gross domestic product (GDP), as a readily available indicator to derive three categories of cost-effectiveness. For an intervention to be cost-effective the cost per QALY must be less than GDP per capita, to be cost-effective it must be between one and three times GDP per capita, and if the cost per QALY value is more than three times GDP per capita (the threshold) the intervention would, however, be regarded as not cost-effective (WHO, 2006a; WHO, 2006b).

The WHO-CHOICE reports the costs and effects of a wide variety of health interventions in 14 epidemiological sub-regions i.e. world divisions made based on geographical location and epidemiological profiles, based on the Global Burden of Disease (GBD) regional classification system. Despite the geographical regions, the regions are also classified into mortality strata. The 198 member states have been classified in the following 14 geographical regions and mortality strata: African Region (Afro D and Afro E), Eastern Mediterranean Region (Emro B and Emro D), European Region (Euro A, Euro B and Euro C), Region of the Americas (Amro A, Amro B and Amro D), South-East Asian Region (Searo B and Searo D), and the Western Pacific Region (Wpro A and Wpro B). The results of these cost-effectiveness analyses are assembled in regional databases, and are available on the internet, which policy makers can adapt to their specific country setting (WHO, 2006a).

Table 2-2 summarises the cost-effectiveness threshold for the African, American and European regions. South Africa falls into the Afro E region together with 19 other countries such as Botswana, Kenya, Zimbabwe, Mozambique, Malawi, Lesotho, Rwanda, etc.

Table 2-2: Threshold values for intervention cost-effectiveness by region (WHO, 2006a)

	Cost-effectiveness threshold (in 2000 International \$)									
Threshold value	Afro D*	Afro E*	Amro A*	Amro B*	Amro D	Emro B	Emro D	Euro A	Euro B	Euro C*
GDP per capita	\$1,381	\$1,576	\$31,477	\$7,833	\$3,837	\$7,870	\$2,393	\$23,927	\$5,873	\$6,916
3x GDP per capita	\$4,143	\$4,728	\$94,431	\$23,499	\$11,511	\$23,610	\$7,179	\$71,781	\$17,619	\$20,748

* A-E indicates the Mortality Strata: A – Very low child, very low adult; B – Low child, low adult; C – Low child, high adult; D – High child, high adult; E – High child, very high adult.

An alternative approach to the theoretical and practical problems of determining λ is to estimate λ based on measuring society's willingness to pay (WTP) for additional health outcomes. Gafni & Birch (2006:2098) states that there is no reason to believe that WTP per QALY is constant over a wide range of QALYs. As with other commodities, the marginal utility of QALYs may weaken with the size of QALY production, whilst the opportunity cost of a QALY will increase with the size of QALY production as the available resources from which to fund extra QALYs weakens. Thus it is difficult to see how information on WTP per QALY in a population sample could be used to determine how to allocate resources in order to maximise health gains in the population. It can rather be used to justify the increased expenditures associated with the failure of the existing economic evaluation guidelines (Gafni & Birch, 2006:2098).

In summary the choice of a cost-effectiveness threshold depends on who is making the decision; what the reason of the analysis is; how the decision maker values health, money and risk; and what the available resources are. Thus, the search for a single cost-effectiveness threshold may probably not be rewarding (Owen, 1998:717). Due to the lack of clinical information on the database, the thresholds will be limited to available medication data provided, as presented in Chapter 4.

2.7 LIMITATIONS

It is important to be aware of the limitations as well as the usefulness of pharmacoeconomic analyses. The questions of cost must always be followed by the inquiry "to whom?" A study conducted from different viewpoints may generate different results. Pharmacoeconomic evaluations provide the tools to analyse the economic results of alternative drug therapy decisions. There is always an element of doubt around the aetiology of disease, and diagnostic and curative techniques. Additionally, an agreement may never be reached on such issues as the value of the discount rate, reducing uncertainty, estimation in the face of uncertainty, and taking into account the concept of equity. These uncertain events can under different assumptions, be analysed by using sensitivity analyses. This can indicate the confidence that can be placed in the results, thereby reducing but not totally eliminating uncertainty. This is why such analyses need systematic and rigorous approaches. Therefore it is important for all involved in medicine related decision making to understand the strengths and weaknesses of this new and exciting field, and how to use the available tools appropriately (Osterhaus & Draugalis, 1991:139).

Finally, it is important to remember that an evaluation of any type is costly and therefore even economic evaluations needs to be subjected to a monetary evaluation. For this reason it could

be suggested that most economic evaluation techniques will prove to be useful in situations where programme objectives require explanation or, where the competing alternatives are radically different in nature, or if large resource commitments are under consideration (Drummond *et al.*, 2005:47).

2.8 PHARMACOECONOMICS AND HYPERTENSION: PERSPECTIVES FROM THE LITERATURE

Antihypertensive drug therapy is a common target of cost-cutting efforts, since hypertension is a general disease, and its treatment often requires the use of more than one medication (Elliot, 2003:9). Reeder and colleagues (2000:S116) stated that the treatment of moderate-to-severe hypertension has been proven beneficial and cost effective, while treatment of mild-to-moderate hypertension has not been proven to be cost effective when effectiveness is balanced against risks and benefits of treatment for patients. Economic evaluations of treatment alternatives can be instructive when this type of treatment uncertainty exists (Reeder *et al.* 2000:S116).

Significant clinical outcomes and endpoints, such as therapeutic efficacy, reduced mortality, and decreased morbidity, are important in estimating the economic outcomes of hypertension treatment. Such clinical outcomes are balanced against treatment costs, and an economic ratio of cost per outcome is calculated. A cost-effectiveness methodology is often applied (Reeder *et al.* 2000:S116). The aim of this section is therefore to review the cost-effectiveness analyses in the field of hypertension treatment.

An extensive literature search on the Medline database was performed on articles relating to pharmacoeconomics and hypertension. The following search terms were used:
Pharmacoeconomics AND

Hypertension AND
Cost-effectiveness OR
Cost-minimization OR
Cost-benefit OR
Cost-of-illness.

Articles from 2000-2011 were used. Some of the most relevant studies according to their outcome, including *inter alia*, LYG, QALYs or economic impact, are summarised in Tables 2-3 and 2-4.

Table 2-3: Summary of Cost-effectiveness studies identified in the literature

Study	Year of publication	Country	Type of study	Treatment compared
Maniadakis <i>et al.</i> ,	2010	Greece	Cost-effectiveness	Irbesartan/hydrochlorothiazide vs. Losartan/hydrochlorothiazide or Valsartan/hydrochlorothiazide.
Heidenreich <i>et al.</i>	2008	United States	Cost-effectiveness	Chlortalidone vs. amlodipine/lisinopril
Boersma <i>et al.</i>	2007	The Netherlands	Cost-effectiveness	Losartan vs. Atenolol (LIFE study)
Booth <i>et al.</i>	2007	Finland	Cost-effectiveness	Antihypertensive Current Care Guideline (ACCG) vs. Prior Clinical Practice (PCP)
Gandjour & Stock	2007	Germany	Cost-effectiveness	National hypertension program vs. no program
Coyle <i>et al.</i>	2007	Canada	Cost-effectiveness	Irbesartan 300mg given early vs. irbesartan 300mg given late vs. conventional treatment
McInnes <i>et al.</i>	2006	United Kingdom	Cost-effectiveness	Losartan vs. Atenolol (LIFE study)
Fujikawa <i>et al.</i>	2005	Japan	Cost-effectiveness	Nifedipine plus candesartan vs. up-titrated monotherapy candesartan
Gaziano <i>et al.</i>	2005	South Africa	Cost-effectiveness	South African hypertension guidelines
Lopez <i>et al.</i>	2004	United States	Cost-effectiveness	β -blockers vs. thiazide diuretics vs. calcium antagonists vs. ACEIs
Richardson <i>et al.</i>	2004	England	Cost-effectiveness	Implementation of new guidelines
Jönsson <i>et al.</i>	2003	Sweden	Cost-effectiveness	Adding acetylsalicylic acid (ASA) to hypertension treatment (HOT study)
Nordmann <i>et al.</i>	2003	Canada	Cost-effectiveness	ACEI as first-line vs. β -adrenoceptor antagonists or diuretics as first-line
Simmons	2003	United States	Cost-effectiveness	Olmesartan medoxomil vs. losartan, valsartan and irbesartan

Table 2-3 (cont.): Summary of Cost-effectiveness studies identified in the literature

Study	Year of publication	Country	Type of study	Treatment compared
Da Costa <i>et al.</i>	2002	Brazil	Cost-effectiveness	Diuretics vs. β -blockers vs. ACEIs vs. calcium channel blockers
Reeder <i>et al.</i>	2000	United States	Cost-effectiveness	ACEIs vs. felodipine, beta-blockers and diuretics

Table 2-4: Excerpts from the conclusions of the cost-effectiveness studies

Study	Conclusion
Maniadakis <i>et al.</i>	“Based on efficacy data from clinical trials and lower attainment costs in various hypertensive patient populations, irbesartan in combination with HCTZ compares favourably with losartan and valsartan in combination with HCTZ in the Greek setting.”
Heidenreich <i>et al.</i>	“Significant savings can be achieved by using chlortalidone as the first drug for treatment of hypertension, although the nonsignificant mortality benefit of amlodipine could make it economically attractive compared to chlortalidone.”
Boersma <i>et al.</i>	“In the present cost analysis, treatment with losartan could be considered a cost-effective intervention compared with atenolol based on the reduced risk for stroke observed in the LIFE study for The Netherlands. This notion should be considered in the development of clinical guidelines, in addition to clinical efficacy, tolerability, and experience with treatment options in general clinical practice.”
Booth <i>et al.</i>	“...the ACCG scenario is less costly and produces more life-years than the PCP scenario.”
Gandjour & Stock	“The analysis shows fairly moderate cost-effectiveness ratios even for low-risk groups (less than €12 000 per life year gained). In women at high risk antihypertensive treatment even leads to savings. This suggests that a national hypertension program provides good value for money.”
Coyle <i>et al.</i>	“The early use of irbesartan for patients with hypertension and type 2 diabetes who have yet to develop overt nephropathy is both more effective and less costly than delaying irbesartan treatment until AON and conventional antihypertensive use.”
McInnes <i>et al.</i>	“The incremental cost-effectiveness ration (ICER) for losartan versus atenolol in hypertensive patients with LVH was £2 130 per quality-adjusted life year (QALY) gained (€3 195/QALY), and this increased to £11 352 per QALY gained (€16 450/QALY) when the costs of stroke beyond the first 5 years were excluded. Thus, the clinical benefit of losartan was achieved at a cost well within reported thresholds for cost-effectiveness.”
Fujikawa <i>et al.</i>	“In conclusion, a low-dose combination therapy of controlled release nifedipine and

Table 2-4 (cont.): Excerpts from the conclusions of the cost-effectiveness studies

Study	Conclusion
	candesartan was ‘dominant’ to up-titrated monotherapy with candesartan in essential hypertensives, and as a consequence, the combination treatment strategy could contribute to a decrease in the financial burden on the National Health Insurance system in Japan.”
Gaziano <i>et al.</i>	“The four absolute risk strategies have incremental cost-effectiveness ratios ranging from \$700 per QALY gained to \$11 000 per QALY gained, depending on the risk threshold for initiating treatment.”
Lopez <i>et al.</i>	“In 2002 the VA has saved as estimated \$8.5 million because of changes in medication use.”
Richardson <i>et al.</i>	“...introducing new guidelines for the management and treatment of hypertension in new patients in general practice is likely to be cost-effective.”
Jönsson <i>et al.</i>	“..we have in this study found that the CV-related health care costs increases as the target for blood pressure is lowered. We have also found that it is cost-effective to pursue a more aggressive treatment of hypertension in patients with diabetes. Finally, we have to conclude that, we in our analysis were unable to provide evidence on the cost-effectiveness of adding ASA to antihypertensive treatment.”
Nordmann <i>et al.</i>	“...we feel confident to conclude that prescribing ACE inhibitors as first-line antihypertensive therapy in patients without cardiovascular morbidity cannot be recommended at this time, unless acquisition costs of ACE inhibitors become substantially more attractive.”
Simmons	“Treatment of patients in a managed care setting with olmesartan medoxomil has the potential to decrease overall medical costs of care for patients with uncontrolled hypertension compared with losartan, valsartan and irbesartan.”
Da Costa <i>et al.</i>	“The costs of hypertension care are mainly dependent on the expenditure on blood pressure-lowering drugs. Treatment of hypertension with diuretics or beta blockers was more cost-effective than treatment with ACE inhibitors and calcium channel blockers.”
Reeder <i>et al.</i>	“The treatment of hypertension offers potential cost savings by avoiding some of the longterm costs of morbidity and mortality.”

This review has identified and described 16 cost-effectiveness analyses of hypertension treatment. The studies represent some research carried out since 2000.

Economic evaluation has a long tradition in the hypertension field, and several cost-effectiveness analyses have been published, as seen in table 2.3 and 2.4. However, the lack of methodological consistency between the studies makes comparisons difficult. The only

constant finding among the studies is that the cost-effectiveness increases with higher pre-treatment blood pressure. It is impossible to draw any policy conclusions from the cost-effectiveness analyses comparing different drugs because of inconsistent methodologies and limited data. It is vital to improve the quality of the cost-effectiveness studies in this area by improving both the data and the methods used. There is also a need to add to cost-effectiveness analysis with other approaches, for example on the basis of willingness to pay (Heidenreich *et al.* 2008:515).

In a study conducted by Reeder and colleagues in 2000 pharmacoeconomic evaluations of ACEIs using cost per YLS or QALY as economic outcome were conducted. Data from the Hypertension Optimal Treatment (HOT) study were used to estimate the cost-effectiveness of antihypertensive therapy with felodipine, ACEIs, beta blockers and diuretics. They calculated the overall cost of managing hypertension to range from about \$1 200 for less aggressive treatment to \$1 400 for intensive treatment (Reeder *et al.* 2000:S116).

Reeder *et al.* (2000:S124) concluded that the treatment of hypertension offers potential cost savings by avoiding some of the long-term costs of morbidity and mortality, and It was also noted that the cost-effectiveness ratios examined in their study suggested that hypertension treatment falls within the range of many other medical interventions routinely used in modern health care. They also noted that prescribing an ACE inhibitor is an efficient choice in the treatment of mild-to-moderate hypertension in middle-aged and older patients, and especially in patients with diabetes or congestive heart failure. With regard to quality-of-life they concluded that the ACE inhibitors result in improved quality-of-life outcomes due to the improved side-effect profile of ACEIs compared to older therapies. In general, long-term health-related quality of life in patients with heart failure who were treated with ACE inhibitors showed small improvements or did not differ significantly from placebo (Reeder, *et al.* 2000:S125).

However, a study done by Da Costa *et al.* in 2002 showed that the cost-effectiveness relationship was more favourable for diuretics (116.3) and beta blockers (228.5) than for ACE inhibitors (608,5) or calcium channel blockers (762,0). They calculated that treatment of hypertension with diuretics or beta-receptor blockers was more cost-effective than treatment with ACE inhibitors and calcium channel blockers (Da Costa *et al.* 2002:103).

Nordmann *et al.* (2003) did a similar study to that of Da Costa *et al.* (2002) and their analysis showed that the gain in life expectancy and QALYs by promoting ACE inhibitors as antihypertensive first-line therapy was very small. They found that the incremental cost-effectiveness ratio of ACE inhibitors as first-line antihypertensive therapy was unfavourable

when compared with conventional antihypertensive therapy as first-line therapy for individualised therapy according to the presence or absence of LVH on the ECG (Nordmann *et al.* 2003:581).

A study performed by Heidenreich *et al.* in 2008 on the cost-effectiveness of Chlortalidone (a thiazide diuretic) compared with Amlodipine (a calcium channel blocker) or Lisinopril (an ACE inhibitor) found that large potential savings from widespread initial treatment with a diuretic were possible. They also noted that substantial savings were possible in the treatment of hypertension if chlortalidone was used as first-line treatment (Heidenreich *et al.* 2008:515).

Richardson *et al.* (2004), Gaziano *et al.* (2005), Gandjour and Stock (2007) and Booth *et al.* (2007) all performed cost-effectiveness studies related to hypertension treatment guidelines.

Richardson *et al.* (2004) found that implementing the new guidelines for the detection, management and treatment of hypertension in a primary care setting was more costly than the implementation of previous guidelines, but more effective in reducing the risk of cardiovascular disease. The incremental cost per cardiovascular disease event avoided was £30 000, although sensitivity analysis showed that the estimate was subject to considerable uncertainty (Richardson *et al.* 2004:769).

In a study on the cost-effectiveness analysis of hypertension guidelines in South Africa done by Gaziano *et al.* (2005) they found that current guidelines based on blood pressure levels are both more expensive and less effective than guidelines based on absolute risk of cardiovascular disease (Gaziano *et al.* 2005:3569). The strategies that were compared included two different strategies based on blood pressure levels and four different strategies based on the absolute level of cardiovascular risk, as well as a comparison strategy of no antihypertension prescription therapy. Markov modelling with 62 possible clinical pathways was used, which allows the prediction of disease events over a given length of time for a particular cohort and the adjustment of risks as the population ages. All members of the cohort began free of cardiovascular disease (CVD). In the initial year, each member of the cohort had a certain probability based on treatment status and risk factors of moving along one of four pathways. The member could either stay disease free, dying of a non-CVD cause, or develop fatal or non-fatal coronary heart disease or stroke. In the subsequent years, those with prior CVD followed a separate pathway with adjusted risks for recurrence of CVD or death on the basis of age and prior event. All risks were updated annually on the basis of age. Costs were captured along the way for treatment of hypertension and CVD events. Effects were measured in life-years and quality-adjusted life-years (QALYs) gained that were accumulated for the cohort over the 10

years for each guideline. Strategies that had higher costs and fewer QALYs than at least one other strategy were eliminated from further consideration (Gaziano *et al.* 2005:3571).

Gaziano *et al.* (2005:3572) calculated the four absolute risk strategies to have incremental cost-effectiveness ratios ranging from \$700 per QALY gained to \$11 000 per QALY gained, depending on the risk threshold for initiating treatment.

In a cost-effectiveness study performed by Gandjour and Stock in 2007, their analysis showed that cost-effectiveness ratios for low-risk hypertension groups (less than €12 000 per life year gained) and treatment in high-risk hypertensive women can lead to savings. They concluded that this may suggest that a national hypertensive treatment programme may provide good value for money (Gandjour & Stock, 2007:257).

Cost-effectiveness studies on the use of ARBs for the treatment of hypertension were done by Coyle *et al.* (2007), Fujikawa *et al.* (2005) and Simmons (2003). Simmons (2003:73) found that hypertensive patients treated with olmesartan medoxomil instead of other ARBs, including losartan, valsartan and Irbesartan, had the potential to reduce overall cost of medical care, whilst Coyle *et al.* (2007:1519) found that Irbesartan, when added to a regimen of conventional therapy, was cost-effective and led to cost-savings and increased life expectancy. The team of Fujikawa *et al.* (2005:591) found that a combination of Candesartan and low-dose controlled-release Nifedipine was dominant over Candesartan as monotherapy, and that the Candesartan-Nifedipine combination can contribute to a decrease in the financial burden.

In 2006 McInnes *et al.* performed a cost-effectiveness analysis comparing losartan and atenolol by making use of the LIFE study. The incremental cost-effectiveness ratio (ICER) for losartan versus atenolol in hypertensive patients with LVH was calculated at £2 123 per QALY gained (€3 195/QALY), and increased to £11 352 per QALY gained (€16 450/QALY) when the costs of stroke beyond the first five years were excluded. They concluded that the clinical benefit of losartan was achieved at a cost well within the reported thresholds for cost-effectiveness (McInnes *et al.* 2006:51).

A similar study was done by Boersma *et al.* (2007:966), but with the results of the LIFE study adapted to the Netherlands. They found that losartan treatment was associated with 0,059 life years gained (LYG) per patient treated with losartan. Losartan also reduced stroke-related costs by €1076 (\$1349) per patient. Boersma *et al.* (2007) further calculated that after the inclusion of study medication costs, the net cost per patient was €51 (\$64) higher for losartan than atenolol. They then calculated the net cost per LYG as €864 (\$1 083), which was below

the Dutch pharmacoeconomic threshold of €20 000/LYG (\$25 000/LYG) for accepting interventions (Boersma *et al.* 2007:968).

In 2003 Jönsson, Hansson and Stålhammar examined the marginal cost-effectiveness of the different goals for the reduction of blood pressure and the cost-effectiveness of adding acetylsalicylic acid to the treatment of hypertension (Jönsson *et al.* 2003:473). They observed that the average cost of drugs and visits increased with more intensive treatment, yet the increase in treatment costs was partly but not fully offset by a non-significant reduction in the cost of cardiovascular hospitalisations. They calculated the estimated cost of avoiding a major cardiovascular event to be between SEK41 600 and SEK477 400. Furthermore, researchers were unable to provide conclusive evidence on the cost-effectiveness of adding acetylsalicylic acid to antihypertensive treatment (Jönsson *et al.* 2003:478-479).

From the literature it is therefore clear that pharmacoeconomic studies, especially cost-effectiveness studies, can play an enormous role in the challenge to contain costs in the treatment of hypertension. However, due to a lack of information pertaining these studies, no comments can be made regarding the advantages and or disadvantages of these studies. Furthermore, the usage of other pharmacoeconomic instruments in the determination of threshold values should be investigated further. This aspect will receive attention via several statistical instruments, including CMA methodologies.

2.9 ECONOMIC IMPACT OF HYPERTENSION

The cost of heart disease to a country is twofold. Initially there is the direct cost of the increased health care attributable to a person having heart disease, and secondly there are indirect costs as a person with heart disease cannot be optimally productive at work or is absent from work as a result of the illness or premature death (Steyn, 2007:27).

In the United States hypertension accounts for nearly 500 000 hospital admissions per year, and is also the primary reason for visits to a physician (Dalzell, 2003:10). The economic and public health outcomes of both hypertension and the failure to manage it are massive (Dalzell, 2003:6). The economic, medical and human toll and impact of inadequately controlled hypertension are enormous, not only in the United States, but also in South Africa.

In a study conducted by Pestana *et al.* in 1996 they calculated that the cost of CVD in South Africa had been between R4 135 billion and R5 035 billion in 1991. This did not include the

costs of rehabilitation and follow-up, and this expenditure reflected 2%-3% of gross domestic product (GDP), or roughly 25% of all health-care expenditure for 1991 (Pestana *et al.* 1996:679).

It was estimated that in South Africa in 2000 9% of all deaths of persons 30 years and older were caused by a high BP (Norman *et al.* 2007:695). According to the annual reports of the South African Council for Medical Schemes', hypertension affected 69 cases per 1 000 people in 2005 (SA, 2006), and by 2008 hypertension affected 105,6 cases per 1 000 people (SA, 2009).

This relatively brief discussion has emphasised the fact that when thresholds are calculated, it is important to not only take note of the importance of clinical outcomes but also the treatment cost.

2.10 ASPECTS OF HYPERTENSION AS A DISEASE AND MEDICATION TREATMENT

According to the WHO, raised blood pressure is responsible for an estimated 7,5 million deaths globally every year (or about 12,8% of all deaths per year). In all the WHO regions, the prevalence of hypertension was the highest in the African region, with approximately 46% of people suffering from this disease (WHO, 2012). In South Africa, hypertension afflicts over 25% of adults and increases the risk of suffering a CVD by 20%. In 2000, nearly 14 200 (15,4%) of people that died from a CVD had suffered from hypertension (SA, 2007).

2.10.1 Definition and classification

2.10.1.1 Definition of hypertension

The National Woman's Health Information Centre of the United States (US) Department of Health (2002), describes cardiovascular diseases as diseases that affect the heart and blood vessel system within a person's entire body. Cardio refers to the heart and vascular refers to the blood vessel system.

Levick (1995:301) defines the medical condition 'hypertension' as a chronic, usually progressive, raised arterial pressure, while the Merck Manual of Diagnosis and Therapy describes hypertension as an elevation of systolic and or diastolic blood pressure (Beers & Berkow, 2007).

2.10.1.2 Classification of hypertension

High blood pressure in adults over 18 years of age can be divided into different levels, as is shown in Table 2-5.

Table 2-5: Classification of hypertension (Lip & Chung, 2002; Beers, 2003).

Category	Systolic blood pressure (SBP) mmHg	Diastolic blood pressure (DBP) mmHg
Optimal	<120	<80
Normal	<130	<85
High-normal	130-139	85-89
Stage 1 hypertension (mild)	140-159	90-99
Stage 2 hypertension (moderate)	160-179	99-109
Stage 3 hypertension (severe)	≥180	≥110
ISH subgroup: borderline	140-149	<90

Classification is based on the average of two or more readings taken at each of two or more visits after initial screening.

2.10.2 Risk factors of hypertension

Hypertension is already a highly prevalent risk factor for CVD throughout the industrialised world (Yusuf *et al.* 2001:2746). It is becoming a progressively more common health problem worldwide because of increasing longevity and the prevalence of contributing factors such as obesity, physical inactivity and an unhealthy diet (WHO, International Society of Hypertension Writing, 2003:1983). Hypertension plays a major etiological role in the development of cerebrovascular disease, ischemic heart disease, cardiac and renal failure, whilst treatment of hypertension has been associated with about a 40% reduction in the risk of stroke and about a 15% reduction in the risk of myocardial infarction (WHO, International Society of Hypertension Writing, 2003:1983).

Target-organ disease (TOD) from arterial hypertension can be cardiac, cerebrovascular, peripheral vascular, renal, and ocular. The risk of complications and premature death is related

to the extent of blood pressure elevation. Hypertension is additive with other risk factors in the development of coronary heart disease (CHD) and stroke (Porter & Kaplan, 2010).

In the absence of associated clinical conditions, target-organ damage or very high levels of blood pressure, the exact level of blood pressure at which to begin antihypertensive medicine treatment has changed over time and is still a subject of debate (Seedat & Rayner, 2011:62). In Table 2–6 the major risk factors, target-organ damage and associated clinical conditions are listed.

Table 2-6: Major risk factors, target-organ damage and associated clinical conditions (Seedat *et al.* 2006:340; Seedat & Rayner, 2011:64)

Major risk factors	Target-organ damage	Associated clinical conditions
Levels of systolic and diastolic BP	Left ventricular hypertrophy	Coronary heart disease
Smoking	Microalbuminuria: albumin/creatinine ratio 3:30 mg/mmol	Heart failure
Dyslipidaemia	Slightly elevated creatinine	Chronic kidney disease
Diabetes Mellitus		Stroke or transient ischaemic attack
Family history of early onset of CVD		Peripheral arterial disease
Waist circumference – abdominal obesity		Advanced retinopathy

2.10.3 Pathophysiology

Hypertension is a heterogeneous disorder in which patients can be stratified by pathophysiological characteristics that have a direct bearing on the efficacy or specifically targeted antihypertensive medications, on the detection of potentially curable forms of hypertension, and on the risk of cardiovascular complications. Essential hypertension is characterised by a sustained systolic pressure of greater than 140 mmHg and a diastolic blood pressure of greater than 90 mmHg. The pressure required to move blood through the circulatory bed is provided by the pumping action of the heart (cardiac output) and the tone of the arteries (peripheral resistance) (Vikrant & Tiwari, 2001:140). In figure 2-4 some of the factors involved in the control of blood pressure are illustrated.

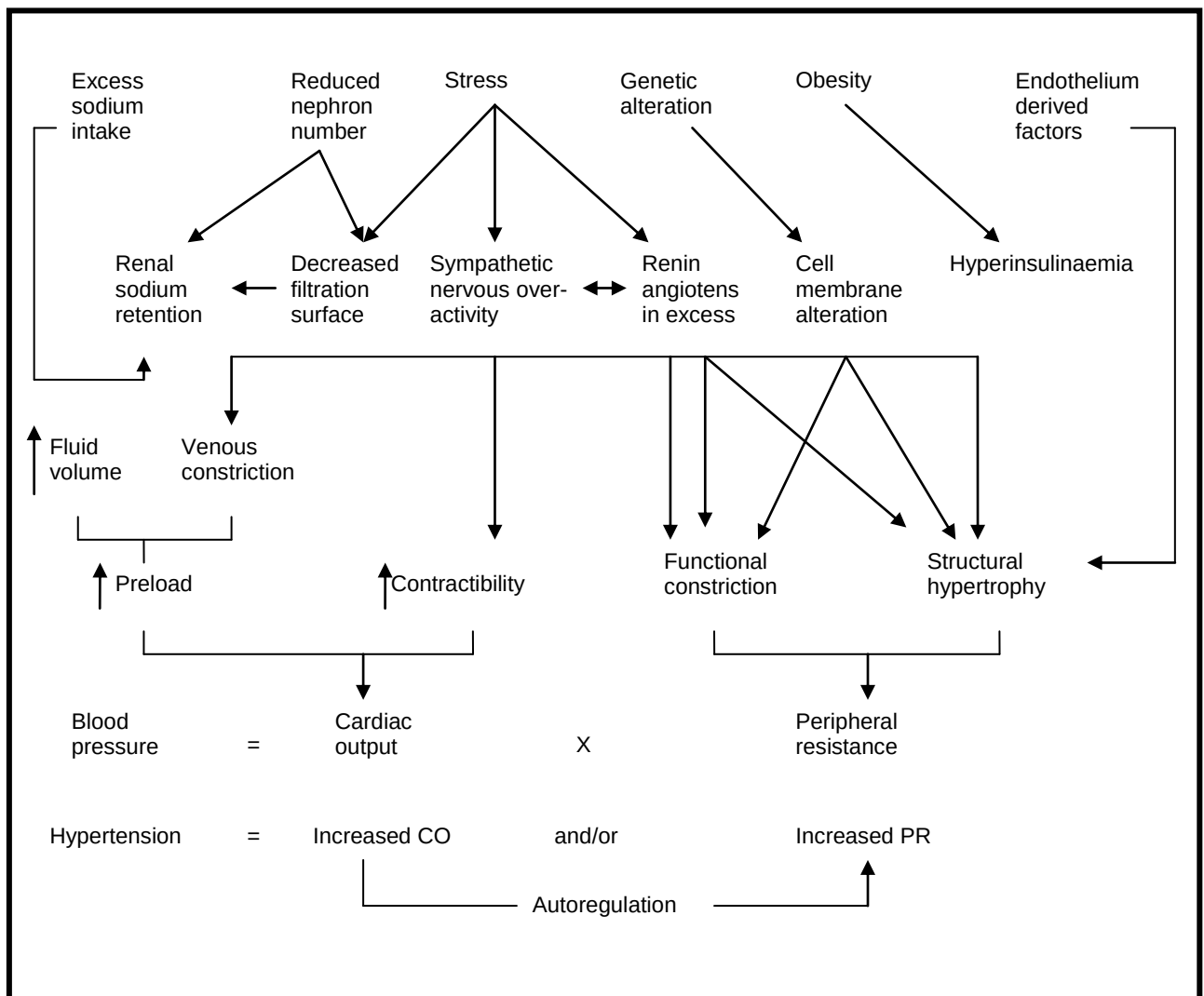


Figure 2-4: Factors involved in the control of blood pressure (adapted from Vikrant & Tiwari, 2001:142); CO = cardiac output, PR = peripheral resistance)

As can be seen in figure 2–4, if cardiac output is responsible for hypertension, the increase in cardiac output can understandably take place in two ways, namely either from an increase in fluid volume (or preload), or from an increase in contractility from neural stimulation of the heart (Vikrant & Tiwari, 2001:141).

There is, however, still a great deal of uncertainty about the pathophysiology of hypertension. A small number of patients, approximately 2% to 5%, have underlying renal or adrenal disease as the cause of their raised blood pressure. In the rest, no clear single particular cause is found and their condition is labelled as ‘essential hypertension’ (Beevers *et al.* 2001:912).

Kopp (2005:782) suggests that there are three metabolic factors that play a major role in the pathogenesis of essential hypertension, namely hyperinsulinaemia/insulin resistance, the sympathetic nervous system (SNS) and the renin-angiotensin-aldosterone system.

If the vasculature is resistant to insulin vasomodulation, just as skeletal muscle is resistant to insulin's metabolic action, insulin resistance may be responsible for the development or continuation of arterial hypertension. On the other hand, insulin could improve vascular responsiveness and prolong arterial hypertension directly by activating the SNS, which acts on the vasculature, heart and kidneys (Osei, 1999:33J).

The influence of the SNS is most noticeable in younger hypertensives, who may show signs of tachycardia and an elevated cardiac output. However, correlations between plasma catecholamines and blood pressure are poor. Insensitivity of the baroreflexes may play a role in the origin of adrenergic hyperactivity (McPhee & Massie, 2006:421).

Figure 2-5 provides a schematic representation of the renin-angiotensin system, showing its key components, the regulators of renin release and the primary effects of angiotensin II, excluding the receptors.

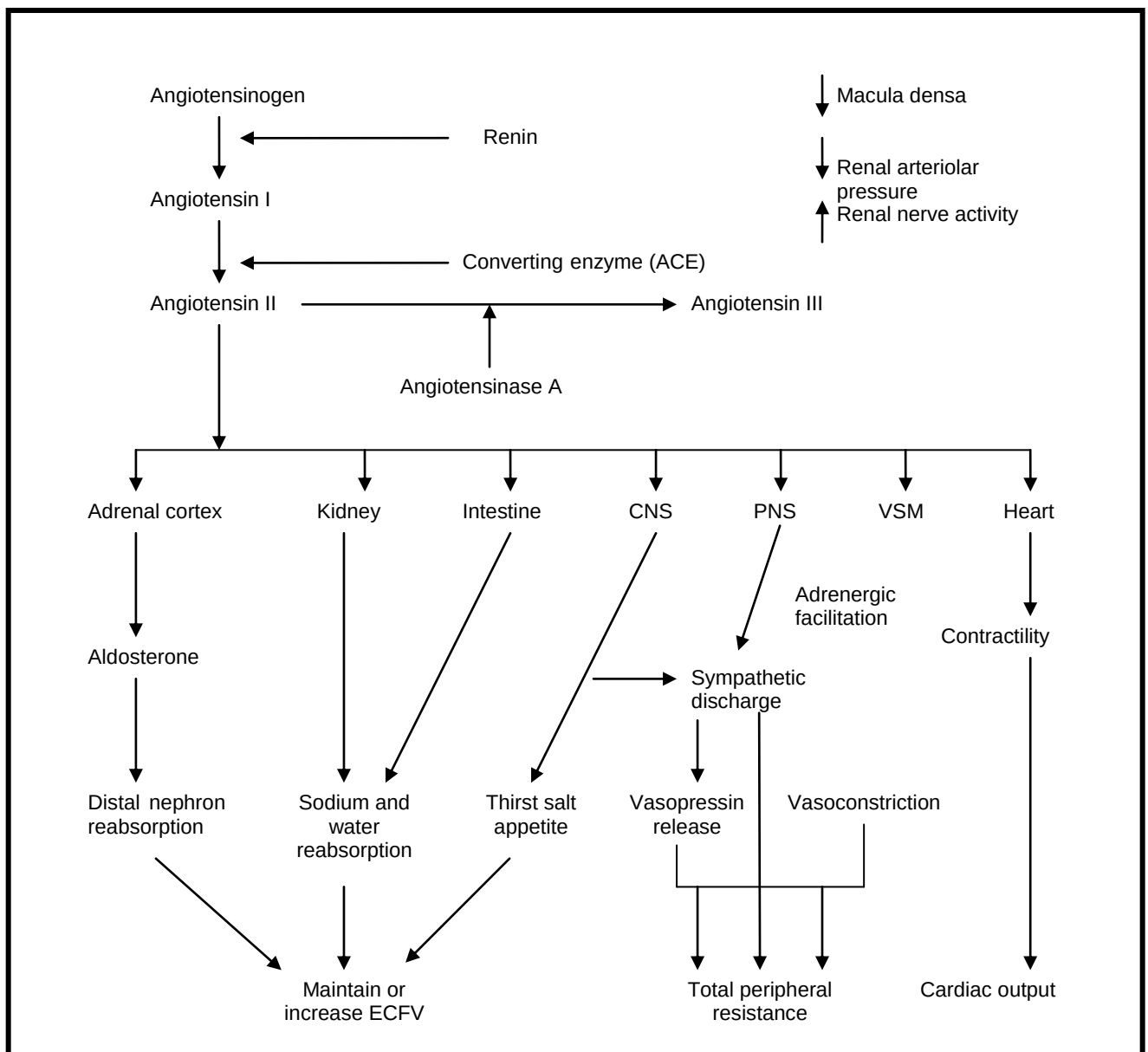


Figure 2-5: Schematic representation of the renin-angiotensin system (adapted from Vikrant & Tiwari, 2001:147); CNS = central nervous system; PNS = peripheral nervous system; VSM = vascular smooth muscle; ECFV = extracellular fluid volume

The renin-angiotensin-aldosterone system helps to regulate blood volume and therefore blood pressure. Renin, an enzyme formed in the juxtaglomerular apparatus (a microscopic structure in the kidney that regulates the function of each nephron), catalyses the conversion of angiotensinogen to angiotensin I. This inactive product is cleaved by angiotensin converting enzyme (ACE), mainly in the lungs but also in the kidneys and brain, to angiotensin II, which is a potent vasoconstrictor that also stimulates autonomic centres in the brain to increase sympathetic discharge and stimulates release of aldosterone and antidiuretic hormone (ADH). The latter two cause sodium (Na) and water retention, elevating blood pressure. Aldosterone also enhances potassium (K) excretion; low plasma K increases vasoconstriction through

closure of K channels. Renin secretion is controlled by at least four mechanisms that are not mutually exclusive, namely a renal vascular receptor responds to changes in tension in the afferent arteriolar wall; a macula densa receptor that detects changes in the delivery rate or concentration of sodium chloride (NaCl) in the distal tubule; circulating angiotensin has a negative feedback effect on renin secretion; and via the renal nerve, the sympathetic nervous system stimulates renin secretion mediated by beta-receptors (Beers & Berkow, 2007).

A number of other conditions that may elevate blood pressure, particularly in predisposed individuals, includes obesity, sodium intake, alcohol, cigarette smoking, polycythemia, non-steroidal anti-inflammatory drugs (NSAIDs) and low potassium intake (Sutters, 2007:432).

2.10.4 Epidemiology

An estimated 16,6 million of total global deaths in 2001 resulted from various forms of cardiovascular disease (CVD), of which 3,9 million were due to hypertensive and other heart conditions (WHO Global strategy on diet, physical activity and health, 2003). Hypertensive heart disease was the seventh leading cause of death in South Africa in 2000, accounting for almost 3,2% (n = 521 082) of all deaths (MRC, 2007). In persons older than 60 years of age, hypertensive heart disease accounted for 7,7% (n = 160 639) of all deaths, following ischaemic heart disease (16,5%) and stroke (15,1%) (MRC, 2007). The Mediscor Medicines Review for 2008 showed that antihypertensives were the top therapeutic group according to total expenditure and utilisation for the years 2006, 2007 and 2008 (Bester & Badenhorst, 2009:15). Hypertension is also more common in older patients, and according to the Framingham Heart Study, individuals older than 55 years have a 90 per cent residual lifetime risk of developing hypertension (Dalzell, 2003:7; Vasan, 2001:1682; Bitton & Gaziano, 2010:69).

2.10.5 Clinical presentation and diagnosis

Essential and secondary hypertension may be caused by genetic or environmental factors (Staessen *et al.* 2003:1629). If environmental factors are taken into account, nutrition can be used as a potential aid in determining and diagnosing hypertensive risk. Variable contributing causes are high salt intake, alcohol, obesity and reduced physical activity (Forrester, 2004:212). Early signs and symptoms of hypertension include headache, vision changes, ringing in the ears, or tingling of the hands and feet. Later signs may include ventricular hypertrophy, haematuria, proteinuria, heart failure, angina, renal failure, or blindness. Secondary hypertension can be caused by diseases of hormonal dysregulation, such as primary aldosteronism, Cushing's syndrome, and pheochromocytoma (Holm *et al.* 2006:112).

Hypertension is diagnosed when blood pressure is consistently elevated above 140/90 mmHg (Elliot, 2007:201). A single elevated blood pressure reading is not sufficient to establish the diagnosis of hypertension. The major exceptions to this rule are hypertensive presentations with unequivocal evidence of life-threatening end-organ damage, as seen in hypertensive emergency, or in hypertensive urgency where blood pressure is >220/125 mmHg, but life-threatening end-organ damage is absent. In less severe cases, the diagnosis of hypertension depends on a series of measurements of blood pressure, since readings can vary and tend to regress toward the mean with time. Patients whose blood pressure is in a hypertensive range typically exhibit the greatest fall toward the normal range between the first and second encounters. Although blood pressure readings may still show variability after the third visit, these later changes are mostly random. The diagnostic correctness needs to be balanced by an appreciation of the importance of establishing the diagnosis of hypertension as quickly as possible, since a three-month delay in treatment of hypertension in high-risk patients is associated with a twofold increase in cardiovascular morbidity and mortality (Sutters, 2007:429).

2.10.6 Complications

Target-organ disease (TOD) from arterial hypertension can be cardiac, cerebrovascular, peripheral vascular, renal, and ocular. The risk of complications and premature death is related to the degree of blood pressure elevation. Hypertension is additive with other risk factors in the development of coronary heart disease (CHD) and stroke. The US Joint National Committee on Detection, Evaluation and Treatment of High Blood Pressure (JNC VII) recommends risk stratification to determine when drug therapy is indicated (United States Department of Health and Human Services, 2004). Risk stratification is based on the presence of TOD, clinical cardiovascular disease (CCD) and other cardiovascular risk factors, including diabetes, dyslipidaemia and smoking. The major complications associated with hypertension are stroke and coronary heart disease (CHD) (Weibert, 2000:797).

2.10.7 Goals of treatment

Treatment should be offered to all persons in whom blood pressure reduction, irrespective of initial blood pressure levels, will reduce overall cardiovascular risk. Blood pressure targets for hypertensive patients at greatest risk of cardiovascular events, particularly diabetic patients, should be lower (<130/80 mmHg) than for individuals at lower cardiovascular risk (<140/90 mmHg) (United States Department of Health and Human Services, 2004).

2.10.8 Management of hypertension

The approach to the management of hypertension has advanced in that it is no longer treated as an individual disease, but treated in the context of a patient's total risk of cardiovascular disease (CVD) (Lip & Chung, 2002;1).

The Southern African Hypertension Society (SAHS) published its first guidelines for the management of hypertension in 1995, followed by the hypertension clinical guideline 2000, which was published in 2001, the third guideline in 2006 and the fourth set of hypertension guidelines was published by the SAHS in 2011 (SAHS, 1995:1321, SAHS, 2001; Seedat *et al.* 2006: 337 & Seedat & Rayner, 2011:60).

Poor management of hypertension is a worldwide problem, with few countries achieving acceptable levels of blood pressure control. In South Africa hypertension is the dominant risk factor for stroke, coronary heart disease, heart failure and chronic kidney disease (Rayner, 2007:30).

2.10.8.1 Non-pharmacologic therapy

Lifestyle modification may have an impact on the morbidity and mortality of patients at risk for CVD due to hypertension. A diet rich in fruit, vegetables, low-fat dietary foods and total fats has been shown to lower systolic blood pressure by up to 5,5 mmHg and diastolic blood pressure by up to 3,0 mmHg (Appel *et al.* 1997:1122). Additional measures that can prevent or mitigate hypertension or its complications include reduction in dietary sodium intake, increase in physical activity, and moderate alcohol consumption (Hagberg *et al.* 2000:204; Sacks *et al.* 2001:8 & Svetkey *et al.* 2003:467).

All patients with high-normal or elevated blood pressures, those who have a family history of cardiovascular complications of hypertension, and those who have multiple coronary risk factors should be counselled about non-pharmacological approaches to lowering blood pressure. Approaches of proven but modest value include weight reduction, reduced alcohol consumption and, in some patients, reduced salt intake. Gradually increasing activity levels should be encouraged, but strenuous exercise training programmes in already active individuals may have less benefit. Calcium and potassium supplements have been advocated, but their ability to lower blood pressure is limited. Smoking cessation will reduce overall cardiovascular risk (Sutters, 2007:437).

2.10.8.2 Pharmacological treatment

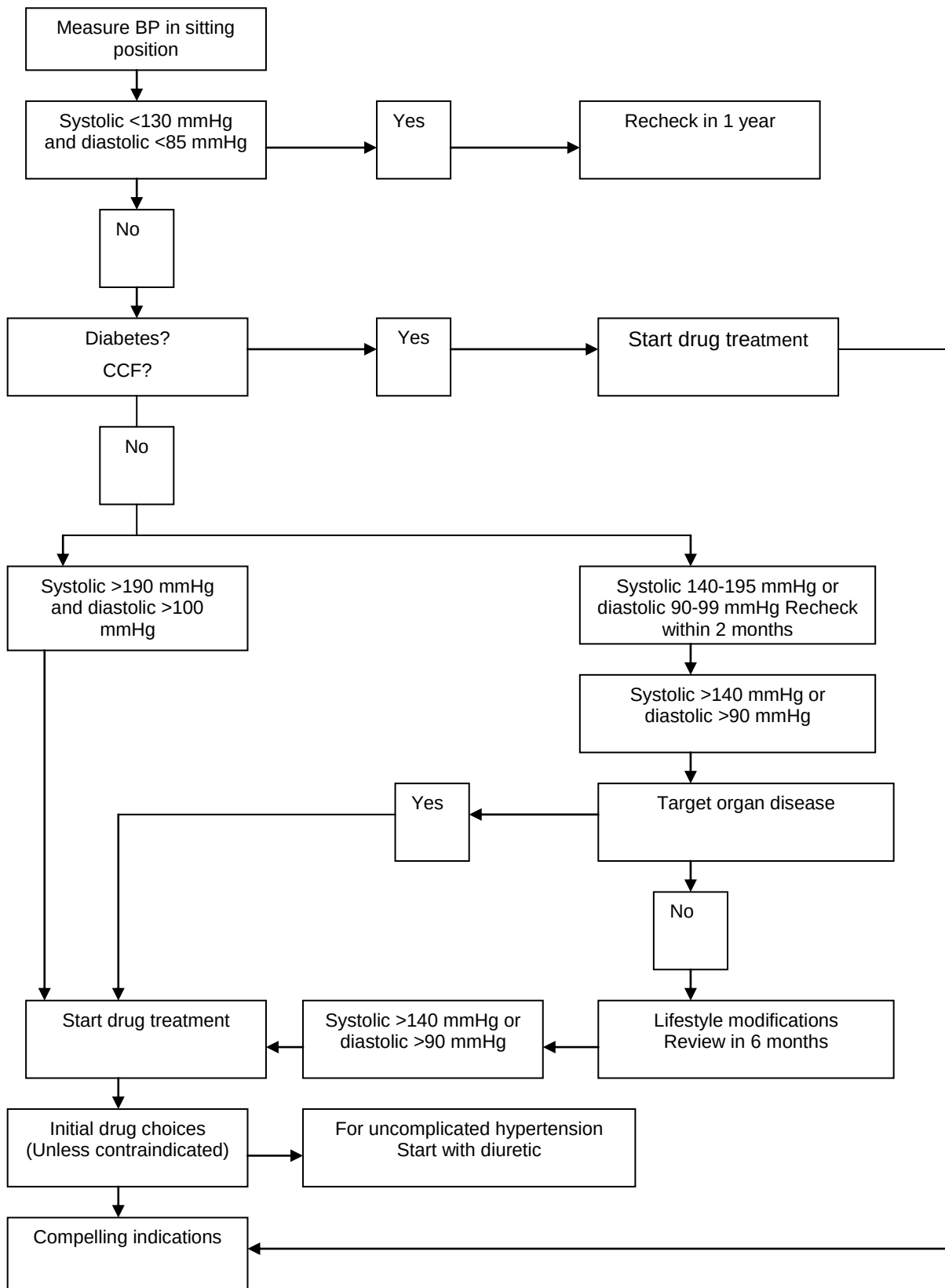
Weibert (2000:801) states that drug therapy should be initiated for stages 2 and 3 hypertension, for all patients with TOD or CCD, and for hypertensive patients with coexisting diabetes. Other hypertensive patients should attempt lifestyle modification for 6 to 12 months, based on risk stratification. Unless hypertension is severe, it is important to start a simple antihypertensive treatment regimen that minimises side effects and encourages long-term compliance, since hypertension is a life-long disease.

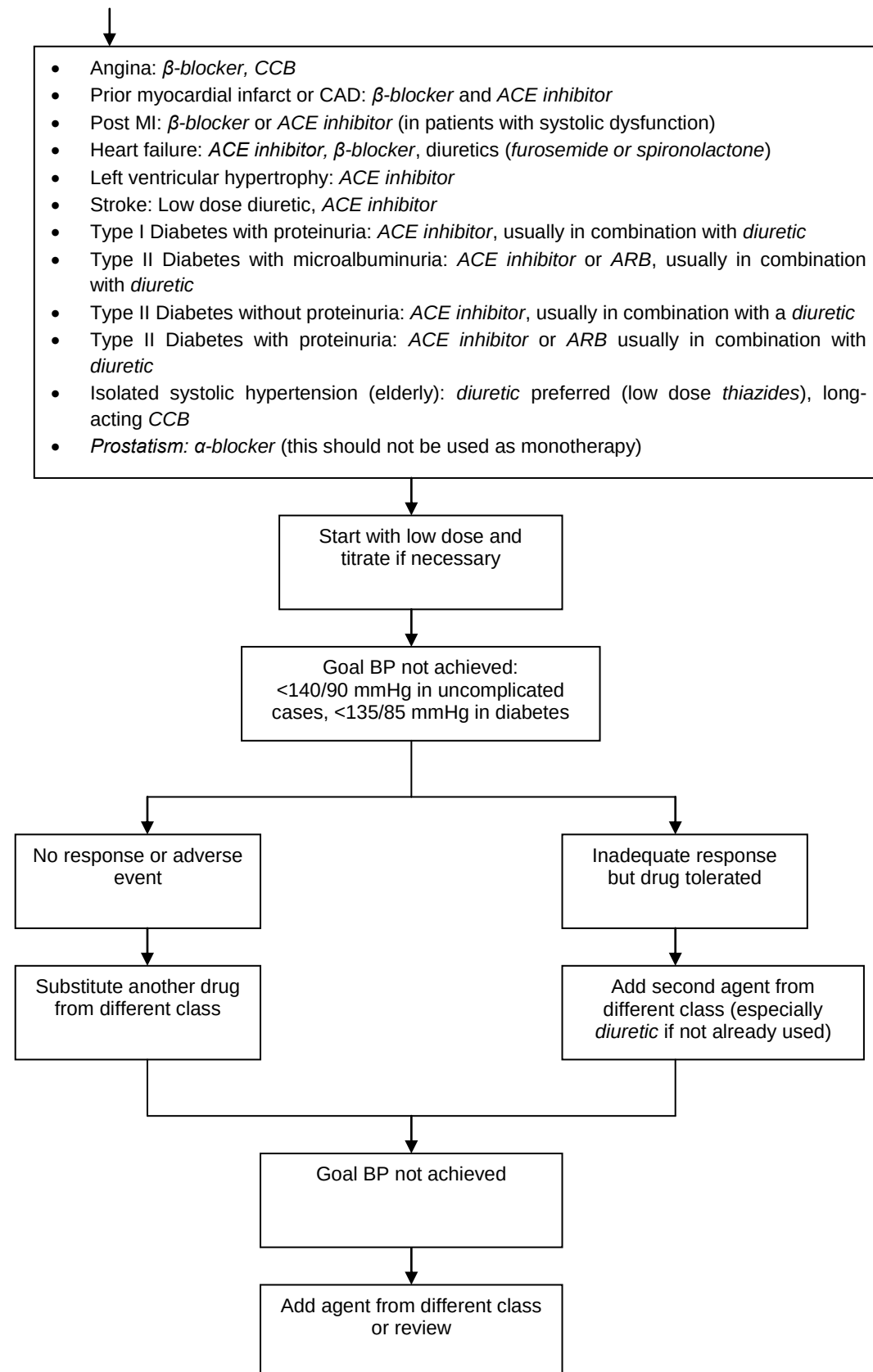
According to the Merck Manual of Diagnosis and Therapy Online (Beers & Berkow, 2007; Porter & Kaplan, 2010), pharmacological therapy should be initiated with a diuretic, unless another pharmacological group is indicated. If these drugs are ineffective, alternative classes suitable for initial therapy include calcium channel blockers, angiotensin-converting enzyme inhibitors (ACEIs), angiotensin II receptor blockers (ARBs), alpha- (α -) 1 adrenergic blockers; and combined α - β -receptor blockers (Beers & Berkow, 2007; Porter & Kaplan, 2010).

The JNC VII (US Department of Health, 2004:30) suggests that therapy begins with lifestyle modification, and if the blood pressure goal is not achieved, thiazide-type diuretics should be used as initial therapy for most patients, either alone or in combination with one of the other classes of antihypertensives that have shown to reduce one or more hypertensive complications. When the use of a single agent in adequate doses fails to achieve the blood pressure goal, the addition of a second agent from a different class should be initiated. The initiation of therapy with more than one drug increases the likelihood of achieving the blood pressure goal in a more timely fashion. The use of multidrug combinations often produces greater blood pressure reduction at lower doses of the component agents, resulting in fewer side effects (Seedat *et al.* 2006:348; Seedat & Rayner 2012:72). The use of fixed-dose combinations may be more convenient and may simplify the treatment regimen, and may also cost less than the individual components prescribed separately (Seedat & Rayner, 2012:72).

The SAHS indicates that in order to follow the recommendations for the treatment of hypertension, it is essential for a patient's added cardiovascular risk to be assessed. Drug treatment should be commenced in the following cases: firstly, in a state of low added risk, despite a period of 6-12 months of lifestyle modification and observation; secondly, moderate additional risk, despite a period of 3-6 months of lifestyle modification and observation; and thirdly, high or very high added risk (Seedat *et al.* 2006:343; Seedat & Rayner, 2012:67). There are three key classes of antihypertensive agents for the management of patients with no compelling indications, namely diuretics (thiazide-like and thiazide), ACE inhibitors, and calcium

channel blockers (CCBs) (Seedat *et al.* 2006:343). The Council for Medical Schemes published the following treatment algorithm for the treatment and management of hypertension as part of the Chronic Disease List (SA, 2003):





In 2008 the South African Department of Health published the fourth edition of the Standard Treatment Guidelines and Essential Drugs List for Primary Health Care (EDL) of the Essential

Drugs Programme. The treatment guidelines for the management of hypertension, according to the EDL, are as follows (Pudifin *et al.* 2008):

Entry to step 1	Treatment	Target
diastolic BP 90 to 99 mmHg and/or systolic BP 140 to 159 mmHg without any existing disease and no major risk factors	lifestyle modification	BP control within 3 months to systolic BP below 140 mmHg and diastolic below 90 mmHg



Entry to step 2	Treatment	Target
diastolic BP 90 – 99 mmHg and systolic BP 140 – 159 mmHg without any existing disease and no major risk factors and failure of lifestyle modification alone to reduce BP after 3 months or mild hypertension with major risk factors or existing disease or moderate hypertension at diagnosis	lifestyle modification and hydrochlorothiazide, oral, 12,5 mg daily	BP control within 1 month to systolic BP below 140 mmHg and diastolic below 90 mmHg



Entry to step 3	Treatment	Target
failure of step 2 after 1 month despite adherence to therapy or severe hypertension	lifestyle modification and hydrochlorothiazide, oral, 12,5 mg daily add ACE-Inhibitor, e.g.: enalapril, 10mg daily	BP control within 1 month to systolic BP below 140 mmHg and diastolic below 90 mmHg

	or Long acting calcium channel blocker, e.g.: amlodipine, oral 5mg daily	



Entry to step 4	Treatment	Target
failure of step 3 after 1 month of compliance	lifestyle modification and hydrochlorothiazide, oral, 12,5 mg daily and ACE-Inhibitor, e.g.: enalapril, 10 – 20 mg daily and long acting calcium channel blocker, e.g.: amlodipine, oral 5mg daily)	BP control within 1 month to systolic BP below 140 mmHg and diastolic below 90 mmHg with no side effects



Entry to step 5	Treatment	Target
failure of step 4 after 1 month of compliance	lifestyle modification and hydrochlorothiazide, oral, 12,5 mg daily and ACE-Inhibitor, e.g.: enalapril, 10 – 20 mg daily and long acting calcium channel blocker, e.g.: amlodipine, oral 5mg daily) and add: atenolol, oral, 50 mg daily	

If not controlled on Step 5 then refer patient to hospital.

The above treatment algorithm must be seen as the threshold treatment plan in the South African setup for the prevention and treatment of hypertension in the public health-care sector of South Africa.

2.10.9 Antihypertensive agents

As was previously discussed, hypertension causes an increased risk of heart attacks and strokes and the treatment of hypertension reduces this risk. There is a wide variety of antihypertensive agents and most of them can be classified into one of six major classes, namely diuretics, beta receptor blockers, calcium channel blockers, ACE inhibitors, alpha receptor blockers and angiotensin receptor blockers (ARBs). Each of these classes has merits and disadvantages, as well as additional properties that influence the choice for a particular patient. However, many patients require more than one agent to control their blood pressure and the choice of combination therapy with the appropriate synergistic effects of the drugs therefore also becomes important (Spencer & Lip, 1999:351). These six major classes of antihypertensives will now be discussed briefly.

In 2003 Law *et al.* conducted a review of 354 trials for antihypertensive medicine. They concluded that the thiazides, beta receptor blockers, ACE inhibitors, ARBs and calcium channel blockers gave similar blood pressure reductions. The mean placebo-adjusted reduction in the analysis was 9,1 mmHg for systolic and 5,5 mmHg for diastolic pressure at standard doses (Law *et al.* 2003:1427).

2.10.9.1 Diuretics

Thiazide diuretics reduce the reabsorption of sodium and chloride in the early part of the distal convoluted tubule of the kidney. This results in the delivery of increased amounts of sodium to the distal tubule, where some of it is exchanged for potassium. The net result is increased excretion of sodium, potassium and water. Circulating volume is diminished, reducing preload on the heart and thus cardiac output and blood pressure. With long-term therapy, auto-regulation by the body's own compensatory mechanism results in vasodilatation, reduction of peripheral vascular resistance and return of the cardiac output to normal. Thiazides also have some direct vasodilator properties (Spencer & Lip, 1999:352).

Another type of diuretic includes loop diuretics, which act on the ascending limb of the loop of Henle and inhibit the reabsorption of chloride, sodium and potassium. They produce a brisk but short-lived diuresis and are therefore unsuitable as first-line agents for hypertension, since they

do not provide 24-hour control. Potassium-sparing diuretics, such as amiloride and triamterene, produce little reduction in blood pressure themselves, but they may be useful in combination with other diuretics to prevent hypokalaemia (Spencer & Lip, 1999:352).

Low-dose diuretics are recommended first-line therapy in uncomplicated cases of hypertension, especially in black patients and elderly patients with isolated systolic hypertension. High doses are not recommended because of biochemical repercussions, including an adverse lipid profile, hyperuricaemia and impaired glucose tolerance (Gibbon *ed.* 2005: 133).

The side effects of thiazides, when they occur, mainly relate to metabolic function, for example: hypokalaemia, hyponatraemia, hyperuricaemia, hyperglycaemia, hyperlipidaemia, occasionally impotence, very rarely blood dyscrasias and pancreatitis and occasionally idiosyncratic reactions, including thrombocytopenia, leucopenia and skin rashes (Lip & Chung, 2002:39).

Diuretics currently available on the South African market include hydrochlorothiazide (e.g. Ridaq®), indapamide (e.g. Natrilix®), furosemide (e.g. Lasix®), spironolactone (e.g. Aldactone®) and amiloride (e.g. Moduretic®) (Gibbon *ed.* 2005:133; Rossiter *ed.* 2010:133).

2.10.9.2 Beta-receptor blockers

Beta receptor blockers are drugs that bind to beta adrenoceptors and thereby block the binding of norepinephrine and epinephrine to these receptors. This inhibits normal sympathetic effects that act through these receptors, and therefore they can be classified as sympatholytic drugs. Some of the beta blockers partially activate the receptor when binding to the beta adrenoceptor, thus preventing norepinephrine from binding to the receptor. These partial agonists therefore provide some background of sympathetic activity while preventing normal enhanced sympathetic activity (Klabunde, 2007).

Another mechanism of antihypertensive action of beta receptor blockers may include reduction of cardiac output, altered baroreceptor reflex sensitivity, depression of plasma renin, decreased release of neurotransmitters such as noradrenalin, or other central or peripheral mechanisms. Mortality benefit in hypertension is not established. In different studies done by Humphreys and Devlin (1968), Seedat and Reddy (1971) and Abson *et al.* (1981) they found that beta receptor blockers may be less effective as monotherapy in black patients. Long-term studies in hypertension suggest an increased risk of type 2 diabetes, especially when they are used in combination with diuretics (Williams *et al.* 2004:154; Gibbon *ed.* 2005:140).

According to Panjra and Messerli (2006:83), beta receptor blockers have a longer list of adverse effects than any of the other antihypertensive medications. This leads to a greater likelihood of poor compliance, discontinuation, and as a consequence, less successful blood pressure control. Some of the organs and systems affected by the adverse effects of beta blockers include the central nervous system (depression, dizziness, hallucinations, headache, insomnia, nightmares, paraesthesia), the eyes (lacrimation, ocular irritation, xerosis), respiratory (bronchospasm, wheezing, dyspnea), the cardiovascular (orthostatic hypotension, peripheral vasoconstriction, peripheral oedema, QT prolongation, sinus bradycardia, syncope, torsade de pointes, ventricular tachycardia, angina, AV block, cardiac arrest), the gastrointestinal (jaundice, diarrhoea, dyspepsia, hepatic necrosis, nausea, vomiting, constipation, flatulence, hypoglycaemia, elevated liver function tests), the sexual (erectile and ejaculation dysfunction, impotence, libido decrease) and the metabolic system (weight gain, increase in cholesterol and triglycerides, increase in insulin resistance) as well as the skin (skin hyperpigmentation, alopecia, exfoliative dermatitis, pruritis). General adverse effects include arthralgias, asthenia, fatigue, diaphoresis, oedema, myalgia, pharyngitis, and urinary retention (Panjra & Messerli 2006:83).

Beta blockers currently available on the South African market include propranolol (e.g. Inderal®, Pur-Bloka®), nadolol (e.g. Corgard®), atenolol (e.g. Tenormin®, Ten-Bloka®), acebutolol (e.g. Sectral®), bisoprolol (e.g. Concor®, Bilacor®), esmolol (e.g. Brevibloc®), metoprolol (e.g. Lopressor®), nebivolol (e.g. Nebilet®) and others (Gibbon *ed.* 2005:141; Rossiter *ed.* 2010:140).

2.10.9.3 Calcium-channel blockers

Calcium channel blockers, also known as calcium antagonists, act by interfering with the action of calcium channels in the cell membrane (Spencer & Lip, 1999:354). This impairs the transport of calcium through the voltage-sensitive calcium channels in vascular smooth muscle cells, which decreases contractile force, vascular smooth muscle tone, and peripheral resistance. The calcium channel blockers are especially effective for patients with low-renin hypertension and they have greater antihypertensive efficacy with higher pre-treatment blood pressure. Calcium antagonists are also used to treat angina, variant angina, certain arrhythmias and migraine headaches. This makes them attractive antihypertensive agents for patients with those conditions (Weibert, 2000:809).

Calcium channel blockers can be divided into two classes, namely the dihydropyridines (e.g. nifedipine and amlodipine) and the non-dihydropyridines (benzothiazepines and

phenylalkylamines) (e.g. Diltiazem and Verapamil) (Lip & Chung, 2002:50; Spencer & Lip, 1999:354).

The most common side effects are flushing, headaches and dizziness associated with the use of short-acting agents, and they may be reduced by using a drug (e.g. amlodipine) or a formulation (e.g. nifedipine LA), with a longer duration of action. Another major side effect is ankle oedema, which appears to be mediated by a change in capillary haemodynamics and does not respond to salt restriction or diuretic therapy (Lip & Chung, 2002:50).

Verapamil reduces intestinal motility and can therefore cause significant constipation. More seriously, it can cause heart block, especially in those with underlying conduction problems. Diltiazem can similarly cause gastrointestinal and conduction problems, although less frequently than verapamil (Spencer & Lip, 1999:354).

Calcium channel blockers currently available on the South African market include nifedipine (e.g. Adalat®, Cardifen®), amlodipine (e.g. Norvasc®, Amloc®), felodipine (e.g. Plendil®), isradipine (e.g. Dynacirc®), lercanidipine (e.g. Zanisip®), nimodipine (e.g. Nimotop®), diltiazem (e.g. Tilazem®, Zildem®) and verapamil (e.g. Isoptin®, Calcard SR®) (Gibbon *ed.* 2005:145-146; Rossiter *ed.* 2010:146).

2.10.9.4 ACE-inhibitors

ACE inhibitors are some of the most commonly prescribed medications for the treatment of hypertension (Vega, 2009).

ACE inhibitors work by blocking the generation of angiotensin II, which is a potent vasoconstrictor and stimulator of aldosterone secretion. According to the Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT) (2002:2981), the antihypertensive efficacy of ACE inhibitors is comparable to that of diuretics and β blockers as monotherapy for the treatment of hypertension. ACE inhibitors are more effective in younger and white patients and somewhat less effective in black patients, unless higher dosages are used or they are used in combination with diuretics (The ALLHAT Officers and Coordinators for the ALLHAT Collaborative Group, 2002:2981). The combination of low-dose diuretic therapy and ACE inhibitors may control blood pressure in up to 85% of patients. Furthermore, ACE inhibitors prolong the survival of patients with severe congestive heart failure, produce regression of left ventricular hypertrophy (LVH) and can also improve insulin sensitivity (Weibert, 2000:808).

The adverse events of ACE inhibitors can be divided into two groups, namely those that are specific to the entire class and those that are related to the specific chemical structure (specifically, related to the presence of a sulfhydryl group). ACE inhibitors, like all other antihypertensive agents, can cause hypotension. However, the frequency of hypotension is greater in renin-dependant states, as is experienced with low sodium intake and diuretic use. It is therefore recommended that a lower initial dose be used under these circumstances. ACE inhibitors can also cause hyperkalaemia because of a decrease in aldosterone. It can also cause a reversible decline in renal function in the setting of decreased renal perfusion. Other frequent side effects of the ACE inhibitors include coughing, angioedema, foetal anomalies when administered in the second or third trimester of pregnancy and dysgeusia. Side effects associated with the presence of a sulfhydryl group include neutropenia, rash and nephrotic-range proteinuria (Benowitz, 2001:174; Brown & Vaughan, 1998:1415-6).

ACE inhibitors currently available include captopril (e.g. Capoten®, Capace®), benazepril (e.g. Cibace®), cilazapril (e.g. Inhibace®), enalapril (e.g. Renitec®, Pharmapress®), fosinopril (e.g. Monopril®), lisinopril (e.g. Zetomax®, Prinivil®), moexipril (e.g. Perdix®), perindopril (e.g. Coversyl®, Prexum®), quinapril (e.g. Accupril®), ramipril (e.g. Tritace®) and trandolapril (e.g. Mavik®) (Gibbon *ed.* 2005:149-150, Rossiter *ed.* 2010:150).

2.10.9.5 Alpha-receptor blockers

Alpha receptor blockers interfere with the sympathetic nervous system and act in the central nervous system (CNS) or peripheral nervous system. These drugs produce a selective postsynaptic alpha-1 adrenoceptor inhibition, causing decreased peripheral resistance and vasodilatation without reducing cardiac output or inducing a reflex tachycardia. Alpha receptor blockers are considered for initial treatment of hypertension for patients with dyslipidaemia and prostatism. Their advantages include a favourable lipid profile effect, equal efficacy in all age and race groups, and a favourable effect on plasma glucose (Weibert, 2000:809).

The main side effect of alpha receptor blockers is postural hypotension, which is more commonly caused by short-acting agents. In women, they may cause urinary incontinence, while in men they may improve the symptoms of benign prostatic hypertrophy. Like most antihypertensive drugs, the alpha receptor blockers can cause headache and fatigue (Spencer & Lip, 1999:356).

Alpha receptor blockers currently available include prazosin (e.g. Pratsiol®), terazosin (e.g. Hytrin®) and doxazosin (e.g. Cardura®, Adco-Doxazosin® and Cardugen®) (Gibbon *ed.* 2005:130, Rossiter *ed.* 2010:130).

2.10.9.6 Angiotensin II receptor antagonists

The newest class of antihypertensive drugs is the angiotensin II receptor antagonists, or blockers, often called A₂RA or ARBs (Kaplan, 1999:1186). As was described in Section 2.7.3, the renin-angiotensin-aldosterone system plays an integral role in the pathophysiology of hypertension because it affects the regulation of fluid volume, electrolyte balance and blood volume. ARBs act by binding to specific membrane-bound receptors that displace the physiologically active angiotensin II (A-II) from its type 1-receptor sub-type (AT₁). Consequently, these drugs function as selective blockers. AT-II pressor effects are mediated by AT₁ receptors. Although these receptors are widespread in organs and tissues, they are found primarily in vascular and myocardial tissue, the liver, the adrenal cortex and some areas of the brain (Kirk, 1999:3140).

ARBs are not significantly associated with coughing compared to the ACE inhibitors, since they do not affect the activity of kinase II or the metabolism of kinins. Life-threatening angioedema has been associated with ARBs, but it is lower with ARBs than with ACE inhibitors. Other infrequent adverse effects with a possible causal association include nausea, headache, upper respiratory tract infection, back pain, fatigue, diarrhoea, dyspepsia, nasal congestion, sinusitis and pharyngitis. ARBs should not be used by pregnant women, since medications that act directly on the renin-angiotensin-aldosterone system have been associated with foetal and neonatal injury (Kirk, 1999:3144).

Even though ARBs are considered to be of equivalent efficacy to ACE inhibitors, these antihypertensive items are often limited to patients in whom ACE inhibitor treatment is contraindicated or inadequately tolerated due to adverse events. This is due to the fact that ARBs have a higher cost (Coca, 2008:215; Mancia *et al.* 2007: 1492).

ARBs currently available in South Africa include losartan (e.g. Cozaar®), candesartan (e.g. Atacand®), eprosartan (e.g. Teveten®), irbesartan (e.g. Approvel®), telmisartan (e.g. Micardis®) and valsartan (e.g. Diovan®). Fixed-dose combinations of these with a diuretic are also available (Gibbon *ed.* 2005:152, Rossiter *ed.* 2010:152).

2.10.10 Other

Other antihypertensive medicine items that may interfere with the sympathetic nervous system and may act in the central nervous system (CNS) or peripheral system include central alpha-2-agonists, peripheral sympatholytics and direct-acting vasodilators (Weibert, 2000:809).

Central alpha-2-agonists stimulate alpha-2-adrenergic receptors in the lower brainstem, which decreases sympathetic outflow to the cardiovascular system. Some agents also block peripheral alpha-2-adrenergic receptors and these combined sympatholytic effects then cause a decrease in peripheral vascular resistance. The efficacy of these drugs is similar to that of other antihypertensives when used as monotherapy for initial hypertension treatment. Unlike peripheral sympatholytics, the central alpha-2-adrenergic agonists do not cause significant sodium and fluid retention, and they also do not adversely affect glucose metabolism. They also have neutral or favourable effects on plasma lipids (Weibert, 2000:809).

Central alpha-2-agonists currently available in South Africa include reserpine (e.g. Reserpine® and Brinerdin®), methyldopa (e.g. Aldomet® and Hy-Po-Tone®) and moxonidine (e.g. Physiotens®) (Gibbon *ed.* 2005:128).

Peripheral sympatholytics are actively transported into the peripheral adrenergic neuron where they deplete norepinephrine and produce postural hypotension. Venous return to the heart as well as cardiac output is decreased. Peripheral sympatholytics also interfere with the sympathetic reflexes that control the resistance and capacitance vessels (Weibert, 2000:811).

Vasodilators directly relax arteriolar smooth muscle and decrease peripheral resistance (Cohn *et al.* 2011:690). They do not interfere with autonomic reflexes or produce postural hypotension. This stimulates carotid sinus baroreceptors, producing reflex increases in heart rate, renin release, and sodium and water retention (Weibert, 2000:811).

2.10.11 Combination therapy

Usually the treatment of hypertension is a step-wise approach, including an upward dose titration and a trial of sequential monotherapy until an effective agent is found. The third option is to use more than one antihypertensive drug, either as individual drugs or as a one-pill-combination therapy (Schultz, 2009:24).

2.11 COMPLIANCE, ADHERENCE AND PERSISTENCE TO ANTIHYPERTENSIVE MEDICATION

Compliance with drug therapy is recognised as essential to the management of chronic diseases such as hypertension (Christensen *et al.* 1997:1164). In 2008 the International Society for Pharmacoeconomics and Outcomes Research (ISPOR) Medication Compliance and Persistence Work Group published definitions for compliance and persistence after three years of international review and discussions (Cramer *et al.* 2008:44). According to this working group, medication compliance refers to the act of conforming to the advice by the prescribing doctor or pharmacist with respect to timing, dosage and rate of medication taking. They therefore defined medication compliance as ‘the extent to which a patient acts in accordance with the prescribed interval and dose of a dosing regimen’ (Cramer *et al.* 2008:46). Cramer *et al.* (2008:46) also stated that medication compliance and medication adherence can be regarded as synonyms. The ISPOR Working Group also described medication persistence as the duration of therapy, or more specifically the time between initiation and discontinuation of medicine therapy (Cramer *et al.* 2008:46).

According to Hess *et al.* (2006:1280), in clinical research, poor adherence can lessen the statistical power to distinguish a difference between treatments and can affect study validity by increasing the risk of false negative results. Poor adherence can also lead to suboptimum treatment of medical conditions and may result in adverse health outcomes (Hess *et al.* 2006:1280).

According to the literature, compliance is considered good when at least 80% of the prescribed doses are taken. Many factors have been described as possible reasons for poor adherence and include the cost of medication, unclear instructions, side effects of medication, inconvenient dosing schedules, etc. (Bittar, 1995:13; Costa, 1996:464; Li *et al.* 2007:326)

Adherence has been calculated using a range of methods. Each method has its limitations, however – no gold standard measure currently exists. Some of the most common measures used are biologic assays of drug in body fluids, pill counts, electronic monitoring and self-report (Grymonpre *et al.* 2006:471).

Prescription claims databases calculate refill medication adherence as opposed to medication consumption, and since pharmacy records are generally computerised, the prospect of using a simple algorithm to assess compliance on the basis of refill patterns is enticing, particularly for

monitoring the progress of patients with chronic diseases (Christensen *et al.* 1997:1164; Grymonpre *et al.* 2006:471).

In a presentation done by Barner at the ISPOR student Forum in 2010, he stated that when secondary databases are used, limited information regarding adherence is given and therefore certain assumptions need to be made, namely that the data that is assessed is only as accurate as the data that was captured. Furthermore the researcher must assume that the patient was in possession of medication, since no evidence is available that the medicine was consumed by the patient and patterns of no drug therapy may not indicate non-adherence, since the doctor could have change the daily regimen or terminated treatment. Databases may, however, provide acceptable estimates of medicine adherence in large populations (Barner, 2010).

Medicine possession rate (MPR) is defined as the number of days of medication supplied within a refill interval. Therefore at least two dates are needed to calculate MPR, for example the index or first date, and at least one other refill date (Barner, 2010).

In a study done by Svensson *et al.* (2000:161) on the reasons for compliance with antihypertensive medication, they found that some of the main reasons for patients complying with antihypertensive medication included the following: confidence or trust in the physician, apprehension of complications such as myocardial infarction and stroke, and a need to control the disease. Some of the reasons reported for patients not complying or stopping their antihypertensive treatment included side effects or symptoms attributed to medication, general aversion to medication, patients did not experience any symptoms of hypertension, and that the patient did not think that it was necessary to use any medicine, since they felt that the hypertension was under control (Svensson *et al.* 2000:161).

These findings seem to correlate with a study done by Wetzels *et al.* (2005:154), where the researchers stated that some of the most common factors for compliance or non-compliance are a patient's positive attitude towards health care and medication, a patient's lack of discipline, aversion to medicine or a patient's ability to actively cope with a health problem. The latter three all indicated non-compliance.

Vlasnik, Aliotta and DeLor (2005:48) stated that poor adherence and non-compliance may be attributable to patient as well as prescriber factors. Patient-centred factors include non-comprehension of prescribing instructions, inability to read, forgetfulness, apathy, physical difficulties limiting access to medication (for example swallowing problems, difficulty in opening containers, et cetera) and limited or no family or social support. Furthermore, the cost of the

treatment, the complexity of dosing regimens, pill burden and side effects may also influence compliance (Vlasnik *et al.* 2005:49).

A study done by Andersson *et al.* in 2005 regarding refill adherence in relation to the patient characteristics found that refill adherence has a tendency to be lower in younger patients and higher in older patients. They also found that the type of medicine a patient received had an influence on the adherence rate. For example, contraceptives had an 81% refill adherence rate, whilst anti-dementia drugs had only a 20% refill adherence rate. Andersson *et al.* (2005:625) also noted that selective beta blockers had a higher refill adherence rate than ACE inhibitors, diuretics and ARBs, even though more side effects can be experienced with the use of beta blockers.

In a study comparing the persistence with fixed-dose combination therapy versus concurrent two-pill therapy, Dezii (2000:4) found that a greater percentage of patients in his study population who received oral combination therapy in a single pill had better persistence with therapy after 12 months, compared to patients who received an ACE-I and a diuretic as separate pills.

Similar results were found in a study done by Jackson *et al.* (2008:1562), where multiple-combination therapies were compared. Jackson *et al.* found that there seems to be a higher adherence rate with the use of a two-pill regimen when compared to a three-pill regimen (Jackson *et al.* 2008:1562). Therefore the conclusion can be drawn that compliance can increase if the treatment regimen is simplified.

As was seen from the literature, it is clear that the analyses of prescription refills can provide valuable insights into a patient's willingness to comply with treatment (Dezii, 2001:42).

2.12 SUMMARY

In this chapter an overview was given of thresholds and the development of a threshold as a tool in decision-making. In the light of this discussion the following concluding remarks and statements can be made regarding aspects of compiling or establishing a threshold.

Firstly, thresholds are not a science-specific instrument, but are rather used in many different contexts, as was seen in Section 2.1. A threshold may be compiled on hard criteria, for example a low pharmacological range. While a threshold may usually be expressed as a number, it is not necessarily true in all cases.

Thresholds have become increasingly important in the medicine world, especially the treatment of diseases, as a supporting mechanism for decision-making, including when to treat, how to treat and who to treat. On the monetary side, pharmacoeconomic research results have become a major information system providing medication treatment cost and outcome information.

Both the private and public health-care sectors use some form of threshold as part of their decision-making process regarding the access to treatment or limitation of treatment. In the private sector some of the medical schemes have regulatory thresholds, or the so-called 'above threshold benefit' (See section 2.1). In the public health-care sector the availability and accessibility of medication can be seen as a threshold.

A threshold may also be an 'information instrument' or a 'range instrument'. In the context of medication a threshold may be an information instrument to dissolve, for example, the disease prevalence and treatment aspects (i.e. medication cost or hospitalisation). A threshold may also not be limited to a specific time or place, and may change from time to time. In this context the threshold values must be realistic and acceptable as a true presentation of an appropriate applicator. While a threshold may be described as a general term, it must be clearly defined for the situation and objectives, and limitations should be set if there should be any.

In the field of medicine, DUR studies have become more important to provide information regarding medicine usage and to improve medicine usage. Thresholds may also play an important role here, especially the establishing of treatment thresholds, which can be either a critical or range threshold. These thresholds can also provide information for DUR studies, especially with reference to retrospective DUR studies.

It is therefore clear that while a threshold may be a general term, it must be clearly defined for the specific situation and must include limitations if there are any.

Furthermore, the economic impact of hypertension as a chronic disease was discussed, as was the pathophysiology, the epidemiology, and the treatment of hypertension. It is clear that the magnitude of blood pressure reduction is almost certainly more important than the choice of drug used to achieve it, and tackling the whole spectrum of risk factors will yield further incremental benefits (Page & Halcox, 2006:293).

A healthy lifestyle remains the basis of the management of hypertension for all levels of blood pressure. A healthy lifestyle reduces blood pressure, improves antihypertensive drug efficiency

and decreases total cardiovascular risk (Seedat *et al.* 2006:343). Since there will be an ever-increasing number of alternatives for the detection, prevention, and treatment of diseases, budgetary constraints will not allow health-care systems to make all of these accessible for everyone, and health-care systems will have to implement a guiding 'instrument' for resource allocation in health care (Eichler *et al.* 2004:518).

From the literature it is clear that pharmacoeconomic studies can play a major role in the challenge of containing costs in the treatment of hypertension.

In this chapter an overview was given of the field of pharmacoeconomics, and hypertension was discussed. In the next chapter an overview and description of the methods that will be used in this study will be given.

CHAPTER 3: EMPIRICAL INVESTIGATION

3.1 INTRODUCTION

In this chapter the empirical research methodology will be discussed. All the procedures followed to obtain the applicable information and the subsequent analysis of the data will also be discussed. The empirical investigation framework includes the statement of general and specific objectives, the selection and construction of the data source and study population, the layout of the research design, the selection of the measurement instruments, the statistical analysis of the data, assessing the reliability and validity of measuring instruments, a description and discussion of the results of the empirical investigation and a conclusion and recommendations.

3.2 RESEARCH OBJECTIVES

The objectives of the empirical investigation will be discussed under a general and specific objectives.

3.2.1 General objective

The general objective of this study was to develop thresholds for the purpose of decision-making in the private health-care sector of South Africa, with specific reference to the treatment of hypertensive patients.

3.2.2 Specific objectives

The specific objectives of the empirical study were as follows:

- To review original pharmacoeconomic studies with reference to the application of hypertension treatment;
- To determine the prevalence and cost implication of hypertension medicine treatment in a section of the private health-care sector of South Africa by means of demographical factors and geographical distribution;

- To analyse the prescription patterns for different types of antihypertensive drugs according to a medicine claims database in the pharmacy benefit management environment;
- To conduct applicable pharmacoeconomic studies on the data in order to make some evaluations on the usage and cost of antihypertensive treatment;
- To investigate patient compliance/adherence with reference to antihypertensive treatment;
- To develop and propose a threshold value/values for the treatment cost of hypertension in South Africa.

3.3 RESEARCH DESIGN

This research is embedded in a drug utilisation review approach supported by various other measuring instruments, classification systems, arithmetical formulas and descriptive statistical methods. This study was done on medicine claims data provided by a South African pharmacy benefit manager (PBM) for a four-year study period ranging from 1 January 2005 to 31 December 2008. Comparisons and analyses were done by using the Statistical Analysis System (SAS for Windows 9.1, 2005).

3.3.1 Drug utilisation review

In this world with its scarce health resources that we live in today, the proper use of medicine is fundamental. One of the measuring tools to help health professionals manage the correct and proper use of medicine is a process called a *drug utilisation review* (DUR).

Wertheimer and Navarro (1999:361) define a DUR as the qualitative and quantitative evaluation of prescription drug use, physician prescribing patterns, or patient drug utilisation to verify the appropriateness of drug therapy. The World Health Organisation defined DUR as follows in 1977: *'the marketing, distribution, prescription, and use of drugs in a society, with special emphasis on the resulting medical, societal and economic consequences'*.

Blackburn *et al.* (2001:6) are of the opinion that a DUR study is a one-time study to assess the suitability of drug therapy. The purpose is to identify whether current patterns of prescribing, dispensing and using drug therapy are consistent with criteria and standards. These criteria and standards demonstrate that drug therapy is effective, safe, appropriate and cost-effective and supports optimal patient outcomes. The study approach here can be seen as a 'one-time study' consisting of sub-time periods (annual data for 2005 to 2008).

Three categories of DUR are recognised. These include the *prospective DUR*, *retrospective DUR* and *concurrent reviews*.

- Prospective DURs involve the evaluation of a patient's planned drug therapy before the medication is dispensed.
- Retrospective DURs are conducted after the patient has received his medication.
- Concurrent reviews are performed during the course of treatment and involve the ongoing monitoring of drug therapy to encourage positive patient outcomes (Academy of Managed Care Pharmacy, 2009).

Since the data used in this study consisted of medicine claims from a medicine claims database of prescriptions already filled, this study was limited to a retrospective DUR. A brief discussion of retrospective DUR will follow to give a better understanding of the scope of this type of research design.

The Academy of Managed Care Pharmacy (2009) defines a retrospective DUR as the '*review of drug therapy after the patient has received the medication*'.

Data is collected and analysed after the prescription has been dispensed and assumed usage of drugs has occurred and is therefore archival in nature. Although retrospective DUR studies have little impact on immediate patient care, they serve to identify tendencies in prescribing practices that may lead to intervention aimed at enhancing prescribing behaviour. Retrospective studies are normally relatively inexpensive and can be conducted rapidly. They can also detect new relationships and problems relating to medications and diseases (Truter, 1995:338).

3.4 RESEARCH METHODOLOGY

The study consisted of two phases. The first phase involved a literature review on aspects of pharmaco-economic issues and hypertension and the treatment thereof. The second phase consisted of the empirical and statistical analysis of the medicine data by applying pharmaco-economic-related methods. The data consisted of membership data and medicine claims data from a private South African pharmaceutical benefit management company.

The empirical study was divided into five steps or phases, namely:

- the selection of the study population (see Section 3.6);
- the selection of the measuring instruments (see Section 3.7.3);
- data analysis (see Section 3.7);
- the report and discussion of the results of the empirical investigation (see Chapter 4); and

- the recommendations based on the results of the empirical investigation (see Chapter 5).

The total population consisted of all the prescriptions on the database, while the study population consisted of all the prescriptions of patients using antihypertensive medicines for a four-year period starting on 1 January 2005 and ending on 31 December 2008. To ensure confidentiality, neither the name of the prescribing doctor nor the patient's name was revealed. A total of 5 863 312 antihypertensive prescriptions over the four-year study period were included for the data analysis.

The different strata were established by following certain steps:

Step 1: All the prescriptions on the database were included in the initial analysis.

Step 2: In this step all the prescriptions containing medicines for the treatment of cardiovascular diseases were selected from the database.

Step 3: In this step the criteria set was selected. This includes all the prescriptions containing at least one antihypertensive medicine item from the database.

Step 4: In this last step the antihypertensive medicine items were classified according to the pharmacological active ingredient.

A detailed description of the data analysis is presented in Appendix A.

3.5 DATA SOURCE

The data for this study was obtained from a medicine claims database. Data was extracted for a period of 48 months, from 1 January 2005 to 31 December 2008. The study period was divided into four time periods, namely January to December 2005, January to December 2006, January to December 2007 and January to December 2008.

The following data fields were used in this study:

- The National Pharmaceutical Product Index (NAPPI) code for the medicine product.
- The description (trade name) of the drug.
- The quantity of medicines that was dispensed.
- The price of the medicines, which was divided into scheme amount, patient levy and total cost.
- The prescription number.
- The date of dispensing.
- Indicator for generic or innovator product.
- Gender of the patient.

- Date of birth of the patient (to determine age).
- Prescriber and provider postal codes.

3.6 STUDY POPULATION

From the total database a study population was selected. After all the prescriptions on the database between 1 January 2005 and 31 December 2008 had been screened, all the prescriptions containing an antihypertensive agent (i.e. medicine items from either MIMS[®] group 7.3 or 16.1) were selected. The patient pool obtained from the selected prescriptions formed the study population. The study population was then further divided into three age groups. Age group 1 included patients ≤ 18 years, age group 2 included patients older than 18 years but younger than 45 years, and age group 3 included patients older than 45 years. According to the PBM an increase in age is usually associated with an increase in medicine usage (Bester & Badenhorst, 2008:10). Furthermore, there are two bimodal peaks in patient age, namely one between 15 and 19 years and another between 35 and 39 years. In the light of these two observations, the chosen age groups took these peaks in medicine usage, as well as the fact that medicine usage, and especially the occurrence of chronic conditions, increases with age, into account.

The study population was also divided into three treatment categories. Treatment category 1 involved all the medicine and prescription information for antihypertensive medicine items prescribed from MIMS[®] group 7.3 alone, while treatment category 2 involved medicines and prescription information for diuretics prescribed only from MIMS[®] group 16.1. Treatment category 3 involved all the medicine and prescription information for the combination of medicine items that were prescribed together from MIMS[®] groups 7.3 and 16.1. A further analysis of the data was conducted to determine the combination of antihypertensive medicine items from MIMS[®] group 7.3 that were prescribed together. No differentiation between the different types of hypertension were possible, due to the lack of ICD-10 codes.

To determine patient adherence to antihypertensive treatment, a sample from all the antihypertensive patients was selected. This was done by merging the patient records of the four study years and including only those records with more than one antihypertensive claim during the four-year study period.

3.7 DATA ANALYSIS

Specific measuring instruments and statistical analyses were applied to the data. These will be discussed briefly.

3.7.1 Data analysis organogram

The data was analysed by employing certain steps as presented in the organogram (see Appendix A). The Statistical Analysis System® SAS 9.1® (SAS institute Inc., 2002-2003) was used to extract and analyse certain data from the database. Microsoft Word 2007® and Microsoft Excel 2007® were used to create basic tables and figures and to compute certain statistical measures.

3.7.2 Classification systems used

Different classification systems were used during this study. These classification systems will subsequently be discussed.

3.7.2.1 The NAPPI Code

A NAPPI code (National Approved Product Pricing Index) is a unique nine-digit product code implemented with electronic transactions in mind (Snyman, 2004:5a). Any given ethical, surgical and consumable product can be uniquely identified by the NAPPI code. This facilitates electronic transfer of information throughout the health-care delivery system. The NAPPI code not only provides information on the manufacturer of the product, but also on the product description, strength and pack size. The first six (6) digits describe the product and the strength whilst the three-digit suffix describes the pack size. For surgical items a range code is allocated (Council for Medical Schemes, 2003, MediKredit, 2010). The NAPPI codes were used to categorise the antihypertensive medicine items into the different pharmacological groups and to determine the strength of the individual antihypertensive medicine items.

3.7.2.2 The MIMS® classification system

The MIMS® (Monthly Index of Medical Specialities) classification system classifies medicine according to its pharmacological action. The MIMS® classifies the antihypertensive medicines into ten groups (7.3.1 – 7.3.10), according to their active ingredient and mechanism of action (Snyman, 2007:122 - 156). The diuretics, which form part of the treatment for hypertension, as was seen in Chapter 2, section 2.10.9.1, are classified in group 16.1.

3.7.2.3 Classification of agents according to the active ingredient

The SAMF® (South African Medicines Formulary) classifies medicine according to its pharmacological active ingredient, and in the case of antihypertensives (C02), according to anti-

adrenergic agents acting centrally, anti-adrenergic agents acting peripherally, and agents acting on arteriolar smooth muscle. Diuretics are classified on their own (C03) and not as part of the antihypertensive medicine items (Rossiter *ed.* 2010:138).

Both the SAMF[®] and MIMS[®] were used to attain and classify the generic and brand names of the different antihypertensive medicines available in the prescribing and usage by the study population.

Appendix B provides a classification of all the antihypertensive drugs with the NAPPI codes according to the MIMS[®] and SAMF[®].

3.7.3 Measuring instruments and statistical analysis

The different measuring instruments and statistical analyses that were used in this study to accomplish the specific objectives stipulated are illustrated below:

3.7.3.1 Measuring instruments

For the purpose of this study, the following measuring instruments were used.

Prevalence

The prevalence illustrates the number of cases of a disease documented in a population during a given period of time (Walley & Strobl, 2004:90). In other words, prevalence can also describe the proportion of people in a specific population with a disease or condition. For the purpose of this study: patients with hypertension.

Prevalence was used in the data analysis as follows:

- To determine the prevalence and cost implication of hypertension treatment in South Africa by means of age, gender and geographical distribution.
- To analyse the prescription patterns for different types of antihypertensive medicine items according to a medicine claims database.

Costs

According to Larson (2005:47), costs can be defined or classified as the resources used to perform an activity or put into effect a decision. Although different types of costs can be defined, this study focused only on the direct costs associated with the treatment of hypertension with medication.

Antihypertensive medicine items were analysed and discussed according to the total cost of the group in comparison with the total database. Costs were analysed according to total cost, average cost per prescription, average cost per medicine item and cost prevalence index (CPI). Total cost included the levy payable by the patient and the amount that the medical scheme had to pay. Medicine cost consists of the single exit price (SEP) as determined by the government, the dispensing fee added by the pharmacist or prescribing doctor and value added tax (VAT) of 14%. Whilst the SEP (determined by the South African Department of Health) changed during the study period, the VAT remained the same. However, for comparison purposes a standard SEP for all medication provided was established at 33% (MUSA, 2011). This was done because different costs by different providers may be applied, as well as maximum prices that can be set by third-party payers or PBM companies. The SEP varied between 26% and 36%, yet certain providers may add up to 75%. The costs that were used in this study helped to determine the cost implication of hypertension treatment in South Africa, to calculate a cost threshold value for the treatment of hypertension, and to determine the cost implication in non-adherence or non-compliance with antihypertension treatment.

Cost-minimisation analysis (CMA)

As was stated in Chapter 2, cost-minimisation analysis can be used when treatments being evaluated have similar health outcomes, with the comparison being limited to analysing the costs. Therefore, only the costs of the two treatments compared will be evaluated. For the purpose of this study CMA will be used to determine possible cost savings after generic substitution and to make some suggestions on the usage and cost of antihypertensive treatment.

Prescribed daily doses (PDD)

The National Health Services (NHS) Information Centre (2011) in England defines the prescribed daily dose as the average daily amount/dose of a drug that is actually prescribed to a specific group of patients for a specific disease or illness, and can be determined from prescription or pharmacy records. It is important to relate the PDD to the diagnosis on which the dosage is based, and whenever there is a big difference in the PDD and the defined daily dose (DDD) it is important to take this into consideration when evaluating DUR figures (WHO, 2003).

In this study the PDD values for antihypertensive medicine items were calculated by multiplying the total number of tablets or capsules dispensed with the strength, and then dividing this by the total days supplied.

Compliance / Refill-based adherence rate

As was seen in Chapter 2, Section 2.11, compliance with drug therapy was defined as the extent to which a person's behaviour corresponds with medical or health advice, and that compliance is essential to the management of chronic diseases such as hypertension (Christensen, *et al.* 1997:1164; Hess, *et al.* 2006:1280).

Since the data used in this study is from a medicine claims database, refill-based adherence can be calculated instead of using medication consumption to determine compliance or adherence, ensuring patient progress can be monitored (Christensen *et al.* 1997:1164; Grymonpre *et al.* 2006:471). The adherence or compliance value obtained from the calculations provides some information on antihypertensive medication consumption, but rather provides information on the possession of antihypertensive medicine. Therefore only an estimate of the highest level of antihypertensive medicine consumption can be made (Hess *et al.* 2006:1281).

For the purpose of this study the refill-adherence rate (RAR) was divided into three categories, as can be seen in Table 3-1. Categories 1 and 3 indicate unacceptably low and high RAR respectively, while Category 2 indicates acceptable RAR.

Table 3-1: Refill-adherence rate (RAR) categories

RAR Category	Criteria
1	$\leq 80\%$
2	$80\% < \text{RAR} \leq 120\%$
3	$\geq 120\%$

The refill-adherence rate (RAR) was calculated per individual medicine item for all antihypertensive (AH) medicine items that were prescribed more than once.

The following equation was used:

$$\text{RAR} = \frac{(\text{total number of days of antihypertensive medicine items supplied} - \text{number of days supplied at last refill})}{\text{days between refills}} \times 100$$

The cost implication is an indication of the monetary value lost if unacceptable refill-based adherence rates are obtained. The cost implication (CI) of individual antihypertensive medication with acceptable or unacceptable refill-adherence rates was determined according to the following formula:

$CI = \frac{\text{Cost of individual AH medication with acceptable RAR}}{(\text{Total cost of AH medication in RAR}-\text{Cost of last refill of AH medication in RAR calculations})} \times 100$

There may be certain limitations when adherence rates are calculated, including the number of days' supply, the inability to determine whether the antihypertensive medicine was in fact consumed by the patient, and when patients decide to pay out of their pocket for their antihypertensive medicine. Medicine claims data is, however, convenient, objective, non-invasive and relatively inexpensive to obtain and therefore suitable for calculating patient adherence (Hess *et al.* 2006:1281).

Threshold determination

As was stated in Chapter 2, a threshold can be used as an information tool for pharmaceutical decision-making. For the purpose of this study to determine or predict a threshold, certain standards and criteria were set to describe prevalence and cost aspects. Two types of threshold were calculated. The first type was a cost range threshold, where the standard deviation to the average cost was used, and the second type of threshold was a net cost ratio threshold, where the cost per household was used as cost threshold. The pharmacoeconomic methods that were used to calculate threshold values included CMA and medication cost. The average cost, standard deviation and median values were used to calculate possible thresholds. The standard deviation was divided by two, and the average cost plus half the standard deviation and the average cost minus half the standard deviation were used as a cost range. The second estimated cost threshold range was calculated by adding a third of the standard deviation to the average cost per item for the upper limit, and subtracting a third of the standard deviation from the average cost per item for the lower limit of the cost threshold range. Different scenarios were sketched, for example, a threshold to use in the treatment of male and female patients was estimated, as well as a threshold for antihypertensive medicine usage in the different age groups. For all the scenarios the threshold was determined by using all four study years combined, and not for individual study years.

A second set of thresholds that was calculated was based on treatment cost per household. For these calculations only the data of study year 2008 was used. It was calculated that there were approximately 2 183 945 households with a relatively high income (the medical aid market) in South Africa during 2008. In order to calculate a threshold, a 'medical aid market' in South Africa was established. Since the data that was used in this study only represents an estimated 35% of the population, the total treatment cost was multiplied by 1,76, to make it more generalisable for the whole private health-care sector of South Africa. The total treatment cost per household was calculated by dividing the total cost for the medical aid market by the

number of relatively high income households. This total treatment cost included value added tax (VAT), which was set at 14%, as well as a 'logistics fee', which was a percentage of the SEP (this can also be seen as the gross profit). This logistics fee is just regulated as a maximum percentage, and hence was set at 33% as a logistics fee.

The 33% SEP that was used for the medical aid market was calculated as follows: five scenarios for SEP values were selected, namely 16%, 26%, 36%, 40% and 50%. These percentages were weighted, namely 0,05 (16%), 0,3 (26%), 0,5 (36%), 0,1 (40%) and 0,05 (50%), and percentages were calculated. These percentages accounted for approximately 33%, hence the 33% SEP used (MUSA, 2011). The final treatment cost per household, which was also the threshold, was the total treatment cost per household minus 14% VAT, minus the 33% logistics fee. It is important to note that these threshold values were used only as illustration and were limited to the private health-care sector and not the total health-care industry. A number of antihypertensive treatment cost thresholds were calculated for the national private health-care sector, including cost thresholds for the different genders, age groups, treatment categories and pharmacological groups.

3.7.3.2 Statistical analysis

For the purposes of this study, the following descriptive statistics and calculations were used:

Arithmetic mean (average)

The arithmetic mean or average can be described as the best-known single numerical value used to indicate the central position or location of a set of numbers. The value of the average is always between the lowest and highest number in a series or range of values (Steyn *et al.* 2003:99).

In this study, the arithmetic mean was calculated for the total number of prescriptions per year and per patient per year, the number of medicine items per prescription and on the total database, the total cost of these medicine items, the total cost per prescription and the total cost of all medicine items. All these calculations were also done for antihypertensive prescriptions and medicine items.

Standard deviation

The standard deviation is a statistic that provides information on how tightly a set of values is clustered around the mean in a set of data (Niles, 2005:2). In other words, the standard deviation is a measure of the spread of the data around the mean.

The formula for the standard deviation differs slightly depending on whether you are using an entire population or only a sample (Brase & Brase, 1999:103).

In this study, the standard deviation was calculated for the total number of prescriptions per year and per patient per year, the number of medicine items per prescription, the total cost of these medicine items, the total cost per prescription and the total cost of all medicine items. All these calculations were done for prescriptions and medicine items on the total database, as well as for antihypertensive prescriptions and antihypertensive medicine items.

The standard deviation was also used in determining a cost threshold range, as was described in Section 3.7.3.1.

The median

According to Niles (2012), the median can be seen as the middle value in a range of values. To determine the median all the values need to be in numerical order and the value in the middle will be the mean. If an even number of values is used, the two middle values are added and then divided by two.

Cost prevalence index

The cost prevalence index can be used as indication to show the relative relationship between the number of medicine items per prescription and the total medicine cost (Serfontein, 1989:180).

To calculate the cost prevalence index, the cost percentage is divided by the prevalence percentage.

$$\text{CPI} = \frac{\text{cost \%}}{\text{prevalence \%}}$$

For the purpose of this study the CPI was interpreted as follows:

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

The cost prevalence index was used to determine which of the antihypertensive medicine items were relatively expensive and which could be described as relatively inexpensive.

Patient prevalence index

The patient prevalence index (PPI) can be used as an indication of the relationship between the number of hypertensive patients and a population or section of the population. The PPI is derived from the CPI and is calculated using the following formula:

$$\text{PPI} = \frac{\text{hypertensive patients \%}}{\text{total patient \%}}$$

For the purpose of this study the PPI was interpreted as follows:

- If the patient index < 1 then the number of hypertensive patients is relative low
- If the patient index = 1 then there is equilibrium between the hypertensive patients and total population.
- If the patient index > 1 then the number of hypertensive patients is relatively high.

Ratios

According to the online Oxford English Dictionary (2012), a ratio is the quantitative relationship between two amounts showing the number of times one value contains or is contained within the other. For the purposes of this study, however, a ratio refers to the difference between the cost and number of patients or antihypertensive medicine items. In other words, it is the number of items in relation to the number of patients, or the relationship of the total cost of antihypertensive medicine items to the number of antihypertensive patients. It was also used to calculate a cost ratio threshold. This was done by dividing the treatment cost by the number of households.

d-values/ effect sizes

According to Talheimer and Cook (2002:3), an effect size is the difference between two means divided by the standard deviation. Ellis and Steyn (2003:51) noted that the effect size is independent of the sample size and is only a determinant of practical significance.

$$d = \frac{x_t - x_c}{S_{\max}}$$

Where:

- d = effect size
- x_t = average cost of treatment (mean)
- x_c = average cost of comparison treatment (mean)
- $S_{\max}$ = maximum standard deviation.

The effect sizes were used to compare two or more treatments or their costs for the treatment of hypertension. This comparison could have been to compare a branded product with its generic equivalent, or two therapeutic similar medicine items.

According to Steyn (1999:3), the following guidelines can be used to evaluate the d-values:

- d = 0,2: small effect with no practically 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.

3.8 ETHICAL CONSIDERATIONS

Permission to conduct this study was granted by the PBM's board of directors as well as the Ethics Committee of the North-West University. The study was approved with the title: 'Hypertension treatment in a section of the prescribed management benefit market in South Africa' by the NWU Ethics Committee and awarded ethical application number NWU-00006-07-A6. To ensure confidentiality, neither the name of the patient nor that of the prescribing doctor was revealed. This was done by the PBM by allocating a random 'dummy' number to each patient. Each prescription record contained an 11-digit reference number, which linked each patient, medical practice or medical aid to scheme line items. This number served as a time stamp of when the transaction was clarified.

3.9 LIMITATIONS IN THE METHODS

Certain limitations were detected and experienced in the analysis of the data. These limitations are summarised in Table 3-2.

Table 3-2: Limitations in the methods

Limitation	Explanation
Data	Data was assumed to be correct, no manipulation was made by the investigator
Cost	Only direct medicine cost was available, therefore a true cost-of-illness could not be calculated
Effectiveness	Since no effectiveness data was available, only CMS could be conducted. A generic indicator was used in these calculations
Effectiveness	Since no effectiveness data was available, a cost-effectiveness threshold could not be established, only a cost threshold could be proposed
ICD-10 code	No ICD-10 codes were available, therefore it was assumed that patients receiving treatment from MIMS group 7.3 and 16.1 were patients with hypertension
SEP	May vary according to specific provider in the calculation for illustration of possible threshold ranges

3.10 RELIABILITY AND VALIDITY OF DATA

The data used in this study was obtained directly from the database provided by the PBM, and there was no direct manipulation of the data. Research was conducted from the perspective that all data obtained from the medicine claims database was reliable and valid. The database was, however, verified by testing for outliers as well as certain random data checks.

Since only one PBM's data was used, no cost or prevalence comparisons could be made with other PBM's, and only direct medicine cost was used throughout the study.

3.11 RESULTS AND DISCUSSION

The results and discussion with regard to the empirical investigation of this study will be discussed in Chapter 4. Certain relevant data will be provided in the appendices.

3.12 CONCLUSIONS AND RECOMMENDATIONS

The conclusion and recommendations of this study with specific reference to the general and specific objectives will be discussed in Chapter 5.

3.13 SUMMARY

Various aspects pertaining to the empirical investigation of this study were discussed in this chapter in order to provide information on the specific approaches followed in this research project.

In Chapter 4 the results of the study as well as some discussions on the data will be provided.

CHAPTER 4: RESULTS AND DISCUSSION

4.1 INTRODUCTION

In this chapter the results of the empirical investigation are reported and discussed. The results are for the period from 1 January 2005 until 31 December 2008. The results are presented according the following categories:

- The prevalence and cost of medicine items recorded in the database.
- The prevalence and cost of cardiovascular system agents in the total database.
- The prevalence and cost of the antihypertensive medicine items in the cardiovascular system.
- The prevalence and cost of antihypertensive agents in the total database and according to a practical pharmacological classification.
- Determination of the average prescribed daily dose (PDD) for combination antihypertensive treatment according to active ingredients.
- The prevalence, type and cost of combinations between different antihypertensive agents.
- Refill-based adherence rate of antihypertensive medication.

4.2 DEFINITIONS

For the purpose of this study certain definitions were standardised and explained. These definitions include the following:

- *Medicine item or medication item or items:* An agent or preparation that contains at least one pharmacological active ingredient and is used to internally or externally treat or prevent an illness.
- *Antihypertensive medicine items:* Medication that is used in the management of hypertension (see Chapter 2), and categories in the MIMS[®] under Sections 7.3 and 16.1.
- *Active ingredient:* The part of the antihypertensive medicine item responsible for a pharmaceutical effect.
- *Prescription:* A written instruction from a legal prescriber to a legal registered provider (e.g. a pharmacist) to dispense a specific medication. A prescription may contain one or more

medicine items. The abbreviation Rx will be used in tables and figures to indicate a prescription.

- *Patient:* A patient is a person receiving medication on prescription, for the purpose of this study especially antihypertensive medication and during the period 1 January 2005 to 31 December 2008.
- *Total database:* All the prescriptions recorded in the database as provided by the PBM for this study.
- *Total population:* All the patients in the database representing a section of the population of the private health-care sector in South Africa.
- *Study population:* The total antihypertensive patient records and antihypertensive medication claims used during this study.
- *Threshold:* The monetary value with regard to antihypertensive medicine usage and cost. Two different types of thresholds will be calculated, namely a cost threshold range, which will have an upper and lower limit that will be calculated using the standard deviation, average cost and median, and secondly a cost ratio threshold that will be calculated per household. This cost ratio threshold will not have an upper and lower value but will consist of a single value calculated for different scenarios.
- *Indicators:* Measuring instruments that will be used to describe and explain the data, and that include prevalence, average cost, standard deviation, median, ratio, total cost and number of prescriptions.

4.3 NOTES RELATED TO THE STUDY FRAMEWORK

Descriptive statistics were applied and used during this study (as was described in Chapter 3) and the results are given in table or figure format. Some of the tables will not add up to one hundred per cent due to rounding off. Due to the nature and scope of the data some values contain one decimal value whilst other contain two decimal values (especially monetary values).

Except if otherwise indicated the tables and figures refer to the study years 1 January 2005 to 31 December 2008.

In the database medicine items as well as non-medicine items (e.g. needles, plasters, etc.) were observed in the database. For the purpose of this study only the medicine items as defined in Section 4.2 were analysed. The terms prevalence and frequency will be regarded as synonyms. Both refer to the number of times a certain value occurs in a set of data. It is assumed that all the data obtained from the database is correct. No direct or indirect manipulation of the base data was done by the researcher. The total costs used in this study include both the patient levy (if there was any levy to be paid by the patient) and the total

amount paid by the medical scheme on behalf of the patient. The indicators used in this study to describe and explain the results include prevalence, average cost, standard deviation, median, ratio, total cost and number of prescriptions.

Table 4-1: Indicators used in this study

	Prevalence	Average cost	Standard deviation	Median	Ratio	Total cost	Number of Rx
Age group	√	√	√	x	√	√	√
Gender	√	√	√	x	x	√	√
Generic indicator	√	√	√	x	x	√	x
Combination treatment	√	√	√	x	x	√	√
Compliance	√	√	√	x	x	√	√
Thresholds	x	√	√	√	√	√	x

Certain information and results are given in tables and figures in the appendices, and include the following:

- Appendix A provides a schematic outline of the steps in the data analysis.
- Appendix B is a summary of all the pharmacological groups in the MIMS.
- Appendix C, Table C1 to Table C11, summarises the prevalence and cost of the different antihypertensive pharmacological groups.
- Appendix D, Table D1, summarises the number of items according to each pharmacological group, and gives an indication of drug status (Generic, Innovator, or Original).
- Appendix E, Table E1, summarises the number of items according to each pharmacological group as utilised by the different age groups.
- Appendix F, Table F1 to Table F4, summarises the number of items according to pharmacological group but with special reference to treatment category, age group and generic indicator.
- Appendix G, Table G1, summarises the prescribing patterns of antihypertensive medicine items between the different genders.
- Appendix H, Table H1 to Table H4, summarises the number of items according to pharmacological group but with special reference to treatment category, gender and generic indicator.
- Appendix I, Table I1 to I15, summarises the top 10 antihypertensive combinations (single antihypertensive medicine item per prescription to eight antihypertensive medicine items per prescription) according to age group.
- Appendix J, Table J1 and J2, summarises the results of calculations made in order to determine cost thresholds for treatment category, gender, age group and generic indicator.

- Appendix K, Table K1 to K11, summarises the results of calculations made in order to determine a cost threshold for the different pharmacological groups within each province.

4.4 MEDICINE ITEMS ON THE DATABASE

4.4.1 Number of individual patients on the database

Figure 4-1 shows the number of patients on the total database. It can be seen that the patient population firstly increased from the first study year (2005) to the second year (2006) (1 903 110 to 1 964 381) and then decreased by approximately 20,8% (N = 1 555 900) to 2007, with a further decrease in 2008 to 1 290 017 patients (17,1%). However, according to the Council for Medical Schemes (CMS, 2006; CMS, 2007; CMS, 2008; CMS, 2009), there was an increase in the number of medical aid members or beneficiaries. This decrease in the total number of patients in the database can be due to a decrease in the number of medical schemes managed by the PBM or a change in the number of medical scheme patients. This aspect falls outside the scope of this research, however, as it may also imply a change in the commercial activity of the PMB.

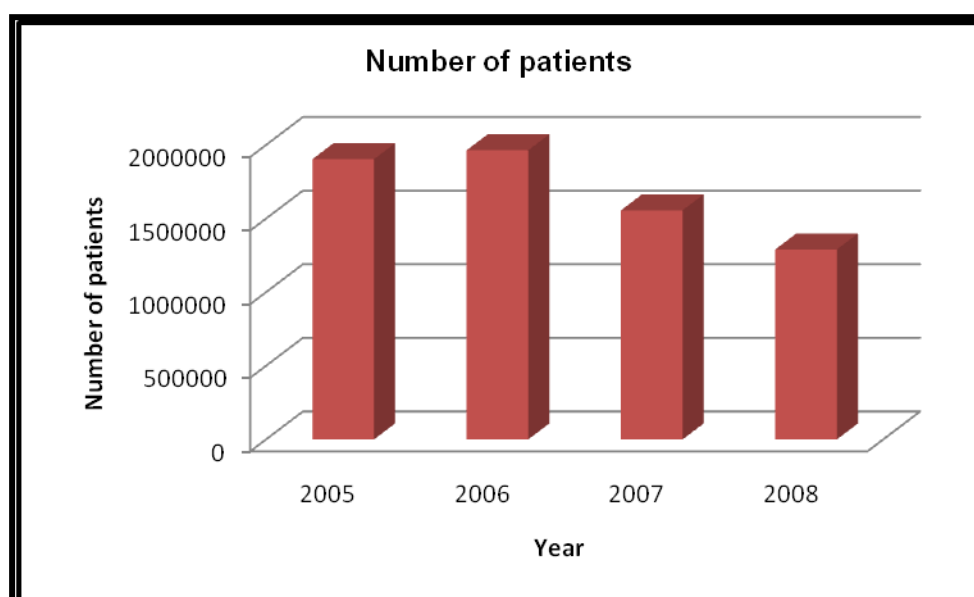


Figure 4-1: Total number of patients recorded on the database

4.4.2 An overview of the total medicine items recorded on the database

In this section the total number of medicine items recorded in the database will be discussed briefly. Table 4-2 summarises the prevalence and cost of medicine items in the database for the period 1 January 2005 to 31 December 2008.

Table 4-2: Prevalence and cost of the total medicine items on the database (2005 - 2008)

Description	Year	Frequency
Number of prescriptions (N)	2005	8 684 984
	2006	9 223 281
	2007	8 261 018
	2008	7 120 095
Average number of prescriptions per patient per year	2005	4,56 ± 6,01
	2006	4,70 ± 6,15
	2007	5,31 ± 6,60
	2008	5,52 ± 6,87
Total number of medicine items prescribed (N)	2005	19 500 774
	2006	21 113 422
	2007	19 075 724
	2008	16 439 253
Average number of medicine items per prescription	2005	2,25 ± 1,46
	2006	2,29 ± 1,50
	2007	2,31 ± 1,53
	2008	2,31 ± 1,56
Total cost of items in Rand value (R) (N)	2005	1 819 865 251,63
	2006	2 046 911 091,23
	2007	1 918 284 176,66
	2008	1 785 871 013,85
Average cost per item in Rand value (R)	2005	93,32 ± 166,36
	2006	92,82 ± 196,42
	2007	100,56 ± 324,11
	2008	108,63 ± 436,75
Median cost per item in Rand value (R)	2005	52,57
	2006	51,22
	2007	54,54
	2008	59,30
Average cost per prescription (R)	2005	209,54 ± 332,14
	2006	221,93 ± 611,58
	2007	232,21 ± 584,40
	2008	250,82 ± 765,55

A number of complex variables were observed. Any of the variables could either increase or decrease throughout the study period, independently of the trends seen with any other variable.

These variables included the number of patients, number of items and number of prescriptions, as well as the average and total costs. The following trends were seen:

- The number of patients **decreased** by approximately 32,2% ($N_{2005} = 1\,903\,110$, $N_{2008} = 1\,290\,017$) during the four-year study period (as seen in Figure 4.1).
- The average number of prescriptions per patient **increased** by approximately 21,1% ($N_{2005} = 4,56 \pm 6,01$; $N_{2008} = 5,52 \pm 6,87$)
- The total number of medicine items in the database has shown a **decrease** of almost 16% ($N_{2005} = 19\,500\,774$; $N_{2008} = 16\,439\,253$).
- There was a slight **decrease** in the total cost of all medicine items.
- There was an **increase** in the average cost per item per year, as well as in the average cost per prescription per year (as was seen in Table 4.2). Calculated d-values between averages indicated no practical significance, since d-values ranged between 0,01 and 0,03. Reasons for this increase could have been due to normal inflation, the application of SEP or differences in the SEP. However, this falls outside the scope of this study.

4.4.3 Prevalence of medicine items of the total database according to age and gender

In this section all aspects relating to the prescribing patterns and cost of prescriptions and medicine items in the total database are discussed briefly.

4.4.3.1 Aspects of medicine usage amongst different age groups

As was described in Chapter 3, all patients in the database were divided into three age categories, namely age groups 1, 2 and 3. AG1 included all patients younger than 18 years of age, while AG2 included patients between 18 and 45 years, and AG3 included all patients of 45 years and older.

Table 4-3 illustrates the total number of patients per age group as well as the number of medicine items dispensed to these patients.

Table 4-3: Summary of prescribing patterns according to age group

Year	Age group	Number of patients	Number of items	Number of Rx	Average cost per Rx (R)	Total cost (R)
2005	AG1	418 992	2 733 847	1 143 946	145,73 $\pm$ 163,77	166 706 489,03
	AG2	750 697	5 918 006	2 737 736	170,94 $\pm$ 285,38	467 990 269,82
	AG3	733 421	10 848 921	4 803 302	246,74 $\pm$ 378,75	1 185 168 492,78

Table 4-3 (Cont.): Summary of prescribing patterns according to age group

Year	Age group	Number of patients	Number of items	Number of Rx	Average cost per Rx (R)	Total cost (R)
2006	AG1	421 484	2 888 098	1 190 246	147,07 ± 182,04	175 052 127,19
	AG2	772 633	6 361 957	2 897 278	171,08 ± 305,13	495 655 123,83
	AG3	770 264	11 863 367	5 135 757	250,99 ± 449,45	1 289 031 483,07
2007	AG1	336 371	2 418 287	1 007 507	153,63 ± 257,90	154 785 430,82
	AG2	590 652	5 428 633	2 469 102	183,74 ± 440,21	453 672 211,90
	AG3	628 877	11 186 365	4 784 409	273,77 ± 686,61	1 309 826 533,94
2008	AG1	243 323	1 688 333	721 282	164,14 ± 252,11	118 392 695,73
	AG2	462 699	4 227 180	1 949 502	197,54 ± 580,04	385 100 704,63
	AG3	583 995	10 523 740	4 449 311	288,22 ± 881,07	1 282 377 613,49

Table 4-4 was compiled from table 4-3, illustrating certain ratios.

Table 4-4: Summary of cost ratios according to age group

Year	Age group	Cost per patient ratio (R)	Cost per item ratio (R)
2005	AG1	397,88	60,98
	AG2	623,41	79,08
	AG3	1 615,95	109,24
2006	AG1	415,32	60,61
	AG2	641,51	77,91
	AG3	1 673,49	108,66
2007	AG1	460,16	64,01
	AG2	768,09	83,57
	AG3	2 082,80	117,09
2008	AG1	486,57	70,12
	AG2	832,29	91,10
	AG3	2 195,87	121,86

From table 4-3 and table 4-4 the following can be concluded:

- During 2005 and 2006 AG2 recorded the highest percentage of patients, i.e. 39,4% (N = 1 903 110; n = 750 697) and 39,3% (N = 1 964 381; n = 772 633) respectively.
- During 2007 and 2008, AG3 recorded the highest percentage of patients i.e. 40,4% (N = 1 555 900; n = 628 877) and 45,3% (N = 1 290 017; n = 583 995) respectively. AG3 (i.e. patients older than 45 years) had the highest total cost, ranging between 62,9% and 71,8% of the total cost of all medicine items throughout all four study years.

- There was an increase in the cost per patient ratio through all four study years, as well as in the cost per item ratio.
- For AG3 the cost per patient ratio was approximately four times higher than for AG1.
- For AG3 the cost per item ratio was approximately 1,7 times higher than for AG1.

Even though AG2 presented with the highest number of patients during 2005 and 2006, AG3 had more prescriptions filled than any of the other age groups throughout all four study periods. Prescriptions for AG3 also recorded the highest average cost throughout the four study years, with the highest average cost in 2008 (R288,22 ± R881,07).

A summary of the average number of prescriptions per patient and number of items per prescription according to age group is presented in Table 4-5

Table 4-5: Summary of prescription possession according to age groups

Year	Age group	Average number of Rx per patient per year	Average number of items per Rx	Total number of Rx	Total number of items
2005	AG1	2,73 ± 2,84	2,39 ± 1,32	1 143 938	2 733 847
	AG2	3,65 ± 4,51	2,16 ± 1,30	2 737 718	5 918 006
	AG3	6,55 ± 7,86	2,26 ± 1,58	4 803 276	10 848 921
2006	AG1	2,82 ± 2,93	2,43 ± 1,34	1 190 240	2 888 098
	AG2	3,75 ± 4,66	2,20 ± 1,32	2 897 261	6 361 957
	AG3	6,67 ± 7,96	2,31 ± 1,62	5 135 729	11 863 367
2007	AG1	3,00 ± 3,10	2,41 ± 1,34	107 500	2 424 843
	AG2	4,18 ± 4,95	2,20 ± 1,33	2 469 083	5 440 128
	AG3	7,61 ± 8,39	2,34 ± 1,65	4 784 344	11 210 753
2008	AG1	2,96 ± 3,13	2,34 ± 1,33	721 273	1 688 333
	AG2	4,21 ± 5,04	2,17 ± 1,32	1 949 482	4 227 180
	AG3	7,62 ± 8,45	2,37 ± 1,68	4 449 280	10 523 740

From table 4-5 the following observations can be made:

- Patients in AG3 received on average the highest number of prescriptions per year for all four study years.
- Patients in AG3 also consumed the highest number of medicine items per year for all four study years – i.e. 55,6% (N = 19 500 774) in 2005, 56,2% (N = 21 113 422) during 2006, 58,8% (N = 19 075 724) during 2007 and 64,0% (N = 16 439 256) during 2008.

According to the literature, people of a higher age consume more medicine items than people from younger age groups and therefore would also account for the highest cost consumption (Anon, 2010a; Cohen, 2001; Daban *et al.* 2010:17; Roe *et al.* 2002:30).

4.4.3.2 Aspects of medicine usage between genders

More female than male patients have been recorded in the database. These findings are illustrated in Figure 4-2.

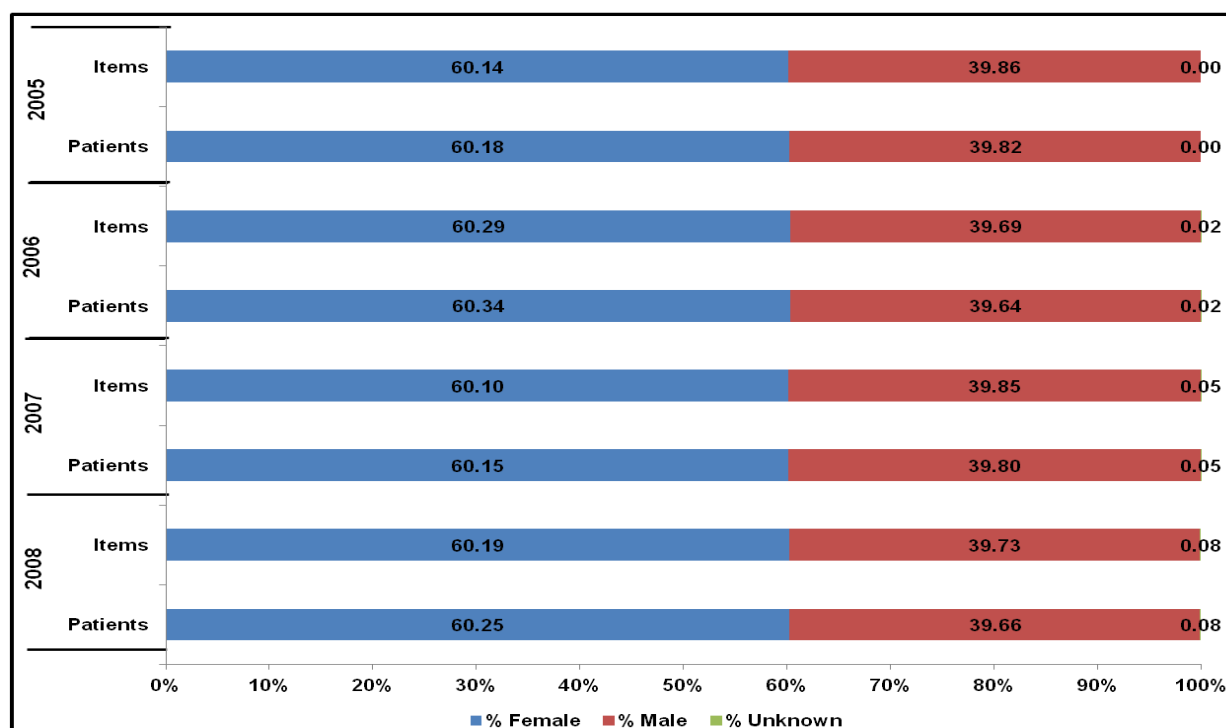


Figure 4-2: Total number of patients and items on the database according to gender (F = female, M = male, U = unknown)

From figure 4-2 it is therefore clear that female patients accounted for approximately 60,2% (N = 76 129 173; n = 45 853 171), whilst their male counterparts accounted for only 39,7% (N = 76 129 173; n = 30 245 410) in the total data base. Female patients also utilised more antihypertensive medicine items than their male counterparts.

4.5 FREQUENCY AND COST OF ANTIHYPERTENSIVE MEDICINE ITEMS

4.5.1 Introduction

In this section the second and third research questions will be answered, namely to determine the prevalence and medicine treatment cost of hypertension and to analyse the prescription

patterns of antihypertensive medicine items. Antihypertensive medicine is classified according to medicine items listed in the MIMS® under Section 7.3 as well as 16.1 (Diuretics) (Snyman, 2010).

4.5.2 Prevalence and cost of antihypertensive medicine items compared to the total database and cardiovascular medicine items

In this section the prevalence and cost of antihypertensive medicine items will be compared to those of all medicine items as well as cardiovascular medicine items. The number of antihypertensive medicine items is included in the total number of items in the database and total number of cardiovascular medicine items.

Table 4-6: Relationship of antihypertensive medicine items to total database and cardiovascular items. (MIMS group 7)

	Year	Prevalence (%)	Total costs in Rand (%)
Total medicine items on the database	2005	19 500 774	1 819 865 251,63
	2006	21 113 422	1 959 738 734,09
	2007	19 075 724	1 918 284 176,66
	2008	16 439 253	1 785 871 013,85
Total number of cardiovascular system medicine items	2005	2 635 003 (13,5)*	355 307 457,65 (19,5) [#]
	2006	2 915 092 (13,8)*	380 646 597,78 (19,4) [#]
	2007	2 766 553 (14,5)*	368 164 055,53 (19,2) [#]
	2008	2 669 759 (16,2)*	342 565 308,41 (19,2) [#]
Total number of antihypertensive medicine items	2005	1 938 496 (9,9)	212 638 495,37 (11,7) [#]
	2006	2 140 779 (10,1)	225 347 237,67 (11,5) [#]
	2007	2 022 771 (10,60)	221 851 892,34 (11,57) [#]
	2008	1 593 105 (12,0)*	207 364 638,58 (11,6) [#]
Total number of prescriptions	2005	8 684 984	1 819 865 25,63
	2006	9 223 281	1 959 738 734,09
	2007	8 261 018	1 918 284 176,66

Table 4-6 (cont.): Relationship of antihypertensive medicine items to total database and cardiovascular items (MIMS group 7)

	Year	Prevalence (%)	Total costs in Rand (%)
	2008	7 120 095	1 785 871 013,85
Number of antihypertensive prescriptions	2005	1 438 528 (16,6) ^{\$}	212 638 495,37 (11,7) [‡]
	2006	1 563 304 (17,0) ^{\$}	225 347 237,67 (11,5) [‡]
	2007	1 460 701 (17,7) ^{\$}	221 851 892,34 (11,6) [‡]
	2008	1 400 779 (19,7) ^{\$}	207 364 638,58 (11,6) [‡]

* N = Total medicine items on the database; # N = Cost of total medicine items; \$ N = Total number of prescriptions; ‡ N = Cost of total number of prescriptions

From Table 4-6 the following can be calculated:

- The antihypertensive medicine items accounted for between 7,7% and 9,7% of all medicine items in the database and for between 10,9% and 11,1% of the total cost (n = R201 114 842,60 (2005), R214 456 322,02 (2006), R212 994 957,25 (2007) and R198 215 798,24 (2008)) during the four study years.
- The cardiovascular system medicine items (MIMS[®] group 7) accounted for between 13,5% and 16,2% of the total medicine items in the database. The total cost for the cardiovascular system medicine items was R355 307 457,65 for the first study year, then it increased to R380 646 597,78 during 2006. During 2007 the total cost of the cardiovascular medicine items decreased to R368 164 055,53, with a further decrease to R342 565 308,41 during 2008.
- CPI values for cardiovascular medicine items were calculated at 1,4, 1,4, 1,3 and 1,2 for the four study years and for the antihypertensive medicine items the CPI values ranged between 0,6 and 0,7 during the four-year study period. These values indicate that cardiovascular medicine items and antihypertensive medicine items were relatively expensive.
- Antihypertensive medicine items constituted 7 695 151 (70,0% N = 10 986 407) of all the cardiovascular medicine items and 59,9% (n = R867 202 263,96; N = R1 446 683 419,37) of the total cost for all four study years collectively for these medicine items.

It was also calculated that between 16,6% and 19,7% of all the prescriptions contained antihypertensive medicine items, and the cost of these antihypertensive prescriptions accounted for between 11,5% and 11,7% of the total cost of all medicine items claimed during the four-year study period.

4.5.3 Prevalence and cost of antihypertensive medicine items

From Table 4-6 it was seen that the antihypertensive medicine items accounted for between 9,9% and 12,0% of the total number of items in the database. Respectively, these medicine items accounted for between 11,5% and 11,7% of the total cost of all medicine items over the four-year study period.

4.5.3.1 Prescribing patterns according to treatment categories

The antihypertensive medicine items were divided into three treatment categories, namely treatment category 1 (TC1), treatment category 2 (TC2) and treatment category 3 (TC3). TC1 represented antihypertensive items from MIMS[®] group 7.3 prescribed alone, TC2 represented antihypertensive items from MIMS[®] group 16.1 (diuretics) prescribed alone and TC3 represented antihypertensive items from both MIMS[®] groups 7.3 and 16.1 prescribed together. The data was analysed according to the number of patients, average cost per patient per year, number of medicine items and average cost per medicine item, as well as number of prescriptions (Rx) and average cost per prescription. Table 4-7 illustrates these findings.

Table 4-7: Summary of prescribing patterns according to treatment categories

Year	TC	Number of patients	Average cost per patient per year (R)	Number of items	Average cost per item (R)	Total cost (R)
2005	TC1	119 742	1 084,35 ± 1169,92	943 821	137,57 ± 69,09	129 842 061,21
	TC2	46 512	183,33 ± 407,55	200 940	42,44 ± 54,45	8 527 075,00
	TC3	53 024	1 400,67 ± 1493,03	793 735	93,57 ± 78,96	74 269 359,16
2006	TC1	126 583	1 086,29 ± 1149,33	1 057 096	130,08 ± 67,95	137 506 213,85
	TC2	44 528	181,90 ± 396,67	198 609	40,78 ± 53,08	8 099 831,79
	TC3	55 813	1 428,72 ± 1480,64	885 074	90,10 ± 76,32	79 741 192,03
2007	TC1	110 670	1 252,05 ± 1212,06	1 056 156	131,20 ± 67,12	138 564 839,86
	TC2	35 209	197,57 ± 437,75	163 494	42,55 ± 56,61	6 956 394,17
	TC3	47 353	1 611,95 ± 1593,35	803 121	95,04 ± 78,94	76 330 658,31
2008	TC1	104 379	1 229,39 ± 1195,89	1 019 442	125,88 ± 64,79	128 322 980,33
	TC2	31 535	199,12 ± 434,80	152 043	41,30 ± 56,91	6 279 192,65
	TC3	46 771	1 555,72 ± 1557,09	798 953	91,07 ± 76,36	72 762 465,60

From table 4-7 Table 4-8 was compiled to give an indication of the ratio of items per patient during each of the study years

Table 4-8: Items per patient ratio

Year	Treatment category	Items per patient ratio
2005	TC1	7,9
	TC2	4,3
	TC3	15,0
2006	TC1	8,4
	TC2	4,5
	TC3	15,9
2007	TC1	9,5
	TC2	4,6
	TC3	17,0
2008	TC1	9,8
	TC2	4,8
	TC3	17,1

Table 4-7 and Table 4-8 revealed that:

- Throughout all four study years TC1 treated the highest number of patients and even though they consumed the highest number of items, patients from TC3 had a higher items per patient per year ratio than TC1 and TC2. This was possibly due to the fact that TC3 consisted of patients receiving medicine items from both MIMS group 7.3 and 16.1.
- TC2 treated the lowest number of patients during all four study years, and they consumed the lowest number of items. As was stated previously, TC2 was antihypertensive medicine items from MIMS group 16.1, the diuretics. According to the literature (Section 2.10.8.2), diuretics are recommended as first-line therapy, but the 2011 South African Hypertension Guideline indicates that uncomplicated essential hypertension should be treated with a diuretic, ACE inhibitor or calcium channel blocker as monotherapy (Seedat & Rayner, 2012:67). From Table 4–7 it can therefore be seen that more patients receive antihypertensive medicine items as monotherapy from TC1 than from TC2.
- On average, antihypertensive medicine items from TC1 (MIMS[®] group 7.3) had the highest average cost. Antihypertensive medicine items from TC2 (MIMS[®] group 16.1) had the lowest average cost, whilst the average cost per item was also lower than medicine items from TC1, i.e. medicine items from MIMS[®] category 7.3. In a study done by Greene *et al.* (2007:131), where the underutilisation of diuretic therapy was investigated, they found that only 20,3% of the patients in their study population received a diuretic as monotherapy and these diuretics accounted for only 0,8% of the total monthly cost of antihypertensive medicine items, compared to ACE inhibitors (20,3% of the cost), calcium channel blockers (58,8% of the cost), beta-receptor blockers (5,1% of the cost) and other items (15,0% of the cost). ACE inhibitors, calcium channel blockers and beta-receptor blockers all fall in TC1.

Fretheim *et al.* (2003:18) also stated that diuretics are by far the lowest-priced antihypertensive medicine items. From this study and from the literature it can therefore be seen that diuretics are relatively less expensive than other antihypertensive medicine items.

- d-values calculated for the difference in average cost between items in TC1 and TC2, indicated that it was of practical significance (d-values ranging from 1,31 to 1,37). This is also true when comparing items in TC1 and TC3 (d-values ranging from 0,46 to 0,56) and TC2 and TC3 (d-values ranging from 0,65 to 0,66).

4.5.3.2 Prescribing patterns of antihypertensive medicine items according to generic indicator

A perspective that needs to be kept in mind is the issue of generic prescribing. According to the WHO (2011), a generic drug is a pharmaceutical product or medicine item that is manufactured without a licence from the innovator company and marketed after the patent right of the specific drug has expired. These generic medicine items are supposed to be just as effective as the originator product, but are usually less expensive. All items sold in South Africa need to be registered by the Medicines Control Council (MCC), ensuring that generic medicine items adhere to the same safety, quality and effectiveness standards as the original product (Anon, 2010b). Table 4–9 summarises the number of generic and innovator antihypertensive medicine items, as well as the number of items with no generic equivalent available. The prevalence percentage and cost percentage were also calculated, as were the CPI and d-values. For the purpose of this study the innovator products are represented by an 'O', the generic equivalent of the innovator is represented with a 'Y' and the products without generic equivalents are indicated with an 'N'. In this section the fourth research question, namely to conduct certain pharmacoeconomic studies on the data in order to make some suggestions on the usage and cost of antihypertensive treatment, will be answered.

Table 4-9: Prescribing patterns according to generic indicator

Year	Generic indicator	Number of items	Average cost per item(R)	Total cost (R)	Prevalence %	Cost %	CPI	d-values
2005	N	674 056	173,21 ± 67,77	116 750562,24	34,8	57,8	1,7	-
	O	289 133	138,97 ± 61,78	40 180 154,76	14,9	26,1	1,8	0,61
	Y	975 307	57,12 ± 45,69	55 707 778,37	50,3	16,1	0,3	

Table 4-9(Cont.): Prescribing patterns according to generic indicator

Year	Generic indicator	Number of items	Average cost per item(R)	Total cost (R)	Prevalence %	Cost %	CPI	d-values
2006	N	548 682	171,89 ± 3,73	94 314 959,05	25,6	46,3	1,8	-
	O	344 248	146,98 ± 1,03	50 598 560,58	16,1	29,05	1,8	0,57
	Y	1 247 849	64,46 ± 48,18	80 433 718,04	58,3	24,66	0,4	
2007	N	470 028	177,88 ± 7,34	83 607 956,41	23,2	41,72	1,8	-
	O	301 523	148,39 ± 4,54	44 743 289,80	14,9	30,54	2,1	0,67
	Y	1 251 220	74,73 ± 52,51	93 500 646,13	61,9	27,75	0,5	
2008	N	408 449	171,95 ± 81,38	70 234 226,61	20,7	36,57	1,8	-
	O	230 565	146,02 ± 66,92	33 666 702,03	11,7	25,76	2,2	0,75
	Y	1 331 424	77,71 ± 52,70	103 463709,94	67,6	37,66	0,6	

From table 4–9 the following conclusions can be drawn:

- During all four study years the generic medicine items (indicated with a 'Y') accounted for more than 50% of all the antihypertensive medicine items (i.e. 50,3% in 2005, 58,3% in 2006, 61,9% in 2007 and 67,6% in 2008). However, the total cost of these generic items was less than 50% (between 26,2% and 49,9%) during the four study years.
- For 2005 and 2006 the antihypertensive medicine items with no generic substitute available accounted for 54,9% and 41,9% respectively.
- The number of generic medicine items utilised by antihypertensive patients increased from 50,3% in 2005 to 67,6% in 2008, an increase of 17,3% over the four-year period. This was in line with trends seen from PBM, where an increase in generic usage of 43,7% during 2005 to 47,4% in 2008 was reported (Bester & Hammann, 2008:6; Bester & Badenhorst, 2009:12).
- The number of innovator products decreased by approximately 3,2% from 2005 to 2008, while the number of items without generic equivalents decreased by 14,0% during the four-year study period. This increase in generic utilisation can be attributed to several factors, including the introduction of several generic medicine items to the ARB class (7.3.9) of

antihypertensive medicine during the course of 2006 and more awareness of generic medicine by the patients, and mandatory generic substitution enforced by medical schemes may have influenced the results.

- The generic medicine items had on average a lower cost than the innovator antihypertensive medicine items. This was also reflected in the d-values calculated for comparison between the innovator and generic equivalents. The d-values, which range between 0,57 and 0,75, indicate that the difference in the average cost is of medium to high effect and may be significant.
- The generic medicine items can also be classified as relatively inexpensive according to the CPI, which was less than 1.
- Those antihypertensive medicine items without generic equivalents available can be seen as relatively expensive according to the CPI, which was more than 1, ranging between 1,7 and 1,8.

Table 4-10 summarises the number of items prescribed for the different treatment categories but with an indication of how many items per category were for a generic product (Y) or the original product (O), and for how many items no generic equivalent (N) was available. For the scenario where no generic equivalent was available, the originator was still patented. Note that some of the results discussed in this section also refer to Appendix D.

Table 4-10: Generic indicator and treatment category

Year	TC	Generic indicator	Number of items	Prevalence percentage	Average cost (R)	Total cost (R)	Cost percentage
2005	TC1	N	422 442	44,8 (N = 943 821)	185,36 ± 53,08	78 304 471,66	60,3 (N = 129 842 061,21)
	TC1	O	172 930	18,3 (N = 943 821)	138,10 ± 58,23	23 881 692,92	18,4 (N = 129 842 061,21)
	TC1	Y	348 449	43,9 (N = 943 821)	79,37 ± 40,90	27 655 896,63	21,3 (N = 129 842 061,21)
	TC2	N	40 163	19,9 (N = 200 940)	92,85 ± 69,70	3 729 043,88	43,7 (N = 8 527 075,00)
	TC2	O	12 283	6,1 (N = 200 940)	123,12 ± 71,57	1 512 223,06	17,7 (N = 8 527 075,00)
	TC2	Y	148 494	73,9 (N = 200 940)	22,13 ± 25,23	3 285 808,06	38,5 (N = 8 527 075,00)
	TC3	N	211 451	26,6 (N = 793 735)	164,18 ± 80,54	34 717 046,70	46,7 (N = 74 269 359,16)
	TC3	O	103 920	13,1 (N = 793 735)	142,28 ± 65,79	14 786 238,78	19,9 (N = 74 269 359,16)
	TC3	Y	478 364	60,3 (N = 793 735)	51,77 ± 45,50	24 766 073,68	33,3 (N = 74 269 359,16)
	Total		1 938 496		109,69 ± 8,34	212 638 495,37	
2006	TC1	N	329 516	31,2 (N = 1057 096)	186,32 ± 8,44	61 394 133,99	44,6 (N = 137 506 213,85)
	TC1	O	217 838	20,6 (N = 1057 096)	148,12 ± 8,16	32 266 271,63	23,5 (N = 137 506 213,85)
	TC1	Y	509 742	48,2 (N = 1057 096)	86,02 ± 42,38	43 845 808,23	31,9 (N = 137 506 213,85)

Table 4–10 (cont.): Generic indicator and treatment category

Year	TC	indicator	of items	percentage	(R)	Total cost (R)	Cost percentage
	TC2	N	36 224	18,2 (N = 198 609)	88,40 ± 67,95	3 202 120,06	39,5 (N = 8 099 831,79)
	TC2	O	12 296	6,2 (N = 198 609)	123,93 ± 71,80	1 523 838,65	18,8 (N = 8 099 831,79)
	TC2	Y	150 089	75,6 (N = 198 609)	22,48 ± 27,25	3 373 873,08	41,7 (N = 8 099 831,79)
	TC3	N	182 942	20,7 (N = 885 074)	162,45 ± 6,00	29 718 705,00	37,3 (N = 79 741 192,03)
	TC3	O	114 114	12,9 (N = 885 074)	147,30 ± 4,54	16 808 450,30	21,1 (N = 79 741 192,03)
	TC3	Y	588 018	66,4 (N = 885 074)	56,48 ± 47,58	33 214 036,73	41,7 (N = 79 741 192,03)
	Total		2 140 779		105,26 ± 5,72	225 347 237,67	
2007	TC1	N	297 386	28,2 (N = 1056 156)	187,21 ± 3,76	55 674 815,81	40,2 (N = 138 564 839,86)
	TC1	O	178 100	16,9 (N = 1056 156)	150,15 ± 1,81	26 740 994,43	19,3 (N = 138 564 839,86)
	TC1	Y	580 670	55,0 (N = 1056 156)	96,70 ± 45,08	56 149 029,62	40,5 (N = 138 564 839,86)
	TC2	N	25 351	15,5 (N = 163 494)	89,44 ± 71,43	2 267 284,25	32,6 (N = 6 956 394,17)
	TC2	O	14 482	8,9 (N = 163 494)	125,08 ± 73,63	1 811 411,85	26,0 (N = 6 956 394,17)
	TC2	Y	123 661	75,6 (N = 163 494)	23,27 ± 30,58	2 877 698,07	41,4 (N = 6 956 394,17)
	TC3	N	147 291	18,3 (N = 803 121)	174,25 ± 92,01	25 665 856,35	33,6 (N = 76 330 658,31)
	TC3	O	108 941	13,6 (N = 803 121)	148,62 ± 66,98	16 190 883,52	21,2 (N = 76 330 658,31)
	TC3	Y	546 889	68,1 (N = 803 121)	63,04 ± 51,89	34 473 918,44	45,2 (N = 76 330 658,31)
	Total		2 022 771		109,68 ± 76,00	221 851 892,34	
2008	TC1	N	257 603	63,1 (N = 1019 442)	180,04 ± 67,43	46 380 044,89	36,1 (N = 128 322 980,33)
	TC1	O	132 042	32,3 (N = 1019 442)	146,71 ± 64,34	19 372 460,04	15,1 (N = 128 322 980,33)
	TC1	Y	629 797	61,8 (N = 1019 442)	99,35 ± 45,52	62 570 475,40	48,8 (N = 128 322 980,33)
	TC2	N	21 267	14,0 (N = 152 043)	90,64 ± 87,52	1 927 604,02	30,7 (N = 6 279 192,65)
	TC2	O	10 981	7,2 (N = 152 043)	123,23 ± 74,48	1 353 135,24	21,5 (N = 6 279 192,65)
	TC2	Y	119 795	78,8 (N = 152 043)	25,03 ± 30,51	2 998 453,39	47,8 (N = 6 279 192,65)
	TC3	N	129 579	16,2 (N = 798 953)	169,21 ± 96,72	21 926 577,70	30,1 (N = 72 762 465,60)
	TC3	O	87 542	11,0 (N = 798 953)	147,83 ± 69,19	12 941 106,75	17,8 (N = 72 762 465,60)
	TC3	Y	581 832	72,8 (N = 798 953)	65,13 ± 73,50	37 894 781,15	52,1 (N = 72 762 465,60)
	Total		1 970 438		105,24 ± 73,50	20 7364 638,58	

The following observations were made from Table 4–10:

- It was also noted from Table 4–10 that for 2005, 2006 and 2007, for each treatment category the generic items constituted the highest percentage, ranging between 43,9% and 55,0% for TC1, 73,9% and 75,6% for TC2 and for TC3 the generic items constituted between 60,3% and 68,1%. For 2008, the generic items also contributed the most for TC2

and TC3 with 78,8% and 72,8% respectively, but for TC1 the items with no generic available (indicated with an 'N') were slightly higher than the generic items, with 63,1% vs. 61,8% (generics).

- It can also be seen that for TC1 the medicine items with no generic equivalent available constituted the highest percentage of the total cost during 2005 and 2006 with 60,3% and 44,6% respectively. During 2007 and 2008 the total cost of the generic medicine items prescribed in TC1 constituted the highest percentage of the total cost with 40,5% (2007) and 48,8% (2008).
- For TC2 it was seen that through all four study years the generic medicine items contributed the highest number of items and made the highest contribution to the total cost for this treatment category. The medicine items prescribed in TC2 include medicine items from MIMS® group 16.1 (the diuretics). As is presented in Appendix D, the generic items constituted the highest number of medicine items for medicine in group 16.1 (2005:74,6%; N = 524 938, 2006: 76,2%; N = 553 771; 2007: 76,0%; N = 476 984 and 2008: 78,8%; N = 460 150). With a CPI of approximately 0,5 over the four-year study period it is therefore clear that the generic diuretics are relatively inexpensive. The originator items ('O') had CPI values greater than 1 (for 2005 CPI = 2,9, for 2006 CPI = 3,0, for 2007 CPI = 2,9 and for 2008 CPI = 3,0), indicating that these items are more expensive than the generic items.
- For TC3 (the scenario where patients received medicine items from pharmacological group 7.3 in combination with 16.1), yet again generic medicine items constituted the highest percentage of items through all four study years (60,3% in 2005; 66,4% in 2006; 68,1% in 2007 and 72,8% in 2008).
- If the cost of medicine items in TC3 is considered, it can be seen that even though the cost of the generic items (generic indicator 'Y') constituted the highest percentage for all four years, these generic items for TC3 are relatively inexpensive since the CPI of these items is less than 1 (for 2005 CPI = 0,6, for 2006 CPI = 0,6, for 2007 CPI = 0,7 and for 2008 CPI = 0,7). The originator products ('O') had CPI values greater than 1 (for 2005 CPI = 1,5, for 2006 CPI = 1,6, for 2007 CPI = 1,6 and for 2008 CPI = 1,6), indicating that these items are more expensive than the generic items.

In table 4-11 a summary is given of the number of prescriptions per treatment category, the average cost of these prescriptions, the average number of prescriptions per patient per year and the total cost of these prescriptions.

Table 4-11: Prescribing patterns according to treatment category

Year	TC	Number of prescriptions	Average cost per prescription (R)	Average number of Rx per patient per year	Total cost (R)
2005	TC1	794 791	163,37 ± 101,53	6.64 ± 4,93	129 842 061,21
	TC2	191 786	44,46 ± 62,26	4.12 ± 4,12	8 527 075,00
	TC3	451 951	164,33 ± 132,09	8.52 ± 5,44	74 269 359,16
2006	TC1	877 523	156,70 ± 100,02	6.93 ± 4,89	137 506 213,85
	TC2	188 572	42,95 ± 61,34	4.23 ± 4,16	8 099 831,79
	TC3	497 209	160,38 ± 130,55	8.91 ± 5,31	79 741 192,03
2007	TC1	859 214	161,27 ± 102,40	7.76 ± 4,79	138 564 839,86
	TC2	154 176	45,12 ± 66,28	4.38 ± 4,26	6 956 394,17
	TC3	447 311	170,64 ± 137,45	9.45 ± 5,36	76 330 658,31
2008	TC1	817 865	156,90 ± 100,94	7.84 ± 4,78	128 322 980,33
	TC2	143 407	43,79 ± 66,82	4.55 ± 4,29	6 279 192,65
	TC3	439 507	165,55 ± 136,31	9.40 ± 5,28	72 762 465,60

Table 4–11 clearly indicates the following:

- Prescriptions containing only medicine items from category 2, i.e. diuretics, had the lowest average cost per item.
- The total number of prescriptions was the highest for TC1 (MIMS® group 7.3) throughout all four study years. These prescriptions also accounted for the highest cost throughout the study period and accounted for between 61,0% and 62,5% of the total cost.
- If d-values were calculated for the difference in average cost between prescriptions in TC1 and TC2, it is clear that it is of practical significance (d-values ranging from 1,17 to 1,13). This is also true when comparing prescriptions in TC2 and TC3 (d-values ranging from 0,89 to 0,91). However, when d-values are calculated for the difference in average cost between prescriptions in TC1 and TC3, it can be seen that these differences are of no statistical significance, since the values range between 0,01 and 0,07.

4.5.3.3 Prescribing patterns of antihypertensive medicine items according to pharmacological group

In this section the prevalence and cost of the different pharmacological groups will be discussed. Some of the results discussed here refer to Appendix C. As was stated in section 4.3. Appendix C summarises the prevalence and cost of the different active ingredients as observed within the pharmacological groups.

Table 4-12 describes the cost and prevalence of the different pharmacological groups of antihypertensive medicine items.

Table 4-12: Prescribing patterns of the antihypertensive pharmacological groups

Pharmacological group	Number of items (N)	Total cost (R)	Prevalence percentage*	Cost percentage**	CPI ***
2005					
Central-acting inhibitors	23 243	2 359 388,85	1,2	1,1	0,9
Alpha-receptor blockers	38 570	6 744 878,32	2,0	3,2	1,6
Beta-receptor blockers	234 538	22 963 725,13	12,1	10,8	0,9
Alpha- and Beta-receptor blockers	56 196	6 638 650,96	2,9	3,2	1,1
Sympathetic nervous blockers	18 195	22 963 725,13	1,0	0,8	0,8
Direct-acting vasodilators	2 339	209 031,26	0,1	0,1	0,8
Calcium channel blockers	131 856	20 892 719,11	6,8	9,8	1,4
ACE inhibitors	649 438	74 212 058,65	33,6	34,9	1,0
Angiotensin-receptor antagonists	255 199	53 386 468,70	13,3	25,2	1,9
Other	3 984	640 004,85	0,2	0,3	1,5
Diuretics	524 938	22 911 036,32	26,8	10,7	0,4
Total	1 938 496	233 921 657,28	100	100	-
2006					
Central-acting inhibitors	25 299	2 673 336,45	1,1	1,1	1,0
Alpha-receptor blockers	44 146	7 611 784,68	2,0	3,2	1,6
Beta-receptor blockers	272 573	24 598 115,30	12,3	10,5	0,9
Alpha- and Beta-receptor blockers	71 311	7 813 341,15	3,2	3,3	1,0
Sympathetic nervous blockers	16 802	1 442 512,24	0,8	0,6	0,8
Direct-acting vasodilators	2 855	251 653,99	0,1	0,1	0,8
Calcium channel blockers	139 623	22 091 143,58	6,3	9,4	1,5
ACE inhibitors	779 328	83 381 944,02	35,1	35,5	1,0
Angiotensin-receptor antagonists	285 653	59 796 391,39	12,9	25,4	2,0
Other	5 820	1 053 063,65	0,3	0,5	1,7

Table 4.12 (cont.): Prescribing patterns of the antihypertensive pharmacological groups

Pharmacological group	Number of items (N)	Total cost (R)	Prevalence percentage*	Cost percentage**	CPI ***
Diuretics	578 456	24 456 927.99	26,0	10,4	0,4
Total	2 221 866	235 170 214.44	100	100	-
2007					
Central-acting inhibitors	20 883	2 495 919.17	0,98	1,06	1,09
Alpha-receptor blockers	40 324	7 319 281.91	1,90	3,11	1,65
Beta-receptor blockers	265 075	23 812 089.10	12,41	10,13	0,82
Alpha- and Beta-receptor blockers	74 779	8 230 197.90	3,50	3,50	1,00
Sympathetic nervous blockers	9 246	105 9178.40	0,43	0,45	1,04
Direct-acting vasodilators	2 489	227 985.30	0,12	0,10	0,83
Calcium channel blockers	199 589	28 571 538.70	9,34	12,16	1,30
ACE inhibitors	730 521	81 693 170.61	34,20	34,75	1,02
Angiotensin-receptor antagonists	286 367	57 690 757.08	13,41	24,54	1,83
Other	9 147	1 894 839.08	0,43	0,81	1,88
Diuretics	497 813	22 064 459.37	23,30	9,39	0,40
Total	2 136 233	235 059 416.62	100	100	-
2008					
Central-acting inhibitors	20 083	2 495 959.87	0,98	1,11	1,14
Alpha-receptor blockers	37 657	6 813 279.70	1,83	3,03	1,66
Beta-receptor blockers	244 192	22 068 382.39	11,86	9,81	0,83
Alpha- and Beta-receptor blockers	75 939	8 323 731.36	3,69	3,70	1,00
Sympathetic nervous blockers	8 627	881 045.99	0,42	0,39	0,93
Direct-acting vasodilators	2 157	171 157.72	0,10	0,08	0,73
Calcium channel blockers	208 638	27 394 634.50	10,13	12,17	1,20
ACE inhibitors	705 225	77 638 969.69	34,24	34,50	1,01
Angiotensin-receptor antagonists	271 162	56 738 422.31	13,17	25,21	1,91
Other	8 769	1 879 001.82	0,43	0,83	1,96
Diuretics	477 256	20 649 271.78	23,17	9,18	0,40
Total	2 059 705	225 053 857.10	100	100	-

* % Prevalence was determined by dividing N with the total (prevalence) per period and then multiply it by 100 (e.g. $(25\,481/1\,728\,446) \times 100$)

** Cost % was determined by dividing R-value with the total cost in Rand per period and then multiplies it with 100 (e.g. $(2\,530\,431.32/208\,829\,630.90) \times 100$)

*** CPI = Cost prevalence index. CPI is determined dividing the cost % by the % prevalence per period (see Chapter 3).

From table 4-12 the following can be seen:

- Angiotensin-converting enzyme (ACE) inhibitors (pharmacological group 7.3.8) were the most frequently prescribed antihypertensive medicine items over all four study years.
- ACE inhibitors also constituted the highest percentage of the cost of antihypertensive medicine items over the four study years.
- The direct-acting vasodilators (pharmacological group 7.3.6) and the pharmacological group labelled 'Others' (7.3.10) were the least prescribed.
- It can also be noted that over the four-year study period there was no explicit increase or decrease in the prevalence of any of the pharmacological groups of antihypertensive medicine items.
- For all four study years the pharmacological groups 7.3.2 (alpha-receptor blockers), 7.3.4 (Alpha- and beta-receptor blockers), 7.3.7 (Calcium channel blockers), 7.3.8 (ACE inhibitors), 7.3.9 (Angiotensin receptor antagonists) and 7.3.10 (Others) were relatively expensive when the cost percentage is compared to the prevalence percentage, since the CPI of these six classes was greater than 1. The diuretics (16.1) were the least costly, since the CPI of these products was 0,40 for all four study years.

From table 4-12 cost ratios for the different pharmacological groups were calculated. These cost ratios are summarised in Table 4-13

Table 4-13: Cost ratios for the different pharmacological groups

Pharmacological group	2005 (R)	2006 (R)	2007 (R)	2008 (R)
Central-acting inhibitors	101,51	105,67	119,52	124,28
Alpha-receptor blockers	174,87	172,42	181,51	180,93
Beta-receptor blockers	97,91	90,24	89,83	90,37
Alpha- and Beta-receptor blockers	118,13	109,57	110,06	109,61
Sympathetic nervous blockers	85,85	85,85	114,56	102,13
Direct-acting vasodilators	89,37	88,15	90,60	79,35
Calcium channel blockers	158,45	158,22	143,15	131,30
ACE inhibitors	114,27	106,99	111,83	110,09
Angiotensin-receptor antagonists	209,20	209,33	201,46	209,24
Other	160,64	180,94	207,15	214,28
Diuretics	43,65	42,88	44,32	43,27

Table 4-13 revealed that:

- The angiotensin-receptor antagonists had the highest cost ratio throughout all four study years, whilst the diuretics had the lowest cost ratio throughout the total study period.
- The cost ratio of the central acting inhibitors showed an increase of approximately 22% and the pharmacological group others showed an increase of approximately 33% over the four-year study period. This can be due to the application of SEP and normal inflation. Although this falls outside the scope of this study, it needs to be further investigated.
- The cost ratio of calcium channel blockers decreased by approximately 17% during the four-year study period, while the cost ratios of beta-receptor blockers and alpha- and beta-receptor blockers decreased by 7,7% and 7,2% respectively.
- Angiotensin-receptor blockers and diuretics showed no real change in the cost ratios.

In Appendix C a summary is given of the frequency, average cost and total cost of the different active ingredients within each pharmacological group.

From Appendix C, Table C2, it can be seen that in the pharmacological group 7.3.2 (the alpha-receptor blockers) products containing the active ingredient doxazosin accounted for between 62,5% and 65,6% of the total number of items and for between 54,8% and 57,7% of the cost of the alpha-receptor blockers. The calculation of d-values (using the average cost for all antihypertensive medicine items per year) for products that fall under category 7.3.2 revealed that alfuzosin and terazosin had d-values greater than 1, indicating that these values were

practically significant. These products also have a CPI of greater than 1, indicating that they were relatively expensive.

In Table C4 it was calculated that antihypertensive medicine items containing the active ingredient carvedilol accounted for approximately 99,8% of all the alpha- and beta-receptor blocking agents as well as the cost within the group. The CPI, however, indicated that there was equilibrium between the cost and prevalence of this antihypertensive medicine product. Labetalol, on the other hand, had a relatively high CPI ranging from 2,2 to 3,6, indicating that labetalol is relative expensive.

A study of the calcium channel blockers (Table C7) revealed that although amlodipine had the highest frequency and cost percentage, the CPI ranged between 0,8 and 0,9, indicating that they were relatively inexpensive.

Nisoldipine was the calcium channel blocker with the highest relative cost compared to the frequency, with a CPI value ranging from 1,9 to 2,2. The d-value of 2,4 to 2,5 was also an indication that there were statistically significant differences between the two average costs. It is interesting to note that there were only seven observations for nisoldipine during 2005, and that no observations of nisoldipine were made for the remaining three study years.

As was previously stated, it was seen from Table 4–12 that the ACE inhibitors (group 3.7.8 in the MIMS®) had the highest cost and prevalence. Table C8 in Appendix C summarises the cost, usage, CPI and d values of the active ingredients of all the ACE inhibitors. From Table C8 it can be seen that enalapril and perindopril were the active ingredients with the highest frequency as well as the highest cost. Since the CPI of enalapril was only approximately 0,5 throughout the study period, it is an indication that these products are relatively inexpensive. Perindopril on the other hand, had a CPI of approximately 1,2, indicating that these items are relative expensive.

An investigation of the generic prescribing and utilising of these medicine items indicated that for all the pharmacological groups, throughout all four study years, the generic items had the lowest average cost when compared to innovator products and medicine items with no generic equivalent available. These findings can be seen in Appendix D, Table D1. From Table D1 it is clear that for the 'older' antihypertensive medications, for example the diuretics, between 74,58% and 78,82% of the items prescribed were generic medicine items. The CPI of between 0,5 and 0,6 is also an indication that these medicine items were relatively less expensive. It was also observed that the 'newer' antihypertensive medicine, for example the angiotensin-receptor blockers, showed an increase in the number of generic items prescribed during the

four-year study period. This may have been due to the expiry of the patents of some of the ARBs. In 2005 there were no generic ARB items claimed, but this changed during 2006 with the availability of the generic valsartan and the first generic losartan in 2007 (Bester & Badenhorst, 2009:15).

Table D1 reveals that there was an increase in the usage of available generic equivalent medicine items for all the pharmacological groups over the four-year study period. The biggest movers were the calcium channel blockers with a 39,64% increase in generic utilisation, the ACE inhibitors with a 24,46% increase in generic utilisation and the alpha- and beta-receptor blockers with a 21,3% increase in generic utilisation since 2005 through to 2008. While there was an increase in the utilisation of these generic items, there was a simultaneous decrease in the utilisation of the innovator products of these pharmacological groups. This was most probably due to more generics that became available.

If the innovator antihypertensive medicine items had been substituted with their generic equivalents, there could have been substantial cost savings. To determine these possible cost savings, two scenarios were sketched. The first scenario involved a 100% substitution, meaning that all innovator items were substituted with a generic product containing the same active ingredient. These potential cost savings were calculated by multiplying the difference in the average cost of the innovator and generic items with the number of innovator medicine items. In cases where the innovator was less expensive than the generic equivalent available, or where no generic equivalent was available, the item was excluded from the study.

According to Bester and Badenhorst (2009:12), only approximately 45% of innovator products were being substituted for the less expensive generic product, therefore scenario 2 entailed the generic substitution of only 45% of the innovator items. These possible cost savings were summarised in Appendix D, Table D2, and it was seen that for all four study years the biggest cost savings could have been possible if the innovator ACE inhibitors and diuretics had been substituted with their generic equivalents.

Total generic substitution of the innovator ACE inhibitors would have led to the following possible cost savings:

- R7 362 197,44 (42%, N = R17 350 942,20) in 2005,
- R8 433 372,00 (45%, N = R18 947 403,68) in 2006,
- R4 748 813,32 (28%, N = R15 573 800,80) in 2007 and
- R3 058 369,84 (23%, N = R13 284 449,55) in 2008.

Total generic substitution for the diuretics could have led to the following possible cost savings:

- R3 685 119,36 (21%, N = R17 350 942,20) in 2005,
- R4 075 199,20 (21%, N = R18 947 403,68) in 2006,
- R5 810 968,67 (34%, N = R15 573 800,80) in 2007 and
- R4 731 947,66 (36%, N = R13 284 449,55) in 2008.

The highest estimated cost saving due to generic substitution could have been for 2006, approximately R18 947 403,68. A total overall cost saving of R65 156 596,23 through all four study years could have been achieved if all the innovator items had been substituted with their generic equivalent.

If scenario two had been followed, namely only substituting 45% of the innovator items, there would have been a smaller margin of cost savings. These savings would have amounted to approximately R29 955 389,30 over the four-year study period.

The generic substitution for the different active ingredients was also studied and cost savings were calculated if the innovator items had been substituted with the generic equivalents. Table 4-14 summarises the potential cost savings if innovator products is substituted with the generic equivalents.

Table 4-14: Summary of estimated cost savings due to generic substitution (2005)

Pharmacological group	Active ingredient	Generic indicator	Number of items	Average cost per item (R)	Difference in average cost (R)	Estimated cost saving @ 100% (R)	Estimated cost saving @ 45% (R)
Central-acting inhibitors	Methyldopa	O	712	180,89 ± 102,23	114,97	81 859,96	36 836,98
	Methyldopa	Y	17 180	65,92 ± 47,11			
Alpha-receptor blockers	Doxazosin	O	4 365	191,70 ± 41,09	111,81	488 037,82	219 617,02
	Doxazosin	Y	7 887	79,89 ± 44,11			
	Prazosin	O	44	171,67 ± 118,44	79,43	3 494,81	1 572,67
	Prazosin	Y	5 885	92,24 ± 68,34			
Beta-receptor blockers	Acebutolol	O	1 846	229,93 ± 50,40	64,23	118 570,24	53 356,61
	Acebutolol	Y	35	165,70 ± 22,68			
	Atenolol/Chlortalidone	O	2 992	198,93 ± 49,71	129,56	387 636,07	174 436,23
	Atenolol/Chlortalidone	Y	44 783	69,37 ± 21,37			
	Bisoprolol	O	46 389	81,04 ± 30,20	23,46	1 088 445,78	489 800,60
	Bisoprolol	Y	20 144	57,57 ± 19,88			
	Sotalol	O	3 467	185,97 ± 79,81	101,85	353 114,39	158 901,47
	Sotalol	Y	8 607	84,12 ± 32,87			
	Timolol/Amiloride	O	1 264	241,90 ± 59,40	22,38	28 293,17	12 731,93
	Timolol/Amiloride	Y	2 799	219,52 ± 49,40			

Table 4-14 (cont.): Summary of estimated cost savings due to generic substitution (2005)

Pharmacological group	Active ingredient	Generic indicator	Number of items	Average cost per item (R)	Difference in average cost (R)	Estimated cost saving @ 100% (R)	Estimated cost saving @ 45% (R)
Alpha- and beta-receptor blockers	Carvedilol	O	13 468	158,47 ± 56,27	59,39	799 894,03	359 952,31
	Carvedilol	Y	38 801	99,07 ± 41,10			
Direct-acting vasodilators	Hydralazine	O	229	195,63 ± 72,08	150,38	34 436,61	15 496,48
	Hydralazine	Y	1 558	45,25 ± 21,40			
Calcium channel blockers	Amlodipine	O	54 019	152,00 ± 33,67	36,60	1 976 835,45	889 575,95
	Amlodipine	Y	29 094	115,41 ± 26,52			
	Felodipine	O	9 070	215,88 ± 38,24	105,18	954 016,26	429 307,32
	Felodipine	Y	13 034	110,69 ± 22,37			
ACE inhibitors	Captopril	O	1 250	148,88 ± 88,14	114,01	142 510,12	64 129,56
	Captopril	Y	33 811	34,88 ± 21,46			
	Captopril/HTCZ	O	182	224,04 ± 54,36	154,86	28 184,13	12 682,86
	Captopril/HTCZ	Y	4 135	69,18 ± 18,15			
	Enalapril	O	19 284	68,72 ± 31,00	15,10	291 171,60	131 027,22
	Enalapril	Y	101 033	53,62 ± 21,64			
	Enalapril /HTCZ	O	13 092	107,05 ± 17,12	29,31	383 757,65	172 690,94
	Enalapril /HTCZ	Y	46 930	77,73 ± 10,32			
	Lisinopril	O	4 802	130,84 ± 54,22	69,07	331 671,71	149 252,27

Table 4-14 (cont.): Summary of estimated cost savings due to generic substitution (2005)

Pharmacological group	Active ingredient	Generic indicator	Number of items	Average cost per item (R)	Difference in average cost (R)	Estimated cost saving @ 100% (R)	Estimated cost saving @ 45% (R)
	Lisinopril	Y	95 257	61,77 ± 21,39			
	Lisinopril /HTCZ	O	10 553	144,69 ± 51,18	50,53	533 207,50	239 943,38
	Lisinopril /HTCZ	Y	4 224	94,17 ± 25,62			
	Perindopril	O	26 856	140,29 ± 36,84	11,48	308 259,08	138 716,59
	Perindopril	Y	90 724	128,81 ± 27,71			
	Ramipril	O	18 234	208,01 ± 59,24	63,97	1 166 481,36	524 916,61
	Ramipril	Y	11 521	144,04 ± 59,10			
Diuretics	Acetazolamide	O	905	56,60 ± 44,28	17,76	16 071,75	7 232,29
	Acetazolamide	Y	934	38,84 ± 31,53			
	Amiloride/HTCZ	O	2 717	110,37 ± 40,82	98,54	267 744,95	120 485,23
	Amiloride/HTCZ	Y	126 897	11,82 ± 9,85			
	HTCZ/Triamterene	O	775	54,66 ± 16,41	30,44	23 594,06	10 617,33
	HTCZ/ Triamterene	Y	6 191	24,21 ± 8,64			
	Indapamide	O	2 337	117,72 ± 28,03	94,55	220 959,91	99 431,96
	Indapamide	Y	104 404	23,18 ± 9,40			
	Indapamide /Perindopril	O	18 600	181,35 ± 18,39	0,37	6 900,06	3 105,03
	Indapamide /Perindopril	Y	32	180,98 ± 12,30			

Table 4-14 (cont.): Summary of estimated cost savings due to generic substitution (2005)

Pharmacological group	Active ingredient	Generic indicator	Number of items	Average cost per item (R)	Difference in average cost (R)	Estimated cost saving @ 100% (R)	Estimated cost saving @ 45% (R)
	Spironolactone	O	3 019	150,48 ± 103,62	98,22	296 519,49	133 433,77
	Spironolactone	Y	43 227	52,26 ± 47,40			
Total cost saving						10 331 668,00	4 649 250,58

From table 4-14 the following conclusions can be drawn:

- A possible cost saving of R10 331 668,00 could have been achieved if all the innovator products had been substituted with a generic equivalent during 2005. This is a saving of approximately 4,42% on the total cost of antihypertensive medicine items for 2005.
- If 45% of the innovator products had been generically substituted, the possible cost savings would only have been R4 649 250,58 or 1,99%.
- The highest cost saving would have been with generic substitution of the calcium channel blocker, amlodipine. For a 100% saving, 54 019 items could have been substituted with a saving of R1 976 835,45, and approximately 24 309 items could have been substituted for a 45% cost saving of R889 575,95.
- The generic equivalent of the amiloride-hydrochlorothiazide combination had the lowest average cost of R11,82 ± R9,85.

In table 4-15 the possible cost savings due to generic substitution for 2006 is summarised.

Table 4-15: Summary of estimated cost savings due to generic substitution (2006)

Pharmacological group	Active ingredient	Generic indicator	Number of items	Average cost per item (R)	Difference in average cost (R)	Estimated cost saving @ 100% (R)	Estimated cost saving @ 45% (R)
Central-acting inhibitors	Methyldopa	O	668	173,87 ± 105,20	105,73	70 628,95	31 783,03
	Methyldopa	Y	17 406	68,14 ± 49,67			
Alpha-receptor blocker	Doxazosin	O	11 639	187,44 ± 34,92	102,66	1 194 908,58	537 708,86
	Doxazosin	Y	11 161	84,77 ± 45,86			
Beta-receptor blocker	Acebutolol	O	1 173	225,53 ± 49,53	53,47	62 725,94	28 226,67
	Acebutolol	Y	525	172,05 ± 41,12			
	Atenolol/Chlortalidone	O	2 599	197,81 ± 51,81	128,38	333 662,36	150 148,06
	Atenolol/Chlortalidone	Y	43 869	69,43 ± 20,57			
	Bisoprolol	O	43 245	78,83 ± 31,46	27,58	1 192 719,44	536 723,75
	Bisoprolol	Y	54 025	51,25 ± 19,23			
	Sotalol	O	3 413	187,47 ± 76,84	102,94	351 345,21	158 105,34
	Sotalol	Y	8 895	84,52 ± 32,74			
	Timolol/Amiloride	O	938	239,71 ± 57,59	22,71	21 297,47	9 583,86
	Timolol / Amiloride	Y	2 289	217,01 ± 50,68			
Alpha- and beta-receptor blockers	Carvedilol	O	11 691	158,79 ± 60,33	60,45	706 693,94	318 012,27
	Carvedilol	Y	54 830	98,34 ± 39,84			
Direct-acting vasodilators	Hydralazine	O	229	191,89 ± 65,24	146,23	33 487,44	15 069,35
	Hydralazine	Y	1 856	45,66 ± 21,54			
Calcium channel blockers	Amlodipine	O	48 512	145,03 ± 30,31	33,29	1 615 148,46	726 816,81
	Amlodipine	Y	65 548	111,73 ± 23,74			
	Felodipine	O	6 216	213,46 ± 40,84	100,90	627 189,08	282 235,09
	Felodipine	Y	16 714	112,56 ± 24,88			
ACE inhibitors	Captopril	O	1 121	156,72 ± 87,92	123,33	138 254,30	62 214,43
	Captopril	Y	34 750	33,38 ± 19,77			

Table 4-15 (cont.): Summary of estimated cost savings due to generic substitution (2006)

Pharmacological group	Active ingredient	Generic indicator	Number of items	Average cost per item (R)	Difference in average cost (R)	Estimated cost saving @ 100% (R)	Estimated cost saving @ 45% (R)
	Captopril/HTCZ	O	139	213,16 ± 43,23	145,48	20 221,32	9 099,60
	Captopril/HTCZ	Y	4 628	67,68 ± 17,81			
	Enalapril	O	13 624	67,57 ± 30,80	14,32	195 077,54	87 784,89
	Enalapril	Y	119 191	53,25 ± 20,95			
	Enalapril /HTCZ	O	9 847	105,63 ± 18,25	28,22	277 929,75	125 068,39
	Enalapril /HTCZ	Y	57 451	77,40 ± 10,72			
	Fosinopril	O	1 374	185,72 ± 48,82	59,02	81 088,05	36 489,62
	Fosinopril	Y	74	126,70 ± 24,24			
	Lisinopril	O	4 265	86,66 ± 34,08	25,42	108 401,61	48 780,72
	Lisinopril	Y	106 365	61,25 ± 21,21			
	Lisinopril /HTCZ	O	11 660	105,61 ± 28,03	20,46	238 590,80	107 365,86
	Lisinopril /HTCZ	Y	20 288	85,14 ± 20,52			
	Perindopril	O	21 537	140,37 ± 35,79	11,76	253 194,33	113 937,45
	Perindopril	Y	121 097	128,61 ± 28,51			
	Quinapril	O	8 890	139,56 ± 43,52	44,74	397 729,23	178 978,15
	Quinapril	Y	3 100	94,82 ± 25,22			
	Ramipril	O	15 780	212,57 ± 62,70	85,80	1 353 907,32	609 258,29
	Ramipril	Y	17 584	126,77 ± 50,63			
Angiotensin-receptor blockers	Valsartan	O	18 168	210,11 ± 28,33	16,85	306 081,14	137 736,51
	Valsartan	Y	16	193,26 ± 53,79			
Diuretics	Acetazolamide	O	857	61,43 ± 51,88	23,71	20 321,91	9 144,86
	Acetazolamide	Y	1 046	37,72 ± 30,36			
	Amiloride/HTCZ	O	2 254	107,99 ± 39,86	96,68	217 912,29	98 060,53
	Amiloride /HTCZ	Y	129 234	11,31 ± 9,57			
	Furosemide	O	27 752	134,14 ± 70,49	104,83	2 909 334,37	1 309 200,47

Table 4-15 (cont.): Summary of estimated cost savings due to generic substitution (2006)

Pharmacological group	Active ingredient	Generic indicator	Number of items	Average cost per item (R)	Difference in average cost (R)	Estimated cost saving @ 100% (R)	Estimated cost saving @ 45% (R)
	Furosemide	Y	56 794	29,31 ± 19,94			
	HTCZ/Triamterene	O	707	51,96 ± 15,68	27,79	19 647,85	8 841,53
	HTCZ/Triamterene	Y	5 805	24,17 ± 9,01			
	Indapamide	O	1 970	113,21 ± 32,20	90,71	178 708,15	80 418,67
	Indapamide	Y	115 337	22,50 ± 9,53			
	Indapamide /Perindopril	O	38 992	180,41 ± 25,39	30,95	1 206 852,20	543 083,49
	Indapamide /Perindopril	Y	50 903	149,46 ± 17,80			
	Spironolactone	O	2 736	147,04 ± 103,01	96,39	263 729,64	118 678,34
	Spironolactone	Y	50 225	50,65 ± 46,01			
Total cost saving						14 396 788,68	6 478 554,90

From table 4-15 the following conclusions can be drawn:

- A possible cost saving of R14 396 788,68 could have been achieved if all the innovator products had been substituted with a generic equivalent during 2006. This is a saving of approximately 6,39% on the total cost of antihypertensive medicine items for 2006.
- If 45% of the innovator products had been generically substituted, the possible cost savings would only have been R6 478 554,90.
- It was also seen that generic substitution of all 27 752 innovator items of furosemide, which is a diuretic, with its generic equivalent would have led to a possible cost saving of R2 909 334,37, and that if only 12 488 (45%) furosemide innovator items had been substituted with a generic equivalent, a cost saving of R1 309 200,47 would have been achieved. The difference in average cost for furosemide was R104,83. However, in 2003 the Medicines Control Council (MCC) issued new guidelines regarding non-substitutable medicines. These guidelines determine that exchangeable use of different brands of chemically equivalent medications could under certain conditions compromise therapeutic effect and patient safety. The recommendations not to substitute a medicine item with a generic equivalent is indicated for medicines with a narrow therapeutic range that have been known to show inconsistent intra- and inter-patient response. Such a substitution is contraindicated in dosage forms that are likely to give rise to clinically significant bioavailability problems, e.g. extended or delayed-release preparations, as well as those known to be super bio-available, or that are intended for the critically ill and/or geriatric or paediatric patients. One such medicine item on the non-substitutable list is furosemide, and therefore no generic cost savings would have been possible.
- Generic equivalent angiotensin-receptor blockers, specifically medicine items containing valsartan, also became available during 2006. Even though 18 168 valsartan items could have been generically substituted, the cost savings would only have been R306 081,14, since the difference in average cost between the innovator and generic items was only R16,85.
- The largest difference in average cost between innovator and generic medicine items was R146,23, which was calculated for hydralazine medicine items (a direct-acting vasodilator).

In table 4-16 the possible cost savings due to generic substitution for 2007 are summarised.

Table 4-16: Summary of estimated cost savings due to generic substitution (2007)

Pharmacological group	Active ingredient	Generic indicator	Number of items	Average cost per item (R)	Difference in average cost (R)	Estimated cost saving @ 100%	Estimated cost saving @ 45%
Central-acting inhibitors	Methyldopa	O	302	146,79 ± 98,31	71,99	21 742,48	9 784,12
	Methyldopa	Y	13 192	74,80 ± 56,06			
Alpha-receptor blockers	Doxazosin	O	10 226	194,00 ± 40,18	109,22	1 116 933,08	502 619,88
	Doxazosin	Y	10 994	84,78 ± 47,75			
Beta-receptor blockers	Acebutolol	O	863	242,51 ± 74,28	68,20	58 860,84	26 487,38
	Acebutolol	Y	670	174,31 ± 46,79			
	Atenolol/Chlortalidone	O	1 969	202,07 ± 67,35	127,88	251 793,87	113 307,24
	Atenolol/Chlortalidone	Y	36 103	74,19 ± 23,39			
	Bisoprolol	O	36 494	79,87 ± 33,89	26,15	954 306,29	429 437,83
	Bisoprolol	Y	72 657	53,72 ± 20,81			
	Sotalol	O	2 663	192,19 ± 91,88	100,87	268 627,21	120 882,24
	Sotalol	Y	8 260	91,32 ± 36,63			
	Timolol/Amiloride	O	553	253,69 ± 70,49	15,23	8 422,51	3 790,13
	Timolol / Amiloride	Y	1 882	238,46 ± 58,92			
Alpha- and beta-receptor blockers	Carvedilol	O	8 901	159,78 ± 61,40	57,65	513 182,71	230 932,22
	Carvedilol	Y	60 899	102,13 ± 40,33			
Direct-acting vasodilators	Hydralazine	O	163	192,46 ± 76,16	142,96	23 303,00	10 486,35
	Hydralazine	Y	1 614	49,50 ± 24,68			
Calcium channel blockers	Amlodipine	O	35 821	149,89 ± 35,90	34,85	1 248 484,49	561 818,02
	Amlodipine	Y	98 820	115,03 ± 28,16			
	Felodipine	O	4 472	221,12 ± 50,08	101,77	455 098,05	204 794,12
	Felodipine	Y	17 119	119,36 ± 27,91			
ACE inhibitors	Captopril	O	682	146,99 ± 109,36	118,44	80 776,20	36 349,29

Table 4-16 (cont.): Summary of estimated cost savings due to generic substitution (2007)							
Pharmacological group	Active ingredient	Generic indicator	Number of items	Average cost per item (R)	Difference in average cost (R)	Estimated cost saving @ 100%	Estimated cost saving @ 45%
	Captopril	Y	18 197	28,55 ± 19,46			
	Captopril/HTCZ	O	91	220,00 ± 51,87	151,07	13 747,71	6 186,47
	Captopril/HTCZ	Y	3 733	68,92 ± 21,04			
	Enalapril	O	10 520	69,16 ± 32,22	12,91	135 767,20	61 095,24
	Enalapril	Y	99 787	56,26 ± 23,44			
	Enalapril /HTCZ	O	7 510	107,56 ± 19,56	25,37	190 497,39	85 723,82
	Enalapril /HTCZ	Y	54 425	82,19 ± 13,70			
	Fosinopril	O	1 478	189,01 ± 56,27	63,36	93 644,41	42 139,98
	Fosinopril	Y	279	125,65 ± 29,37			
	Lisinopril	O	3 163	88,02 ± 37,37	23,30	73 699,38	33 164,72
	Lisinopril	Y	92 961	64,72 ± 23,78			
	Lisinopril /HTCZ	O	9 299	109,89 ± 32,15	21,56	200 486,47	90 218,91
	Lisinopril /HTCZ	Y	26 282	88,33 ± 23,64			
	Perindopril	O	15 774	139,00 ± 38,81	10,52	165 870,33	74 641,65
	Perindopril	Y	124 538	128,49 ± 30,78			
	Quinapril	O	6 310	128,10 ± 34,77	20,23	127 639,82	57 437,92
	Quinapril	Y	4 316	107,88 ± 29,77			
	Quinapril /HTCZ	Y	8 474	101,57 ± 21,64	58,26	715 663,18	322 048,43
	Quinapril /HTCZ	O	12 285	159,82 ± 36,93			
	Ramipril	O	9 647	216,88 ± 75,63	84,65	816 657,85	367 496,03

Table 4-16 (cont.): Summary of estimated cost savings due to generic substitution (2007)

Pharmacological group	Active ingredient	Generic indicator	Number of items	Average cost per item (R)	Difference in average cost (R)	Estimated cost saving @ 100%	Estimated cost saving @ 45%
	Ramipril	Y	20 631	132,22 ± 48,53			
Angiotensin-receptor blockers	Losartan	O	3 009	145,19 ± 32,95	32,49	97 754,60	43 989,57
	Losartan	Y	219	112,71 ± 27,51			
	Valsartan	O	22 112	207,57 ± 39,84	40,85	903 249,33	406 462,20
	Valsartan	Y	5 277	166,72 ± 33,70			
	Valsartan /HTCZ	O	18 328	207,37 ± 40,47	39,37	721 511,00	324 679,95
	Valsartan /HTCZ	Y	5 427	168,00 ± 28,25			
Diuretics	Acetazolamide	O	894	65,92 ± 53,48	23,25	20 781,37	9 351,62
	Acetazolamide	Y	948	42,67 ± 34,05			
	Amiloride/HTCZ	O	1 705	107,75 ± 44,97	97,80	166 756,16	75 040,27
	Amiloride /HTCZ	Y	99 861	9,95 ± 7,93			
	Furosemide	O	33 463	134,96± 72,86	110,50	3 697 612,20	1 663 925,49
	Furosemide	Y	51 667	24,46 ± 16,17			
	HTCZ/Triamterene	O	595	52,23 ± 17,72	27,24	16 205,51	7 292,48
	HTCZ/Triamterene	Y	4 908	24,99 ± 8,97			
	Indapamide	O	1 642	111,35 ± 33,15	88,70	145 644,04	65 539,82
	Indapamide	Y	101 207	22,65 ± 10,68			
	Indapamide /Perindopril	O	23 536	177,98 ± 32,47	27,69	651 762,61	293 293,18
	Indapamide / Perindopril	Y	88 688	150,28 ± 22,06			

Table 4-16 (cont.): Summary of estimated cost savings due to generic substitution (2007)

Pharmacological group	Active ingredient	Generic indicator	Number of items	Average cost per item (R)	Difference in average cost (R)	Estimated cost saving @ 100%	Estimated cost saving @ 45%
	Spironolactone	O	2 349	143,04 ± 92,58	90,46	212 495,16	95 622,82
	Spironolactone	Y	49 430	52,58 ± 47,32			
Total cost saving						14 168 976,45	6 376 039,40

From table 4-16 the following observations regarding generic substitution were made:

- A possible cost saving of R14 168 976,45 could have been achieved if all the innovator products had been substituted with a generic equivalent during 2007. This is a saving of approximately 6,39% on the total cost of antihypertensive medicine items for 2007.
- If 45% of the innovator products had been generically substituted, the possible cost savings would only have been R6 376 039,40 or 2,87% of the total cost (R221 851 892,30).
- The highest cost saving would have been achieved if all of the 33 463 innovator furosemide medicine items had been substituted with a generic equivalent, but as stated previously, furosemide is on the list of non-substitutable medicines, and therefore generic substitution was not possible.
- If all the amlodipine innovator medicine items had been substituted with generic equivalents, a possible cost saving of R1 248 484,49 or 0,53% (N = R235 059 416,62) could have been possible.
- If only 45% of the 33 463 amlodipine items had been generically substituted, a possible cost saving of R561 818,02 or 0,24% (N = R235 059 416,62) could have been achieved.

During 2007 more generic angiotensin-receptor blockers became available for possible substitution. These included generic equivalents for losartan and the valsartan/HCTZ combination. Total generic substitution of the innovator of the latter could have resulted in a saving of R721 511,00, while generic substitution of all the losartan innovator items could have given a R97 754,60 saving. It can also be seen that there was an increase in the number of generic valsartan items utilised when compared with 2006.

In table 4-17 the possible cost savings due to generic substitution for 2008 is summarised.

Table 4-17: Summary of estimated cost savings due to generic substitution (2008)

Pharmacological group	Active ingredient	Generic indicator	Number of items	Average cost per item (R)	Difference in average cost (R)	Estimated cost saving @ 100% (R)	Estimated cost saving @ 45% (R)
Central-acting inhibitors	Methyldopa	O	82	91,00 ± 90,68	12,25	1 004,28	451,93
	Methyldopa	Y	12713	78,75 ± 56,05			
	Moxonidine	O	1 909	220,04 ± 51,17	46,22	88 226,49	39 701,92
	Moxonidine	Y	77	173,82 ± 51,69			
Alpha-receptor blockers	Doxazosin	O	9 210	199,46 ± 39,91	121,00	1 114 369,15	501 466,12
	Doxazosin	Y	11 134	78,47 ± 46,01			
Beta-receptor blockers	Acebutolol	O	951	235,55 ± 64,94	52,94	50 345,79	22 655,61
	Acebutolol	Y	177	182,61 ± 66,69			
	Atenolol/Chlortalidone	O	2 445	208,19 ± 66,58	131,22	320 843,47	144 379,56
	Atenolol/Chlortalidone	Y	26 080	76,96 ± 24,98			
	Bisoprolol	O	31 166	83,34 ± 36,18	27,45	855 623,52	385 030,59
	Bisoprolol	Y	83 715	55,88 ± 21,96			
	Sotalol	O	2 083	205,51 ± 95,74	110,25	229 644,69	103 340,11
	Sotalol	Y	7 253	95,26 ± 36,84			
Alpha- and beta-receptor blockers	Carvedilol	O	6 863	167,60 ± 64,81	64,47	442 441,00	199 098,45
	Carvedilol	Y	64 609	103,13 ± 39,80			
Direct-acting vasodilators	Hydralazine	O	7	222,70 ± 126,77	170,95	1 196,68	538,51
	Hydralazine	Y	1 590	51,74 ± 24,93			
Calcium channel blockers	Amlodipine	O	22 976	147,24 ± 41,99	43,96	1 009 954,91	454 479,71
	Amlodipine	Y	124 965	103,28 ± 27,79			
	Felodipine	O	3 229	228,37 ± 57,58	105,37	340 250,01	153 112,51
	Felodipine	Y	16 559	123,00 ± 28,95			
ACE inhibitors	Captopril	O	307	152,98 ± 142,56	122,99	37 757,27	16 990,77

Table 4-17 (cont.): Summary of estimated cost savings due to generic substitution (2008)

Pharmacological group	Active ingredient	Generic indicator	Number of items	Average cost per item (R)	Difference in average cost (R)	Estimated cost saving @ 100% (R)	Estimated cost saving @ 45% (R)
	Captopril	Y	21 413	29,99 ± 17,80			
	Captopril /HTCZ	O	58	227,66 ± 42,36	155,02	8 991,44	4 046,15
	Captopril /HTCZ	Y	3 491	72,63 ± 23,81			
	Enalapril	O	8 214	69,64 ± 32,78	10,61	87 188,89	39 235,00
	Enalapril	Y	107 234	59,03 ± 23,17			
	Enalapril /HTCZ	O	5 933	108,26 ± 19,12	22,77	135 119,75	60 803,89
	Enalapril /HTCZ	Y	59 007	85,49 ± 13,75			
	Fosinopril	O	1 116	188,29 ± 58,84	45,33	50 583,90	22 762,76
	Fosinopril	Y	246	142,97 ± 33,88			
	Lisinopril	O	2 565	89,28 ± 37,91	22,74	58 332,48	26 249,62
	Lisinopril	Y	94 496	66,54 ± 23,87			
	Lisinopril /HTCZ	O	7 180	114,83 ± 33,30	22,95	164 787,17	74 154,23
	Lisinopril /HTCZ	Y	28 374	91,87 ± 24,43			
	Perindopril	O	10 534	141,01 ± 38,20	11,53	121 427,64	54 642,44
	Perindopril	Y	112 363	129,48 ± 32,13			
	Quinapril	O	4 188	130,90 ± 36,43	31,91	133 632,92	60 134,81
	Quinapril	Y	5 209	98,99 ± 31,65			
	Quinapril /HTCZ	Y	7 163	105,10 ± 23,39	58,45	412 891,81	185 801,32
	Quinapril /HTCZ	O	7 064	163,55 ± 40,53			
	Ramipril	O	6 419	225,15 ± 79,30	90,22	579 108,56	260 598,85
	Ramipril	Y	21 337	134,94 ± 47,68			
Angiotensin-receptor blockers	Losartan	O	12 963	114,70 ± 31,44	22,10	286 446,11	128 900,75
	Losartan	Y	8 955	92,60 ± 22,60			
	Valsartan	O	12 815	212,10 ± 41,16	47,82	612 778,43	275 750,29
	Valsartan	Y	13 443	164,28 ± 36,47			

Table 4-17 (cont.): Summary of estimated cost savings due to generic substitution (2008)

Pharmacological group	Active ingredient	Generic indicator	Number of items	Average cost per item (R)	Difference in average cost (R)	Estimated cost saving @ 100% (R)	Estimated cost saving @ 45% (R)
	Valsartan /HTCZ	O	10 734	211,32 ± 39,21	42,87	460 130,91	207 058,91
	Valsartan /HTCZ	Y	13 634	168,45 ± 31,76			
Diuretics	Acetazolamide	O	836	66,98 ± 50,72	21,03	17 578,53	7 910,34
	Acetazolamide	Y	768	45,96 ± 35,62			
	Amiloride/HTCZ	O	1 165	105,61 ± 49,09	93,79	109 259,57	49 166,81
	Amiloride /HTCZ	Y	99 745	11,82 ± 9,21			
	Furosemide	O	28 264	135,31 ± 75,49	110,63	3 126 980,00	1 407 141,00
	Furosemide	Y	53 391	24,68 ± 15,75			
	HTCZ/Triamterene	O	427	52,74 ± 21,54	27,10	11 570,07	5 206,53
	HTCZ/ Triamterene	Y	4 281	25,64 ± 8,76			
	Indapamide	O	1 146	113,45 ± 37,27	89,34	102 388,81	46 074,96
	Indapamide	Y	97 346	24,11 ± 10,41			
	Indapamide /Perindopril	O	14 190	179,53 ± 33,70	27,43	389 288,28	175 179,72
	Indapamide / Perindopril	Y	95 907	152,10 ± 22,38			
	Spironolactone	O	1 776	141,22 ± 90,01	87,31	155 068,04	69 780,62
	Spironolactone	Y	50 545	53,90 ± 48,29			
Total cost savings						11 515 210,60	5 181 844,77

From table 4-17 the following observations regarding generic substitution were made:

- A possible cost saving of R11 515 210,60 could have been achieved if all the innovator products had been substituted with a generic equivalent during 2008. This is a saving of approximately 5,55% on the total cost of antihypertensive medicine items for 2008.
- If 45% of the innovator products had been generically substituted, the possible cost savings would only have been R5 181 844,77 or 2.50% of the total cost (R207 364 638,60).
- The highest cost saving would have been achieved if all of the 9 210 innovator doxazosin medicine items had been substituted with a generic equivalent. This possible saving could have been R1 114 639,15.
- If only 45% of the innovator doxazosin items had been generically substituted, a saving of R501 466,12 could have been achieved.

To summarise, total possible cost savings with 100% generic substitution over a four-year study period could have amounted to R50 412 643,73. If only 45% of innovator antihypertensive medicine items had been substituted with a generic equivalent, a saving of R22 685 689,65 could have been possible during the four-year study period.

4.5.4 Average number of antihypertensive items and average number of prescriptions according to age-group and gender.

In this section all the prescribing patterns of antihypertensive medicine items relating to age group and gender will be discussed.

4.5.4.1 Prescribing patterns according to age group

As was seen in Section 4.4.3, all the patients were divided into three age groups. Age group 1 (AG1) included all the patients aged 1 - ≤ 18, age group 2 (AG2) included patients aged 19 - ≤ 45 and age group 3 (AG3) included all the patients aged 45 years and older. In Table 4–18 the average cost and number of antihypertensive items according to age group are summarised.

Table 4-18: Prescribing patterns of antihypertensive medicine items according to age group

Year	Age group	Number of patients	Number of items	Average cost per item (R)	Item per patient ratio
2005	AG1	1 906	2 339	83,36 ± 71,80	1,2
	AG2	140 423	174 863	101,59 ± 79,36	1,2
	AG3	1 296 199	1 761 294	110,53 ± 78,20	1,2
	Total	1 438 528	1 938 496	109,69 ± 78,34	1,3
2006	AG1	2 058	2 660	81,65 ± 73,09	1,3
	AG2	151 158	191 002	99,07 ± 76,30	1,3
	AG3	1 410 088	1 947 117	105,90 ± 75,64	1,4
	Total	1 563 304	2 140 779	105,26 ± 75,72	1,4
2007	AG1	1 544	1 959	89,15 ± 84,83	1,3
	AG2	129 439	165 530	104,73 ± 77,35	1,3
	AG3	1 329 718	1 855 282	110,14 ± 75,85	1,4
	Total	1 460 701	2 022 771	109,68 ± 76,00	1,4
2008	AG1	1 254	1 632	85,12 ± 79,43	1,3
	AG2	112 980	146 847	100,80 ± 73,86	1,3
	AG3	1 286 545	1 821 959	105,61 ± 73,45	1,4
	Total	1 400 779	1 970 438	105,24 ± 73,50	1,4

From table 4-18 the following observations can be made:

- Patients in AG3 (age 45 years and older), had the highest usage of antihypertensive medicine items, accounting for more than 90% of all the antihypertensive medicine items throughout the four-year study period. This is in accordance with literature, where it is suggested that hypertension is more common amongst older people (Dalzell, 2003:7; Vasan, 2001:1682; Bitton & Gaziano, 2010:69).
- Even though patients from AG3 consumed a higher number of antihypertensive medicine items, the item per patient ratio was only slightly higher for AG3.

4.5.4.2 Generic antihypertensive medicine usage according to age groups

In this section the usage of generic antihypertensive medicine items by the different age groups is discussed. Possible cost savings due to this generic substitution are also calculated.

Table 4-19 summarises the number of items utilised by the different age groups, but with an indication of how many items per age group were for a generic product (Y) or the original product (O), and for how many items no generic equivalent (N) was available. In cases where no generic equivalent was available, the originator was still patented.

Table 4-19: Number of generic and innovator items according to age group

Year	Generic indicator	Age group	Number of items	Average cost per item (R)	Total cost (R)	Prevalence % #	Cost % #	CPI
2005	N	AG1	477	145,33 ± 78,41	69 324,58	20,39	35,56	1,74
	N	AG2	58 321	167,63 ± 73,40	9 776 230,89	33,35	55,03	1,65
	N	AG3	615 258	173,76 ± 67,18	106 905 006,80	34,93	54,91	1,57
	O	AG1	585	108,48 ± 65,74	63 462,92	25,01	32,55	1,30
	O	AG2	20 734	138,53 ± 62,98	2 872 213,78	11,86	16,17	1,36
	O	AG3	267 814	139,07 ± 61,66	37 244 478,06	15,21	19,13	1,26
	Y	AG1	1 277	48,70 ± 47,40	62 188,28	54,60	31,90	0,58
	Y	AG2	95 808	53,40 ± 45,65	5 116 023,21	54,79	28,80	0,53
	Y	AG3	878 222	57,54 ± 45,67	50 529 566,88	49,86	25,96	0,52
2006	N	AG1	410	127,25 ± 92,89	52 171,03	15,41	24,02	1,56
	N	AG2	46 529	163,19 ± 81,65	7 593 043,89	24,36	40,13	1,65
	N	AG3	501 743	172,74 ± 72,87	86 669 744,13	25,77	42,03	1,63
	O	AG1	705	115,90 ± 70,86	81 708,74	26,50	37,62	1,42
	O	AG2	26 373	146,38 ± 63,06	3 860 556,28	13,81	20,40	1,48
	O	AG3	317 170	147,10 ± 60,82	46 656 295,56	16,29	22,63	1,39
	Y	AG1	1 545	53,92 ± 52,61	83 302,79	58,08	38,36	0,66
	Y	AG2	118 100	63,24 ± 49,99	7 468 855,45	61,83	39,47	0,64
	Y	AG3	1 128 204	64,60 ± 47,98	72 881 559,80	57,94	35,34	0,61
2007	N	AG1	210	160,34 ± 127,07	33 670,57	10,72	19,28	1,80
	N	AG2	37 331	170,70 ± 86,88	6 372 403,41	22,55	36,76	1,63
	N	AG3	432 487	178,51 ± 76,39	77 201 882,43	23,31	37,78	1,62
	O	AG1	579	119,67 ± 78,64	69 289,33	29,56	39,68	1,34
	O	AG2	21 063	142,03 ± 65,55	2 991 611,67	12,72	17,26	1,36
	O	AG3	279 881	148,93 ± 64,39	41 682 388,80	15,09	20,40	1,35
	Y	AG1	1 170	61,26 ± 62,92	71 677,44	59,72	41,04	0,69
	Y	AG2	107 136	74,41 ± 55,31	7 971 518,91	64,72	45,98	0,71
	Y	AG3	1 142 914	74,77 ± 52,23	85 457 449,78	61,60	41,82	0,68
2008	N	AG1	133	129,78 ± 84,81	17 260,52	8,15	12,43	1,52
	N	AG2	28 136	165,50 ± 88,76	4 656 525,69	19,16	31,46	1,64
	N	AG3	380 180	172,45 ± 80,78	65 560 440,40	1,54	34,07	22,06
	O	AG1	392	126,80 ± 85,35	49 705,35	24,02	35,78	1,49
	O	AG2	13 434	138,82 ± 72,70	1 864 903,20	9,15	12,60	1,38
	O	AG3	216 739	146,50 ± 66,48	31 752 093,48	11,90	16,50	1,39
	Y	AG1	1 107	64,99 ± 67,90	71 946,14	67,83	51,79	0,76
	Y	AG2	105 277	78,66 ± 55,11	8 281 305,84	71,69	55,94	0,78
	Y	AG3	1 225 040	77,64 ± 52,47	95 110 457,96	67,24	49,43	0,74

Prevalence % and cost % were calculated using the total number of items and total cost per age group (see Table 4-11 for total number of items per age group and total cost per age group)

From table 4-19 the following observations were made:

- For all four study years and through all age groups the generic items had the highest prevalence percentage and cost percentage.
- Calculated CPIs for these items indicated that the generic items were less expensive than the originator items and items with no generic equivalent available ($CPI < 1$).
- The average cost of the generic items indicated that for all four years the generic items had a lower average cost than the overall average cost (see average cost in 'Total' row for all study years) for all antihypertensive medicine items for a specific year.
- For 2005 the average cost of the generic items was between 48% and 56% lower than the overall average cost; for 2006 this figure lay between 41% and 51%. For 2007 the average cost of the generic items was between 32% and 44% lower than the overall average cost, while for 2008 the average cost of the generic items was only between 25% and 40% lower than the overall average cost of all the antihypertensive medicine items. This was calculated by subtracting the average cost per item (per age group) from the total or overall average cost of all antihypertensive medicine items. This difference was then divided by the overall average cost and multiplied by 100.

Since the generic items have a lower average cost, relatively large savings are possible through generic substitution. These savings were calculated by multiplying the number of original items by the average cost of the generic items for each age group. This total was then subtracted from the total cost of the original items. These findings are summarised in table 4-20.

Table 4-20: Possible cost savings through generic substitution per age group

Year	Generic indicator	Age group	Number of items	Average cost (R)	Total cost (R)	New total cost (R) *	Possible saving (R)
2005	O	AG1	585	108.48 ± 65.74	63 462.92	28 488.76	34 974.16
	O	AG2	20 734	138.53 ± 62.98	2 872 213.78	1 107 168.767	1 765 045.01
	O	AG3	267 814	139.07 ± 61.66	37 244 478.06	15 409 002.99	21 835 475.07
	Y	AG1	1 277	48.70 ± 47.40	62 188.28	-	-
	Y	AG2	95 808	53.40 ± 45.65	5 116 023.21	-	-
	Y	AG3	878 222	57.54 ± 45.67	50 529 566.88	-	-
2006	O	AG1	705	115.90 ± 70.86	81 708.74	38 011.95	43 696.79
	O	AG2	26 373	146.38 ± 63.06	3 860 556.28	1 667 875.74	2 192 680.54
	O	AG3	317 170	147.10 ± 60.82	46 656 295.56	20 489 064.32	26 167 231.24
	Y	AG1	1 545	53.92 ± 52.61	83 302.79	-	-
	Y	AG2	118 100	63,24 ± 49,99	7 468 855,45	-	-
	Y	AG3	1 128 204	64,60 ± 47,98	72 881 559,80	-	-

Table 4-20 (cont.): Possible cost savings through generic substitution per age group

Year	Generic indicator	Age group	Number of items	Average cost (R)	Total cost (R)	New total cost (R) *	Possible saving (R)
2007	O	AG1	579	119,67 ± 78,64	69 289,33	35 471,14	33 818,19
	O	AG2	21 063	142,03 ± 65,55	2 991 611,67	1 567 205,26	1 424 406,41
	O	AG3	279 881	148,93 ± 64,39	41 682 388,80	20 927 135,81	20 755 252,99
	Y	AG1	1 170	61,26 ± 62,92	71 677,44	-	-
	Y	AG2	107 136	74,41 ± 55,31	7 971 518,91	-	-
	Y	AG3	1 142 914	74,77 ± 52,23	85 457 449,78	-	-
2008	O	AG1	392	126,80 ± 85,35	49 705,35	25 476,86	24 228,49
	O	AG2	13 434	138,82 ± 72,70	1 864 903,20	1 056 746,13	808 157,07
	O	AG3	216 739	146,50 ± 66,48	31 752 093,48	16 827 324,45	14 924 769,03
	Y	AG1	1 107	64,99 ± 67,90	71 946,14	-	-
	Y	AG2	105 277	78,66 ± 55,11	8 281 305,84	-	-
	Y	AG3	1 225 040	77,64 ± 52,47	95 110 457,96	-	-

* New total cost was calculated by multiplying the number of original items per age group with the average cost per corresponding age group for generic medicine items.

The following calculations were made and conclusions were drawn from Table 4-20:

- Cost savings due to generic substitution for 2005 could have been R34 974,16 (approximately 55%, N = R63 462,92) for AG1, while the cost saving for AG 2 could have been R1 765 045,01 or approximately 61%, and for age group3 the cost saving due to generic substitution could have been R21 835 475,07 (58.6%, N = R37 244 478,06).
- Patients from AG1 could have contributed to a 54,5% (n = R43 696,79, N = R81 708,74) cost saving during 2006 if they had opted for generic equivalent antihypertensive medicine items. If patients from AG2 had opted for generic substitution, a saving of R2 192 680,54 (approximately 57%, N = R3 860 556,28) could have been achieved, while patients in AG3 opting for a generic equivalent could have achieved a 56% cost saving (n = R26 167 231,47, N = R46 656 295,56).
- Patients from AG1 could have contributed to a R33 818,19 (approximately 49%, N = R69 289,33) cost saving during 2007 if they had opted for generic equivalent antihypertensive medicine items. If patients from AG2 had opted for generic substitution, a saving of approximately 48% (n = R2 192 680,54; N = R3 860 556,28) could have been achieved, while patients in AG3 opting for a generic equivalent could have achieved a 49,8% cost saving (n = R20 755 252,99, N = R41 682 388,80).
- If generic substitution had been implemented during 2008, the possible cost savings could have been R24 228,49 (48,7%, N = R49 705,35) for patients in AG1, R808 157,07 (43,3%, N = R1 864 903,20) for patients in AG2 and R14 924 769,03 (47%, N = R31 752 093,48) for patients in AG3.

4.5.4.3 Antihypertensive prescriptions prescribed to patients in different age groups

In this section the number of prescriptions, average number of prescriptions per patient per year and total cost for each age group are analysed and discussed. The results are summarised in Table 4-21.

Table 4-21: Number of antihypertensive prescriptions per year according to age group

Year	Age group	Number of Rx	Average number of Rx per patient per year	Average cost per Rx (R)	Total cost (R)
2005	AG1	1 005	1,90 ± 2,28	194,01 ± 382,28	194 975,78
	AG2	35 641	3,94 ± 4,00	498,43 ± 833,26	17 764 467,88
	AG3	182 632	7,10 ± 5,15	1065,96 ± 1270,70	194 679 051,71
	Total	219 278	6,56 ± 5,12	969,72 ± 1226,75	212 638 495,37
2006	AG1	973	2,12 ± 2,73	22,21 ± 554,63	217 182,56
	AG2	35 982	4,20 ± 4,12	525,89 ± 850,30	18 922 455,62
	AG3	189 969	7,42 ± 5,11	1085,48 ± 1259,18	260 207 599,49
	Total	226 924	6,89 ± 5,10	993,05 ± 1219,66	279 347 237,67
2007	AG1	752	2,05 ± 2,65	232,23 ± 622,68	174 637,34
	AG2	28 354	4,57 ± 4,28	611,40 ± 955,08	17 335 533,99
	AG3	164 126	8,10 ± 5,08	1245,03 ± 1343,51	204 341 721,01
	Total	193 232	7,56 ± 5,12	1148,11 ± 1312,25	221 851 892,34
2008	AG1	557	2,25 ± 3,11	249,39 ± 602,93	138 912,01
	AG2	23 541	4,80 ± 4,36	628,81 ± 959,33	14 802 734,73
	AG3	158 587	8,11 ± 5,04	1213,36 ± 1319,60	192 422 991,84
	Total	182 685	7,67 ± 5,08	1135,09 ± 1293,09	207 364 638,58

From table 4-21 the following trends can be seen:

- Patients in AG3 had the highest number of prescriptions, average number of prescriptions per patient and average cost per patient per year.
- The patients in AG3 were responsible for between 83,2% and 86,8% of all the antihypertensive prescriptions during the four-year study period, which accounted for between 91,6% and 93,1% of the total cost during the four-year study period.

4.5.4.4 Prescribing patterns of different antihypertensive pharmacological groups to patients in different age groups

In this section the number of medicine items per pharmacological group is discussed according to the different age groups. These findings are summarised in Table E1 in Appendix E.

From Table E1 the following observations were made:

- For all pharmacological groups and for all four years, patients in AG3 showed the highest prevalence percentage and cost percentage for antihypertensive medicine.
- Antihypertensive medicine items prescribed to patients in AG3 accounted for 91% of all antihypertensive medicine items during 2005 and 2006. During 2007 and 2008 antihypertensive medicine items prescribed to patients in AG3 accounted for 92% of all the antihypertensive medicine items.
- CPI values calculated showed that there was an equilibrium in the prevalence and cost of antihypertensive medicine items prescribed and dispensed to patients in AG3 (CPI = 1).
- The most frequently prescribed antihypertensive medicine items for patients in AG1 during the four-year study period were (in order of highest to lowest prevalence) diuretics, ACE inhibitors, beta-receptor blockers, calcium channel blockers and ARBs. According to the literature, diuretics and beta-receptor blockers are safe and effective for the treatment of hypertension in children and young adolescents, but ACE inhibitors are more commonly prescribed for diabetic children (Luma & Spiotta, 2006:1565; Zarbock, 2005).
- During 2005 the utilisation of diuretics by patients in AG1 accounted for 40,7% of all the medicine items consumed by AG1 patients, totalling R58 595,51 (30,1%, N = R194 975,78).
- During 2006 the utilisation of diuretics by patients in AG1 accounted for 38,3% of all the medicine items consumed by AG1 patients, totalling R61 762,11 (33,1%, N = R186 326,37).
- During 2007 the utilisation of diuretics by patients in AG1 was approximately 781, or 39,9% of the total antihypertensive medicine items utilised by patients in AG1, totalling R54 569,77 (31,4%, N = R173 872,11).
- During 2008 the utilisation of diuretics by patients in AG1 was approximately 707, or 43,3% (N = 1 632) of the total antihypertensive medicine items utilised by patients in AG1, with a total cost of R52 824,89 (38%, N = R138 912,01).
- The most frequently prescribed antihypertensive medicine items for patients in AG2 during the four-year study period were (in order of highest to lowest prevalence) ACE inhibitors,

diuretics, ARBs, beta-receptor blockers and calcium channel blockers. Williams *et al.* (2004:157) stated that younger patients, i.e. patients younger than 55 years, tend to have higher renin levels compared to patients older than 55 years, and therefore ACE inhibitors are more effective in younger patients.

- During 2005 the utilisation of ACE inhibitors by patients in AG2 accounted for 35,8% of all the medicine items consumed by AG2 patients, totalling R6 894 101,93 (38,8%, N = R17 764 467,88).
- During 2006 the utilisation of ACE inhibitors by patients in AG2 accounted for 38,1% (n = 72 693) of all the medicine items consumed by AG2 patients, and 40,3% (n = R7 633 619,79, N = R18 922 455,62) of the total cost for antihypertensive medicine items for patients in AG2.
- During 2007 the patients from AG2 utilised 64 035 (38,7%, N = 1 855 282) ACE inhibitors with a total cost of R6 983 064,81 or 40,3% (N = R17 335 533,99) of the total cost for antihypertensive medicine items for patients in AG2.
- During 2008 the patients from AG2 utilised 39,3% (n = 57 518, N = 1 821 959) ACE inhibitors with a total cost of R6 162 940,31 or 41,6% (n = R6 162 940,31, N = R14 802 734,73) of the total cost for antihypertensive medicine items for patients in AG2.
- The most frequently prescribed antihypertensive medicine items for patients in AG3 during the four-year study period were (in order of highest to lowest prevalence) ACE inhibitors, diuretics, ARBs, beta-receptor blockers and calcium channel blockers. Even though it is stated in the literature that younger patients (i.e. patients ≤ 55 years) have a better response to ACE inhibitors (Williams *et al.* 2004:157), various studies (SCOPE trial, STOP-2 trial, ALLHAT trial, LIFE trial) have proven that older antihypertensive patients show a substantial decrease in cardiovascular morbidity and mortality when treated for hypertension with any antihypertensive medicine item (Lithell *et al.* 2003:875; Hannsson *et al.* 1999:1754; The ALLHAT Officers, 2002:2994; and Dahlof *et al.* 2002:1000).
- During 2005 the utilisation of ACE inhibitors by patients in AG3 accounted for 33,3% of all the medicine items consumed by AG3 patients, totalling R67 255 931,62 (34,5%, N = R194 679 051,70).
- During 2006 the utilisation of ACE inhibitors by patients in AG3 accounted for 34,1% (n = 664 325, N = 1 947 117) of all the medicine items consumed by AG3 patients, and R71 111 292,82 or 34,5% (N = R194 679 051,70) of the total cost.
- During 2007 the utilisation of ACE inhibitors by patients in AG3 accounted for 33,8% (n = 627 153, N = 1 855 282) of all the medicine items consumed by AG3 patients, and R70 167 493,44 or 34,3% (N = R204 341 721,00) of the total cost.

- During 2008 the utilisation of ACE inhibitors by patients in AG3 accounted for 33,7% (n = 613 523, N = 1 821 959) of all the medicine items consumed by AG3 patients, and R67 497 683,88 or 35,1% (N = R192 422 991,80) of the total cost.

4.5.4.5 Prescribing patterns of antihypertensive medicine items according to pharmacological group, treatment category, generic indicator and age group

In this section the influence of generic substitution on the usage of antihypertensive medicine is investigated according to the disease and age group of the different pharmacological groups. These findings are summarised in Appendix F.

Tables F1 – F4 in Appendix F summarise the number of antihypertensive medicine items according to pharmacological group, treatment category, generic indicator and age group. From Tables F1 – F4 the following observations were made:

- Throughout all four study years the generic items seemed to have a higher prevalence than the original antihypertensive medicine items.
- It was also noted that the average costs of the generic products were substantially lower than the average costs of the original products across all age groups and study years. The practical and statistical significance of these differences are proven in the calculated d-values.
- Medicine items prescribed in TC2 (i.e. MIMS group 16.1) had the lowest prevalence for all three age groups and generic indicators, but it was noticed that the generic products had a slightly higher prevalence and cost percentage.
- For diuretic products the prevalence and cost percentages were the lowest in TC1, which is expected since the treatment category includes only antihypertensive medicine items from MIMS group 7.3. However, throughout all four study years it was seen that diuretic items prescribed as part of TC3 showed a higher prevalence and cost percentage than those prescribed as part of TC2.

4.5.4.6 Prescribing patterns of antihypertensive medicine to patients of different genders

Another aspect that needs to be taken into consideration is the gender of the patients. In this section all aspects of antihypertensive medicine usage amongst patients of different genders are discussed.

Table 4-22 summarises the number of patients, items, average cost per item and total cost according to gender.

Table 4-22: Antihypertensive medicine item prescribing patterns according to gender

Year	Gender	Number of patients	Number of items	Average cost per antihypertensive item (R)	Total cost (R)
2005	F	833 393	1 114 978	104,58 ± 76,86	116 606 870,51
	M	604 350	822 469	116,65 ± 79,78	95 943 956,66
	U	785	1 049	83,57 ± 84,82	87 668,20
2006	F	869 522	1 217 175	100,69 ± 74,32	122 561 012,39
	M	666 149	922 773	111,31 ± 77,13	102 710 075,68
	U	633	831	91,64 ± 70,69	76 149,60
2007	F	839 521	1 152 423	104,98 ± 74,38	120 986 599,79
	M	621 136	870 290	115,89 ± 77,66	100 858 694,92
	U	44	58	113,75 ± 62,87	6 597,63
2008	F	794 764	1 106 101	101,59 ± 71,69	112 372 194,63
	M	606 015	864 337	109,90 ± 75,51	94 992 443,95
	U	-	-	-	-

The following observations were made from Table 4-22:

- More female than male patients received antihypertensive medicine during the four-year study period. Even though men are at greater risk of developing cardiovascular disease, the incidence of uncontrolled hypertension is also greater in male patients than in female patients (Reckelhoff, 2001:1199). Men are also generally less aware of their hypertension and receive less treatment than women (Fodor & Tzerocska, 2004:34; Wolf-Maier *et al.* 2004:12).
- Female patients accounted for approximately 57,2% (N = 5 836 312, n = 3 337 200) of all hypertension patients during the four-year study period, but antihypertensive medicine prescribed to female patients accounted for approximately 54% of the total cost of antihypertensive medicine. This is in line with the total database, which indicated that there were more female than male patients during all four study years (as seen in Figure 4.2). This is also in line with the CMS reports of 2005-6, 2006-7 and 2008-9, which stated that there were more female than male patients in the age groups older than 19 years (CMS, 2006; CMS, 2007; CMS, 2009). These results are also in line with a study on estimating the burden of disease attributable to hypertension in 2000 by Norman *et al.* (2007:695). In their study Basu *et al.* (2010:115) state that more women suffer from hypertension than

men, while Lunet and Barros (2002:15) state that treatment and control of hypertension are more common among women than among their male counterparts.

As with the different age groups it is once again important to look at the influence of generic substitution with respect to male and female patients. Table 4-23 summarise these findings.

Table 4-23: Number of generic and innovator antihypertensive medicine items utilised by the different genders

Year	Generic indicator	Gender	Number of items	Average cost per item (R)	Total cost (R)	Prevalence % [#]	Cost% [#]	CPI
2005	N	F	386 689	167,00 ± 66,46	64 576 947,50	34,68	55,38	1,60
	N	M	287 103	181,57 ± 68,57	52 128 866,61	34,91	54,33	1,56
	N	U	264	169,50 ± 104,27	44 748,13	25,17	51,04	2,03
	O	F	158 218	136,52 ± 60,09	21 599 548,20	14,19	18,52	1,31
	O	M	130 774	141,94 ± 63,64	18 562 479,71	15,90	19,35	1,22
	O	U	141	128,56 ± 56,22	18 126,85	13,44	20,68	1,54
	Y	F	570 071	53,38 ± 44,80	30 430 374,81	51,13	26,10	0,51
	Y	M	404 592	62,42 ± 46,41	25 252 610,34	49,19	26,32	0,54
	Y	U	644	38,50 ± 32,90	24 793,22	61,39	28,28	0,46
	Total		1 938 496	109,69 ± 78,34	212 638 495,40			
2006	N	F	319 802	164,62 ± 71,60	52 645 154,67	26,27	42,95	1,63
	N	M	228 720	182,07 ± 75,44	41 643 023,31	24,79	40,54	1,64
	N	U	160	167,38 ± 72,05	26 781,07	19,25	35,17	1,83
	O	F	183 135	144,65 ± 60,02	26 490 815,34	15,05	21,61	1,44
	O	M	160 972	149,64 ± 62,06	24 088 307,74	17,44	23,45	1,34
	O	U	141	137,85 ± 67,38	19 437,50	16,97	25,53	1,50
	Y	F	714 238	60,80 ± 47,70	43 425 042,38	58,68	35,43	0,60
	Y	M	533 081	69,37 ± 48,39	36 978 744,63	57,77	36,00	0,62
	Y	U	530	56,47 ± 39,17	29 931,03	63,78	39,31	0,62
	Total		2 140 779	105,26 ± 75,72	225 347 237,70			
2007	N	F	273 237	169,81 ± 73,97	46 397 212,38	23,71	38,35	1,62
	N	M	196 773	189,09 ± 80,45	37 207 731,38	22,61	36,89	1,63
	N	U	18	167,37 ± 61,93	3 012,65	31,03	45,66	1,47
	O	F	162 071	146,69 ± 62,94	23 774 706,85	14,06	19,65	1,40
	O	M	139 438	150,37 ± 66,30	20 966 839,44	16,02	20,79	1,30
	O	U	14	124,54 ± 31,10	1 743,51	24,14	26,43	1,09
	Y	F	717 115	70,86 ± 52,46	50 814 680,56	62,23	42,00	0,67
	Y	M	534 079	79,92 ± 52,14	42 684 124,10	61,37	42,32	0,69
	Y	U	26	70,83 ± 43,00	1841,47	44,83	27,91	0,62
	Total		2 022 771	109,68 ± 76,00	221 851 892,30			
2008	N	F	237 842	163,82 ± 75,48	38 962 835,22	21,50	34,67	1,61

Table 4-23 (cont.): Number of generic and innovator antihypertensive medicine items utilised by the different genders

Year	indicator	Gender	items	per item (R)	Total cost (R)	% [#]	Cost% [#]	CPI
	N	M	170 607	183,29 ± 87,70	31 271 391,39	19,74	32,92	1,67
	O	F	123 036	144,83 ± 65,32	17 819 180,82	11,12	15,86	1,43
	O	M	107 529	147,38 ± 68,68	15 847 521,21	12,44	16,68	1,34
	Y	F	745 223	74,60 ± 53,22	55 590 178,59	67,37	49,47	0,73
	Y	M	586 201	81,67 ± 51,77	47 873 531,35	67,82	50,40	0,74
	Total		1 970 438	105,24 ± 73,50	207 364 638,60			

Prevalence % and cost % were calculated using the total number of items and total cost of the different genders

The following points were observed from Table 4-23:

- On average, generic antihypertensive medicine items had a lower average cost and a higher prevalence percentage than the innovator antihypertensive medicine items.
- The CPI of these items was below 1 throughout all four study years, indicating that these items were relatively less expensive than the original items or the items with no generic equivalent available.

As was stated in Section 4.5.3, potential cost savings can be achieved through generic substitution. These savings were calculated by multiplying the number of original items by the difference in average cost of the originator and generic items for each gender group. These findings are summarised in Table 4-24.

Table 4-24: Possible cost savings due to generic substitution per gender

Year	Generic indicator	Gender	Number of items	Average cost per item (R)	Total cost (R)	Difference in average cost (R)	Possible saving (R)
2005	O	F	158 218	136,52 ± 60,09	21 599 548,20	83,14	13 154 244,52
	O	M	130 774	141,94 ± 63,64	18 562 479,71	79,52	10 399 148,48
	O	U	141	128,56 ± 56,22	18 126,85	90,06	12 698,46
	Y	F	570 071	53,38 ± 44,80	30 430 374,81	-	-
	Y	M	404 592	62,42 ± 46,41	25 252 610,34	-	-
	Y	U	644	38,50 ± 32,90	24 793,22	-	-
2006	O	F	183 135	144,65 ± 60,02	26 490 815,34	83,85	15 355 869,75
	O	M	160 972	149,64 ± 62,06	24 088 307,74	80,27	12 921 222,44
	O	U	141	137,85 ± 67,38	19 437,50	81,38	11 474,58
	Y	F	714 238	60,80 ± 47,70	43 425 042,38	-	-

Table 4-24 (cont.): Possible cost savings due to generic substitution per gender							
Year	Generic indicator	Gender	Number of items	Average cost per item (R)	Total cost (R)	in average cost (R)	Possible saving (R)
	Y	M	533 081	69,37 ± 48,39	36 978 744,63	-	-
	Y	U	530	56,47 ± 39,17	29 931,03	-	-
2007	O	F	162 071	146,69 ± 62,94	23 774 706,85	75,83	12 289 843,93
	O	M	139 438	150,37 ± 66,30	20 966 839,44	70,45	9 823 407,10
	O	U	14	124,54 ± 31,10	1 743,51	53,71	751,94
	Y	F	717 115	70,86 ± 52,46	50 814 680,56	-	-
	Y	M	534 079	79,92 ± 52,14	42 684 124,10	-	-
	Y	U	26	70,83 ± 43,00	1 841,47	-	-
2008	O	F	123 036	144,83 ± 65,32	17 819 180,82	70,23	8 640 818,28
	O	M	107 529	147,38 ± 68,68	15 847 521,21	65,71	7 065 730,59
	Y	F	745 223	74,60 ± 53,22	55 590 178,59	-	-
	Y	M	586 201	81,67 ± 51,77	47 873 531,35	-	-

From Table 4-24 the following observations were made:

- If all female patients opted for substitution with generic equivalent antihypertensive medicine a cost saving of almost 60% (n = R13 154 244,52, N = R21 599 548,20) could have been achieved during 2005.
- If all male patients opted for substitution with generic equivalent antihypertensive medicine during 2005, a cost saving of 44% (n = R10 399 148,48, N = R21 599 548,20) could have been achieved.
- During 2006 a cost saving of almost 54% (n = R15 355 869,75, N = R28 288 566,77) could have been achieved if female patients had opted for substitution with generic equivalent antihypertensive medicine items, and if all male patients had asked for substitution with generic equivalent antihypertensive medicine a cost saving of R12 921 222.44 could have been possible.
- During 2007 generic substitution by female patients could have achieved savings of almost 56%, while savings of up to 44% could have been achieved if male patients had opted for substitution with generic equivalent medicine items.
- If all female patients had opted for substitution with generic equivalent antihypertensive medicine, a cost saving of almost 55% (n = R8 640 818,28, N = R15 706 548,87) could have been achieved during 2008, and if all male patients opted for substitution with generic

equivalent antihypertensive medicine during the same year, a cost saving of 45% (n = R7 065 730,59, N = R15 706 548,87) could have been achieved.

- A total possible cost saving of R89 675 210,07 (18%, N = R502 294 559,65) could have been achieved over the four-year study period if generic substitution had been implemented.

Thus far in this section, the number of male and female hypertensive patients and generic substitution of antihypertensive medicine items to the different genders have been discussed, and possible cost savings that can be achieved if generic substitution is implemented have been estimated. In Table 4-25 the average number of prescriptions per patients and average number of items per prescription for the different genders are summarised.

Table 4-25: Summary of antihypertensive prescription statistics according to gender

Year	Gender	Number of prescription	Average number of prescriptions per patient	Average number of items per prescription	Average cost per antihypertensive prescription (R)
2005	F	127 441	6,54 ± 5,14	1,34 ± 0,60	139,92 ±111,54
	M	91 717	6,59 ± 5,10	1,36 ± 0,63	158,76 ± 119,86
	U	120	6,54 ± 4,94	1,34 ± 0,59	111,68 ± 119,25
2006	F	130 165	6,89 ± 5,13	1,36 ± 0,62	136,71 ± 109,60
	M	96 660	6,89 ±5,07	1,39 ± 0,66	154,18 ± 117,98
	U	99	6,39 ± 5,46	1,31 ± 0,50	120,31 ± 84,30
2007	F	111 684	7,52 ± 5,15	1,37 ± 0,64	144,11 ± 112,70
	M	81 537	7,62 ± 5,08	1,40 ± 0,68	162,38 ± 122,67
	U	11	4,00 ± 4,43	1,32 ± 0,52	149,95 ± 81,91
2008	F	103 650	7,67 ± 5,14	1,39 ± 0,66	141,39 ±111,03
	M	79 035	7,67 ± 5,01	1,43 ± 0,70	156,75 ±122,00
	U	-	-	-	-

From Table 4-25 the following observations were made:

- More prescriptions were issued to female patients than to their male counterparts. According to Fodor and Tzerovska (2004:34), men are generally less aware of their hypertension and consequently receive less therapy than women. This can possibly be a reason for the higher number of antihypertensive medicine prescriptions and items issued to female patients.

- The average number of prescriptions per patient per year was, however, more equal between male and female patients, namely 6,54 prescriptions per female patient as opposed to 6,59 prescriptions per male patient during 2005 and 7,52 prescriptions per female patient as opposed to 7,62 prescriptions per male patient during 2007.
- During 2006 and 2008 the average number of prescriptions per patient was equal for female and male patients.
- From the average number of prescriptions per patient it can be assumed that patients only refilled their prescriptions every second month. However, since hypertension is a chronic disease that needs treatment every day, it can therefore be assumed that not all patients complied with their treatment. Compliance or adherence will, however, be determined in a later section.
- The average cost per prescription was higher for male patients than for female patients throughout the four-year study period, but if d-values are calculated, this difference in the average cost per prescription can be seen as not practically significant (d-values ranging between 0,12 and 0,15).

4.5.4.7 Prescribing patterns of antihypertensive medicine items according to pharmacological group, treatment category, generic indicator and gender

In this section the number of antihypertensive medicine items are discussed according to pharmacological group, treatment category, generic indicator and gender. These findings are summarised in Appendix G and Appendix H.

Table G1 in Appendix G summarises the number of antihypertensive medicine items according to pharmacological group and patient gender. From Table G1 the following observations were made:

- Throughout all four study years more beta-receptor blockers were prescribed to female patients than to male patients. Both the prevalence percentage (for 2005 = 61,3%, for 2006 = 61%, for 2007 = 60% and for 2008 = 59,1%) and cost percentage (for 2005 = 62%, for 2006 = 61,3%, for 2007 = 61,5% and for 2008 = 61%) were higher for female patients. The calculated CPIs (CPI = 1) indicated that there was an equilibrium between the cost and prevalence of beta-receptor blockers prescribed to female patients.
- Female patients showed a higher usage of calcium channel blockers than their male counterparts throughout all four study years. The average cost for calcium channel blockers was higher for those prescribed and dispensed to male patients, but the small d-values (<0,2) indicated that these differences were of no practical or statistical significance.

- Throughout all four study years more ACE inhibitors were prescribed to female patients than to their male counterparts. Both the prevalence percentage (for 2005 = 53%, for 2006 = 52%, for 2007 = 52% and for 2008 = 55%) and cost percentage (for 2005 = 56%, for 2006 = 52%, for 2007 = 52% and for 2008 = 54%) were higher for female patients. The calculated CPIs (CPI = 1) indicated that there was an equilibrium between the cost and prevalence of the ACE inhibitors prescribed to female patients.
- Female patients showed a higher usage of angiotensin-receptor blockers (ARBs) than their male counterparts throughout all four study years. During 2005 approximately 56% of ARBs were prescribed to female patients, accounting for R29 961 525,64 (56%, N = R53 380 408,70) of the total cost of ARBs. The same trends can be seen for 2006, 2007 and 2008, with the prevalence percentage and cost percentage almost in equilibrium.
- During 2005 66% of all diuretics that were prescribed were prescribed to female patients, accounting for 63% of the total cost of the diuretics (N = R22 911 035,73). This trend continued during 2006, 2007 and 2008. The average cost of the diuretic medicine items was higher for male patients than for their female counterparts. However, the calculated d-values for these average costs showed that the difference in these values was of no practical or statistical significance (d-values<0.2).

Table H1 – H4 in Appendix H summarises the number of antihypertensive medicine items according to pharmacological group, treatment category, generic indicator and patient gender. From table H1 – H4 the following observations were made:

- Throughout all four study years the generic items seemed to have a higher prevalence than the original antihypertensive medicine items.
- It was also noted that the average cost of the generic products were substantially lower than the average cost of the original products. The practical and statistical significance of these differences is proofed in the calculated d-values.
- Medicine items prescribed in treatment category 2 (i.e. MIMS group 16.1) had the lowest prevalence for both genders and generic indicators, but it was noticed that the generic products had a slightly higher prevalence and cost percentage.
- For diuretic products the prevalence and cost percentages were the lowest in treatment category 1, which was expected, since the treatment category included only antihypertensive medicine items from MIMS group 7.3. However, throughout all four study years it was seen that diuretic items prescribed as part of treatment category 3 showed a higher prevalence and cost percentage than those prescribed as part of treatment category 2.

To summarise, Section 4.5.4 investigated aspects of antihypertensive medicine usage among patients of different genders. In Section 4.5.5 the different combinations of antihypertensive medicine items observed in the database are examined.

4.5.5 Combination antihypertensive therapy

As was stated in Chapter 2, Paragraphs 2.10.8.2 and 2.10.11, when a patient is diagnosed with 'high blood pressure' a step-wise approach is used in the treatment thereof. Usually, step one of treating hypertension is for the patient to make some lifestyle changes, including reduction in salt intake, increase in exercise, etc. Once the patient has made these lifestyle changes and the hypertensive state stays unchanged after three months, medicine treatment is started (see Paragraph 2.10.8.2). Treatment is usually started with a thiazide diuretic, if the patient has no other major risk factors such as diabetes, chronic heart failure, angina, prostatism, to name a few (see Chapter 2, Paragraph 2.10.8.2). According to the South African Hypertension Society (SAHS), the three classes or types of antihypertensive medicine that can be used to treat patients with no compelling risk factors include diuretics, ACE inhibitors and calcium channel blockers (Seedat *et al.* 2006:344).

If treatment to control hypertension fails and upward dose-titration was not successful, a trial of sequential monotherapy can be followed until an effective agent is found. Lastly, more than one antihypertensive drug can be used to control hypertension (Schultz, 2009:24). According to the South African Department of Health's fourth edition of the Standard Treatment Guidelines and Essential Drugs List for Primary Health Care (EDL) of the Essential Drugs Programme, published in 2008, the treatment for the management of hypertension indicates that treatment is started with a diuretic. Failure to reach blood pressure goals can lead to the addition of an ACE inhibitor or calcium channel blocker. If the blood pressure goal is achieved, both the ACE inhibitor and the calcium channel blocker are added to the thiazide. Further failure to reach the blood pressure goal can lead to the addition of atenolol 50 mg (a beta-receptor blocking agent) (Pudifin *et al.* 2008). The SAHS Guidelines (Seedat & Rayner, 2012:72) state that regardless of the classes of antihypertensive items that are combined, combination therapy will as a rule result in the lowering of blood pressure. The usage of one-pill combination (fixed-dose combination) products is encouraged because it will lead to better adherence, since the number of daily tablets is reduced. These fixed-dose combinations should not elicit additive adverse effects. The most effective blood pressure-reducing antihypertensive medicine combinations are diuretics and beta-receptor blockers, diuretics and ACE inhibitors or angiotensin-receptor blockers, calcium channel blockers with ACE inhibitors, and beta-receptor blockers with alpha-receptor blockers. Synergistic effects can also be achieved with ACE inhibitors or angiotensin-receptor blockers combined with either calcium channel blockers or diuretics (Seedat *et al.*

2006:348; Seedat & Rayner, 2012:72). In this section the combination therapy observed in the data is discussed (the third research question). In Table 4-25 an illustration is given of the number of observations for prescriptions containing one and more antihypertensive medicine items.

Table 4-26: Number of observations for prescriptions containing one or more antihypertensive items in combination

Year	One item	Two items	Three items	Four items	Five items	Six items	Seven items	Eight items
2005	5 849	23 042	15 780	3 688	487	48	5	1
2006	5 567	22 472	17 037	4 500	661	92	15	2
2007	4 416	18 935	15 757	4 339	682	91	12	-
2008	4 120	17 688	15 408	4 639	829	104	11	3

From Table 4-26 it can be seen that most observations were made for prescriptions containing two or three antihypertensive agents. For the purposes of this study only the top ten combinations for each year and age group will be discussed. These results are summarised in Appendix I, Table I1 – Table I31. The PDDs (prescribed daily dosages) of the antihypertensive items used will be discussed. In Table 4-27 the recommended daily dosages, together with the maintenance dose and maximum daily dosages of the most frequently prescribed antihypertensives, are summarised (Rossiter *ed.* 2010:130-164).

Table 4-27: Summary of the recommended-, maintenance- and maximum daily dose of the most frequently prescribed antihypertensives

Pharmacological group	Active ingredient	Recommended daily dose	Maintenance dose per day	Maximum dose per day
Diuretics	Spironolactone	100-400mg	-	400mg
	Furosemide	40-200mg	20-40mg	200mg
	Indapamide	2.5mg	-	5mg
	HCTZ	25-50mg	-	100mg
	Bumetanide	1mg	0.5 – 2mg	2mg
	Bumetanide/KCl	0.5/573mg	-	1/1146mg (2 tablets daily)
	Torsemide	2.5mg	2.5mg	5mg
	Amiloride*	2.5-10mg		-
	Triamterene/HCTZ	50/25mg two times per day	50/25mg	-

Table 4.27 (cont.): Summary of the recommended-, maintenance- and maximum daily dose of the most frequently prescribed antihypertensives

Pharmacological group	Active ingredient	Recommended daily dose	Maintenance dose per day	Maximum dose per day
Central acting inhibitors	Methyldopa	250mg	1500 – 2000mg	3000mg
	Moxonidine	0.2mg	-	0.4mg
Alpha-receptor blocker	Doxazosin	1mg		16mg
	Prazosin	1mg	-	16mg
	Alfuzosin	10mg		10mg
Beta-receptor blocker	Bisoprolol	5-10mg	-	20mg
	Bisoprolol/HCTZ	2.5/6.25mg	-	10/6.25mg
	Nebivolol	5mg		
	Sotalol	160mg		600mg
Alpha- and beta-receptor blocker	Carvedilol**	12.5mg	25 – 50mg	50mg
Sympathetic nervous blockers	Ergocristine/Clopidamide/ Reserpine	1/10/0.2mg	0.5/5/0.1mg	
Direct-acting vasodilator	Hydralazine	10 – 20mg two to four times per day	100 – 200mg	300 mg
	Minoxidil	5 – 40mg	-	100mg
Calcium channel blocker	Amlodipine	5mg	-	10mg
	Nifedipine	10mg three times per day	-	60 – 80mg in divided doses
	Lercanidipine	10mg	-	20mg
	Verapamil	80-120mg three times daily	-	480mg
ACE-inhibitor	Perindopril	4mg	-	8mg
	Enalapril	10-20mg	20mg	20mg
	Lisinopril	10mg	20mg	40mg
	Captopril	12.5mg three times daily	-	150mg
	Quinapril	10mg		20-40mg
	Trandolapril/Verapamil	2/180mg		2/180mg
	Ramipril/Felodipine	2.5/2.5mg or 5.5mg	2.5/2.5mg or 5.5mg	-
Angiotensin-receptor blockers	Valsartan	80mg or 160mg	-	320mg
	Eprosartan	600mg	-	800mg
	Candesartan	8mg	8 – 16mg	32mg

Table 4.27 (cont.): Summary of the recommended-, maintenance- and maximum daily dose of the most frequently prescribed antihypertensives

Pharmacological group	Active ingredient	Recommended daily dose	Maintenance dose per day	Maximum dose per day
	Irbesartan	150mg	-	300mg
	Candesartan/HCTZ	16/12.5mg	-	16/12.5mg
	Losartan/HCTZ	50/12.5mg	-	100/25mg
	Valsartan/HCTZ	80/12.5mg	Clinical appropriate dose	320/25mg
	Telmisartan/HCTZ***	40/12.5mg	-	80/12.5mg

*Amiloride is only available in combination with HCTZ

**Carvedilol must be administered in divided doses to elderly patients

***Telmisartan/HCTZ can only be prescribed after stabilising on individual components

The recommended daily dose for spironolactone usage in children is 3 mg/kg body weight per day, not exceeding 120 mg per day. For furosemide, the dosage for use in children is between 1 and 3 mg/kg body weight per day, and not exceeding 120 mg per day (Snyman, 2010).

4.5.5.1 Single agents prescribed

Tables I1 to I4 analyse prescriptions where single antihypertensive items were observed. From these tables it can be seen that the most frequently prescribed antihypertensive medicine items as single agents included ACE inhibitors, diuretics, calcium channel blockers, beta-receptor blockers and one-pill combination products, e.g. an indapamide/perindopril combination product. The ACE inhibitors most frequently prescribed as monotherapy included perindopril, enalapril and lisinopril. The prescribed daily doses (PDDs) for these ACE inhibitors corresponded with the dosing guidelines provided in Table 4-27. For perindopril the PDD was 4 mg, while for enalapril and lisinopril the PDDs were 10 mg and 20 mg respectively.

The diuretic products most frequently prescribed included medicine items containing the active ingredients spironolactone, furosemide and indapamide, as well as the one-pill combination product consisting of amiloride and HCTZ. The PDD for spironolactone was 25 mg or 100 mg per day. Furosemide had a PDD of 20 mg per day and therefore falls within the guidelines. For indapamide a PDD of 37,5 mg per day was observed in 2005. This is an indication of possible over-use, since the recommended daily dose is only 2,5 mg per day. However were other observations made where the PDD for indapamide ranged between 1,5 mg and 2,5 mg per day. In 2005 the one-pill combination of amiloride and HCTZ showed a PDD of 75/750 mg per day, meaning that the patient would have to take 15 tablets per day. This is an indication of possible over-usage. This was also observed for patients in AG1, and according to Snyman *et al.* (2010), this one-pill combination product is contra-indicated in children. During 2006-2008 the amiloride/HCTZ combination product had a PDD of 5/50 mg per day, which falls within the dosing guidelines (see Table 4-27).

The only calcium channel blocker prescribed was amlodipine, with a PDD of 5 mg or 10 mg per day, while the only beta-receptor blocker prescribed was bisoprolol, with a PDD of 2,5 mg or 5 mg per day. For both these products the PDDs observed were within the recommended daily dosage.

According to the South African Hypertension Guidelines (2011), hypertension treatment should be started or initiated with a diuretic, an ACE inhibitor or a calcium channel blocker. Therefore it can be concluded that all the antihypertensive products that were prescribed as monotherapy were in line with the guidelines provided by the SAHS (Seedat & Rayner, 2012:67). The average cost of all the prescriptions containing one antihypertensive medicine item ranged between R107,80 ± R67,39 and R113,25 ± R75,20 during the four-year study period.

4.5.5.2 Prescriptions containing two antihypertensive medicine items

The top ten prescriptions containing two antihypertensive medicine items are summarised in Tables I5 to I8. The most frequently prescribed combination of antihypertensive medicine items was an ACE inhibitor in combination with a diuretic. In a number of combinations the one antihypertensive medicine item was a product containing two active ingredients, usually diuretics. There were also a number of prescriptions containing two diuretic medicine items (e.g. furosemide and spironolactone or HCTZ and spironolactone). However, this combination occurred only for patients treated for hypertension that fell in AG1.

Antihypertensive combination prescriptions prescribed to patients in age group 1

During 2005 the following antihypertensive combination prescriptions had the highest prevalence:

- The ACE inhibitor-diuretic combination products that were most often prescribed were the combination of captopril and furosemide.
- There were 17 prescriptions observed containing this combination with a PDD of 25/20 mg.
- There were also 11 prescriptions with the captopril furosemide combination with a PDD of 12,5/20 mg and 37,5/300 mg. As stated by Snyman (2010), the furosemide dosage in children should be between 1 and 3 mg/kg body weight and should not exceed 120 mg per day. However, since the actual age of the specific patient was not known, and the patients in AG1 were aged between 1 year and 18 years, it cannot be determined whether the PDD exceeded the maximum daily dose.

During 2006 the following antihypertensive combination prescriptions had the highest prevalence:

- The combination amlodipine 5 mg (a calcium channel blocker) with perindopril 4 mg (an ACE inhibitor) had the highest frequency with 22 prescriptions.
- There were two other combinations of a calcium channel blocker and an ACE inhibitor, namely amlodipine 5 mg with lisinopril 10 mg and amlodipine 10 mg with enalapril 10 mg. There were nine prescriptions containing the first combination, at an average cost of R153,90 ± R2,08 per prescription, and there were eight prescriptions containing the amlodipine/enalapril combination at an average cost of R210,72 ± R0,37.

During 2007 the following antihypertensive combination prescriptions had the highest prevalence:

- The combination of the calcium channel blocker amlodipine 5 mg with the ACE inhibitor perindopril 4 mg had the highest prevalence, with a total of 17 prescriptions at a total cost of R4 932,10 and an average cost of R290,12 ± R6,61.
- There were 16 prescriptions for the combination of furosemide with spironolactone.
- Eight of these prescriptions were for furosemide 20 mg and spironolactone 25 mg, while for the other eight prescriptions furosemide had a PDD of 40 mg.
- The furosemide 20 mg spironolactone 25 mg combination prescriptions had a higher average cost per prescription (R119,55 ± R2,11) than the prescriptions containing furosemide 40 mg (R51,16 ± R4,36). This can be attributable to the fact that where furosemide 40 mg was prescribed, a generic equivalent was dispensed.
- In total there were 20 prescriptions containing captopril and furosemide. The PDDs for five of these prescriptions were 250 mg captopril and 21,42 mg furosemide. This exceeded the maximum daily dose for captopril, which is set at 150 mg per day in divided doses. This can lead to adverse effects and possible patient non-compliance.

During 2008 the following antihypertensive combination prescriptions had the highest prevalence:

- The highest prevalence was seen for the combination of an ACE inhibitor with a diuretic.
- The ACE inhibitor/diuretic combination products that were most often prescribed were the combination of furosemide and lisinopril.
- There were 13 prescriptions observed containing this combination, with a PDD of 40/10 mg. These prescriptions had an average cost of R90,92 ± R2,16.

- There were nine prescriptions each of the calcium channel blocker/diuretic combination of amlodipine 5 mg with spironolactone 25 mg and the alpha- and beta-receptor blocker/ACE inhibitor combination of carvedilol 12,5 mg with lisinopril 10 mg.

Antihypertensive combination prescriptions prescribed to patients in age group 2

During 2005 the following antihypertensive combination prescriptions had the highest prevalence for patients in AG2:

- 525 prescriptions containing the combination enalapril with indapamide were prescribed. The PDD of enalapril was 20 mg for 279 of these prescriptions, while the remaining 246 prescriptions' enalapril had a PDD of 10 mg. For all 525 prescriptions the PDD of indapamide was 2,5 mg. The combination that occurred the most for AG2 during 2005 was indapamide 2,5 mg, with perindopril 4 mg with a frequency of 749, and accounting for a total cost of R111 854,70.

During 2006 the following antihypertensive combination prescriptions had the highest prevalence:

- All but one of the top ten prescriptions containing two antihypertensive items for AG2 during 2006 was a combination between an ACE inhibitor and diuretic.
- The second highest number of prescriptions in this age group was a combination of a diuretic (the one-pill combination amiloride/HCTZ 5/50 mg) with a central acting inhibitor (reserpine 0,25 mg). This combination accounted for 529 of all the two-antihypertensive-item combination prescriptions and had an average cost of R52,38 ± R17,24 per prescription.
- The combination of indapamide 2,5 mg with perindopril 4 mg had the highest prevalence of 848 prescriptions, with a total cost R 128 073,17.
- Indapamide 2,5 mg and amiloride/HCTZ 5/50 mg were the two antihypertensive items most commonly prescribed in combination with another antihypertensive medicine item.

During 2007 the following antihypertensive combination prescriptions had the highest prevalence:

- The diuretic/ACE inhibitor combination of indapamide 2,5 mg with perindopril 4 mg had the highest prevalence.
- This combination accounted for 595 of the prescriptions, with an average cost of R150,27 ± R18,71 and a total cost of R89 412,27.
- The second highest number of prescriptions was for the combination of amlodipine 5 mg with the one-pill combination indapamide/perindopril 2,5/4 mg. Approximately 435

prescriptions were for this combination, accounting for approximately 0,16% (n = R107 700,36, N = R721 32 873,03) of the total cost for two-item combination prescriptions during 2007.

During 2008 the following antihypertensive combination prescriptions had the highest prevalence:

- The calcium channel blocker-diuretic/ACE inhibitor combination of amlodipine 5 mg with indapamide/perindopril 1,25/4 mg had the highest prevalence.
- This combination accounted for 582 of all the prescriptions with an average cost of R234,52 ± R49,16 and a total cost of R136 491,26.
- The second highest number of prescriptions in this age group was for the same combination of amlodipine with the one-pill combination indapamide/perindopril.
- Amlodipine had a PDD of 10 mg, while the PDD for the one-pill combination indapamide/perindopril was 1,25/4 mg per day. Approximately 451 prescriptions were for this combination, accounting for approximately 0,18% (n = R121 800,65, N = R68 816 568,47) of the total cost for two-item combination prescriptions during 2008.

Antihypertensive combination prescriptions prescribed to patients in age group 3

During 2005 the following antihypertensive combination prescriptions had the highest prevalence for patients in AG3:

- The combination indapamide 2,5 mg with perindopril 4 mg had the highest frequency, with 6 281 prescriptions containing this combination. The total cost was R947 794,15, with an average cost of R150,90 ± R14,66 per prescription. The total cost for all two-item combination prescriptions in all age groups containing two antihypertensive medicine items amounted to R67 859 319,49 with an average cost of R203,95 ± R116,15 per prescription for 2005.

During 2006 the following antihypertensive combination prescriptions had the highest prevalence for patients in AG3:

- The indapamide 2,5 mg and perindopril 4 mg combination had the highest number of prescriptions with 6 795 with an average cost of R152,21 ± R12,75.
- This combination accounted for 1,42% (n = R1 034 265,68, N = R72 685 539,04) of the total cost for prescriptions consisting of two antihypertensive medicine items.

During 2007 the following antihypertensive combination prescriptions had the highest prevalence:

- The diuretic-ACE inhibitor combination of indapamide 2,5 mg with perindopril 4 mg had the highest prevalence.
- The indapamide 2,5 mg/perindopril 4 mg combination prescriptions accounted for 5 324 of the total two-item combination prescriptions for 2007. On average these prescriptions cost R153,07 ± R16,84 per prescription, totalling R814 942,48.
- The second highest number of two-item prescriptions in AG3 was for the combination of amlodipine 5 mg with indapamide/perindopril 1,25/4 mg.

During 2008 the following antihypertensive combination prescriptions had the highest prevalence:

- The calcium channel blocker-diuretic/ACE inhibitor combination of amlodipine 5 mg with indapamide/perindopril 1,25/4 mg had the highest prevalence.
- The amlodipine 5 mg/indapamide/perindopril 1,25/4 mg combination prescriptions accounted for 28,12% (n = 4 469, N = 17 688) of the total two-item combination prescriptions, with an average cost of R245,32 ± R29,41 per prescription, totalling R1 096 322,83.
- The second highest number of two-item prescriptions was the combination of indapamide 2,5 mg with perindopril 4 mg.

Summary of the two-item combination prescriptions

- During all four study years the combination of an ACE inhibitor and diuretic was the most frequently prescribed.
- During 2005 indapamide was the most prescribed antihypertensive medicine item, with approximately 56 106 prescriptions containing indapamide as one of the antihypertensive medicine items in the prescription.
- HCTZ was second with approximately 37 345 prescriptions.
- The total cost for all two-item combination prescriptions in 2005 amounted to R67 859 319,49, with an average cost of R203,98 ± R116,15 per prescription.
- A total of 332 676 prescriptions were observed.
- During 2006 indapamide was the most prescribed antihypertensive medicine item. Approximately 61 161 prescriptions contained indapamide as one of the antihypertensive items in the prescription.
- The total cost for all two-item combination prescriptions in all age groups amounted to R72 685 539,04, with an average cost of R195,75 ± R110,19 per prescription for 2006.

- A total of 371 325 prescriptions were observed.
- During 2007 the calcium channel blocker amlodipine was the most prescribed antihypertensive item in two-item combination prescriptions. Approximately 65 123 prescriptions contained amlodipine as one of the antihypertensive items in the prescription.
- The total cost in all age groups for all two-item combination prescriptions containing two antihypertensive medicine items amounted to R72 132 873,03 with an average cost of R207,87 ± R107,41 per prescription for 2007.
- A total of 347 015 prescriptions were observed.
- During 2008 the calcium channel blocker amlodipine was the most prescribed antihypertensive item in two-item combination prescriptions. Approximately 73 211 prescriptions contained amlodipine as one of the antihypertensive items in the prescription.
- The total cost in all age groups for all two-item combination prescriptions containing two antihypertensive medicine items amounted to R68 819 568,47 with an average cost of R198,47 ± R104,28 per prescription for 2008.
- A total of 346 732 prescriptions in 17 688 different combinations were observed.

As was stated previously, the South African Hypertension Guidelines (Seedat & Rayner, 2012:67) suggest that hypertension treatment should be initiated with a low-dose diuretic, and if target blood pressure or control is not achieved, combination therapy should be introduced with another first-choice antihypertensive drug. It can therefore be concluded that all the prescriptions consisting of two antihypertensive medicine items were in line with the guidelines for the combination treatment of hypertensive patients.

4.5.5.3 Prescriptions containing three antihypertensive medicine items

The top ten prescriptions containing three antihypertensive medicine items for all four study years are summarised in Tables I9 to I12.

Antihypertensive prescriptions prescribed to patients in age group 1

During 2005 the following three-item antihypertensive combination prescriptions had the highest prevalence for patients in AG1:

- The most prevalent combination was for an ACE inhibitor in combination with two diuretics; 11 of these prescriptions were observed.

- Five prescriptions consisted of the following products: enalapril 4,67 mg, furosemide 40 mg and spironolactone 25 mg.
- The average cost of these prescriptions was R242,31 ± R0,01, totalling R1 211,57.
- One observation, accounting for eight prescriptions, consisted of the combination amlodipine 10 mg, enalapril 20 mg and HCTZ 12,5 mg. These eight prescriptions had an average cost of R263,12 ± R0,01 per prescription with a total cost of R2 104,94.

During 2006 the following three-item antihypertensive combination prescriptions had the highest prevalence for patients in AG1:

- 103 prescriptions were prescribed to patients in AG1 in 41 different combinations.
- The most prevalent combination was for an ACE inhibitor in combination with two diuretics, totalling 21 prescriptions in three different combinations.
- Ten prescriptions consisting of captopril 12,5 mg, HCTZ 12,5 mg and spironolactone 12,5 mg had an average cost of only R35,27 ± R0,01. This may be due to the fact that for all three of these active ingredients a generic equivalent was prescribed.
- Five prescriptions consisting of captopril 25 mg, furosemide 40 mg and spironolactone 25 mg had an average cost of only R14,12 ± R0,04. All of these active ingredients were also prescribed as a generic equivalent.
- Six prescriptions consisting of enalapril 4,67 mg, furosemide 40 mg and spironolactone 25 mg had an average cost of R231,79 ± R1,04. In these prescriptions only the spironolactone product was a generic equivalent, while the enalapril product was an original and the furosemide product was one for which no generic equivalent was available.

During 2007 the following three-item antihypertensive combination prescriptions had the highest prevalence for patients in AG1:

- Seventy-three prescriptions in 39 different combinations were prescribed to patients in AG1.
- The combination of an ACE inhibitor with two diuretics had the highest prevalence, accounting for 16 prescriptions in four different combinations among the top 10 combinations.
- The combination of enalapril 5 mg, furosemide 20 mg and spironolactone 25 mg had the highest prevalence, with eight prescriptions and an average cost of R146,22 ± R0,57 per prescription and a total cost of R1 169,76. For both enalapril and spironolactone a generic equivalent product was prescribed.

- The combination with the highest prevalence was the combination for amlodipine 10 mg, doxazosin 4 mg and HCTZ 12,5 mg with 11 prescriptions. These 11 prescriptions had an average cost of R466,38 ± R3,23 per prescription with a total cost of R5 130,18.

During 2008 the following three-item antihypertensive combination prescriptions had the highest prevalence for patients in AG1:

- Sixty-two prescriptions in 27 different combinations were prescribed to patients in AG1.
- The combination of an ACE inhibitor with two diuretics had the highest prevalence, accounting for 19 prescriptions in four different combinations among the top 10 combinations.
- Nine prescriptions consisted of enalapril 10 mg, HCTZ 12,5 mg and spironolactone 100 mg, with a total cost of R1 776,15 and an average cost of R197,35 ± R3,87 per prescription. All the items in these prescriptions were generic equivalents.
- The other 10 prescriptions consisted of enalapril, furosemide and spironolactone, but with different PDDs.

Combination prescriptions prescribed to patients in age group 2

During 2005 the following three-item combination prescriptions had the highest prevalence for patients in AG2:

- In AG2 there were 3 028 prescriptions observed with a total cost of R1 033 368,04.
- The combination of the one-pill fixed-dose combination product amiloride/HCTZ 5/50 mg, perindopril 4 mg and reserpine 0,25 mg was the most frequently prescribed combination to patients, with 22 prescriptions. These combinations had an average cost of R152,13 ± R0,51 and a total cost of R3 346,88.

During 2006 the following observations were made for three-item combination prescriptions for patients in AG2:

- 3 974 three-item combination prescriptions were prescribed in 1 179 different combinations.
- The combination with the highest prevalence in the top 10 for AG 2 was the combination of a calcium channel blocker, a diuretic and an ACE inhibitor.
- The three-item combination prescription with the highest prevalence, i.e. 39 prescriptions, consisted of the following antihypertensive medicine items: amlodipine 5 mg, indapamide 2,5 mg and perindopril 4 mg, with an average cost of R249,60 ± R6,88 per prescription, totalling R9 734,56. The PDDs of all the items in these prescriptions were in line with the recommended guidelines as summarised in Table 4-27.

During 2007 the following observations were made for three-item combination prescriptions for patients in AG2:

- The highest prevalence was seen for combination prescriptions consisting of a calcium channel blocker, a diuretic and an ACE inhibitor. Approximately 131 prescriptions in the top 10 combinations consisted of antihypertensive items from these pharmacological groups.
- The highest prevalence was 40 prescriptions, consisting of amlodipine 5 mg, indapamide 2,5 mg and spironolactone 4 mg, with an average cost of R240,96 ± R15,50 per prescription with a total cost of R9 638,53.
- Seventy-three prescriptions consisted of a calcium channel blocker, a beta-receptor blocker and the fixed-dose combination of a diuretic with an ACE inhibitor.
- The specific combination of amlodipine 10 mg, bisoprolol 10 mg and the fixed-dose combination indapamide/perindopril 1,25/4 mg had the highest prevalence for this combination, i.e. 41 prescriptions. These 41 prescriptions had a total cost of R15 387,97 with an average cost of R375,32 ± R7,34 per prescription. The PDDs in these prescriptions were all in line with the recommended dosages, as summarised in Table 4-27.

During 2008 the following observations were made for three-item combination prescriptions for patients in AG2:

- Four thousand and ninety-six three-item combination antihypertensive prescriptions were prescribed to patients in AG2.
- The combination of a calcium channel blocker, beta-receptor blocker and fixed-dose combination of a diuretic and an ACE inhibitor had the highest prevalence, accounting for 126 prescriptions in three different combinations.
- Sixty-one prescriptions consisted of amlodipine 10 mg, bisoprolol 5 mg and the fixed-dose combination of indapamide/perindopril 1,25/4 mg, with an average cost of R332,78 ± R18,36 per prescription, totalling R20 299,81.
- Ninety-nine prescriptions consisted of a calcium channel blocker with a diuretic and an ACE inhibitor.
- Thirty prescriptions consisted of amlodipine 5 mg, indapamide 2,5 mg and perindopril 4 mg, with an average cost of R237,37 ± R29,37 per prescription with a total cost of R7 121,00.

Combination prescriptions prescribed to patients in age group 3

During 2005 the following observations were made for three-item combination prescriptions for patients in AG3:

- For patients in AG3 the most prevalent combination was an alpha- and beta-receptor blocker, a diuretic and an ACE inhibitor.
- Four different observations were made for this combination.
- Twenty-two prescriptions consisted of the active ingredients carvedilol 25 mg, indapamide 2,5 mg and perindopril 4 mg, and accounted for 0,23% ($n = R49\ 510,28$, $N = R21\ 506\ 187,81$) of the total cost of all three-item combination prescriptions, with an average cost of $R246,32 \pm R17,26$ per prescription.
- The second highest prevalence was for a calcium channel blocker, a diuretic and an ACE inhibitor.
- This combination accounted for 295 prescriptions in three different combinations.
- The highest prevalence in this combination was 154 prescriptions with the active ingredients amlodipine 5 mg, indapamide 2,5 mg and perindopril 4 mg with an average cost of $R253,41 \pm R13,50$ per prescription with a total cost of $R39\ 025,63$.

During 2006 the following observations were made for three-item combination prescriptions for patients in AG3:

- There were 72 164 prescriptions in 15 817 different combinations prescribed and dispensed.
- Of these, 772 were for the combination of a calcium channel blocker, a diuretic and an ACE inhibitor.
- Four hundred of these prescriptions contained the active ingredients amlodipine 5 mg, indapamide 2,5 mg and perindopril 4 mg, These prescriptions accounted for 0,41% ($n = R102\ 056,02$, $N = R24\ 906\ 246,38$) of the total cost for three-item combination prescriptions.
- A total of 519 prescriptions consisted of an alpha- and beta-receptor blocker, a diuretic and an ACE inhibitor. The combination of carvedilol 25 mg, indapamide 2.5 mg and perindopril 4 mg accounted for 203 prescriptions, and had a total cost of $R50\ 489,67$ with an average cost of $R248,72 \pm R25,21$ per prescription.

During 2007 the following observations were made for three-item combination prescriptions for patients in age group 3:

- There were 72 264 prescriptions in 14 622 different combinations prescribed.

- The most frequently prescribed combination was a calcium channel blocker with a diuretic and an ACE inhibitor.
- The specific combination of amlodipine 5 mg, indapamide 2,5 mg and perindopril 4 mg were prescribed 433 times and had a total cost of R109 796,20 with an average cost of R253,57 ± R24,91 per prescription.

During 2008 the following observations were made for three-item combination prescriptions for patients in AG3:

- Three-item combination prescriptions accounted for 76 430 prescriptions in 14 289 different combinations.
- The combination of a calcium channel blocker, diuretic and ACE inhibitor had the highest prevalence. 1 275 prescriptions containing these three classes of antihypertensive medicine items were observed.
- 342 prescriptions consisted of amlodipine 5 mg, indapamide 2,5 mg and perindopril 4 mg at a total cost of R81 570,93 with an average cost of R238,51 ± R26,98 per prescription.
- 603 prescriptions consisted of a calcium channel blocker, beta-receptor blocker and fixed-dose combination of a diuretic and an ACE inhibitor.
- 281 prescriptions consisted of amlodipine 5 mg, bisoprolol 5 mg and the fixed-dose combination of indapamide/perindopril 1,25/4 mg, with an average cost of R297,05 ± R23,44 per prescription, totalling to R83 472,25.

Summary of the three-item combination prescriptions

- During 2005, 63 219 prescriptions consisting of three antihypertensive medicine items were observed in 15 780 different combinations with an average cost of R340,19 ± R153,14 per prescription and a total cost of R21 506 187,81.
- Fifty of these 63 219 prescriptions were prescribed to patients in AG 1 in 27 different combinations.
- During 2006, 76 241 prescriptions consisting of three antihypertensive medicine items were observed in 17 037 different combinations with an average cost of R326,68 ± R147,16 per prescription and a total cost of R24 906 246,38.
- During 2007, 78 484 prescriptions consisting of three antihypertensive medicine items were observed in 15 757 different combinations with an average cost of R337,20 ± R144,75 per prescription, totalling R26 465 030,69.

- During 2008, 80 588 prescriptions consisting of three antihypertensive medicine items were observed in 15 408 different combinations with an average cost of R324,58 ± R144,49 per prescription and a total cost of R26 157 169,23.

The South African Hypertension Guidelines (Seedat & Rayner, 2012:72) suggests that hypertension treatment should be initiated with a low-dose diuretic, and if target blood pressure or control is not achieved, combination therapy should be introduced with another first-choice antihypertensive drug. If target blood pressure is still not achieved, a third first-choice antihypertensive agent may be added (Schultz, 2009:26, Seedat & Rayner, 2012:72). It can therefore be concluded that all the prescriptions consisting of three antihypertensive medicine items was in line with the guidelines for the combination treatment of hypertensive patients.

4.5.5.4 Prescriptions containing four antihypertensive medicine items

The top ten prescriptions containing four antihypertensive medicine items for all four study years are summarised in Table I13 to I16.

Combination prescriptions prescribed to patients in age group 1

During 2005 the following observations were made for four-item combination prescriptions for patients in AG1:

- Four different combinations for prescriptions consisting of four antihypertensive medicine items were observed for hypertensive patients in AG1 during 2005, totalling 10 prescriptions.
- Six of these prescriptions, with an average cost of R331,52 per prescription and a total cost of R1 989,12, consisted of enalapril 5 mg, furosemide 33,33 mg, HCTZ 12.5 mg and spironolactone 25 mg.
- A further two prescriptions consisted of bumetanide 5 mg, captopril 37,5 mg, furosemide 120 mg and spironolactone 50 mg, These two prescriptions had an average cost of R271,22 per prescription.
- As can be seen from Table 4-27, all the PDDs for the items in these prescriptions were in line with the recommended guidelines.

During 2006 the following observations were made for four-item combination prescriptions for patients in AG1:

- Thirteen four-item combination prescriptions were prescribed to patients in AG1.

- Four of these prescriptions consisted of captopril 25 mg, furosemide 60 mg, sotalol 160 mg and spironolactone 25 mg. On three of these prescriptions the furosemide 60 mg that was prescribed had no generic equivalent available, and these prescriptions had an average cost of R585,44 per prescription, while the one prescription with an original product (in other words a furosemide product for which a generic equivalent is available) had a lower average cost, i.e, R455,68. A d-value to determine the significance could not be calculated, since no standard deviations on the average costs were measured.

During 2007 the following observations were made for four-item combination prescriptions for patients in AG1:

- It can be seen from Table I15 that there were only a total of 12 prescriptions prescribed in five different combinations.
- Nine prescriptions consisted of captopril 25 mg, furosemide 60 mg, sotalol 160 mg and spironolactone 25 mg.
- In six of these prescriptions all the items were original products with an average cost of R631,55 ± R79,87 per prescription.
- Two prescriptions contained a generic equivalent for captopril 25 mg and these prescriptions had an average cost of R611,89 per prescription.
- The remaining prescription had generic equivalents prescribed for both the captopril 25 mg and the spironolactone 25 mg, with a total cost of R546,81. As was seen from Table 4-27, all the PDDs in these prescriptions correlate with the suggested daily doses.
- Two prescriptions with the lowest average cost per prescription (R54.11) consisted of two ACE inhibitors and two diuretics, namely enalapril 5 mg, enalapril 10 mg, HCTZ 12.5 mg and spironolactone 50 mg. All the items in these prescriptions were generic equivalents, and this may be a reason for the low average cost of these prescriptions.

During 2008 the following observations were made for four-item combination prescriptions for patients in AG1:

- There were 19 four-item combination prescriptions prescribed to patients in AG1.
- Three observations, accounting for six prescriptions consisted of an alpha- and beta-receptor blocker, two diuretics and an ACE inhibitor.
- Four observations, accounting for 12 prescriptions, consisted of a beta-receptor blocker, an ACE inhibitor and two diuretics. The highest prevalence for this combination, i.e. eight prescriptions, contained bisoprolol 5 mg, enalapril 5 mg, furosemide 40 mg and

spironolactone 25 mg, with an average cost of R220,66 ± R69,43 per prescription and a total cost of R1 765,29.

Combination prescriptions prescribed to patients in age group 2

During 2005 the following observations were made for four-item combination prescriptions for patients in AG2:

- There were 545 prescriptions prescribed to hypertensive patients in AG2.
- Sixteen of the 545 prescriptions contained an alpha-receptor blocker (carvedilol 8 mg), a diuretic (indapamide 2,5 mg), a calcium channel blocker (nifedipine 60 mg) and an ACE inhibitor (perindopril 8 mg), with an average cost of R774,65 and a total cost of R12 394,40.
- Thirty-two prescriptions contained an alpha- and beta-receptor blocker, two diuretics and an ACE inhibitor. The only difference was in the active ingredients.
- Twelve of the 32 prescriptions consisted of carvedilol 25 mg, enalapril 20 mg, furosemide 240 mg and spironolactone 100 mg and accounted for 0,29% (n = R15 192,93, N = R5 190 360,09) of the total cost for four-item combination prescriptions, with an average cost of R1 266,08 ± R55,23.
- Ten of the 32 prescriptions consisted of carvedilol 25 mg, furosemide 160 mg, ramipril 5 mg and spironolactone 25 mg, with an average cost of R841,60 ± R8,04 per prescription.
- The last 10 prescriptions consisted of carvedilol 50 mg, furosemide 60 mg, perindopril 4 mg and spironolactone 25 mg, with an average cost of R369,00. The d-value of 58,8 between the average costs of these two sets of prescriptions is an indication that this difference is of practical significance. A possible reason for this difference may be the price difference in average cost between ramipril (R192,26 ± R66,31) and perindopril (R131,43 ± R30,42). This is emphasised by the d-value of 0,9 between these two products, which indicates that the difference is significant and of practical importance. Another reason may be the fact that the furosemide 60 mg is a generic equivalent of the innovator product and may therefore have a much lower average cost.

During 2006 the following observations were made for four-item combination prescriptions for patients in AG2:

- There were 734 prescriptions prescribed to patients in AG2.
- From Table I14 it can be seen that the most frequently prescribed groups of antihypertensive medicine items were combinations of alpha- and beta-receptor blockers, an ACE inhibitor and two diuretics.

- The combination of carvedilol 12,5 mg, furosemide 40 mg, perindopril 4 mg and spironolactone 25 mg accounted for 25 prescriptions.
- Thirteen of the 25 prescriptions contained an original furosemide product, while all the other medicine items were for generic equivalents, with an average cost of R367,70 ± R17,62 per prescription.
- Twelve of the 25 prescriptions consisted of only generic medicine items with an average cost of R250.61 ± R6.37. The high d-value (calculated between the average cost per prescription) of 6.6 is an indication that this difference in average cost is of practical significance.
- Twenty-three prescriptions consisted of the combinations carvedilol, enalapril, furosemide and spironolactone.
- Thirteen of 23 prescriptions, with an average cost of R1 255,22 ± R22,05 per prescription and a total cost of R16 317,86, had the following PDDs: carvedilol 25 mg, enalapril 20 mg, furosemide 240 mg and spironolactone 100 mg.
- The other 10 prescriptions consisted of carvedilol 12,5 mg, enalapril 10 mg, furosemide 40 mg and spironolactone 25 mg and had an average cost of R139,54 ± R33,37 per prescription, with a total cost of R1 395,44. Possible reasons for the difference in average cost could include the use of generic medicine items, smaller dosages, etc.
- Fourteen prescriptions consisted of amlodipine 10 mg, carvedilol 50 mg, indapamide 2,5 mg and perindopril 4 mg, totalling R6 340,89, with an average cost of R367,70 ± R17,62 per prescription.

During 2007 the following observations were made for four-item combination prescriptions for patients in AG2:

- The four-item combination prescriptions accounted for 699 prescriptions in 233 different combinations that were prescribed to patients in AG 2.
- The top 10 combinations are summarised in Table I15.
- Eighteen prescriptions consisted of the one-pill fixed-dose combination ergocristine/clopamide/reserpine 0,5/5/0,1 mg, the one-pill fixed-dose combination of losartan/HCTZ 100/25 mg, moxonidine 0,4 mg and nifedipine 60 mg, with an average cost of R174,02 ± R4,05 per prescription, totalling R3 132,42. All of the PDDs are within the suggested guidelines, as summarised in Table 4,23. All of the items on these prescriptions were antihypertensive medicine items with no generic equivalent available.

- Twelve prescriptions consisted of furosemide 80 mg, minoxidil 10 mg, nifedipine 60 mg and perindopril 8 mg, with an average cost of R402,61 ± R16,37 per prescription and a total cost of R4 831,32.
- From Table I15 it can also be seen that the fixed-dose combination of bisoprolol/HCTZ, with different PDDs, was the most prescribed antihypertensive medicine item in combination – it was prescribed in 88 prescriptions.

During 2008 the following observations were made for four-item combination prescriptions for patients in AG2:

- There were 738 four-item antihypertensive prescriptions prescribed and dispensed in 265 different combinations.
- Three observations, accounting for 35 prescriptions, consisted of an alpha- and beta-receptor blocker, an ACE inhibitor and two diuretics.
- Fourteen of the 35 prescriptions consisted of carvedilol 25 mg, furosemide 160 mg, lisinopril 10 mg and spironolactone 50 mg, with an average cost of R317,71 ± R12,99 per prescription, totalling R4 377,98.

Combination prescriptions prescribed to patients in age group 3

During 2005 the following observations were made for four-item combination prescriptions for patients in AG3:

- 10 210 prescriptions in 3 469 different combinations were prescribed.
- Four observations in the top 10 combinations, totalling 88 prescriptions, consisted of an alpha- and beta-receptor blocker, two diuretics and an ACE inhibitor.
- Forty-five of these 88 prescriptions consisted of carvedilol, furosemide, lisinopril and spironolactone.
- Twenty-seven of the 45 prescriptions consisted of carvedilol 25 mg, furosemide 40 mg, lisinopril 5 mg and spironolactone 25 mg, with an average cost of R214.60 ± R15.26 per prescription. As was seen in Table 4-27 the recommended daily dose for lisinopril is 10 mg. We see, however, that in 27 prescriptions lisinopril was under-utilised, since the PDD was only 5 mg.
- Eighteen of the 45 prescriptions consisted of carvedilol 50 mg, furosemide 80 mg, lisinopril 20 mg and spironolactone 25 mg.
- Forty-three of 88 prescriptions consisted of carvedilol, furosemide, perindopril and spironolactone.

- Twenty-seven of 43 prescriptions contained carvedilol 25 mg, furosemide 40 mg, perindopril 2 mg and spironolactone 25 mg, with an average cost of R235,72 ± R23,52 per prescription, totalling R6 364,55.
- The other 16 prescriptions' average cost was R372,06 ± R0,01, and they consisted of carvedilol 12,5 mg, furosemide 40 mg, perindopril 4 mg and spironolactone 50 mg. The items on all 43 prescriptions had PDDs in line with the suggested daily dosages (see Table 4-27).

During 2006 the following observations were made for four-item combination prescriptions for patients in AG3:

- 13 237 prescriptions consisting of four antihypertensive medicine items were prescribed to patients in AG3.
- From Table I14 it can be seen that the most frequently prescribed groups of antihypertensive medicine items were combinations of alpha- and beta-receptor blockers, an ACE inhibitor and two diuretics.
- Seven of the observations, accounting for 199 prescriptions, in the top ten four-item combination prescriptions for AG3 consisted of carvedilol, furosemide, perindopril and spironolactone. In Table 4-28 the PDDs of these combinations are summarised, as are the number of prescriptions for each specific combination.

Table 4-28: Summary of the PDDs for the different combinations

	PDD Rx [#] 1	PDD Rx2	PDD Rx3	PDD Rx4	PDD Rx5	PDD Rx6	PDD Rx7
Carvedilol	25mg	12.5mg	12.5mg	25mg	25mg	25mg	12.5mg
Furosemide	40mg	40mg*	40mg**	80mg	40mg	40mg	40mg
Perindopril	4mg	4mg	4mg	4mg	2mg	4mg	2mg
Spironolactone	25mg	25mg	25mg	25mg	25mg	12.5mg	25mg
Number of prescriptions	35	34	30	30	25	24	21

Rx abbreviation for prescription

* A generic furosemide product was prescribed

** An original furosemide product was prescribed instead of the generic.

The average cost of the combination with the generic furosemide product was R248,12 ± R18,86 per prescription, while the combination with the original furosemide product was R370,22 ± R17,85 per prescription – a difference of R122,10 per prescription. This difference can also be regarded as of statistical and practical significance, since the d-value for the difference between the two averages was 6,5.

During 2007 the following observations were made for four-item combination prescriptions for patients in AG3:

- 14 303 prescriptions in 4 101 different combinations were prescribed and dispensed to patients in AG3 during 2007.
- Sixty-five prescriptions consisting of alfuzosin 10 mg, the fixed-dose combination ergocristine/clopamide/reserpine 0,5/5/0,1 mg, lercanidipine 20 mg and the fixed-dose losartan/HCTZ 100/25 mg were observed, with an average cost of R268,44 ± R32,05 per prescription, totalling R17 448,87 (approximately 0,25%, N = R7 078 319,80).
- Forty-seven prescriptions, with an average cost of R233,79 ± R25,98 and a total cost of R10 987,90, consisted of amlodipine 10 mg, the one-pill fixed-dose combination of losartan/HCTZ 100/25 mg, telmisartan 80 mg, and another one-pill fixed-dose combination trandolapril/verapamil 180/2 mg.
- The one-pill fixed-dose combination of bisoprolol with HCTZ was the most prescribed antihypertensive item in combination – it was prescribed in 168 prescriptions, but with different PDDs.

During 2008 the following observations were made for four-item combination prescriptions for patients in AG3:

- 15 263 prescriptions were prescribed and dispensed.
- There were 326 prescriptions in seven different observations consisting of an alpha- and beta-receptor blocker, two diuretics and an ACE inhibitor.
- The most common active ingredients used in these combinations were carvedilol, furosemide, perindopril and spironolactone.
- There were 131 prescriptions consisting of carvedilol 12,5 mg, furosemide 40 mg, perindopril 4 mg and spironolactone 25 mg.
- 68 of 131 prescriptions consisted of only generic equivalents and had an average cost of R268,61 ± R31,59 per prescription, accounting for 0,25% (n = R18 265,36, N = R7 348 481,21) of the total cost of all four-item combination prescriptions during 2008.
- In 63 of 131 prescriptions an original furosemide product was prescribed, with an average cost of R380,56 ± R40,03 per prescription, totalling R23 975,20.
- There is therefore a difference of R111,95 in the average costs of the 68 and 63 prescriptions. The high d-value of 2,8 is an indication that this difference has practical and statistical significance. As was stated previously, furosemide is on the list of non-substitutable medicine items, and therefore generic substitution is not possible.

Summary of four-item prescriptions

- During 2005, 10 765 prescriptions consisting of four antihypertensive medicine items were observed in 3 688 different combinations, with an average cost of R482,15 ± R191,47 per prescription and a total cost of R5 190 360,09.
- During 2006, 13 984 prescriptions consisting of four antihypertensive medicine items were observed in 4 500 different combinations, with an average cost of R454,89 ± R185,65 per prescription, totalling R6 361 206,17.
- During 2007, 15 014 prescriptions consisting of four antihypertensive medicine items were observed in 4 339 different combinations. These 15 014 prescriptions had an average cost of R471,45 ± R191,14 per prescription and a total cost of R7 078 319,80.
- During 2008, 16 020 prescriptions consisting of four antihypertensive medicine items were observed in 3 688 different combinations, with an average cost of R458,71 ± R193,85 per prescription, totalling R7 348 481,21.

As was seen in the literature, the most effective blood pressure-reducing antihypertensive medicine combinations are diuretic and beta-receptor blockers, diuretic and ACE inhibitors or angiotensin-receptor blockers, calcium channel blockers with ACE inhibitors, and beta-receptor blockers with alpha-receptor blockers (Seedat & Rayner, 2012:72). Therefore it can be concluded that the four-item combination prescriptions are in line with the guidelines for hypertension treatment as stipulated by the SAHS.

4.5.5.5 Prescriptions containing five antihypertensive medicine items

The top ten prescriptions containing four antihypertensive medicine items for all four study years are summarised in Tables I17 to I20.

Five-item antihypertensive combination prescriptions prescribed to patients in AG1

During 2005 no observations were made for five-item combination antihypertensive prescriptions for patients in AG1.

During 2006 the following observations were made for five-item combination prescriptions for patients in AG1:

- Only one prescription consisting of five antihypertensive medicine items was observed for patients in AG1, and consisted of enalapril 10 mg, enalapril 20 mg, hydralazine 100 mg, the one-pill fixed-dose combination product telmisartan/HCTZ 80/12.5 mg and verapamil 480 mg, with an average cost of R655,03. As was seen from Table 4-27, the

maximum dose per day for enalapril is set at 20 mg per day, while 30 mg was prescribed to this patient. The maximum daily dose for verapamil was also prescribed. This possible over-utilisation may have led to the patient experiencing possible adverse effects, which may have led to patient non-compliance.

During 2007 the following observations were made for five-item combination prescriptions for patients in AG1:

- One observation was made for patients in AG1 receiving a combination of five antihypertensive medicine items consisting of enalapril 10 mg, enalapril 20 mg, hydralazine 100 mg, the one-pill fixed-dose combination telmisartan/HCTZ 80/12,5 mg and verapamil 480 mg, with a total cost of R625,52.

During 2008 no observations were made for five-item antihypertensive combination prescriptions for patients in AG1.

Five-item antihypertensive combination prescriptions prescribed to patients in AG2

During 2005 the following observations were made for five-item combination prescriptions for patients in AG2:

- Fifty-six five-item combination prescriptions were observed for patients in AG2.
- Seven of these prescriptions consisted of amlodipine 10 mg, carvedilol 12,5 mg, doxazosin 1 mg, indapamide 2,5 mg and perindopril 4 mg, with an average cost of R425,57 ± R31,22, totalling R2 979,00. As was seen from Table 4-27, the PDDs for these items were all in line with the guidelines for daily dosages.
- Six prescriptions consisted of amlodipine 10 mg, doxazosin 8 mg, furosemide 80 mg, minoxidil 5 mg and perindopril 4 mg, with an average cost of R854,69 ± R2,62, accounting for 0,62% (n = R5 128,13, N = R828 168,14) of the total cost of five-item antihypertensive combination prescriptions.
- Six prescriptions consisting of five antihypertensive medicine items consisted of amlodipine 10 mg, bisoprolol 10 mg, furosemide 40 mg, indapamide 2,5 mg and the one-pill fixed-dose combination item valsartan/HCTZ 160/12,5 mg. These six prescriptions had a total cost of R3 287,94 and an average cost of R547,99. As was seen from Table 4-27, all the PDDs for these prescriptions were in line with the recommended dosages for these antihypertensive medicine items.

During 2006 the following observations were made for five-item combination prescriptions for patients in AG2:

- Seventy-four prescriptions were prescribed to patients in AG2; these 74 prescriptions were observed in 29 different combinations.
- Two combinations representing a total of 17 prescriptions consisted of exactly the same antihypertensive medicine items but with different PDDs. These antihypertensive medicine items included candesartan, carvedilol, furosemide, HCTZ and spironolactone.
- Nine of the 17 prescriptions, accounting for 0,72% ($n = R7\ 682,59$, $N = R1\ 069\ 974,11$) of the total cost, with an average cost of R853,62, consisted of candesartan 8 mg, carvedilol 12.5 mg, furosemide 160 mg, HCTZ 50 mg and spironolactone 50 mg.
- The other eight of 17 prescriptions consisted of candesartan 16 mg, carvedilol 25 mg, furosemide 40 mg, HCTZ 12.5 mg and spironolactone 50 mg with an average cost of $R494,87 \pm R0,01$ per prescription, accounting for 0,38% ($n = R3\ 958,98$, $N = R1\ 069\ 974,11$) of the total cost. It is therefore clear that the strength or dosage of any combination antihypertensive prescription can play a major role in the overall cost of antihypertensive treatment.

During 2007 the following observations were made for five-item combination prescriptions for patients in AG2:

- There were 124 prescriptions containing a combination of five antihypertensive medicine items prescribed.
- Fourteen of the 124 prescriptions consisted of the one-pill fixed-dose combinations of ergocristine/cloпамide/reserpine 0,5/5/0,1 mg and losartan/HCTZ 100/25 mg, moxonidine 0,4 mg, nifedipine 60 mg and spironolactone 25 mg with an average cost of $R1\ 045,15 \pm R61,85$ per prescription and accounted for approximately 1,13% ($n = R14\ 632,16$, $N = R1\ 294\ 047,97$) of the total cost of five-item antihypertensive prescriptions.
- Eleven prescriptions with an average cost of $R934,75 \pm R18,34$ and a total cost of R10 282,22 consisted of bisoprolol 2,5 mg, irbesartan 300 mg, perindopril 8 mg, perindopril 4 mg and spironolactone 25 mg. The PDD of perindopril is 12 mg in total, while a maximum daily dose of not more than 8 mg is suggested.

During 2008 the following observations were made for five-item combination prescriptions for patients in AG2:

- There were 118 prescriptions prescribed and dispensed to hypertensive patients in AG2.
- Eleven prescriptions consisted of amlodipine 10 mg, doxazosin 8 mg, furosemide 80 mg, minoxidil 5 mg and perindopril 4 mg, with an average cost of $R968,07 \pm R23,33$ per prescription, accounting for 0,73% ($n = R10\ 648,74$, $N = R1\ 458\ 710,70$) of the total cost for five-item combination prescriptions during 2008.

- Eight prescriptions with an average cost of R1 091,73 ± R40,38 per prescription and a total cost of R8 733,82 consisted of candesartan 8 mg, carvedilol 12,5 mg, furosemide 160 mg, HCTZ 50 mg and spironolactone 50 mg.
- Eleven prescriptions consisted of bumetanide 2 mg, carvedilol 50 mg, HCTZ 25 mg, ramipril 10 mg and spironolactone 12,5 mg.
- In five of these 11 prescriptions a generic equivalent for carvedilol was prescribed. However, these five prescriptions had a higher average cost than the other six prescriptions (R728,65 vs. R698,22 ± R96,58). A relatively small d-value (0,3) indicates that this difference is of no real practical significance. This is probably due to the high standard deviation in the average cost of the six prescriptions containing the original carvedilol.

Five-item antihypertensive combination prescriptions prescribed to patients in AG3

During 2005 the following observations were made for five-item combination prescriptions for patients in AG3:

- There were 1 221 prescriptions observed for a combination of five antihypertensive medicine items for patients in AG3.
- Fourteen prescriptions, with an average cost of R646,39 ± R48,11 and a total cost of R9 049,49, consisted of alfuzosin 10 mg, bisoprolol/HCTZ 5/6,25 mg, ergocristine/clopamide/reserpine 0,5/5/0,1 mg, felodipine 5 mg and lisinopril 20 mg. The PDDs for all of these items was in line with the guidelines summarised in Table 4-27.
- Two observations, representing 25 prescriptions, consisted of the following antihypertensive items: amlodipine 5 mg, carvedilol 25 mg, furosemide 40 mg, spironolactone 25 mg and valsartan 160 mg. For 12 of the prescriptions valsartan was in a fixed-dose combination with HCTZ with a PDD of 160/12,5 mg and carvedilol had a PDD of 6,25 mg. The average cost of these 12 prescriptions was R464,63 ± R10,26, with a total cost of R5 575,59. Those 13 prescriptions with a higher carvedilol dosage and single valsartan had an average cost of R432,75 ± R9,03 and a total cost of R5 625,70.

During 2006 the following observations were made for five-item combination prescriptions for patients in AG3:

- A total of 1 632 prescriptions in 631 different combinations were observed.
- One such combination, which accounted for 16 prescriptions with a total cost of R10 146,24 (0,95%, N = R1 069 974,11) and an average cost of R634,14 per prescription, consisted of the one-pill fixed-dose combination of bisoprolol/HCTZ 10/6,25 mg,

lercanidipine 10 mg, another fixed-dose combination losartan/HCTZ 100/25 mg, nebivolol 5 mg and torasemide 2,5 mg.

- Fifteen prescriptions consisting of alfuzosin 10 mg, the one-pill fixed-dose combinations of bisoprolol/HCTZ 5/6,25 mg, ergocristine/clopamide/reserpine 0,5/5/0,1 mg, felodipine/ramipril 5/5 mg and lisinopril 20 mg, with an average cost of R731,27 ± R11,60 had a total cost of R10 969,11.
- Another 15 prescriptions with an average cost of R625,96, totalling R9 389,40, consisted of the one-pill fixed-dose combination of bumetanide/KCl 1/1 146 mg, candesartan 16 mg, the one-pill fixed-dose combination felodipine/ramipril 5/5 mg, furosemide 80 mg and methyldopa 1 000 mg.

During 2007 the following observations were made for five-item combination prescriptions for patients in AG3:

- A total of 1 851 prescriptions were prescribed in 635 different combinations.
- Eighteen prescriptions consisted of the one-pill fixed-dose combinations of bisoprolol/HCTZ 2,5/6,25, bisoprolol/HCTZ 5/6,25, indapamide 1,5 mg and the one-pill fixed-dose combinations of trandolapril/verapamil 2/180 mg and valsartan/HCTZ 160/12,5 mg, accounting for 0,93% (n = R12 065,92, N = R1 294 047,97) of the total cost of five-item combination prescriptions for the treatment of hypertensive patients, with an average cost of R670,33 ± R24,11 per prescription. The PDDs of these antihypertensive medicine items indicate that they are all in line with the recommended daily dosages as seen in Table 4-27.
- Fourteen prescriptions, with an average cost of R346,95 ± R0,01 per prescription totalling R4 857,36, consisted of the one-pill fixed-dose combination of bisoprolol/HCTZ 5/6,25 mg, doxazosin 8 mg, minoxidil 5 mg, moxonidine 0,4 mg and the one-pill fixed-dose combination of trandolapril/verapamil 2/180 mg.
- Another 14 prescriptions consisting of the one-pill fixed-dose combination bisoprolol/HCTZ 10/6.25, the one-pill fixed-dose felodipine/ramipril 5/5 mg combination, furosemide 60 mg, the one-pill fixed-dose combination of losartan/HCTZ 50/12,5 mg and moxonidine 0,2 mg, had an average cost of R413,30 ± R7,59 per prescription and a total cost of R5 786,18. It can therefore be seen that the PDDs for all these prescriptions are in line with the prescribing guidelines, as summarised in Table 4-27.

During 2008 the following observations were made for five-item combination prescriptions for patients in AG3:

- A total of 2 154 prescriptions were prescribed and dispensed to patients in AG3.

- Sixteen prescriptions, consisting of carvedilol 50 mg, doxazosin 1 mg, enalapril 10 mg, furosemide 40 mg and spironolactone 25 mg, had an average cost of R340,34 ± R6,01 per prescription and a total cost of R5 445,46. All the antihypertensive medicine items on these prescriptions were generic equivalents for the originator products. This can be a possible reason for the relatively low average cost. As was seen from Table 4-27, all the antihypertensive medicine items on these prescriptions had the correct PDDs.

Summary of the five-item combination prescriptions

- During 2005, 1 277 prescriptions consisting of five antihypertensive medicine items were prescribed and dispensed with an average cost of R648,53 ± R219,45 per prescription and a total cost of R828 168,14.
- No five-item combination prescriptions were prescribed to patients in AG1 during 2005.
- During 2006, 1 707 prescriptions consisting of five antihypertensive medicine items were prescribed and dispensed in 661 different combinations, with an average cost of R626,82 ± R215,49 per prescription, totalling R1 069 974,41.
- During 2007 1 976 prescriptions were observed, in 682 different combinations, consisting of five antihypertensive medicine items prescribed and dispensed. These 1 976 prescriptions had an average cost of R654,88 ± R225,03 per prescription and a total cost of R1 294 047,97.
- During 2008, 2 272 prescriptions consisting of five antihypertensive medicine items were prescribed and dispensed, with an average cost of R642,04 ± R239,90 per prescription totalling R1 458 710,70.
- During 2008 no five-item combination antihypertensive prescriptions were prescribed to patients in AG1.

As was seen in the SAHS Guidelines, no provision is made for combinations consisting of five or more antihypertensive medicine items. However, the guidelines of the British Hypertension Society suggest that after failure to achieve target blood pressure with the combination of an ACE inhibitor, beta-receptor blocker, calcium channel blocker and diuretic, an alpha-receptor blocker, or spironolactone (a diuretic) or any other diuretic should be added (Williams *et al.* 2004:158). It can therefore be seen that even though no guidelines for a combination of more than five antihypertensive medicine items exist in South Africa, the five-item combinations discussed in this section comply with guidelines set by the British Hypertension Society.

4.5.5.6 Prescriptions containing six antihypertensive medicine items

The top ten prescriptions containing six antihypertensive medicine items for all four study years are summarised in Table I21 to I24.

Six item combination antihypertensive prescriptions prescribed to patients in AG1

No six-item antihypertensive prescriptions were observed for patients in AG1 during the total study period.

Six-item combination antihypertensive prescription prescribed to patients in AG2

During 2005 no six-item antihypertensive combination prescriptions were observed for patients in AG2.

During 2006 the following observations were made for six-item combination prescriptions for patients in AG2:

- A total of 219 prescriptions containing six antihypertensive medicine items were observed with a total cost of R169 499,26, and an average cost of R773,97 ± R237,24 per prescription.
- Four different 6-item combinations were observed for patients in AG2, totalling 14 prescriptions.
- Six of the 14 prescriptions consisted of bisoprolol 10 mg, furosemide 40 mg, hydralazine 100 mg, the fixed-dose combination of losartan/HCTZ 25/100 mg and nifedipine 60 mg, with an average cost of approximately R918,52, contributing 3,25% (n = R5 511,12, N = R169 499,26) of the total cost of the six-item combination antihypertensive prescriptions. All the PDDs for the antihypertensive medicine items in these prescriptions were in line with the guidelines suggested in Table 4-27.

During 2007 the following observations were made for six-item combination prescriptions for patients in AG2:

- Seven different six-item combinations were observed for patients in AG2, totalling 21 prescriptions.
- Seven of these 21 prescriptions consisted of carvedilol 25 mg, doxazosin 4 mg, furosemide 120 mg, lercanidipine 10 mg, perindopril 4 mg and spironolactone 25 mg, contributing 2,59% (n = R4 572,40, N = R176 460,30) of the total cost of the six-item combination antihypertensive prescriptions, with an average cost of approximately R653,20. All the PDDs for the antihypertensive medicine items in these prescriptions are in line with the guidelines suggested in Table 4-27.
- Another nine prescriptions consisted of a beta-receptor blocker (bisoprolol), a diuretic (furosemide), a direct-acting vasodilator (hydralazine), the one-pill fixed-dose

combination of an angiotensin-receptor blocker and a diuretic (losartan/HCTZ), a central acting inhibitor and a calcium channel blocker (nifedipine).

- For five of these nine prescriptions the PDD for furosemide was 40 mg, and for the other four prescriptions the PDD of furosemide was 20 mg.
- The prescriptions with the higher furosemide dosage had a higher average cost per prescription than those with the 20 mg furosemide (R817,24 ± R32,86 vs, R779,20 ± R37,57). The d-value for the difference between the average costs is 1,01, which is an indication that the difference is of practical significance, and it can be seen that a higher dose in only one item can make a substantial difference to the average cost.

During 2008 the following observations were made for six-item combination prescriptions for patients in AG2:

- Seven different six-item combinations were observed for patients in AG2, totalling 17 prescriptions.
- Eight prescriptions consisted of bisoprolol 10 mg, furosemide 20 mg, hydralazine 300 mg, the one-pill combination of losartan/HCTZ 100/25 mg, methyldopa 500 mg and nifedipine 60 mg, accounting for 2,85% (n = R6 024,72, N = R221 718,77) of the total cost for six-item combination prescriptions for 2008. These prescriptions showed no abnormality regarding the PDDs for the different antihypertensive medicine items.

Six-item combination antihypertensive prescriptions prescribed to patients in AG3

During 2005 the following observations were made for six-item combination prescriptions for patients in AG3:

- All 134 prescriptions consisting of six antihypertensive medicine items prescribed and dispensed during 2005 were for patients in AG3. These 134 prescriptions had an average cost of R794,98 ± R246,04 per prescription and a total cost of R106 526,94.
- Fifteen of the 134 prescriptions consisted of the one-pill fixed-dose combination amiloride/HCTZ 5/50, the one-pill fixed-dose combination atenolol/chlortalidone 100/25, doxazosin 1 mg, enalapril 40 mg, furosemide 40 mg and methyldopa 250 mg, with an average cost of R331,34 ± R27,73 per prescription, accounting for approximately 4,67% (n = R4 970,10, N = R106 526,94) of the total cost of the six-item antihypertensive prescriptions for 2005. The PDD for enalapril was double the recommended maximum dose and therefore these patients should have been monitored for adverse effects, which may have led to patient non-compliance.
- Eight prescriptions, with an average cost of R914,44 ± R30,53 per prescription and a total cost of R7 315,49, consisted of an angiotensin-receptor blocker, an alpha- and

beta-receptor blocker, an alpha-receptor blocker, two diuretics and a fixed-dose diuretic combination. The diuretics prescribed in this prescription were torasemide 10 mg and torasemide 5 mg. From Table 4-27 it can be seen that the maximum daily dose for torasemide was 5 mg, clearly indicating an over-utilisation of torasemide, but if torasemide is prescribed as treatment for oedema the maximum daily dose may be as high as 40 mg/day. For the other antihypertensive items in the prescription the PDDs were in line with recommended daily dose guidelines.

During 2006 the following observations were made for six-item combination prescriptions for patients in AG3:

- A total of 203 prescriptions in 88 different six-item antihypertensive item combinations were observed.
- Nine prescriptions consisted of bisoprolol 1,25 mg, bumetanide/KCl 0,5/573 mg, doxazosin 8 mg, indapamide 1,5 mg, spironolactone 25 mg and valsartan 149,33 mg. Except for bisoprolol with a lower than recommended PDD (1,25 mg), all the other items in these prescriptions showed acceptable PDDs. The effectiveness of this low-dose bisoprolol must be questioned, but since no clinical data was available, this could not be investigated further.
- Eight prescriptions consisted of a diuretic, a fixed-dose combination of angiotensin-receptor blocker with a diuretic, an alpha- and beta-receptor blocker, two alpha-receptor blockers and a calcium channel blocker, with an average cost of R712,48 ± R6,65 per prescription, and accounted for 3,36% (n = R4 699,80, N = R169 499,26) of the total cost for six-item prescriptions for the 2006 study year. All the PDDs for the individual items were within the guidelines. For another eight prescriptions the diuretic (bumetanide) was substituted for the one-pill combination bumetanide/KCl. These prescriptions had a higher average cost per prescription (R849,62 ± R7,55) than the six-item combination containing bumetanide. A d-value of 18,16 was obtained for the average costs of these two sets of combinations. This indicates that there was some statistical significance in the difference.

During 2007 the following observations were made for six-item combination prescriptions for patients in AG3:

- There were 211 six-item combination prescriptions prescribed to patients in AG3.
- Eleven of the 211 prescriptions consisted of the one-pill fixed-dose combinations of bisoprolol/HCTZ 2,5/10 mg and candesartan/HCTZ 16/6,25, carvedilol 25 mg, felodipine 5 mg, furosemide 40 mg and another one-pill fixed-dose combination product,

lisinopril/HCTZ 10/12,5 mg, with a cumulative total cost of R7 070,41 (approximately 4,01%, N = R176 460,30), and an average cost of R642,76 ± R12,86 per prescription.

- Another 11 prescriptions, with an average cost of R418,04 ± R5,06 per prescription totalling R4 598,49, consisted of the following bumetanide 1 mg, the one-pill fixed-dose combination product candesartan/HCTZ 16/12,5 mg, carvedilol 25 mg, doxazosin 1 mg, doxazosin 4 mg and felodipine 5 mg. All the items in the PDDs for these prescriptions were in line with the guidelines stipulated in the literature (see Table 4-27).

During 2008 the following observations were made for six-item combination prescriptions for patients in AG3:

- A total of 251 six-item antihypertensive combination prescriptions were prescribed to patients in AG3, totalling R196 735,45.
- Fourteen six-item prescriptions were prescribed, consisting of the one-pill fixed-dose combination of bisoprolol/HCTZ 6,25/2,5, doxazosin 8 mg, minoxidil 10 mg, nifedipine 60 mg, quinapril 40 mg and the diuretic spironolactone 50 mg, with an average cost of R386,92 ± R11,00 per prescription and a total cost of R5 416,88. These prescriptions also showed no abnormality regarding the PDDs for the different antihypertensive medicine items in these prescriptions.
- Eleven six-item prescriptions consisting of the same active ingredients in the same dosages as the abovementioned 14 prescriptions had an average cost of R662,21 ± R13,91 per prescription with a total cost of R7 284,31. The only difference was that a generic equivalent for spironolactone 50 mg was prescribed. As was seen, the average cost per prescription was substantially higher than the combination with the original spironolactone product. The extremely high d-value (19,79) was an indication of the practical and statistical significance of this seemingly small difference.

Summary of the six item combination prescriptions

- During 2005 there were 134 prescriptions consisting of six antihypertensive medicine items prescribed and dispensed, totalling R106 526,94, with an average cost of R794,98 ± R246,04. All these prescriptions were for patients in AG3.
- During 2006, 219 prescriptions were observed in 92 different combinations with an average cost of R773,97 ± R237,24, totalling R169 499,26.
- During the 2007 study year, 232 prescriptions containing six antihypertensive medicine items were observed. These 232 prescriptions had a total cost of R176 460,30, with an average cost of R760,60 ± R273,33 per prescription.

- During the 2008 study year 268 prescriptions containing six antihypertensive medicine items were observed in 104 different combinations. These 268 prescriptions had a total cost of R211 718,77, with an average cost of R790,00 ± R307,23 per prescription.

4.5.5.7 Prescriptions containing seven antihypertensive medicine items

The top ten prescriptions containing seven antihypertensive medicine items for all four study years are summarised in Tables I25 to I28. During all four study periods there were no seven-item antihypertensive medicine items prescribed to patients in AG1.

Seven-item antihypertensive combination prescriptions prescribed to patients in AG2

During 2005 and 2006 no seven-item combination prescriptions were observed for patients in AG2.

During 2007 the following observations were made for seven-item combination prescriptions prescribed and dispensed to patients in AG2:

- One seven-item prescription was prescribed in AG2 with a total cost of R1 473,77 and consisted of carvedilol 25 mg, doxazosin 8 mg, furosemide 80 mg, furosemide 40 mg, moxonidine 0,4 mg, nifedipine 60 mg and perindopril 8 mg. The PDDs for all these antihypertensive medicine items were in line with the recommended dosages suggested in Table 4-27.

During 2008 the following observations were made for seven-item combination prescriptions prescribed and dispensed to patients in AG2:

- Only 1 of seven-item combination prescription was prescribed to patients in AG2 with a total cost of R1 211,45. This prescription consisted of amlodipine 20 mg, bisoprolol 10 mg, bisoprolol 10 mg, hydralazine 150 mg, methyldopa 1 500 mg, perindopril 4 mg and prazosin 15 mg.
- The PDD of amlodipine is double the maximum recommended daily dose, and this may have led to side effects, including but not limited to headache, oedema, flushing, palpitations, etc., which may have led to patient non-compliance.

Seven-item antihypertensive combination prescriptions prescribed to patients in AG3

During 2005 the following observations were made for seven-item combination prescriptions prescribed and dispensed to patients in AG3:

- Eight prescriptions with an average cost of R995,85 ± R296,89 per prescription and a total cost of R106 526,94 were prescribed to patients in AG3.

- Four prescriptions consisted of atenolol/chlortalidone 62,5/250 mg, doxazosin 4 mg, enalapril 42,86 mg, enalapril 20 mg, HCTZ 93,75 mg, methyldopa 1 500 mg and perindopril 8 mg (the strengths given here are the actual PDDs as they were dispensed). It is important to note that these prescriptions contained four ACE inhibitors in high doses. As was seen in Table 4-27, the maximum daily dose for enalapril is set at 20 mg, while the maximum daily dose for perindopril is 8 mg. This over-utilisation of enalapril (i.e. 62,86 mg per day) may have led to side effects, of which the most common is coughing, and subsequently may have led to patient non-compliance.

During 2006 the following observations were made for seven-item combination prescriptions prescribed and dispensed to patients in AG3:

- A total of 23 prescriptions with a total cost of R23 703,92 and an average cost of R1030,61 ± R334,74 were prescribed to patients in AG3.
- Six prescriptions consisted of the combination of a one-pill fixed-dose combination of a beta-receptor blocker with a diuretic, an alpha-receptor blocker, three ACE inhibitors, a diuretic and a central acting inhibitor. The PDDs of these combinations included atenolol/chlortalidone 250/62,5 mg, doxazosin 4 mg, enalapril 42,86 mg, enalapril 20 mg, HCTZ 93,75 mg, methyldopa 1 500 mg and perindopril 8 mg.
- From these PDDs it can be seen that patients receiving these prescriptions utilised on average 62,86 mg enalapril, which was more than three times the maximum daily dose.
- Patients also received the maximum daily dose of perindopril.
- Three prescriptions consisted of two calcium channel blockers (amlodipine 10 mg and nifedipine 60 mg), a beta-receptor blocker (bisoprolol 5 mg), an ACE inhibitor (enalapril 20 mg), two diuretics (furosemide 80 mg and methyldopa 1 500 mg) and an angiotensin-receptor blocker (irbesartan 300 mg), with an average cost of R1 155,69 per prescription totalling R3 467,07.

During 2007 the following observations were made for seven-item combination prescriptions prescribed and dispensed to patients in AG3:

- Only 22 seven-item antihypertensive combination prescriptions were issued.
- Eleven of the 22 prescriptions consisted of bisoprolol 10 mg, the one-pill fixed-dose combination of bisoprolol/HCTZ 10/12,5, candesartan 16 mg, hydralazine 10 mg, indapamide 2,5 mg, methyldopa 500 mg and the one-pill fixed-dose combination of valsartan/HCTZ 160/12,5 mg, with an average cost of R1 188,63 ± R48,21, totalling R13 074,90, were observed. As was seen from Table 4-27, all these antihypertensive items had a PDD that was in line with guidelines and recommendations.

- Three prescriptions consisted of bisoprolol, enalapril, furosemide, minoxidil, nifedipine, spironolactone and telmisartan/HCTZ.
- Two of the three prescriptions had the same PDDs for all seven items.
- However, one prescription had larger PDDs for the diuretics (furosemide 160 mg vs. furosemide 80 mg, and spironolactone 200 mg vs. spironolactone 100 mg), as well as for the direct-acting vasodilator minoxidil (i.e. minoxidil 15 mg vs. minoxidil 10 mg). Even though one prescription had higher PDDs, they still lay within the recommended doses.
- The average cost of the combination with higher doses of diuretics was R804,69, and was R279,10 lower than the average cost of the combination with the lower diuretic dosages.

During 2008 the following observations were made for seven-item combination prescriptions prescribed and dispensed to patients in AG3:

- Only 12 prescriptions were prescribed to patients in AG3.
- Two of the seven-item antihypertensive medicine item prescriptions consisted of bisoprolol 10 mg, furosemide 160 mg, minoxidil 15 mg, moxonidine 0,4 mg, nifedipine 60 mg, prazosin 6 mg and telmisartan/HCTZ 80/12,5 mg and have an average cost of R1 908,65.
- Three seven-item antihypertensive prescriptions consisted of the same antihypertensive medicine items, i.e. bisoprolol, furosemide, minoxidil, moxonidine, nifedipine, spironolactone and telmisartan/HCTZ. For all three prescriptions the PDDs of the different items were the same, except for minoxidil. In two of the prescriptions minoxidil had a PDD of 15 mg, and in the third prescription minoxidil had a PDD of 20 mg. The prescription with the higher minoxidil dose had a substantially higher average cost (R1 816,50) than the two prescriptions with the 15 mg minoxidil (R742,29).

Summary of the seven-item combination prescriptions

- During all four study years there were 67 seven-item antihypertensive medicine prescriptions totalling R96 335,92.
- During 2005 eight seven-item antihypertensive combination prescriptions were observed, with an average cost of R995,85 ± R296,89, totalling R7 966,77. All of these prescriptions were prescribed to patients in AG3.
- For the 2006 study year there were 23 prescriptions consisting of seven antihypertensive items, with an average cost of R1 030,61 ± R334,74 and a total cost of R23 703,92. All the seven-item antihypertensive combination prescriptions were prescribed to patients in AG3.

- During 2007 there were also only 23 prescriptions observed with an average cost of R1 075,38 ± R281,60, with a total cost of R49 467,47.
- During 2008 13 prescriptions consisting of seven antihypertensive medicine items were observed, with an average cost of R1 169,06 ± R499,36, totalling R15 197,76.

4.5.5.8 Prescriptions containing eight antihypertensive medicine items

During the four-year study period there were only 10 observations for prescriptions with eight antihypertensive medicine items. However during 2007 there were no eight-item antihypertensive prescriptions. No eight-item antihypertensive prescriptions were prescribed to patients in AG1. The eight-item combination prescriptions are summarised in Table I29 – Table I30.

Eight-item antihypertensive combination prescriptions prescribed to patients in AG2

During 2005, 2006 and 2007 no eight-item combination prescriptions were observed for patients in AG 2.

During 2008 one prescription consisting of eight antihypertensive medicine items was observed. This prescription, which amounted to a total cost of R1 236,32, consisted of carvedilol 25 mg, carvedilol 25 mg, doxazosin 8 mg, furosemide 120 mg, furosemide 120 mg, nifedipine 60 mg and perindopril 4 mg. As was seen in Table 4-27, the maximum daily dose for furosemide is 200 mg per day. For this prescription the PDD of furosemide was 240 mg. This over-prescribing might have led to some adverse effects, such as muscle cramps, etc., which may then have led to patient non-compliance.

Eight-item antihypertensive combination prescriptions prescribed to patients in AG3

During 2005 only one prescription consisting of eight antihypertensive medicine items were observed. This prescription consisted of amiloride/HCTZ 5/50 mg, bisoprolol 5 mg, bumetanide 1 mg, doxazosin 8 mg, methyldopa 1 500 mg, methyldopa 1 500 mg, nifedipine 60 mg and valsartan 160 mg, totalling R1 443,77. It can therefore be seen that in this prescription the maximum daily dose for methyldopa (3 000 mg per day) and nifedipine (60 mg per day) was prescribed.

During 2006 there were three observations for prescriptions containing 8 items.

- Two of these prescriptions consisted of carvedilol 50 mg, furosemide 40 mg, hydralazine 75 mg, indapamide 2,5 mg, lisinopril 40 mg, losartan/HCTZ 100/25 mg, moxonidine 0,4 mg and spironolactone 25 mg and accounted for a total cost of R2 301,52.

- The remaining eight-item antihypertensive prescription observed during 2006 consisted of amlodipine 10 mg, amlodipine 10 mg, bisoprolol 10 mg, bisoprolol 10 mg, candesartan/HCTZ 16/12,5 mg, furosemide 20 mg, moxonidine 0,3 mg and spironolactone 25 mg. This prescription had a total cost of R1 043,26. For this prescription it can be seen that one of the amlodipine containing products as well as one of the bisoprolol containing products was a generic equivalent.

During 2007 no eight-item antihypertensive combination prescriptions were observed.

During 2008 there were two observations made for prescriptions containing eight antihypertensive medicine items prescribed to patients in AG3.

- Three prescriptions containing the amlodipine 10 mg, amlodipine 5 mg, bisoprolol 5 mg, bisoprolol 10 mg, bumetanide/KCl 0,5/573 mg, eprosartan 160 mg, torasemide 10 mg and torasemide 5 mg accounted for a total cost of R2 853,18, with an average cost of R951,06. Bumetanide and torasemide are both high-ceiling loop diuretics that selectively inhibit sodium chloride re-absorption, and even though the PDDs of both bumetanide and torasemide fall within the recommended and maximum doses, and bumetanide is in a one-pill fixed-dose combination with potassium, patients should be monitored for adverse effects.
- Two prescriptions consisting of bisoprolol 10 mg, furosemide 160 mg, minoxidil 15 mg, moxonidine 0,4 mg, nifedipine 60 mg, prazosin 6 mg, spironolactone 50 mg and the one-pill fixed-dose combination of telmisartan/HCTZ 80/12,5 mg had a total cost of R3 920,28, with an average cost of R1 960,14. As was seen in Table 4-27, telmisartan/HCTZ can only be prescribed after the patient has been stabilised on both the components individually. Since the patient's individual medication history was not available, the investigation into this observation falls outside the scope of this study.

4.5.5.9 Summary of the antihypertensive combination prescriptions

In this section the different combinations of antihypertensive treatment were discussed, and it is therefore clear that there is a vast difference of combinations prescribed to hypertensive patients and that no fixed regimen exists. However, the SAHS Guidelines make recommendations for combinations of antihypertensive medicine items, and it is important to adhere to these guidelines in order to minimise adverse effects and drug-drug interactions that may lead to patient non-compliance. The ideal should be to treat hypertension, or any other chronic condition, with the least possible medication in the least effective dose to ensure optimal patient compliance.

4.6 GEOGRAPHICAL DISTRIBUTION OF ANTIHYPERTENSIVE PATIENTS

For the purpose of this study the data was analysed according to geographical distribution, i.e. provinces. The mid-year estimates conducted by Statistics South Africa indicated that KwaZulu-Natal had the highest population during 2005, 2006 and 2007, followed by Gauteng and the Eastern Cape provinces. Table 4-29 summarises the findings of the mid-year estimates conducted by Stats SA for 2005, 2006, 2007 and 2008.

Table 4-29: Distribution of the South African population (StatsSA, 2005, 2006, 2007, 2008)

Province	2005 Population	2006 Population	2007 Population	2008 Population
Eastern Cape	7 039 300	6 894 300	6 906 200	6 579 300
Free State	2 953 100	2 859 800	2 965 600	2 877 700
Gauteng	9 018 100	9 526 200	9 688 100	10 447 100
KwaZulu-Natal	9 651 100	9 924 000	10 014 500	10 105 500
Limpopo	5 635 000	5 365 400	5 042 900	5 274 800
Mpumalanga	3 219 900	3 505 800	3 536 300	3 590 000
North West	3 823 900	3 374 200	3 394 200	3 425 000
Northern Cape	1 941 500	1 094 500	1 102 200	1 125 900
Western Cape	4 645 600	4 745 500	4 839 800	5 262 000
Total	46 888 200	47 390 900	47 849 800	48 687 300

From table 4-29 the following observations were made:

- There was a gradual increase in the South African population over the four-year study period.
- During 2005, 2006 and 2007 KwaZulu-Natal was the province with the highest population (approximately 21% of the population), while Gauteng was the highest populated province in 2008 (21,5% of the population).
- The Northern Cape had the lowest population for all study years.

Table 4-30 illustrates the distribution of patients throughout South Africa, as well as the distribution of antihypertensive patients in a section of the private health-care sector of South Africa.

Table 4-30: Estimated distribution of all patients and antihypertensive patients on the database in South Africa

Year	Province	Number of patients	% of total population	Number of antihypertensive patients	% of antihypertensive patients [#]	PPI
2005	Eastern Cape	1 500 695	7.70	110 279	7.67	1.0
	Free State	923 514	4.74	76 824	5.34	1.1
	Gauteng	7 688 460	39.43	595 084	41.37	1.0
	KwaZulu-Natal	3 052 011	15.65	198 642	13.81	0.9
	Limpopo	1 231 222	6.31	51 872	3.61	0.6
	Mpumalanga	954 853	4.90	52 776	3.67	0.7
	North West	1 088 284	5.58	69 148	4.81	0.9
	Northern Cape	291090	1.49	24 055	1.67	1.1
	Western Cape	2 513 005	12.89	255 826	17.78	1.4
	Not indicated	257 640	1.32	4 022	0.28	0.2
	Total	19 500 774	100	1 438 528	100	1
2006	Eastern Cape	1 516 411	7.18	117 256	7.50	1.0
	Free State	1 024 829	4.85	83 440	5.34	1.1
	Gauteng	8 545 665	40.48	644 598	41.23	1.0
	KwaZulu-Natal	3 158 899	14.96	217 549	13.92	0.9
	Limpopo	1 337 434	6.33	54 347	3.48	0.5
	Mpumalanga	1 102 747	5.22	63 858	4.08	0.8
	North West	1 333 599	6.32	79 868	5.11	0.8
	Northern Cape	317 515	1.50	25 438	1.63	1.1
	Western Cape	2 703 483	12.80	274 761	17.58	1.4
	Not indicated	72 840	0.34	2 189	0.14	0.4
	Total	21 113 422	100	1 563 304	100	1
2007	Eastern Cape	1 366 013	7.16	108 883	7.45	1.0
	Free State	912 088	4.78	77 967	5.34	1.1
	Gauteng	7 687 720	40.30	588 533	40.29	1.0
	KwaZulu-Natal	2 981 474	15.63	212 821	14.57	0.9
	Limpopo	1 131 964	5.93	51 871	3.55	0.6

Table 4.30 (cont.): Estimated distribution of all patients and antihypertensive patients on the database in South Africa

Year	Province	Number of patients	% of total population	Number of antihypertensive patients	% of antihypertensive patients [#]	PPI
	Mpumalanga	1 018 008	5.34	60 598	4.15	0.8
	North West	1 209 542	6.34	78 010	5.34	0.8
	Northern Cape	282 918	1.48	21 500	1.47	1.0
	Western Cape	2 443 558	12.81	258 999	17.73	1.4
	Not indicated	42 439	0.22	1 519	0.10	0.5
	Total	19 075 724	100	1 460 701	100	1
2008	Eastern Cape	1 198 226	7.29	104 502	7.46	1.0
	Free State	779 955	4.74	71 560	5.11	1.1
	Gauteng	6 700 970	40.76	569 351	40.65	1.0
	KwaZulu-Natal	2 622 032	15.95	214 763	15.33	1.0
	Limpopo	869 606	5.29	45 807	3.27	0.6
	Mpumalanga	852 837	5.19	60 834	4.34	0.8
	North West	991 484	6.03	68 842	4.91	0.8
	Northern Cape	254 492	1.55	25 876	1.85	1.2
	Western Cape	2 138 087	13.01	237 984	16.99	1.3
	Not indicated	31 564	0.19	1 260	0.09	0.5
	Total	16 439 253	100	1 400 779	100	1

[#] The % of antihypertensive patients is calculated as a % of the total database

From table 4-30 it can be seen that Gauteng, KwaZulu-Natal and the Western Cape had the highest representation of patients in the total database, as well as hypertensive patients. The patient prevalence index (PPI) was calculated for hypertension patients in South Africa. As was stated in Chapter 3, Section 3.7.3.2, the PPI is an indication of the relationship between hypertension patients and the population. If the PPI is <1, then the number of hypertension patients is relatively small (as seen for Limpopo, Mpumalanga and North West). A PPI of >1, however, indicates a relatively high number of hypertensive patients in a population (as seen for Northern Cape and Western Cape), while a PPI = 1 indicates that there is an equilibrium between the number of hypertensive patients and the population (as seen for Eastern Cape, Free State, Gauteng and KwaZulu-Natal).

4.6.1 Hypertension medicine possession rate in a section of the private healthcare sector in South Africa

As was stated in Section 4.5.6, for the purpose of this study the data was analysed according to geographical distribution, i.e. provinces. Figure 4–3 illustrates the usage/distribution of all medicine items in the total database through the nine provinces of South Africa for the four study years.

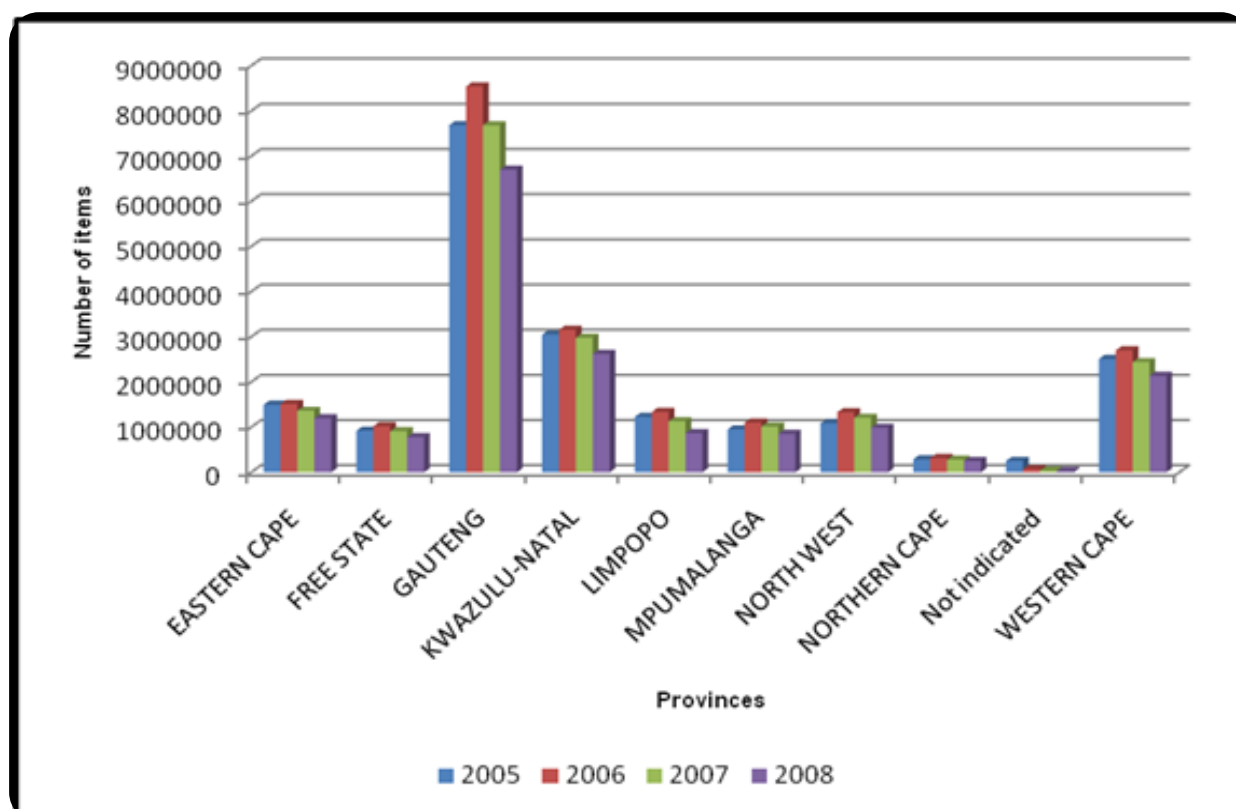


Figure 4-3: Distribution of medicine items used in a section of the private healthcare sector of South Africa.

According to the annual reports of the Council for Medical Schemes (2006, 2007, 2009), the provinces with the highest number of medical scheme member during the four study years (2005-2008) were Gauteng (37,1%, 36,4%, 36,5% and 36,1%), the Western Cape (16,4%, 16,2%, 16,3% and 16,1%) and KwaZulu-Natal (15,2%, 15,3%, 15,3% and 15,3%). The province with the lowest number of medical scheme members was the Northern Cape with 2,1% through all four study years. The same trend can be seen from Figure 4.3. It can be clearly seen that Gauteng had the highest usage of medicine items (39,45, 40,5%, 40,3% and 40,8%), followed by KwaZulu-Natal (15,7%, 15,0%, 15,6% and 15,9%) and the Western Cape (12,9%, 12,8%, 12,8% and 13,0%).

In Table 4-31 the distribution of antihypertensive medicine items is illustrated between the different provinces.

Table 4-31: Geographical distribution of antihypertensive medicine items (MIMS® group 7.3)

Year	Province	Number of items	Average cost per item (R)	Total cost (R)
2005	Eastern Cape	111 775	124.09 ± 67.27	13 870 294.01
	Free State	81 751	133.78 ± 70.25	10 936 776.34
	Gauteng	632 583	139.09 ± 70.92	87 988 229.20
	KwaZulu-Natal	199 129	132.45 ± 73.66	26 314 199.88
	Limpopo	50 005	127.74 ± 71.22	6 387 577.68
	Mpumalanga	56 542	130.56 ± 69.03	7 381 932.94
	North West	71 927	134.45 ± 69.03	9 670 553.99
	Northern Cape	24 844	116.19 ± 69.59	2 886 557.52
	Western Cape	265 289	133.17 ± 68.16	35 328 771.92
	Not indicated	3 440	101.73 ± 80.28	349 949.07
	Total	1 497 285	134.32 ± 5.21	201 114 842.60
2006	Eastern Cape	124 034	116.99 ± 64.43	14 510 914.35
	Free State	89 010	126.15 ± 69.57	11 228 776.44
	Gauteng	708 771	132.60 ± 69.28	93 985 103.21
	KwaZulu-Natal	229 129	124.70 ± 71.68	28 573 094.89
	Limpopo	55 049	122.76 ± 68.29	6 757 789.55
	Mpumalanga	68 051	120.68 ± 66.67	8 212 163.03
	North West	87 237	128.72 ± 67.31	11 228 822.59
	Northern Cape	26 147	111.15 ± 67.97	2 906 168.44
	Western Cape	292 817	125.56 ± 66.50	36 764 775.39
	Not indicated	2 320	124.45 ± 69.06	288 714.12
	Total	1 682 565	127.46 ± 5.17	214 456 322.00
2007	Eastern Cape	119 752	120.55 ± 63.77	14 436 070.52
	Free State	85 704	130.02 ± 69.38	11 143 477.94
	Gauteng	675 513	136.73 ± 68.33	92 361 792.15

Table 4.31 (cont.): Geographical distribution of antihypertensive medicine items (MIMS® group 7.3)

Year	Province	Number of items	Average cost per item (R)	Total cost (R)
	KwaZulu-Natal	233 391	121.18 ± 71.47	28 283 246.26
	Limpopo	53 794	126.73 ± 67.23	6 817 222.64
	Mpumalanga	66 735	124.01 ± 66.16	8 275 835.25
	North West	87 583	129.90 ± 65.87	11 377 263.64
	Northern Cape	22 785	121.64 ± 65.94	2 771 679.36
	Western Cape	291 288	128.01 ± 66.09	37 287 629.83
	Not indicated	1 875	128.39 ± 74.14	240 739.66
	Total	1 638 420	130.00 ± 6.31	212 994 957.25
2008	Eastern Cape	116 107	114.36 ± 60.45	13 277 638.62
	Free State	77 576	122.79 ± 67.15	9 525 306.77
	Gauteng	661 757	131.00 ± 66.10	86 689 950.13
	KwaZulu-Natal	242 570	116.69 ± 69.59	28 304 387.74
	Limpopo	48 964	123.71 ± 64.14	6 057 492.91
	Mpumalanga	67 709	117.91 ± 62.01	7 983 855.28
	North West	78 634	125.43 ± 63.81	9 863 366.52
	Northern Cape	26 155	106.81 ± 62.31	2 793 684.47
	Western Cape	272 028	123.24 ± 63.51	33 525 513.92
	Not indicated	1 605	121.25 ± 75.26	194 601.88
	Total	1 593 105	124.42 ± 6.39	198 215 798.24

From Table 4-31 it can be seen that, like with the overall medicine usage among the provinces, the most antihypertensive items were used in Gauteng, the Western Cape and KwaZulu-Natal. Between 41,2% and 43,5% of all the antihypertensive items claimed for during the study period was for patients in the Gauteng Province. These items accounted for between 43,6% and 43,8% of the total cost of antihypertensive medicine items during the four-year study period.

Table 4-32: Geographical distribution of antihypertensive medicine items (MIMS® group 16.1)

Year	Province	Number of items	Average cost per item(R)	Total cost (R)
2005	Eastern Cape	44 338	32.94 ± 47.88	1 460 413.95
	Free State	29 604	48.51 ± 61.71	1 436 109.60
	Gauteng	217 700	49.70 ± 62.73	10 819 040.19
	KwaZulu-Natal	78 555	41.61 ± 54.58	3 268 912.15
	Limpopo	22 896	30.72 ± 41.35	703 413.46
	Mpumalanga	19 470	40.65 ± 54.87	791 537.19
	North West	27 056	41.74 ± 55.73	1 129 384.46
	Northern Cape	10 226	37.33 ± 35.39	330 592.59
	Western Cape	96 065	41.45 ± 53.32	3 981 808.81
	Not indicated	2 337	26.40 ± 50.31	61 702.16
	Total	548 247	43.74 ± 57.29	23 982 914.56
2006	Eastern Cape	46 578	30.00 ± 40.13	1 397 481.71
	Free State	30 592	44.48 ± 56.84	1 360 738.12
	Gauteng	228 253	46.68 ± 62.68	11 111 000.15
	KwaZulu-Natal	81 549	40.73 ± 57.33	3 321 757.02
	Limpopo	22 873	30.73 ± 44.15	762 970.21
	Mpumalanga	24 115	37.88 ± 56.30	913 532.17
	North West	30 473	41.50 ± 57.32	1 264 559.91
	Northern Cape	10 916	29.40 ± 34.50	326 821.68
	Western Cape	102 179	39.30 ± 51.92	4 016 018.51
	Not indicated	928	45.31 ± 71.80	42 048.51
	Total	578 456	42.28 ± 56.95	24 456 927.99
2007	Eastern Cape	40 346	30.99 ± 43.63	1 250 445.55
	Free State	26 898	46.97 ± 63.62	1 263 365.21
	Gauteng	185 166	52.95 ± 68.94	9 805 423.33
	KwaZulu-Natal	75 591	41.36 ± 63.55	3 126 236.48

Table 4.32 (cont.): Geographical distribution of antihypertensive medicine items (MIMS® group 16.1)

Year	Province	Number of items	Average cost per item(R)	Total cost (R)
	Limpopo	20 460	32.75 ± 48.63	669 963.21
	Mpumalanga	20 949	39.88 ± 58.21	835 512.69
	North West	28 484	41.33 ± 64.60	1 177 320.93
	Northern Cape	8 451	32.50 ± 39.66	274 680.28
	Western Cape	90 858	40.03 ± 53.69	3 637 096.96
	Not indicated	610	40.02 ± 50.73	24 414.73
	Total	497 813	44.32 ± 62.01	22 064 459.37
2008	Eastern Cape	38 868	29.67 ± 40.90	1 153 300.06
	Free State	25 682	44.32 ± 61.92	1 138 263.55
	Gauteng	178 425	51.35 ± 70.27	9 162 324.72
	KwaZulu-Natal	75 675	40.94 ± 64.78	3 098 214.40
	Limpopo	18 380	35.61 ± 52.72	654 580.42
	Mpumalanga	21 461	39.25 ± 58.26	842 448.69
	North West	25 119	39.16 ± 63.43	983 573.23
	Northern Cape	11 790	30.57 ± 56.29	360 374.92
	Western Cape	81 389	39.79 ± 55.00	323 8718.10
	Not indicated	467	37.42 ± 52.01	17 473.69
	Total	477 256	43.27 ± 63.03	20 649 271.78

From Table 4-32 it can be clearly seen that Gauteng, KwaZulu-Natal and the Western Cape had the highest usage of diuretic medicine items, accounting for between 70,3% and 71,6% of all the diuretic medicine items during all four study years. The cost of the diuretics in these three provinces amounted to approximately 75% of the total cost of diuretic medicine items throughout the four-year study period.

Since these three provinces, Gauteng, KwaZulu-Natal and the Western Cape, have the highest number of people of the population, these trends can be expected.

In the next section the compliance with or adherence to antihypertensive medicine items will be discussed.

4.7 COMPLIANCE AND ADHERENCE

In this section the fifth research question, namely to determine the refill-adherence rate (AR) or compliance of patients in the database receiving antihypertensive medicine items, will be investigated and discussed. Unacceptable low or high adherence rates may be an indication of monetary wastage and may have a vast impact on the financial burden of patients and medical schemes or funders. From the literature, satisfactory RAR can be defined as the percentage of patients who had refills dispensed covering 80-120% of the prescribed treatment. Under-supply can be seen as <80%, while oversupply is >120% (Krigsman *et al.* 2007:20; Anderson *et al.* 2005:622). The RAR was determined from 2005 to 2008 for antihypertensive medicine items that were prescribed more than once and will be expressed as a percentage.

As was seen in Chapter 3, Section 3.7.3.1, the RAR will be divided in three categories, as can be seen in Table 4-33.

Table 4-33: Refill-adherence rate (RAR) categories

RAR Category	Criteria
1	$\leq 80\%$
2	$80\% < AR \leq 120\%$
3	$\geq 120\%$

The RAR will be calculated for all antihypertensive medicine items, the different genders, and age groups and the top 10 antihypertensive medicine items according to prevalence, according to the three treatment categories.

4.7.1 Total number of antihypertensive medicine items used in RAR calculations and their associated costs

In this section the RAR of all the antihypertensive medicine items that were dispensed more than once during the total study period are examined according to the three treatment categories that were discussed in Section 4.5.3.

Table 4-34 summarises the total number of antihypertensive medicine items and their total costs that were used in the RAR calculations. These results are presented according to the three treatment categories.

Table 4-34: Total cost and number of all antihypertensive items

Treatment category	Number of items	Average cost per item (R)	Total cost (R)
TC1	434 037	1215.02 ± 1843.92	527 364 190.00
TC2	139 812	208.28 ± 661.22	29 119 372.27
TC3	410 361	757.18 ± 1507.83	310 718 702.00

Table 4-34 revealed that antihypertensive medicine items prescribed for TC1 had the highest average cost. TC1 included antihypertensive medicine items from MIMS group 7.3, while antihypertensive medicine items from TC2, which included the items in MIMS group 16.1, had the lowest average cost.

Table 4-35 summarises the total number of antihypertensive medicine items and the costs related to these antihypertensive medicine items that were not included in RAR calculations. These items were typically prescribed only once during the study period.

Table 4-35: Total cost and number of items not included in the RAR calculations

Treatment category	Number of items	Average cost (R)	Total cost (R)
TC1	136 533	118.06 ± 182.13	16 118 824.83
TC2	78 612	70.06 ± 380.64	5 507 891.10
TC3	136 489	68.65 ± 72.78	9 370 234.49

From Table 4-35 it can be seen that for TC1 and TC3, approximately a third of the total number of medicine items that were prescribed occurred only once during the study period and were therefore not included in the RAR calculations. Almost half of the medicine items prescribed to patients in TC2 occurred only once during the study period.

In Table 4-36 the total number of antihypertensive medicine items and the costs relating to these antihypertensive medicine items that were included in RAR calculations are summarised. These are all the antihypertensive medicine items from MIMS group 7.3, 16.1 and a combination of 7.3 and 16.1 that were prescribed more than once during the total study period.

Table 4-36: Total cost and number of items used in RAR calculations

Treatment category	Number of items	Average cost (R)	Total cost (R)
TC1	297 504	1 718.45 ± 2 034.58	511 245 365.00
TC2	61 200	385.81 ± 869.86	23 611 481.17
TC3	273 872	1 100.33 ± 1 746.42	301 348 468.00

From Table 4-36 it can be calculated that the total number of antihypertensive medicine items that were prescribed more than once during the study period amounted to 632 577, with an associated cost of R836 205 314,17. Only 43,77% (n = 61 200, N = 139 812) of items prescribed in TC2 (i.e. MIMS group 16.1, Diuretics) were prescribed more than once. Since hypertension is a chronic disease and diuretics are often prescribed as first-line therapy, this can be seen as non-compliance by patients.

4.7.2 Refill-adherence rate for all the antihypertensive medicine items according to treatment category.

In this section the RAR for the different treatment categories are summarised and discussed.

Table 4-37 summarises the adherence rates of all three treatment categories.

Table 4-37: Adherence rates of all three treatment categories during the study period

Treatment category	Total number of items used in AR calculations	RAR1	RAR2	RAR3	Average RAR
TC1	297 504	38.52%	53.19%	8.30%	86.19% ± 119.47
TC2	61 200	58.12%	33.36%	8.52%	70.20% ± 135.16
TC3	273 872	41.61%	48.53%	9.87%	85.49% ± 138.50

Table 4-37 indicated that the average refill-based adherence rate for TC1 was 86,19%, for TC2 it was 70,20% and for TC3 the average refill-based adherence rate was 85,49%. According to Table 4.33 it was noted that only 53,19% of all the items that were used in TC1 (i.e. antihypertensive medicine items from MIMS group 7.3) had acceptable refill-adherence rates during the four-year study period. The RAR was the lowest for antihypertensive medicine items dispensed in TC2 (i.e. medicine items from MIMS group 16.1) with only 33,36% of these items with acceptable AR. TC2 also had the highest unacceptably low refill-adherence rate with 58,12%. Between 8,3% and 9,87% of all the antihypertensive medicine items had unacceptably high adherence rates indicating that patients had an oversupply of more than 120%. This may have been an indication that patients overused their medicines, but it may also have indicated stockpiling of antihypertensive medicine items. This may also have led to unnecessarily high costs.

A study conducted by Sung *et al.* (2009:1318) on the treatment adherence of antihypertensive medicine in Korea indicated that patients treated with a combination of antihypertensive medicine items and a diuretic (TC3 in this study) showed a lower adherence rate than those treated with a combination of antihypertensive medicine items without a diuretic (TC1 in this study). According to Sung *et al.* (2009:1318,) the AR was similar in patients treated with an

ACE inhibitor or ARB and those treated with a combination of antihypertensive medicine items without a diuretic (TC1).

4.7.3 Refill-adherence rate of antihypertensive medicine items for the different age groups

In this section the RAR for antihypertensive usage among the different age groups is discussed according to the three treatment categories.

Tables 4-38, 4-39 and 4-40 summarise the RAR of all three treatment categories for age groups 1, 2 and 3 respectively.

Table 4-38: Refill-adherence rates of all three treatment categories for patients in AG1

Treatment category	Total number of items used in RAR calculations for patients in AG1	RAR1	RAR2	RAR3	Average RAR
TC1	350	56.29%	32.29%	11.43%	82.21% ± 130.76
TC2	225	64.44%	24.00%	11.56%	68.05% ± 97.78
TC3	308	52.92%	33.77%	13.31%	87.27% ± 162.00

According to the RAR of patients in AG1 (i.e. age ≤18 years), summarised in Table 4-38, patients receiving antihypertensive medicine items from TC2 had the lowest average adherence rate, i.e. 68,05%. Only 24% of the antihypertensive medicine items from TC2 dispensed to patients from AG1 had acceptable refill-adherence rates, while 64,44% of these items had unacceptably low refill-adherence rates and 11,56% had unacceptably high (>120%) refill adherence rates. Patients from AG1 receiving antihypertensive medicine items from TC3 had the highest refill-adherence rate, namely i.e. 87,27%.

Table 4-39: Refill-adherence rates of all three treatment categories for patients in AG2

Treatment category	Total number of items used in RAR calculations for patients in AG2	RAR1	RAR2	RAR3	Average RAR
TC1	34 577	47.47%	42.71%	9.82%	85.28% ± 163.59
TC2	8 628	66.49%	23.13%	10.38%	66.00% ± 171.43
TC3	22 057	51.41%	36.96%	11.63%	82.45% ± 177.79

An investigation into the refill-adherence rate of patients in AG2, i.e. patients between 18 and 45 years of age, showed that treatment with antihypertensive medicine items from TC1 had the highest average adherence rate (see Table 4-39). Despite the high adherence rate of 85,28%,

only 42,71% of items dispensed to patients in AG2 receiving antihypertensive medicine items from TC1 had acceptable adherence. Only 23,13% of medicine items from TC2 dispensed to patients in AG2 had acceptable adherence rates. The average RAR for patients receiving antihypertensive medicine items from TC2 was a relatively low 66%, indicative of an unacceptably low RAR.

Table 4-40: Refill-adherence rates of all three treatment categories for patients in AG3

Treatment category	Total number of items used in RAR calculations for patients in AG3	RAR1	RAR2	RAR3	Average RAR
TC1	262 577	37.31%	54.60%	8.09%	86.31% ± 112.36
TC2	52 293	56.71%	35.10%	8.20%	70.91% ± 128.64
TC3	251 508	40.74%	49.56%	9.71%	85.75% ± 134.47

Table 4-40 revealed that patients in AG3 who received antihypertensive treatment from TC1 had the highest average RAR, even though only 54,6% of these medicine items had acceptable refill-adherence rates. TC2 again showed the lowest average refill-adherence rate, with only 35,1% of all items having acceptable refill-adherence rates, while 56,71% of items in TC2 had unacceptably low RAR and only 8,20% showed unacceptably high RAR ($80\% < AR \leq 120\%$). It can therefore be concluded that patients in AG3 showed the best RAR. These findings were also in line with studies done internationally showing that adherence increases as age increases (Andersson *et al.* 2005:625; Jackson *et al.* 2008:1562).

4.7.4 Refill-adherence rate of antihypertensive medicine usage for the different genders

In this section the RAR for antihypertensive medicine usage among the different genders are discussed according to the three treatment categories. Table 4-41 summarises the refill-adherence rate among **female** patients.

Table 4-41: Refill-adherence rates of all three treatment categories amongst female patients

Treatment category	Total number of items used in RAR calculations for female patients	RAR1	RAR2	RAR3	Average RAR
TC1	148 930	38.32%	53.62%	8.06%	85.98% ± 118.15
TC2	43 485	58.75%	33.62%	7.63%	68.97% ± 127.60
TC3	162 583	41.89%	48.80%	9.31%	84.32% ± 128.58

From Table 4-41 it was noted that just over half (53,62%) of the female patients that were using antihypertensive medicine items from TC1 had acceptable RAR, while approximately a third

(33,62%) of female patients receiving antihypertensive treatment from TC2 had acceptable RAR.

The average RAR for female patients receiving treatment from TC1 and TC3 was 85,98% and 84,23% respectively. Female patients that received antihypertensive treatment from TC2 had an average RAR that fell below the acceptable level of 80%.

Table 4-42 summarises the RAR for **male** patients who received antihypertensive medicine items during the study period.

Table 4-42: Refill-adherence rates of all three treatment categories amongst male patients

Treatment category	Total number of items used in RAR calculations for male patients	RAR1	RAR2	RAR3	Average RAR
TC1	148 499	38.71%	52.76%	8.53%	86.40% ± 120.80
TC2	17 689	56.60%	32.69%	10.71%	73.23% ± 153.10
TC3	111 197	41.89%	48.80%	9.31%	87.19% ±151.88

Table 4-42 revealed that the average ARs for male patients receiving treatment from TC1 and TC3 were 86,40% and 87,19% respectively. Male patients that received antihypertensive treatment from TC2 had an average RAR that fell below the acceptable level of 80%, i.e. 73,23%. It was also seen that just over half (52,76%) of the male patients that were using antihypertensive medicine items from TC1 had an acceptable RAR, while approximately a third (32,69%) of male patients receiving antihypertensive treatment from TC2 had an acceptable RAR.

Overall, male patients showed better adherence to antihypertensive treatment than their female counterparts, but male patients that received antihypertensive medicine from TC1 and TC2 showed a higher incidence of oversupply (AR3) than female patients. In contrast to this study, a similar study done by Andersson *et al.* (2005:625) found that there was no gender difference in total refill adherence rates, but that male patients had a higher oversupply of antihypertensive medicine items than females. Sung *et al.* (2009:1312) also found that the probability of good adherence did not vary between male and female patients. In a systematic qualitative review of the literature, Jin *et al.* (2008:276) concluded that gender may not be a good predictor of compliance or non-compliance because of inconsistencies in adherence studies.

4.7.5 Refill-adherence rate for usage of the top 10 antihypertensive medicine items

In this section the refill-adherence rate for the most frequently dispensed antihypertensive medicine items during the total study period is examined according to the three treatment categories. The top 10 are listed according to prevalence.

Table 4-43: Refill-adherence rates of the top 10 active ingredients for each TC

Treatment category	Active ingredient	Number of items	Average RAR
TC1	Indapamide/Perindopril	27 495	86.32% ± 123.63
	Amlodipine	26 354	90.41% ± 128.56
	Bisoprolol	25 235	84.81% ± 106.94
	Perindopril	24 225	85.13% ± 136.70
	Enalapril	22 564	84.96% ± 115.89
	Lisinopril	19 550	85.87% ± 97.92
	Enalapril/HCTZ	14 135	86.38% ± 123.45
	Bisoprolol/HCTZ	13 486	84.00% ± 94.88
	Valsartan/HCTZ	10 277	86.81% ± 99.71
	Carvedilol	9 296	85.75% ± 108.81
TC2	Amiloride/HCTZ	21 125	66.70% ± 126.41
	Indapamide	16 732	72.52% ± 120.38
	Furosemide	8 481	72.00% ± 159.85
	HCTZ	6 021	69.40% ± 146.05
	Spironolactone	4 290	78.54% ± 150.91
	Bumetanide/KCl	2 048	62.92% ± 158.21
	Torasemide	1 045	72.85% ± 139.74
	Triamterene/HCTZ	562	76.59% ± 158.94
	Acetazolamide	476	64.03% ± 144.64
	Piretanide	182	67.48% ± 78.08
TC3	Indapamide	28 056	83.18% ± 140.56

Table 4.43 (cont.): Refill-adherence rates of the top 10 active ingredients for each treatment category

Treatment category	Active ingredient	Number of items	Average RAR
	Amiloride/HCTZ	24 341	74.12% ± 114.29
	Furosemide	24 081	79.46% ± 170.75
	Enalapril	18 471	85.72% ± 118.66
	HCTZ	17 085	82.00% ± 141.14
	Perindopril	16 727	88.02% ± 142.81
	Amlodipine	15 251	94.27% ± 154.18
	Lisinopril	14 391	89.84% ± 129.14
	Spironolactone	12 734	83.11% ± 121.81
	Bisoprolol	12 097	90.32% ± 123.92

From Table 4-43 the following was observed:

- For TC1 the one-pill fixed-dose combination of indapamide/perindopril had the highest prevalence, but only the fourth highest RAR of 86,32% after amlodipine (90,412%), valsartan/HCTZ (86,81%) and enalapril/HCTZ (86,38%).
- All the antihypertensive medicine items prescribed in TC1 showed acceptable RAR, i.e. RAR above 80% but lower than 120%.
- For TC2 spironolactone showed the highest RAR with 78,54%, followed by the one-pill fixed-dose combination of triamterene/HCTZ with 76,59% and torasemide (72,85%).
- Not any of the top 10 antihypertensive medicine items prescribed in TC2 had an acceptable refill-adherence rate above, i.e. $80\% < \text{RAR} \leq 120\%$.
- For TC3 amlodipine showed the highest RAR with 94,27%, followed by bisoprolol (90,32%) and lisinopril (89,84%).
- It was further observed that only two medicine items from TC3 had unacceptably low RAR (i.e. $\leq 80\%$), namely furosemide (79,46%) and the one-pill fixed-dose combination of amiloride/HCTZ (74,12%).

A study conducted by Andersson *et al.* (2005:625) found that there was a higher RAR with beta-receptor blockers than with ACE inhibitors, diuretics and ARBs. Sung *et al.* (2009:1312) found that patients receiving ACE inhibitors, ARBs or a combination without diuretics had higher odds of good adherence, while in patients receiving beta-receptor blockers, calcium channel blockers, diuretics or combinations with diuretics the likelihood of good adherence was lower. In their report on the 2005 American Society of Hypertension scientific meeting, Andros and

Weintraub (2005:S398) stated that better adherence was achieved in patients treated with ARBs than any other antihypertensive medicine items.

4.7.6 Cost implication of unacceptable high or low adherence rates

In this section the cost or monetary implication of the over- or under-supply of antihypertensive medicine items is discussed in terms of the three different treatment categories. This cost implication was calculated against the total cost for the medicine items included in the RAR calculations. Over- or under supply of antihypertensive medicine may have led to a wastage of funds and a larger financial burden on patients and medical schemes.

As was seen from Chapter 3, the cost implication was calculated by dividing the cost of the antihypertensive medication by acceptable or unacceptable RAR, with the difference in the cost of all antihypertensive medicine items included in the RAR calculations and the cost of the last refill of all items included in the RAR calculations and expressed as a percentage. Table 4-36 shows the cost used in the denominator of the cost implication formula (i.e. cost of antihypertensive medicine items used in the RAR calculations minus the cost of the last refill).

Table 4-44: Financial implications of the use of antihypertensive medicine items

Treatment category	Cost of items repeated more than once (R)	Cost of items with unacceptable low RAR (R)	Cost of items with acceptable RAR (R)	Cost of items with unacceptable high RAR (R)
TC1	511 245 365.00	134 427 457.00	320 248 665.00	19 419 203.66
TC2	23 611 481.17	8 810 550.13	11 583 406.44	910 929.11
TC3	301 348 468.00	78 468 489.61	184 621 857.00	14 656 226.87

From Table 4-44 the following can be concluded:

- The 38,52% (Table 4-37) of antihypertensive medicine items prescribed in TC1 with an unacceptably low RAR accounted for approximately 26,3% (n = R134 427 457,00, N = R511 245 365,00) of the total cost.
- The 53,19% of antihypertensive medicine items prescribed to patients in TC1 with acceptable RAR had a total cost of R320 248 665,00 (62,6%, N = R511 245 365,00).
- The cost contribution for the antihypertensive medicine items in TC1 with an unacceptably high RAR was approximately 3,80% (n = R19 419 203,66, N = R511 245 365,00).
- TC2 showed the same trends for the unacceptably low RAR, acceptable RAR and unacceptably high RAR.

- For TC3 the 41,61% (Table 4-37) of antihypertensive medicine items with an unacceptably low RAR had a cost of R78 468 489,61, while the 9,87% of items with an unacceptably high RAR had a cost of R14 656 226,87.
- The 48,53% antihypertensive medicine items in TC3 with an acceptable RAR contributed to 61,27% ($n = R184\,621\,857,00$, $N = R301\,348\,468,00$) of the total cost.

From this section it was clear that the unacceptable levels (high and low) of antihypertensive adherence rate had a relatively large cost and therefore a large financial impact on members and medical schemes. Efforts should be made to minimise this wastage of funds by promoting patient adherence and compliance. Better adherence will also lead to better therapeutic benefits and effects.

4.8 THRESHOLDS AS PLANNING AND CONTROL INSTRUMENTS

4.8.1 Introduction

As was seen in Section 2.1 of Chapter 2, there are a number of definitions for the term 'threshold'. As was stated in Chapter 2, for the purpose of this study a threshold can be defined as follows: *A threshold analysis determines the monetary value with regard to the medicine usage and cost of antihypertension treatment.*

In this section a range of thresholds for pharmaceutical decision-making for the treatment of hypertension are calculated and suggested, answering the sixth research objective. Different scenarios are used, and for each scenario at least one threshold is suggested. The thresholds that are selected depend on the needs of the patients and their willingness to pay. The threshold may have an upper and lower limit.

4.8.2 Threshold calculation for antihypertensive medication

For the purpose of this study, the average cost, standard deviation and median were used to calculate possible thresholds. For almost all of the average costs that were used the standard deviations were more than 50% of the average cost. For this reason the standard deviation was divided and used as a range: the average cost plus half the standard deviation and the average cost minus half the standard deviation. A second cost threshold range was calculated where a third of the standard deviation was added to the average cost and subtracted from the average cost.

These relatively large standard deviations were also an indication of the skewness and diversity of the data, and therefore the median can also be used to determine a threshold, since the median is the middle value in any range of values. For all the scenarios the threshold was determined for the individual study years. It must also be remembered that a prescriber has a free choice among a limited number of antihypertensive medicine items that can be prescribed, depending on various factors including benefit range of the medical scheme and the willingness of the patient to pay for treatment, an indication that a relatively large standard deviation may be created. Therefore, for threshold purposes it is important to limit threshold values within reasonable ranges.

4.8.2.1 Calculation of threshold by using the total antihypertensive medicine items

The first threshold that was determined calculated by using the average cost and median for all the antihypertensive medicine items found in the database during the four-year study period. Table 4-45 summarises these findings and was compiled from Table 4-16.

Table 4-45: Threshold estimation using total antihypertensive medicine items

Year	Average cost (R)	Average cost + $\frac{1}{2}$ standard deviation (R)	Average cost - $\frac{1}{2}$ standard deviation (R)	Median (R)	Average cost + $\frac{1}{3}$ standard deviation (R)	Average cost - $\frac{1}{3}$ standard deviation (R)
2005	106.69 $\pm$ 78.34	145.86	67.52	95.49	132.54	80.84
2006	105.26 $\pm$ 75.72	144.43	67.40	89.80	130.25	80.27
2007	109.68 $\pm$ 76.00	147.68	71.68	102.57	134.76	84.60
2008	105.24 $\pm$ 73.50	141.99	68.49	95.97	129.50	80.99

To suggest a threshold for pharmaceutical decision-making, a range of values was used, namely the median value, the average cost plus half the standard deviation for all four study years as upper limit, and the average cost minus half the standard deviation for all four study years as the lower limit. The second scenario that was used was the average cost plus 33% of the standard deviation and the average cost minus 33% of the standard deviation. The second scenario gave a smaller threshold range. If Table 4-45 is used to suggest a cost threshold for pharmaceutical decision-making in the treatment of hypertension, a threshold value ranging between R68,50 and R142,00 or R80,99 and R129,50 is suggested for the total four-year study period, depending on the scenario used.

For the 50% scenario with a cost threshold range of R68,50 and R142,00, the following was observed:

- Approximately 35% of the average costs for antihypertensive medicine items was equal to or less than R68,49, while approximately 27% of the average costs was equal to or above R141,99.
- Thirty-eight per cent of all the average costs was within the proposed cost threshold range.

For the 33% scenario with a cost threshold range of R80,99 and R129,50, the following was observed:

- Approximately 41% of the average costs was lower than or equal to the lower limit of the proposed cost threshold range, while approximately 36% of all average costs for antihypertensive medicine items was equal to or above the upper limit of the cost threshold range.
- Approximately 24% of the antihypertensive costs was within the proposed cost threshold range.

4.8.2.2 Calculation of threshold in terms of patient gender

The second threshold that can be proposed to use as decision-making tool can be determined according to the gender of the patient. Table 4-46 summarises the average costs and medians for antihypertensive treatment for each gender.

Table 4-46: Threshold estimation of antihypertensive usage according to gender

	Female					
Year	Average cost (R)	Average cost +½ standard deviation (R)	Average cost -½ standard deviation (R)	Median (R)	Average cost + ⅓ standard deviation (R)	Average cost - ⅓ standard deviation (R)
2005	104.58 ± 76.86	143.01	66.15	87.64	129.94	79.22
2006	100.69 ± 74.32	137.85	63.53	85.60	125.22	76.16
2007	104.98 ± 74.38	142.17	67.79	96.11	129.53	80.43
2008	101.90 ± 71.69	137.75	67.05	94.13	125.56	78.24
	Male					
Year	Average cost (R)	Average cost +½ standard deviation (R)	Average cost -½ standard deviation (R)	Median (R)	Average cost + ⅓ standard deviation (R)	Average cost - ⅓ standard deviation (R)
2005	116.65 ± 79.78	155.54	76.76	108.61	142.98	90.32
2006	111.31 ± 77.31	149.97	72.65	100.16	136.82	85.80
2007	115.87 ± 77.66	154.70	77.04	110.55	141.50	90.24
2008	109.90 ± 75.51	147.66	72.14	99.90	134.82	84.98

The same formula and criteria that were used to determine the threshold for all antihypertensive medicine items was used again to determine a threshold for male and female patients. For female patients the threshold for pharmaceutical decision-making ranged between R67,01 and R137,75 or R78,24 and R125,56, and for male patients this threshold ranged between R72,14 and R147,66 or R84,98 and R134,82, depending on the scenario used.

For the 50% scenario with a cost threshold range of R67,50 and R137,00 the following was observed for female patients:

- Approximately 36% of the average costs per item was equal to or below R66,15.
- Approximately 29% of the average costs per item was equal to or above R143,01.
- Approximately 35% of the average costs per item lay within the threshold range of R66,15 to R143,01.

For the 33% scenario with a cost threshold range of R78,24 and R125,56 the following was observed for female patients:

- Approximately 41% of the average costs per item was equal to or below the lower limit.
- Approximately 36% of the average costs per item was equal to or above the upper limit.
- Approximately 23% of the average costs per item was within the cost threshold range.

For male patients, in the 50% scenario with a cost threshold range of R72,14 and R147,66 the following was observed:

- Approximately 34% of the average costs per item was equal to or below the lower limit.
- Approximately 26% of the average costs per item was equal to or above the upper limit.
- Approximately 39% of the average costs per item was within the cost threshold range.

For the 33% scenario with a cost threshold range of R84,98 and R134,82 the following was observed:

- Around 41% of the average costs per item was equal to or above the lower limit.
- About a third of the average costs per item was equal to or above the upper limit.
- Around 26% of the average costs per item was within the cost threshold range.

4.8.2.3 Calculation of threshold for the different age groups

The third threshold that can be projected to use as decision-making tool was determined according to the age of the patient. Table 4-47 summarises the average costs and medians for antihypertensive treatment for the three age groups.

Table 4-47: Threshold estimation for the three age groups

Year		AG1	AG2	AG3
2005	Average cost (R)	83.37 ± 71.80	101.59 ± 79.36	110.53 ± 78.20
	Average cost +½ standard deviation (R)	119.27	141.27	149.63
	Average cost -½ standard deviation (R)	47.47	61.91	71.43
	Median (R)	64.93	84.37	98.48
	Average cost + ⅓ std dev	107.07	127.78	136.34
	Average cost - ⅓ std dev	59.68	75.40	84.72
2006	Average cost (R)	81.65 ± 73.09	99.07 ± 76.30	105.90 ± 75.64
	Average cost +½ standard deviation (R)	118.2	137.22	143.72
	Average cost -½ standard deviation (R)	45.1	60.92	68.08
	Average cost + ⅓ std dev	105.77	124.25	130.86
	Average cost - ⅓ std dev	57.53	73.89	80.94
	Median (R)	59.75	84.37	91.19
2007	Average cost (R)	89.15 ± 84.83	104.76 ± 77.35	110.14 ± 75.85
	Average cost +½ standard deviation (R)	131.56	143.41	148.07
	Average cost -½ standard deviation (R)	46.73	66.05	72.21
	Average cost + ⅓ std dev	117.14	130.29	135.17
	Average cost - ⅓ std dev	61.16	79.23	85.11
	Median (R)	64.64	102.28	102.58

Table 4-48 (cont.): Threshold estimation for the three age groups

Year		AG1	AG2	AG3
2008	Average cost (R)	85.12 ± 79.43	100.80 ± 73.86	105.61 ± 73.45
	Average cost +½ standard deviation (R)	124.84	137.73	142.34
	Average cost -½ standard deviation (R)	45.4	63.87	68.88
	Average cost + ⅓ std dev	111.33	125.17	129.85
	Average cost - ⅓ std dev	58.91	76.43	81.37
	Median (R)	55.67	92.17	96.35

The same formula and criteria that were used to determine the threshold for antihypertensive medicine items used in the treatment of male and female patients, was applied again to determine a threshold for hypertensive patients of different age groups. For patients from AG1, the threshold for pharmaceutical decision making ranged between R46,07 and R122,06 or R57,53 and R117,14, for patients from AG2, the threshold ranged between R62,89 and R137,48 or R73,89 and R130,29 and for patients in AG3 a threshold value was set between R70,16 and R145,90 or R80,94 and R136,34.

For patients in AG1 the data for the 50% scenario with a cost threshold range of R45,40 and R124,84 revealed the following:

- Roughly 43% of the average costs per item was equal to or below the lower cost threshold limit.
- Around 29% of the average costs per item was equal to or above the upper cost threshold limit.
- Only 27% of the average costs per item was within the cost threshold range.

For the 33% scenario with a cost threshold range of R58,91 and R111,33 the data revealed the following:

- Just more than half (52%) of the average costs per item was equal to or below the lower limit.
- About a third (32%) of the average costs per item was equal to or above the upper limit of the cost threshold range.
- Approximately 16% of the average costs per item was within the cost threshold range.

For patients in AG2 the data for the 50% scenario with a cost threshold range of R63,87 and R137,73 revealed the following:

- Approximately 35% of the average costs per item was equal to or below the lower limit of the cost threshold range.

- Approximately 29% of the average costs per item was equal to or above the upper threshold limit, with approximately 36% of the average costs per item within the cost threshold range.

For the 33% scenario with a cost threshold range of R76,43 and R125,17 the data revealed the following:

- Roughly 41% of the average costs per item was equal to or below the lower limit.
- Around 38% of the average costs per item was equal to or above the upper limit of the cost threshold range.
- Only approximately 22% of the average costs per item was within the cost threshold range.

For patients in AG3 the data for the 50% scenario with a cost threshold range of R68,88 and R142,34 revealed the following:

- Approximately 35% of the average costs per item was equal to or below the lower limit of the proposed cost threshold range, while 27% was equal to or above the upper limit.
- Approximately 38% of the average costs per item was within the proposed cost threshold range.

For the 33% scenario with a cost threshold range of R81,37 and R129,85 the data revealed the following:

- Approximately 41% and 35% of the average costs per item was equal to or below the lower limit and equal to or above the upper limit respectively.
- Around 24% of the average costs was within the calculated cost range threshold.

4.8.2.4 Calculation of threshold for the different treatment categories

The fourth threshold that can be used as decision-making tool was determined according to the different treatment categories. Table 4-48 summarises the average costs and medians for antihypertensive treatment for the three treatment categories.

Table 4-49: Threshold determination with regards to treatment category

		TC1	TC2	TC3
2005	Average cost (R)	137.57 ± 69.09	42.44 ± 54.45	93.57 ± 78.96
	Average cost +½ standard deviation (R)	172.12	69.66	133.05
	Average cost -½ standard deviation (R)	103.01	15.22	54.09
	Average cost + ⅓ standard deviation (R)	160.37	60.41	119.63
	Average cost - ⅓ standard deviation (R)	114.77	24.47	67.51
	Median (R)	130.54	26	75.18
2006	Average cost (R)	130.08 ± 67.95	40.78 ± 53.08	90.10 ± 76.32
	Average cost +½ standard deviation (R)	164.06	67.32	128.26
	Average cost -½ standard deviation (R)	96.1	14.24	51.94
	Average cost + ⅓ standard deviation (R)	152.50	58.30	115.29
	Average cost - ⅓ standard deviation (R)	107.66	23.26	64.91
	Median (R)	124.95	25.95	73.09
2007	Average cost (R)	131.20 ± 67.12	42.55 ± 56.61	95.04 ± 78.94
	Average cost +½ standard deviation (R)	164.76	70.86	134.51
	Average cost -½ standard deviation (R)	97.64	14.24	55.57
	Average cost + ⅓ standard deviation (R)	153.35	61.23	121.09
	Average cost - ⅓ standard deviation (R)	109.05	23.87	68.99
	Median (R)	128.63	21	81.34
2008	Average cost (R)	125.88 ± 64.79	41.30 ± 56.91	91.07 ± 76.36
	Average cost +½ standard deviation (R)	158.28	69.76	129.25
	Average cost -½ standard deviation (R)	93.48	12.84	52.89
	Average cost + ⅓ standard deviation (R)	147.26	60.08	116.27
	Average cost - ⅓ standard deviation (R)	104.50	22.52	65.87
	Median (R)	122.6	24.01	76.84

The same formula and criteria that were used to determine the threshold for antihypertensive medicine items used in the treatment of male and female patients, were applied again to determine a threshold for hypertensive patients treated in different treatment categories. For patients from TC1, i.e. antihypertensive medicine items from MIMS group 7.3, the threshold for pharmaceutical decision-making ranged between R93,48 and R164,41 or R104,50 and R147,26, for patients treated with TC2, i.e. antihypertensive medicine items from MIMS group 16.1, the threshold ranged between R12,84 and R69,76 or R22,52 and R60,08, and for patients treated from TC3, i.e. a combination of MIMS groups 7.3 and 16.1, a threshold value of R52,89 and R129,25 or R65,87 and R116,29 was proposed.

For patients receiving treatment from TC1, the data for the 50% scenario with a cost threshold range of R93,48 and R164,41 revealed the following:

- Approximately 35% and 26% of the average costs per item were equal to and lower than the lower, or equal to and higher than the upper limits of the threshold range respectively.

- Approximately 40% of the average costs was within the proposed cost threshold range.

For the 33% scenario with a cost threshold range of R104,50 and R147,26 the data revealed the following:

- Approximately 41% and 33% of the average costs per item were equal to and lower than the lower limit, or equal to and higher than the upper limit of the proposed cost threshold range respectively.
- Only approximately 26% of the average costs per item was within the range of the proposed cost threshold range.

For patients receiving treatment from TC2 the data for the 50% scenario with a cost threshold range of R12,84 and R69,76 revealed the following:

- Almost a third (34%) of the average costs per item was equal to or below the lower limit of the proposed cost threshold range.
- Only 20% of the average costs per item was equal to or above the upper limit of the proposed cost threshold range.
- A total of 46% of the average costs per item was within the proposed cost threshold range.

For the 33% scenario with a cost threshold range of R22,52 and R68,08 the data revealed the following:

- Almost half (49%) the average costs per item was equal to or below the lower limit of the proposed cost threshold range.
- Around 22% of the average costs per item was equal to or above the upper limit.
- Approximately 30% of the average costs per item was within the proposed cost threshold range.

For patients receiving treatment from TC3 the data for the 50% scenario with a cost threshold range of R52,89 and R129,25 revealed the following:

- Approximately 39% of the average costs per item was equal to or below the lower limit of the proposed cost threshold range.
- Roughly 28% of the average costs per item was equal to or above the upper limit of the cost threshold range.
- Almost a third (33%) of the average costs per item was within the proposed cost threshold range.

For the 33% scenario with a cost threshold range of R65,87 and R116,27 the data revealed the following:

- Approximately 44% of the average costs per item was equal to or lower than the lower limit of the proposed cost threshold range, while almost a third (33%) of the average costs was equal to or higher than the upper limit of the cost threshold range.
- Only approximately 23% of the average costs per item was within the proposed cost threshold range.

4.8.2.5 Calculation of threshold for the different pharmacological groups

In this section a threshold for the different pharmacological groups is proposed. In the literature it is stated that the outcomes for the different antihypertensive pharmacological groups are equal, namely to reduce blood pressure. Therefore the costs of the different pharmacological groups can be compared and a threshold for decision-making can be suggested.

Table 4-50: Threshold calculation of the different antihypertensive pharmacological groups

Year	Pharmacological group	Average cost (R)	Average cost +½ std dev (R)	Average cost -½ std dev (R)	Average cost + ⅓ std dev (R)	Average cost - ⅓ std dev (R)	Median (R)
2005	Central-acting inhibitors	102.09 ± 77.83	141.01	63.17	127.77	76.41	64.18
	Alpha-receptor blockers	175.49 ± 92.85	221.92	129.06	206.13	144.85	184.94
	Beta-receptor blockers	98.05 ± 49.31	122.71	73.39	114.32	81.78	89.80
	Alpha- and beta-receptor blockers	118.14 ± 55.54	145.91	90.37	136.47	99.81	97.22
	Sympathetic nervous blocker	89.41 ± 78.39	128.61	50.21	115.28	63.54	38.25
	Direct-acting vasodilators	90.68 ± 86.25	133.81	47.55	119.14	62.22	57.30
	Calcium-channel blockers	158.22 ± 57.33	186.89	129.55	177.14	139.30	140.08
	ACE inhibitors	114.37 ± 65.35	147.05	81.69	135.94	92.80	106.46
	Angiotensin-receptor blockers	209.24 ± 31.34	224.91	193.57	219.58	198.90	211.63
	Others	160.64 ± 24.83	173.06	148.22	168.83	152.45	158.86
	Diuretics	43.74 ± 57.29	72.39	15.09	62.65	24.83	27.21
2006	Central-acting inhibitors	105.67 ± 78.74	145.04	66.3	131.65	79.69	67.33
	Alpha-receptor blockers	172.42 ± 95.15	220.02	124.82	203.82	141.02	184.94
	Beta-receptor blockers	90.24 ± 47.27	113.88	66.60	105.84	74.64	85.60

Table 4.49 (cont.): Threshold calculation of the different antihypertensive pharmacological groups

Year	Pharmacological group	Average cost (R)	cost +½ std dev (R)	cost -½ std dev (R)	cost + ⅓ std dev (R)	cost - ⅓ std dev (R)	Median (R)
	Alpha- and beta-receptor blockers	109.58 ± 51.73	135.45	83.71	126.65	92.51	89.74
	Sympathetic nervous blocker	85.85 ± 78.96	125.33	46.37	111.91	59.79	34.46
	Direct-acting vasodilators	88.15 ± 87.27	131.79	44.51	116.95	59.35	53.17
	Calcium channel blockers	158.22 ± 57.33	186.89	129.55	177.14	139.30	140.08
	ACE inhibitors	106.99 ± 59.21	136.60	77.38	126.53	87.45	95.77
	Angiotensin-receptor blockers	209.33 ± 34.53	226.60	192.06	220.72	197.94	211.63
	Others	180.94 ± 48.06	204.97	185.30	196.80	165.08	158.86
	Diuretics	42.28 ± 56.95	70.76	13.80	61.07	23.49	26.61
2007	Central-acting inhibitors	119.52 ± 83.53	161.29	77.75	147.08	91.96	87.50
	Alpha-receptor blockers	181.51 ± 103.79	233.41	129.61	215.76	147.26	193.01
	Beta-receptor blockers	89.84 ± 48.72	114.20	65.45	105.92	73.76	87.52
	Alpha- and beta-receptor blockers	110.07 ± 50.03	135.09	85.05	126.58	93.56	97.91
	Sympathetic nervous blocker	114.56 ± 90.08	159.60	69.52	144.29	84.83	175.70
	Direct-acting vasodilators	91.60 ± 89.03	136.12	47.08	120.98	62.22	54.36
	Calcium channel blockers	143.14 ± 58.07	172.18	114.10	162.30	123.98	137.56
	ACE inhibitors	111.83 ± 57.85	140.76	82.90	130.92	92.74	114.44
	Angiotensin-receptor blockers	201.46 ± 45.93	224.43	172.94	216.62	186.30	211.63
	Others	207.15 ± 57.03	235.67	178.63	225.97	188.33	206.19
	Diuretics	44.32 ± 62.01	75.33	13.31	64.78	23.86	24.01
2008	Central-acting inhibitors	124.01 ± 85.14	166.58	81.44	152.11	95.91	90.01
	Alpha-receptor blockers	179.61 ± 109.22	234.22	125.00	215.65	143.57	193.01
	Beta-receptor blockers	90.37 ± 49.10	114.92	65.82	106.57	74.16	89.27
	Alpha- and beta-receptor blockers	109.43 ± 47.46	133.16	85.70	125.09	93.77	95.65
	Sympathetic nervous blocker	100.37 ± 92.14	146.44	54.31	130.78	69.97	35.88
	Direct-acting vasodilators	79.85 ± 75.17	117.43	42.26	104.65	55.04	52.84
	Calcium channel blockers	131.22 ± 61.29	161.87	100.58	151.45	110.99	111.73
	ACE inhibitors	109.75 ± 56.78	138.14	81.35	128.48	91.01	102.84

Table 4.49 (cont.): Threshold calculation of the different antihypertensive pharmacological groups

Year	Pharmacological group	Average cost (R)	cost + $\frac{1}{2}$ std dev (R)	cost - $\frac{1}{2}$ std dev (R)	cost + $\frac{1}{3}$ std dev (R)	cost - $\frac{1}{3}$ std dev (R)	Median (R)
	Angiotensin-receptor blockers	209.24 $\pm$ 31.34	206.91	152.00	197.57	161.33	179.88
	Others	179.45 $\pm$ 54.91	242.29	185.05	232.56	194.78	206.19
	Diuretics	43.09 $\pm$ 62.62	74.40	11.78	63.76	22.43	24.36

The same formula and criteria that were used to determine the threshold for antihypertensive medicine items used in the different treatment categories were applied to the individual pharmacological groups to determine a threshold range.

From Table 4-49 the following thresholds can be deduced:

- Antihypertension treatment with central-acting inhibitors should have a cost ranging between R63,17 and R166,58 or R76,41 and R152,11,
- For treatment with alpha-receptor blockers a threshold ranging R124,82 and R234,22 or R141,02 and R215,76 is proposed.
- For beta-receptor blockers a threshold ranging from R65,45 to R122,71 or R73,76 and R114,32 is suggested
- When the combination of alpha- and beta-receptor blockers is used, a threshold of between R83,71 and R145,91 or R92,51 and R136,47 is anticipated.
- For hypertension treatment with sympathetic nervous blockers and direct-acting vasodilators, thresholds of R46,37 to R159,60 or R59,79 and R144,29, and R42,26 to R136,12 or R55,04 and R120,98 are suggested respectively.
- Furthermore, it is proposed that calcium channel blockers as hypertensive treatment have a threshold value of R100,58 to R186,89 or R110,99 and R177,14, while ACE inhibitors have a threshold ranging from R77,38 to R147,05 or R87,45 and R135,94.
- For the ARBs a threshold with a relatively small range, namely R152,00 to R226,60 or R161,33 and R220,72, is suggested, due to the relatively small standard deviations of the average costs.
- Finally, a threshold of R11,78 to R75,33 or R22,43 and R64,78 is proposed for hypertension treatment with diuretics. This is almost the same threshold range that has been proposed for treatment that falls into treatment category 2 (R14,24 to R69,71) which is treatment of hypertension with medicine items from MIMS group 16.1.

4.8.3 Calculation of cost ratio thresholds per household

In a study done by MUSA (2011) it was calculated that there were approximately 2 183 945 households with a relatively high income in South Africa during 2008. In order to calculate a threshold, a 'medical aid market' in South Africa was established. Since the data that was used in this study represents only an estimated 35% of the medical aid population, the total treatment cost (as per gender group, age group, treatment category, etc.) was multiplied by 1,76 to make it more generalisable for the whole private health-care sector of South Africa. The treatment cost per household was calculated by dividing the total cost for the medical aid market by the number of high-income households. However, this treatment cost includes value added tax (VAT), which is set at 14%, as well as a logistics fee, which is a percentage of the SEP (this can also be seen as the gross profit for the provider). This logistics fee is not regulated, and therefore 33% is used as a logistics fee (MUSA, 2011). It is important to take note that these threshold values are only applicable in the private health-care sector and not necessarily the total healthcare industry. A number of antihypertensive treatment cost thresholds will be calculated for the national private healthcare sector, these include cost thresholds for the different genders, age groups, treatment categories and pharmacological groups. As these ratio thresholds indicate a "ratio per household" it makes it extremely useful for planning and control purposes in the medicine usage market, as it focuses on a net ratio threshold medicine cost treatment per household. While the non-medical aid market falls outside the scope of this study, it should be further investigated for possible application in this market, especially as part of the planning of the proposed national health insurance system.

Note that in this section (Section 4.8.3), a threshold refers to a ‘net cost ratio threshold’, except if otherwise indicated. This net cost ratio threshold does not include VAT or SEP and does not have an upper or lower threshold ratio. It focuses especially on factors that may influence a household’s antihypertensive medication treatment cost. It also identifies income for the state (via VAT) and income for the medicine provider (gross profit or logistics fee) from the antihypertensive market in the private sector. For illustration purposes the cost ratio threshold was calculated as follows:

- Step 1: Total treatment cost per household = total cost for the medical aid market / number of high income households
- Step 2: VAT amount= total treatment cost per household x (114/100)
- Step 3: Logistics fee = VAT amount x (135/100)
- Step 4: Threshold = cost per household minus VAT – logistics fee

Table 4-50 summarises the calculations to determine an antihypertensive cost threshold for female and male patients. The number of high-income households used is 2 183 945 (MUSA, 2011).

Table 4-51: Ratio threshold estimation for different genders per household (2008)

Gender	Total cost (R)	Total cost for medical aid market (R)	Total treatment cost per household (R)	VAT (R)	Cost per household minus VAT (R)	Logistics fee (R)	Threshold (R)
F	112 372 194.63	197 775 062.55	90.56	11.12	79.44	19.71	59.73
M	94 992 443.95	167 186 701.35	76.55	9.40	67.15	16.66	50.49

Table 4-50 revealed that a higher threshold will exist for female patients. This however is inconsistent with the threshold determined for the different genders as seen in Section 4.8.2.2, where it was calculated that male patients would have a higher threshold value than their female counterparts.

Table 4-51 sets out the calculation of a cost threshold for antihypertensive treatment for the different age groups used in this study.

Table 4-52: Ratio threshold estimation for age groups per household (2008)

Age group	Total cost (R)	Total cost for medical aid market (R)	Total cost per household (R)	VAT	Cost per household minus VAT (R)	Logistics fee (R)	Threshold (R)
AG1	138 912.01	244 485.14	0.11	0.01	0.10	0.02	0.07
AG2	14 802 734.73	26 052 813.12	11.92	1.46	10.46	2.60	7.87
AG3	192 422 991.84	338 664 465.64	154.93	19.02	135.91	33.72	102.19

Table 4-51 reveals that a higher threshold value for the treatment of hypertensive patients will be needed for older patients. This is in line with threshold calculations made in Section 4.8.2.3. This higher threshold value can be due to the fact that hypertension is a disease more prevalent among older people, as was seen in Section 2.10.4.

A third possible cost threshold that can be calculated is for treatment within the different treatment categories. These calculations are summarised in Table 4-52.

Table 4-53: Ratio threshold estimation according to treatment category per household (2008)

Treatment category	Total cost (R)	Total cost for medical aid market (R)	Total treatment cost per household (R)	VAT	Cost per household minus VAT (R)	Logistics fee (R)	Threshold (R)
TC1	128 322 980.33	225 848 445.38	103.41	12.70	90.71	22.51	68.21
TC2	6 279 192.65	11 051 379.06	5.06	0.62	4.44	1.10	3.34
TC3	72 762 465.60	128 061 939.46	58.64	7.20	51.44	12.76	38.67

Table 4-52 revealed the following:

- If a cost threshold for hypertensive treatment is calculated for the different treatment categories, TC1 will have the highest threshold.
- The threshold for TC2 would only be R3,34. In Section 4.8.2.4 the threshold per treatment category was calculated, and TC2 also showed the lowest threshold, with TC1 having the highest threshold. The threshold for TC2 was approximately R30 below the threshold for TC1. The lower average cost of diuretic medicine items may have had an influence on the difference in threshold values for TC1 compared with TC3.

A fourth threshold that can be calculated is for generic antihypertensive equivalents. As was seen in Section 4.5.3.2, the average of generic antihypertensive medicine items is lower than that of the original antihypertensive medicine items. Table 4-53 summarises the results of calculations made to estimate a cost threshold for generic and innovator antihypertensive medicine items.

Table 4-54: Ratio threshold estimation for generic indicator per household (2008)

Generic indicator	Total cost (R)	Total cost for medical aid market (R)	Total cost per household (R)	VAT (R)	Cost per household minus VAT (R)	Logistics fee (R)	Threshold (R)
N	70 234 226.61	123 612 238.83	56.60	6.95	49.65	12.32	37.33
O	33 666 702.03	59 253 395.57	27.13	3.33	23.80	5.91	17.89
Y	103 463 709.94	182 096 129.49	83.38	10.24	73.14	18.15	54.99

Table 4-53 revealed that the threshold for treatment with generic antihypertensive medicine items should be approximately R54.99, while treatment with originator antihypertensive medicine items should be approximately R17,89.

A fifth way of estimating a cost threshold for hypertensive treatment is when the gender of the patient is combined with the type of antihypertensive medicine item used, namely generic or innovator. Table 4-54 summarises the results of threshold calculations combining gender and generic indicator.

Table 4-55: Ratio threshold estimation for gender and GI per household (2008)

Generic indicator	Gender	Total cost (R)	Total cost for medical aid market (R)	Total treatment cost per household (R)	VAT (R)	Cost per household minus VAT (R)	Logistics fee (R)	Threshold (R)
N	F	38 962 835.22	68 574 589.99	31.40	3.86	27.54	6.83	20.71
N	M	31 271 391.39	55 037 648.85	25.20	3.09	22.11	5.48	16.62
O	F	17 819 180.82	31 361 758.24	14.36	1.76	12.60	3.13	9.47
O	M	15 847 521.21	27 891 637.33	12.77	1.57	11.20	2.78	8.42
Y	F	55 590 178.59	97 838 714.32	44.80	5.50	39.30	9.75	29.55
Y	M	47 873 531.35	84 257 415.18	38.58	4.74	33.84	8.40	25.45

Table 4-54 reveals that a higher threshold is needed to treat a female patient with a generic antihypertensive medicine item than to treat a male patient, and that the threshold is the lowest when a male patient is treated with an originator antihypertensive medicine item.

A sixth way of threshold estimation is the combination of the patient's gender with the treatment category used. As was seen in Section 4.5.3.1, TC2 had the lowest average cost, while TC1 had the highest average cost. Table 4-55 summarises the results of the calculations to determine a threshold if the patient's gender and the treatment category is combined.

Table 4-56: Ratio threshold estimation for gender and TC per household (2008)

Treatment category	Gender	Total cost (R)	Total cost for medical aid market (R)	Treatment cost per household (R)	VAT (R)	Cost per household minus VAT (R)	Logistics fee (R)	Threshold (R)
TC1	F	64 748 966.19	113 958 180.49	52.18	6.41	45.77	11.36	34.41
TC1	M	63 574 014.14	111 890 264.89	51.23	6.29	44.94	11.15	33.79
TC2	F	4 502 851.54	7 925 018.71	3.63	0.45	3.18	0.79	2.39
TC2	M	1 776 341.11	3 126 360.35	1.43	0.18	1.26	0.31	0.94
TC3	F	43 120 376.90	75 891 863.34	34.75	4.27	30.48	7.56	22.92
TC3	M	29 642 088.70	52 170 076.11	23.89	2.93	20.95	5.20	15.76

From Table 4-55 it is revealed that:

- A higher cost threshold is needed to treat female patients, irrespective of the TC that is used.
- Treatment of male patients with TC2 has the lowest proposed cost threshold.
- Treatment of female patients with TC1 have the highest cost threshold.

A seventh way of estimating a cost threshold for hypertensive treatment is when the age of the patient is combined with the type of antihypertensive medicine item used, namely generic or innovator. As was stated previously, hypertensive treatment with a generic antihypertensive medicine item has a lower average cost than treatment with an original item. Table 4-56 summarises the results of calculations combining generic indicator and age group.

Table 4-57: Ratio threshold estimation for age and generic indicator per household (2008)

Generic indicator	Age group	Total cost (R)	Total cost for medical aid market (R)	Treatment cost per household (R)	VAT (R)	Cost per household minus VAT (R)	Logistics fee (R)	Threshold (R)
N	AG1	17 260.52	30 378.52	0.01	0.00	0.01	0.00	0.01
N	AG2	4 656 525.69	8 195 485.21	3.75	0.46	3.29	0.82	2.48
N	AG3	65 560 440.40	115 386 375.10	52.83	6.49	46.35	11.50	34.85
O	AG1	49 705.35	87 481.42	0.04	0.00	0.04	0.01	0.03
O	AG2	1 864 903.20	3 282 229.63	1.50	0.18	1.32	0.33	0.99
O	AG3	31 752 093.48	55 883 684.52	25.59	3.14	22.45	5.57	16.88
Y	AG1	71 946.14	126 625.21	0.06	0.01	0.05	0.01	0.04
Y	AG2	8 281 305.84	14 575 098.28	6.67	0.82	5.85	1.45	4.40
Y	AG3	95 110 457.96	167 394 406.01	76.65	9.41	67.23	16.68	50.55

Table 4-56 reveals the following:

- AG3 has a higher threshold, irrespective of generic indicator.
- The highest threshold is seen for patients in AG3 receiving generic antihypertensive medicine items.
- A lower threshold is proposed for treatment with original antihypertensive medicine items than for treatment with a generic antihypertensive medicine item.

An eighth way of estimating a cost threshold for hypertensive treatment is when the TC to be used is combined with the age of the patient. As was stated previously, hypertensive treatment

with TC2 had a lower average cost than treatment with TC1 or TC3, and antihypertensive treatment cost increases with age. Table 4-57 summarises the results of calculations combining TC and age group.

Table 4-58: Ratio threshold estimation for age and treatment category per household (2008)

Treatment category	Age group	Total cost (R)	Total cost for medical aid market (R)	Total cost per household (R)	VAT (R)	Cost per household minus VAT (R)	Logistics fee (R)	Threshold (R)
TC1	AG1	58 544.52	103 038.36	0.05	0.01	0.04	0.01	0.03
TC1	AG2	10 599 974.10	18 655 954.42	8.54	1.05	7.49	1.86	5.63
TC1	AG3	117 664 461.71	207 089 452.61	94.82	11.64	83.18	20.64	62.54
TC2	AG1	30 498.49	53 677.34	0.02	0.00	0.02	0.01	0.02
TC2	AG2	509 434.49	896 604.70	0.41	0.05	0.36	0.09	0.27
TC2	AG3	5 739 259.67	10 101 097.02	4.63	0.57	4.06	1.01	3.05
TC3	AG1	49 869.00	87 769.44	0.04	0.00	0.04	0.01	0.03
TC3	AG2	3 693 326.14	6 500 254.01	2.98	0.37	2.61	0.65	1.96
TC3	AG3	69 019 270.46	121 473 916.01	55.62	6.83	48.79	12.11	36.68

From Table 4-57 it is clear that irrespective of the TC that is used, a higher cost threshold is proposed for patients from AG3.

Lastly, antihypertensive treatment cost thresholds can also be calculated for the private health-care sector for the nine provinces of South Africa. Table 4-58 summarises the number of high-income households per province with the related antihypertensive medicine cost.

Table 4-598: Number of estimated high income households per province per household (2008)

Province	Number of estimated high income households	Total cost (R)	Total cost for medical aid market (R)
Eastern Cape	182 062	13 896 645.64	24 458 096.33
Free State	121 235	10 043 872.07	17 677 214.84
Gauteng	823 907	90 953 549.92	160 078 247.86
KwaZulu-Natal	282 421	29 729 804.47	52 324 455.87
Limpopo	136 293	6 218 523.10	10 944 600.66
Mpumalanga	145 358	8 295 682.77	14 600 401.68
North West	97 786	10 146 524.69	17 857 883.45
Northern Cape	44 268	2 951 882.03	5 195 312.37
Western Cape	395 355	34 950 477.12	61 512 839.73
Province not indicated	76 495	177 676.77	312 711.12

The treatment cost per household can be calculated by using the number of high income households, and a threshold can be derived. Table 4-59 summarises the results of these calculations.

Table 4-59: Summary of the treatment cost per household per province (2008)

Province	Total cost (R)	Total cost for medical aid sector (R)	Total treatment cost per household (R)	VAT (R)	Cost minus VAT (R)	Logistics fee (R)	Threshold (R)
Eastern Cape	13 896 645.64	24 458 096.33	134.34	16.50	117.84	29.24	88.60
Free State	10 043 872.07	17 677 214.84	145.81	17.91	127.90	31.74	96.17
Gauteng	90 953 549.92	160 078 247.86	194.29	23.86	170.43	42.29	128.14
KwaZulu-Natal	29 729 804.47	52 324 455.87	185.27	22.75	162.52	40.32	122.19
Limpopo	6 218 523.10	10 944 600.66	80.30	9.86	70.44	17.48	52.96
Mpumalanga	8 295 682.77	14 600 401.68	100.44	12.34	88.11	21.86	66.25
North West	10 146 524.69	17 857 883.45	182.62	22.43	160.19	39.75	120.45
Northern Cape	2 951 882.03	5 195 312.37	117.36	14.41	102.95	25.54	77.40
Western Cape	34 950 477.12	61 512 839.73	155.59	19.11	136.48	33.86	102.62
Not indicated	177 676.77	312 711.12	6.98	0.86	6.13	1.52	4.61

Table 4-59 reveals the following:

- The highest cost threshold for antihypertensive treatment is needed for Gauteng, approximately R128,14 per household, followed by KwaZulu-Natal, where a cost threshold of R122,19 per household is estimated.
- The province with the lowest antihypertensive cost threshold is Limpopo, with a threshold of approximately R52,96 per household

The last threshold estimation that is discussed is a threshold based on the pharmacological group. The results of these calculations are summarised in Table 4-60 and Appendix L.

Table 4-600: Ratio threshold estimation according to antihypertensive pharmacological group per household (2008)

Pharmacological group	Total cost (R)	Total cost for medical aid market (R)	Treatment cost per household (R)	VAT (R)	Cost minus VAT (R)	Logistics fee (R)	Threshold (R)
Central acting inhibitors	2 495 959.87	4 392 889.37	2.01	0.25	1.76	0.44	1.33
Alpha-receptor blockers	6 813 279.70	11 991 372.27	5.49	0.67	4.82	1.20	3.62
Beta-receptor blockers	22 068 382.39	38840353.01	17.78	2	16	4	11.73
Alpha- and beta-receptor blockers	8 319 809.18	14 642 864.16	6.70	0.82	5.88	1.46	4.42
Sympathetic nervous blockers	881 045.99	1 550 640.94	0.71	0.62	0.09	0.47	0.07
Direct acting vasodilators	171 157.72	301 237.59	0.14	0.02	0.12	0.03	0.09
Calcium channel blockers	27 394 634.49	48 214 556.70	22.08	2.71	19.37	4.81	14.56
ACE-inhibitors	7 7642 891.87	136 651 489.69	62.57	7.68	54.89	13.62	41.27
Angiotensin receptor blockers	56 738 422.31	99 859 623.27	45.72	5.62	40.11	9.95	30.16
Other	1 879 001.82	3 307 043.20	1.51	0.19	1.33	0.33	1.00
Diuretics	20 649 271.78	36 342 718.33	16.64	2.04	14.60	1.68	12.92
Total	225 053 857.10	396 094 788.53	181.37	22.27	159.09	39.47	119.62

Table 4-60 reveals the following:

- A ratio threshold for antihypertensive treatment can be set at R119,62 per household.
- The most expensive antihypertensive treatment will be the ACE inhibitors. To treat a hypertensive patient with an ACE inhibitor it would cost the private health-care provider approximately R41,27 per household.
- Treatment with an angiotensin-receptor antagonist would cost the private health insurer R30,16 per household per year.
- Treatment with a beta-blocker will cost approximately R11,73 per household.
- To treat a hypertensive patient with a calcium channel blocker would cost R14,56 per household.
- The threshold for diuretics (16.1) can be set at approximately R12,92 per household.

Pharmaceutical thresholds for antihypertensive treatment in the different provinces in South Africa have also been calculated according to the different pharmacological groups (MIMS group 7.3.1 – 7.3.10 and 16.1). The results of these calculations can be seen in Appendix J, Tables J1 to J11.

Table J1 reveals that treatment with a **central-acting inhibitor** may cost R1,95 per household. It will cost the private health-care insurer approximately R4,26 per household to treat patients residing in Gauteng with a central-acting inhibitor. In North West treatment with these antihypertensive medicine items will cost the private health-care insurer R2,05 per household.

From to Table J2 it is seen that treatment with an **alpha-receptor blocker** would cost the private health-care insurer in the region of R3,62 per household. Treating patients in Gauteng with these antihypertensive medicine items will cost approximately R12,29 per household, while treatment of patients living in KwaZulu-Natal will cost in the region of R4,22 per household. For Free State patients a cost ratio threshold of R3,20 per household can be set.

Table J3 reveals that treatment with a **beta-receptor blocker** may cost R11,73 per household. It will cost the private health-care insurer approximately R35,26 per household to treat patients residing in Gauteng with a central acting inhibitor. In North West a cost threshold for treatment with these antihypertensive medicine items can be set at R16,18 per household. For patients residing in KwaZulu-Natal a cost threshold of R14,73 per household can be set, while Western Cape patients can expect an antihypertensive medicine cost ratio threshold of approximately R10,58 per household.

From to Table J4 it is seen that treatment with an **alpha- and beta-receptor blocker** would cost the private health-care insurer in the region of R4,42 per household. Treating patients in Gauteng with these antihypertensive medicine items will cost approximately R14,32 per household, while treatment of patients living in the Western Cape will cost in the region of R4,67 per household. For patients residing in KwaZulu-Natal a cost ratio threshold of R4,21 per household can be set.

Table J5 reveals that a cost threshold for treatment with a **sympathetic nervous blocker** will be only R0,07 per household. The low prevalence (0,1%, n = 2 157; N = 2 051 705) of these antihypertensive medicine items as well as the relatively low total cost may be attributable to the low threshold value. The same low threshold was calculated for treatment with a **direct-acting vasodilator**, as seen in Table J6. The cost ratio threshold for these antihypertensive items can be set at approximately R0,09 per household.

From Table J7 it is clear that treatment with a **calcium channel blocker** would cost the private health-care insurer in the region of R14,56 per household. A cost threshold for treating patients in Gauteng with these antihypertensive medicine items can be set at around R44,49 per household, while treatment of patients living in KwaZulu-Natal will cost in the region of R17,63 per household. For patients residing in North West a cost threshold of R16,78 per household

can be set. For the Eastern Cape and Western Cape a cost ratio threshold of R13,34 per household and R12,86 per household respectively is expected.

Treatment with an **ACE inhibitor** will have the highest overall threshold value, namely R41,27, as seen in Table J8. For patients living in Gauteng a threshold value for treatment with an ACE inhibitor can be set at approximately R123,85 per household. Treating patients residing in North West will cost approximately R42,49 per household, while patients living in KwaZulu-Natal can expect a cost ratio threshold in the region of R42,19 per household. For patients residing in the Western Cape a cost ratio threshold of R40,75 per household is expected.

Table J9 reveals that treatment with an **angiotensin-receptor blocker** may cost R30,16 per household. It will cost the private health-care insurer approximately R97,11 per household to treat patients residing in Gauteng with an angiotensin-receptor blocker. In North West a cost threshold for treatment with these antihypertensive medicine items can be set at R35,90 per household, while a cost ratio threshold of R35,70 is proposed for Free State patients suffering from hypertension.

Table J10 indicates that a cost ratio threshold value of R1,00 per household can be proposed for hypertensive patients treated with antihypertensive medicine items falling under the group 'Others' (MIMS group 7.3.10).

Lastly, Table J11 reveals that treatment with a **diuretic** may cost R12,92 per household. In Gauteng it will cost the private health-care insurer approximately R40,60 per household to treat patients with a diuretic. In KwaZulu-Natal a cost threshold for treatment with these antihypertensive medicine items can be set at R14,99 per household, while a cost ratio threshold of R13,74 is proposed for patients living in North West suffering from hypertension.

To conclude, from the above tables and discussions it can therefore be clearly seen that numerous thresholds can be derived for different scenarios. As was stated in the opening paragraphs of this section, we have used medicine cost, since all the antihypertensive treatment is expected to have the same outcome, namely lowering blood pressure. A threshold/thresholds based on cost-minimisation principles have therefore been derived using the average costs and standard deviations. Since no effectiveness data (e.g. number of myocardial infarcts prevented, etc.) was available, cost-effectiveness threshold could not be calculated and proposed.

4.9 CHAPTER SUMMARY

In this chapter the results of the empirical investigation was outlined and discussed. The focus was on the prescribing patterns of antihypertensive medicine items and the data was analysed according to three age groups, gender and treatment category. Cost savings through generic substitution were investigated, as well as the different combinations of antihypertensive medicine items and patient adherence or compliance. Possible thresholds that can be used as planning instruments were also proposed.

In Chapter 5 some the conclusions drawn in this study are documented and some recommendations are made.

CHAPTER 5:

CONCLUSIONS, LIMITATIONS AND RECOMMENDATIONS

5.1 INTRODUCTION

In this chapter the conclusions and limitations are discussed. Certain recommendations for this study will conclude this chapter.

5.2 CONCLUSIONS

The following conclusions can be discussed on the basis of the specific objectives of the research.

The **first specific research objective** was to review original pharmacoeconomic studies with reference to the application of hypertension treatment.

This was done through an overview of the literature (refer to Chapter 2, Sections 2.2.2 and 2.8). From the literature it can be concluded that pharmacoeconomic studies, especially cost-effectiveness studies and cost-minimisation studies, can play an important role in providing information on the challenges to contain costs in the treatment of hypertension.

The **second specific research objective** was to determine the prevalence and cost implication of hypertension medicine treatment in a section of the private health-care sector of South Africa by means of demographical factors and geographical distribution. From the results and discussion in Chapter 4 (Sections 4.5.2, 4.5.4.1, 4.5.4.6 and 4.6), the following remarks can be made:

- The antihypertensive medicine items accounted for between 7,68% and 9,69% of all medicine items in the database and between 10,94% and 11,10% of the total cost during the four study years.
- Antihypertensive medicine items constituted 7 695 151 (70,04% N = 10 986 407) of all the cardiovascular medicine items and 59,94% of the total cost of cardiovascular medicine items for all four study years collectively for these medicine items.
- Three age groups were identified, namely age group 1 (patients ≤ 18 years), age group 2 (>18 and ≤ 45 years) and age group 3 (>45 years). Regarding the age groups the following was noted:

- The most frequently prescribed antihypertensive medicine items for patients in AG1 during the four-year study period were (in order of highest to lowest prevalence) diuretics, ACE inhibitors, beta-receptor blockers, calcium channel blockers and ARBs.
- The most frequently prescribed antihypertensive medicine items for patients in AG2 during the four-year study period were (in order of highest to lowest prevalence) ACE inhibitors, diuretics, ARBs, beta-receptor blockers and calcium channel blockers.
- The most frequently prescribed antihypertensive medicine items for patients in AG3 during the four-year study period were (in order of highest to lowest prevalence) ACE inhibitors, diuretics, ARBs, beta-receptor blockers and calcium channel blockers.
- Patients in AG3 had the highest usage of antihypertensive medicine items, accounting for more than 90% of all the antihypertensive medicine items throughout the four-year study period.
- As far as gender is concerned, more female than male patients received antihypertensive medication during the four-year study period. An investigation into possible reasons for this observation falls outside the scope of this study.
- Female patients accounted for approximately 57,2% (N = 5 836 312, n = 3 337 200) of all hypertension patients during the four-year study period, and for approximately 54% of the total cost of antihypertensive medicine.
- A geographic distribution of the number of hypertensive patients revealed that the highest number of hypertensive patients resided in Gauteng (between 40,3% and 41,4%), the Western Cape (between 17% and 17,8%) and KwaZulu-Natal (between 13,7% and 15,3%).
- A geographic distribution of the usage of antihypertensive medicine usage revealed that the highest usage of antihypertensive medicine items was in Gauteng, the Western Cape and KwaZulu-Natal.
 - Between 41,2% and 43,5% of all the antihypertensive items claimed for during the study period was for patients in the Gauteng. These items accounted for between 43,6% and 43,8% of the total cost of antihypertensive medicine items during the four-year study period.
 - Gauteng, KwaZulu-Natal and the Western Cape had the highest usage of diuretic medicine items, accounting for between 70,3% and 71,6% of all the diuretic medicine items during all four study years. The cost of the diuretics in these three provinces amounted to approximately 75% of the total cost of diuretic medicine items throughout the four-year study period.

To conclude, even though antihypertensive medicine items constituted a high proportion (approximately 70%) of the cardiovascular medicine items in the database, they can be regarded as relatively expensive. Older patients (patients older than 45 years) and female patients consumed the highest proportion of antihypertensive medicine items. This was found to be in line with the literature (see Chapter 2, Section 2.10.4 and Chapter 4, Section 4.5.4.6). Furthermore, the investigation into the geographical distribution of hypertensive patients is important not only for the private market but also to aid in decision making in the public healthcare sector and the proposed national health insurance system.

The **third research objective** was to analyse the prescription patterns of antihypertensive medicine items according to a medicine claims database in the pharmacy benefit management environment. From the results and discussion in Chapter 4 Section 4.5 the following was noted:

- Between 16,6% and 19,7% of all the prescriptions contained antihypertensive medicine items, and the cost of these prescriptions accounted for between 11,5% and 11,7% of the total cost of all medicine items claimed during the four-year study period.
- Patients in AG3 had the highest number of prescriptions, average number of prescriptions per patient and average cost per patient per year.
- Furthermore, patients in AG3 were responsible for between 83,2% and 86,8% of all the antihypertensive prescriptions during the four year study period, which accounted for between 91,6% and 93,1% of the total cost during the four-year study period.
- Prescription patterns were also analysed for mono and combination hypertension treatment.
- As was stated in Chapter 1, the treatment of hypertension may become a complex process. This was accentuated in the results where prescriptions containing up to eight combinations of antihypertensive items were observed.
- As single agents the most frequently prescribed antihypertensive medicine items were ACE inhibitors, diuretics, calcium channel blockers, beta-receptor blockers and one-pill combination products, e.g. an indapamide/perindopril combination product. The ACE inhibitors most frequently prescribed as monotherapy included perindopril, enalapril and lisinopril. The diuretic products most frequently prescribed included spironolactone, furosemide and indapamide, as well as the one-pill combination product consisting of amiloride and HCTZ. The only calcium channel blocker prescribed was amlodipine
- The most observations were made for prescriptions containing two or three antihypertensive agents.
- For the two-item combination prescriptions the following was revealed:

- The ACE inhibitor-diuretic combination was the most frequently prescribed.
- For 2005 and 2006 indapamide had the highest prevalence as one of the antihypertensive medicine items (56 106 prescriptions in 2005 and 61 161 prescriptions in 2006).
- HCTZ was second with approximately 37 345 prescriptions.
- The total cost for all two-item combination prescriptions in 2005 amounted to R67 859 319,49, with an average cost of R203,98 ± R116,15 per prescription. A total of 332 676 prescriptions were observed.
- For 2006 the total cost for all two-item combination prescriptions in all age groups accounted to R72 685 539,04 with an average cost of R195,75 ± R110,19 per prescription. A total of 371 325 prescriptions were observed.
- During 2007 and 2008 the calcium channel blocker amlodipine had the highest prevalence (65 123 prescriptions in 2007 and 73 211 prescriptions in 2008).
- For 2007 the total cost for all two-item combination prescriptions in all age groups containing two antihypertensive medicine items amounted to R72 132 873,03, with an average cost of R207,87 ± R107,41 per prescription. A total of 347 015 prescriptions were observed.
- For 2008 the total cost for all two-item combination prescriptions in all age groups containing two antihypertensive medicine items amounted to R68 819 568,47, with an average cost of R198,47 ± R104,28 per prescription. A total of 346 732 prescriptions in 17 688 different combinations were observed.
- For the three-item combination prescriptions the following was noted:
 - During 2005, 63 219 prescriptions consisting of three antihypertensive medicine items were observed in 15 780 different combinations, with an average cost of R340,19 ± R153,14 per prescription and a total cost of R21 506 187,81.
 - During 2006, 76 241 prescriptions consisting of three antihypertensive medicine items were observed in 17 037 different combinations, with an average cost of R326,68 ± R147,16 per prescription and a total cost of R24 906 246,38.
 - During 2007, 78 484 prescriptions consisting of three antihypertensive medicine items were observed in 15 757 different combinations, with an average cost of R337,20 ± R144,75 per prescription, totalling R26 465 030,69.
 - During 2008, 80 588 prescriptions consisting of three antihypertensive medicine items were observed in 15 408 different combinations, with an average cost of R324,58 ± R144,49 per prescription and a total cost of R26 157 169,23.

- For four-item prescriptions the following observations can be made:
 - During 2005, 10 765 prescriptions consisting of four antihypertensive medicine items were observed in 3 688 different combinations, with an average cost of R482,15 ± R191,47 per prescription and a total cost of R5 190 360,09.
 - During 2006, 13 984 prescriptions consisting of four antihypertensive medicine items were observed in 4 500 different combinations, with an average cost of R454,89 ± R185,65 per prescription, totalling R6 361 206,17.
 - During 2007, 15 014 prescriptions consisting of four antihypertensive medicine items were observed in 4 339 different combinations with an average cost of R471,45 ± R191,14 per prescription and a total cost of R7 078 319,80.
 - During 2008, 16 020 prescriptions consisting of four antihypertensive medicine items were observed in 3 688 different combinations with an average cost of R458,71 ± R193,85 per prescription, totalling R7 348 481,21.
- For the five-item combination prescriptions the following remarks can be made:
 - During 2005 there were 1 277 five-item combination prescriptions prescribed and dispensed with an average cost of R648,53 ± R219,45 per prescription and a total cost of R828 168,14.
 - During 2006 there were 1 707 five-item combination prescriptions prescribed and dispensed in 661 different combinations, with an average cost of R626,82 ± R215,49 per prescription, totalling R1 069 974,41.
 - During 2007 there were 1 976 five-item combination prescriptions observed, in 682 different combinations with an average cost of R654,88 ± R225,03 per prescription and a total cost of R1 294 047,97.
 - During 2008 there were 2 272 five-item combination prescriptions prescribed and dispensed, with an average cost of R642,04 ± R239,90 per prescription totalling R1 458 710,70.
- For the six-item combination prescriptions the following were revealed:
 - During 2005 there were 134 prescriptions consisting of six antihypertensive medicine items prescribed and dispensed, totalling R106 526,94, with an average cost of R794,98 ± R246,04. All these prescriptions were for patients in age group 3.
 - During 2006, 219 prescriptions were observed in 92 different combinations, with an average cost of R773,97 ± R237,24, totalling R169 499,26.

- During the 2007 study year, 232 prescriptions containing six antihypertensive medicine items were observed, with a total cost of R176 460,30, and an average cost of $R760,60 \pm R273,33$ per prescription.
- During the 2008 study year, 268 prescriptions containing six antihypertensive medicine items were observed in 104 different combinations, with a total cost of R211 718,77, and an average cost of $R790,00 \pm R307,23$ per prescription.
- For the seven-item combination prescriptions the following was observed:
 - During all four study years there were 67 seven-item antihypertensive medicine prescriptions totalling R96 335,92.
 - During 2005, eight seven-item antihypertensive combination prescriptions were observed, with an average cost of $R995,85 \pm R296,89$, totalling R7 966,77. All these prescriptions were prescribed to patients in age group 3.
 - For the 2006 study year there were 23 prescriptions consisting of seven antihypertensive items, with an average cost of $R1\ 030,61 \pm R334,74$ and a total cost of R23 703,92. All the seven-item antihypertensive combination prescriptions were prescribed to patients in age group 3.
 - During 2007 there were also only 23 prescriptions observed with an average cost of $R1\ 075,38 \pm R281,60$, with a total cost of R49 467,47.
 - During 2008 13 prescriptions consisting of seven antihypertensive medicine items were observed, with an average cost of $R1\ 169,06 \pm R499,36$, totalling R15 197,76.
- During the four-year study period there were only 10 observations for prescriptions with eight antihypertensive medicine items.

To conclude, a wide variety of prescribing patterns for the treatment of hypertension exist in the pharmacy benefit management environment. This is accentuated by the differences in age, gender and combination therapy, with a wide variety of averages, standard deviations and cost patterns.

The **fourth research objective** was to conduct applicable pharmacoeconomic studies on the data in order to elucidate on the usage and cost of antihypertensive treatment.

Cost-minimisation analysis (CMA) was used to calculate possible cost savings through generic substitution. These savings were calculated for antihypertensive pharmacological groups, treatment categories, age groups and patient gender. The results observed in Section 4.5.3.2 showed that:

- Generic antihypertensive medicine items accounted for more than 50% of all the antihypertensive medicine items throughout the four-year study period.
- The average costs of generic medicine items were lower than those of the original hypertensive medicine items.
- Total possible cost savings with 100% generic substitution over a four-year study period could have amounted to R50 412 643,73. If only 45% of innovator antihypertensive medicine items had been substituted with a generic equivalent, a saving of R22 685 689,65 could have been possible during the four-year study period.
- The number of generic medicine items utilised by antihypertensive patients increased by 17,26% over the four-year period.
- For each treatment category (TC) the generic items constituted the highest percentage, ranging between 43,9% and 55,0% for TC1, 73,9% to 75,6% for TC2 and for TC3 the generic items constituted between 60,3% and 68,1%.
- The calcium channel blockers had a 39,64% increase in generic utilisation, the ACE inhibitors had a 24,46% increase in generic utilisation and the alpha- and beta-receptor blockers had a 21,3% increase in generic utilisation from 2005 through to 2008. T
- The largest cost savings could have been possible if the innovator ACE inhibitors and diuretics had been substituted with their generic equivalents.
- Total generic substitution of the innovator ACE inhibitors would have led the following possible cost savings:
 - R7 362 197,44 (42%, N = R17 350 942,20) during 2005
 - R8 433 372,00 (45%, N = R18 947 403,68) in 2006
 - R4 748 813,32 (28%, N = R15 573 800,80) during 2007
 - R3 058 369,84 (23%, N = R13 284 449,55) in 2008.
- Total generic substitution for the diuretics could have led to the following possible cost savings:
 - R3 685 119,36 (21%, N = R17 350 942,20) in 2005
 - R4 075 199,20 (21%, N = R18 947 403,68) in 2006
 - R5 810 968,67 (34%, N = R15 573 800,80) during 2007
 - R4 731 947,66 (36%, N = R13 284 449,55) during 2008.
- Possible cost savings of R136 717,63 could have been achieved due to generic substitution by patients in AG1, while possible cost savings of R6 958 563,18 could have been achieved if all patients in AG2 had opted for the generic equivalent antihypertensive medicine items. If patients in AG3 had opted for generic substitution, cost savings of R83 682 728,56 could have been achieved during the four-year study period.

- Possible cost savings of R49 440 776,30 and R40 209 508,61 could have been achieved due to generic substitution by female and male patients respectively during the four-year study period.

To conclude, while the usage of generic substitution increased during the four study years, further cost savings are still possible through more generic substitution.

The **fifth research objective** was to investigate patient compliance/adherence with reference to antihypertensive treatment.

Refill-adherence rates (RAR) were calculated for the different treatment categories (TC), patient age groups (AG), patient gender and top 10 pharmaceutical products per TC. From the results in Chapter 4, Section 4.6, Tables 4–33 to 4–44, the following observations were made:

- The total number of antihypertensive medicine items that had been prescribed more than once during the study period amounted to 632 577 with an associated cost of R836 205 314,17. Only 43,77% (n = 61 200, N = 139 812) of items prescribed in TC2 (i.e. MIMS group 16.1, Diuretics) was prescribed more than once.

For refill-adherence rate according to TC the following was observed (Table 4–34):

- The average refill-based adherence rate for TC1 was 86,19%, for TC2 it was 70,20% and for TC3 the average refill-based adherence rate was 85,49%.
- Only 53,19% of all the items that were used in TC1 (i.e. antihypertensive medicine items from MIMS group 7.3) had acceptable refill-adherence rates during the four-year study period.
- The RAR was the lowest for antihypertensive medicine items dispensed in TC2 (i.e. medicine items from MIMS group 16.1), with only 33,36% of these items with an acceptable AR.
- TC2 also had the highest unacceptably low refill-adherence rate with 58,12%.
- Between 8,3% and 9,87% of all the antihypertensive medicine items had unacceptably high adherence rates, indicating that patients had an oversupply of more than 120%, indicating that patients may have overused their medicines.

For RAR in relation to patient age, the following observations can be made (Table 4–38, Table 4–39 and Table 4–40):

- Patients in AG1 receiving antihypertensive medicine items from TC2 had the lowest average adherence rate, i.e. 68,05%.
- Only 24% of the antihypertensive medicine items from TC2 dispensed to patients from AG1 had acceptable refill-adherence rates, whilst 64,44% of these items had

unacceptably low refill-adherence rates and 11,56% had unacceptably high (>120%) refill adherence rates.

- Patients from age group 1 receiving antihypertensive medicine items from TC3 had the highest refill-adherence rate, i.e. 87,27%.
- Patients in AG2 receiving treatment with antihypertensive medicine items from TC1 had the highest average adherence rate (85,28%).
- The average RAR for patients receiving antihypertensive medicine items from TC2 was a relatively low 66%, indicative of an unacceptably low RAR.
- Patients in AG3 receiving treatment from TC1 had the highest average RAR, even though only 54,6% of these medicine items had acceptable refill-adherence rates.
- TC2 again showed the lowest average refill-adherence rate, with only 35,1% of all items having acceptable refill-adherence rates, whilst 56,71% of items in TC2 had unacceptable low RAR and only 8,20% showed unacceptable high RAR ($80\% < \text{RAR} \leq 120\%$).
- To conclude, patients in age group 3 showed the best RAR.

For an RAR in relation to the gender of the patient, the following was observed (Tables 4–41 and 4–42):

- 53,62% of the female patients that were using antihypertensive medicine items from TC1 had an acceptable RAR, while approximately a third (33,62%) of female patients receiving antihypertensive treatment from TC2 had an acceptable RAR.
- The average RARs for female patients receiving treatment from TC1 and TC3 were 85,98% and 84,23% respectively.
- The average RAR for male patients receiving treatment from TC1 and TC3 were 86,40% and 87,19% respectively.
- Male patients that received antihypertensive treatment from TC2 had an average RAR that was below the acceptable level of 80%, i.e. 73,23%.
- To conclude, in general male patients showed better adherence to antihypertensive treatment than their female counterparts.

For RAR according to pharmacological active ingredient, the following was seen (Table 4–43):

- In TC1 the one-pill fixed-dose combination of indapamide/perindopril had the highest prevalence, but only the fourth highest RAR of 86,32% after amlodipine (90,412%), valsartan/HCTZ (86,81%) and enalapril/HCTZ (86,38%).
- All of the antihypertensive medicine items prescribed in TC1 showed an acceptable RAR.
- For TC2, spironolactone showed the highest RAR with 78,54%, followed by the one-pill fixed-dose combination of triamterene/HCTZ with 76,59% and torasemide (72,85%).

- None of the top 10 antihypertensive medicine items prescribed in TC2 had an acceptable refill-adherence rate above, i.e. $80\% < \text{RAR} \leq 120\%$.
- For TC3, amlodipine showed the highest RAR with 94,27%, followed by bisoprolol (90,32%) and lisinopril (89,84%).
- Only furosemide (79,46%) and the one-pill fixed-dose combination of amiloride/HCTZ (74,12%) had unacceptably low RAR in TC2.

The financial implication of over- or under-medication supply was investigated and the following remarks can be made (Table 4–44):

- The 38,52% (Table 4–37) of antihypertensive medicine items prescribed in TC1 with an unacceptably low RAR accounted for approximately 26,3% ($n = \text{R}134\,427\,457,00$, $N = \text{R}511\,245\,365,00$) of the total cost.
- The 53,19% of antihypertensive medicine items prescribed to patients in TC1 with an acceptable RAR had a total cost of $\text{R}320\,248\,665,00$ (62,6%, $N = \text{R}511\,245\,365,00$).
- The cost contribution for the antihypertensive medicine items in TC1 with an unacceptably high RAR was approximately 3,80% ($n = \text{R}19\,419\,203,66$, $N = \text{R}511\,245\,365,00$).
- TC2 showed the same trends for the unacceptably low RAR, acceptable RAR and unacceptably high RAR.
- For TC3 the 41,61% (Table 4–37) of antihypertensive medicine items with unacceptable low RAR had a cost of $\text{R}78\,468\,489,61$, whilst the 9,87% of items with unacceptable high RAR had a cost of $\text{R}14\,656\,226,87$.
- The 48,53% antihypertensive medicine items in TC3 with an acceptable RAR contributed to 61,27% ($n = \text{R}184\,621\,857,00$, $N = \text{R}301\,348\,468,00$) of the total cost.

To conclude, unacceptable levels (high and low) of an antihypertensive adherence rate may have had a relatively large financial impact on members and medical schemes which may lead to an increase in cost. By promoting adherence and compliance, better therapeutic benefits and effects will be achieved. In this regard patient information and communication systems may support better adherence rates.

The **sixth research objective** was to propose threshold value/values for the treatment cost of hypertension in South Africa. This was calculated in Section 4.8 of Chapter 4.

Two different types of thresholds were calculated and suggested. The first included a cost threshold range that was calculated using the average cost per item and standard deviation. These cost threshold ranges had an upper and lower limit and were calculated for total

antihypertensive medicine items, patient gender, patient age group treatment category and pharmacological group. Two scenarios were used to propose cost threshold ranges. The first range was the average cost per item, plus half the standard deviation (as the upper limit) and the average cost per item less half the standard deviation (as the lower limit). The second range was calculated by adding a third of the standard deviation to the average cost per item (as the upper limit) and subtracting a third of the standard deviation from the average cost per item (as the lower limit) This was done to calculate a 'reasonable threshold' (see Chapter 1, Section1.1). These results are summarised in Table 5–1.

Table 5-1: Summary of the proposed cost threshold ranges

Indicator	Threshold range 1*	Threshold range 2**	% average costs within range 1	% of average costs within range 2
All antihypertensive medicine items	R68.50 – R142.00	R80.90 – R129.50	38%	24%
Female patients	R67.01 – R137.75	R78.24 – R125.56	35%	23%
Male patients	R72.14 – R147.66	R84.98 – R134.82	39%	26%
AG1	R46.07 – R122.06	R57.53 – R117.14	27%	16%
AG2	R62.89 – R137.48	R73.89 – R130.29	36%	22%
AG3	R70.16 – R145.90	R80.94 – R136.34	38%	24%
TC1	R93.48 – R164.41	R104.50 – R147.26	40%	26%
TC2	R12.84 – R69.76	R22.52 – R60.08	46%	30%
TC3	R52.89 – R129.25	R65.87 – R116.29	33%	23%
Central acting inhibitors	R63.17 – R166.58	R76.41 – R152.11	-	-
Alpha-receptor blockers	R124.82 – R234.22	R141.02 – R215.76	-	-
Beta-receptor blockers	R65.45 – R122.71	R73.76 – R114.32	-	-
Alpha- and beta-receptor blockers	R83.71 – R145.91	R92.51 – R136.47	-	-
Sympathetic nervous blockers	R46.37 – R159.60	R59.79 – R144.29	-	-
Direct acting vasodilators	R42.26 – R136.12	R55.04 – R120.98	-	-
Calcium channel blockers	R100.58- R186.89	R110.99 – R177.14	-	-
ACE-inhibitors	R77.38 – R147.05	R87.45 – R135.94	-	-
Angiotensin receptor	R152.00 – R226.60	R161.33 – R220.72	-	-

Table 5-2 (Cont.): Summary of the proposed cost threshold ranges

Indicator	Threshold range 1*	Threshold range 2**	% average costs within range 1	% of average costs within range 2
blockers				
Diuretics	R11.78 – R75.33	R22.43 – R64.78	-	-

*Threshold range 1 is the 50% scenario; **Threshold range 2 is the 33% scenario

The second threshold that was calculated was a cost ratio threshold. The number of estimated high-income households was used to calculate these cost ratio thresholds. Firstly a total cost for the medical aid market was established. This was done by multiplying the total cost by a factor of 1,76 (MUSA, 2011). This total cost for the medical aid market was then divided by the number of households to establish a cost ratio. This ratio included VAT and a logistics fee, which is a percentage of the SEP that needed to be subtracted in order to get a cost ratio per household. These cost ratio thresholds were applicable only to the private health-care sector of South Africa and not necessarily to the total health-care market. These cost ratio thresholds are summarised in Table 5–2.

Table 5-3: Summary of the cost ratio thresholds

Indicator	Cost ratio threshold	Indicator	Cost ratio threshold
Female	R59.73	TC1 (AG1)	R0.03
Male	R50.49	TC1 (AG2)	R5.63
		TC1 (AG3)	R62.54
AG1	R0.07	TC2 (AG1)	R0.02
AG2	R7.87	TC2 (AG2)	R0.27
AG3	R102.19	TC2 (AG3)	R3.05
		TC3 (AG1)	R0.03
TC1	R68.21	TC3 (AG2)	R1.96
TC2	R3.34	TC3 (AG3)	R36.68
TC3	R38.67		
		Eastern Cape	R88.60
N	R37.33	Free State	R96.17
O	R17.89	Gauteng	R128.14
Y	R54.99	KwaZulu-Natal	R122.19
		Limpopo	R52.96

Indicator	Cost ratio threshold	Indicator	Cost ratio threshold
N (Female)	R20.71	Mpumalanga	R66.25
N (Male)	R16.62	North West	R120.45
O (Female)	R9.47	Northern Cape	R77.40
O (Male)	R8.42	Western Cape	R102.62
Y (Female)	R29.55		
Y (Male)	R25.45	Central acting inhibitors	R1.33
		Alpha-receptor blocker	R3.62
TC1 (Female)	R34.41	Beta-receptor blocker	R11.73
TC1 (Male)	R33.79	Alpha-and beta-receptor blocker	R4.42
TC2 (Female)	R2.39	Sympathetic nervous blocker	R0.07
TC2 (Male)	R0.94	Direct acting vasodilator	R0.09
TC3 (Female)	R22.92	Calcium channel blocker	R14.56
TC3 (Male)	R15.76	ACE-inhibitor	R41.27
		Angiotensin receptor inhibitor	R30.16
N (AG1)	R0.01	Others	R1.00
N (AG2)	R2.48	Diuretics	R12.92
N (AG3)	R34.85	Total	R119.62
O (AG1)	R0.03		
O (AG2)	R0.99		
O (AG3)	R16.88		
Y (AG1)	R0.04		
Y (AG2)	R4.40		
Y (AG3)	R50.55		

To conclude, from the above tables and discussions it can therefore be clearly seen that numerous thresholds can be derived for different scenarios. Only medicine costs were used, since no clinical data was available and therefore thresholds based on cost-minimisation principles were calculated. Since medication cost is one of the biggest cost drivers, application of these suggestions or principles in the pharmaceutical benefit management environment may lead to relative large cost savings.

5.3 LIMITATIONS

Based on the results and discussion in Chapter 4, certain limitations were identified, which could restrict or limit the scope of this study. The following limitations were detected:

- Clinical data was limited to pharmacological groups and therefore the relevance of some of the utilisation patterns could not be determined, e.g. specific treatment and diagnosis.
- As was seen from the literature, certain antihypertensive medicine items are not indicated for certain ethnic groups. The race of the patients was not available, and therefore these allegations could not be investigated.
- Since the non-medical aid market falls outside the scope of this study, possible cost threshold ranges or cost ratio thresholds could not be determined for this health-care sector.
- The number of newly diagnosed patients could not be determined.
- The researcher was not responsible for compiling the database and accepted it as correct.
- Due to ethical and patient confidentiality factors, data from MUSA was limited for analysis purposes.

5.4 RECOMMENDATIONS

The following recommendations could be formulated after analysis of the data and research study:

- Methods should be developed to improve adherence rates needs further investigation.
- Patient and prescriber surveys should be conducted to promote an understanding of the difference in prescribing patterns and adherence rates between female and male patients.
- Possible drug/drug interactions of antihypertensive medicine items with other medicine items should be investigated and clinically evaluated.
- An in-depth study should be undertaken into the geographical distribution of hypertensive patients to determine possible reasons for the high prevalence of hypertension in Gauteng, KwaZulu-Natal and the Western Cape.
- Cost threshold ranges and cost ratio thresholds should be further investigated for possible application in the public health-care market, especially as part of the planning of the proposed national health insurance system.
- The usage of other pharmacoeconomic instruments, such as willingness to pay, in the determination of threshold values needs to be investigated further.

- An in-depth investigation on demographical and geographical influence on medication thresholds should be undertaken, not only for hypertension treatment but also for other life threatening diseases.

5.5 SUMMARY

In this chapter the conclusions pertaining to the objectives of the literature review as well as the empirical investigation were presented. Limitations regarding this study as well as some recommendations were also presented.

REFERENCES

Abarca, J. 2005. Assessing pharmacoeconomic studies. (In Bootman, J.L., Townsend, R.J. & McGhan, W.F. eds. *Principles of Pharmacoeconomics* 3rd ed. Cincinnati, OH : Harvey Whitney. p.363-374).

Abson, C.P., Levy, L.M. & Eyherabide, G. 1981. Once-daily atenolol in hypertensive Zimbabwean blacks. *South African medical journal*: 47-48, 11 Jul.

Academy Of Managed Care Pharmacy®. 2009. Drug utilization review.
<http://www.amcp.org/WorkArea/DownloadAsset.aspx?id=9296> Date of access: 10 Sep. 2011.

Andersson, K., Melander, A., Svensson, C., Lind, O. & Nilsson, J.L.G. 2005. Repeat prescriptions: refill adherence in relation to patient and prescriber characteristics, reimbursement level and type of medication. *European journal of public health*, 15(6):621-626.

Andros, V. & Weintraub, H.S. 2005. After the diagnosis: adherence and persistence with hypertension therapy. *American journal of managed care*, 11:S395-S399.

Anisman-Reiner, V. 2008. The allergy threshold. <http://victoria-anisman-reiner.suite101.com/allergy-threshold-a51559> Date of access: 11 May 2008.

Anon. 2008. Discovery Health Executive Plan. <http://www.discovery.co.za/portal/loggedout-provider/executive-plan> Date of access: 3 May 2008.

Anon. 2010a. Must for seniors. Fact sheet: Medicine use and older adults.
www.mustforseniors.org Date of access: 22 Feb. 2012.

Anon. 2010b. About generic medicines. <http://www.specpharm.com/generics.htm> Date of access: 8 Nov. 2011.

Appel, L.J., Moore, T.J., Obarzanek, E., Vollmer, W.M., Svetkey, L.P., Sacks, F.M., Bray, G.A., Vogt, T.M., Cutler, J.A., Windhauser, M.M., Lin, P.-H. & Karanja, N. 1997. A clinical trial of the effects of dietary patterns on blood pressure. *The New England journal of medicine*, 336(16):1117-1124.

Alcocer, L. & Cueto, L. 2008. Review: Hypertension, a health economics perspective. *Therapeutic advances in cardiovascular disease*, 2(3):147-155.

Barner, J.C. 2010. Medication adherence: focus on secondary database analysis. Paper presented at the ISPOR Student Forum, 24 February.
<http://www.ispor.org/student/teleconferences/ISPORStudentForumPresentation022410.pdf>
Date of access: 17 Feb. 2012.

Basu, R., Franzini, L., Krueger, P.M. & Lairson, D.R. 2010. Gender disparities in medical expenditures attributable to hypertension in the United States. *Women's health issues*, 20:114-125.

Beers, M.H., ed. 2003. The Merck manual. 2nd home ed.
<http://www.merck.com/mmhe/print/sec03/ch022/ch022a.html> Date of access: 5 Sep. 2006.

Beers, M.H. & Berkow, R., eds. 2007. The Merck manual of diagnosis and therapy. 17th ed.
<http://www.merck.com/mmpe/print/sec07/ch071/ch071a.html> Date of access: 3 Apr. 2007.

Beevers, G., Lip, G.Y. & O'Brien, E. 2001. ABC of hypertension: the pathophysiology of hypertension. *British medical journal*, 322:912-916.

Benowitz, N.L. 2001. Antihypertensive agents. (*In* Katzung, B.G., Masters, S.B. & Trevor, A.J., eds. Basic & clinical pharmacology. 8th ed. New York : McGrawHill. p155-180).

Bester, M. & Badenhorst, E. 2009. Mediscor Medicines Review 2008. <http://www.mediscor.net>
Date of access: 8 Jan. 2010.

Bester, M., Brews, M & Hammann, E. 2005. Mediscor Medicines Review 2004.
<http://www.mediscor.net> Date of access: 15 Jul. 2007.

Bester, M. & Hammann, E. 2007. Mediscor Medicines Review 2006. <http://www.mediscor.net>
Date of access: 17 Jul. 2007.

Bester, M. & Hammann, E. 2008. Mediscor Medicines Review 2007. <http://www.mediscor.net>
Date of access: 1 Aug. 2008.

Bittar, N. 1995. Maintaining long-term control of blood pressure: the role of improved compliance. *Clinical cardiology*, 18(Suppl III):12-16.

Bitton, A & Gaziano, T. 2010. The Framingham heart study's impact on global risk assessment. *Progress in cardiovascular disease*, 53:68-78.

Blackburn, J., Berner, M., Carruthers, G., Cutler, J., Friesen, E., Thornton, M., Forte, L., Psenicka, E., Shane, L. & McKenzie, E. 2001. Drug utilization review: a Canadian process and methodology for drug utilization studies of community-based drug therapy. Canada : Canada's Research Based Pharmaceutical Companies.

Blecher, M. & Harrison, S. 2006. Health care financing. (*In* Ijumba, P. & Padarath, A., eds. South African health review – 2006. Durban : Health Systems Trust. p 31-64).

Boersma, C., Carides, G.W., Atthobari, J., Voors, A.A & Postma, M.J. 2007. An economic assessment of losartan-based versus atenolol-based therapy in patients with hypertension and left-ventricular hypertrophy: results from the Losartan Intervention for Endpoint reduction (LIFE) study adapted to The Netherlands. *Clinical therapeutics*, 29(5):963-971.

Booth, N., Jula, A., Aronen, P., Kaila, M., Klaukka, T., Kukkonen-Harjula, K., Reunanen, A., Rissanen, P., Sintonen, H. & Mäkelä, M. 2007. Cost-effectiveness analysis of guidelines for antihypertensive care in Finland. *Health services research*, 7:172-185.

Bootman, J.L., Townsend, R.J. & McGhan, W.F., eds. 2005. Introduction to pharmacoeconomics. (*In* Bootman, J.L., Townsend, R.J. & McGhan, W.F., eds. Principles of pharmacoeconomics 3rd ed. Cincinnati, OH : Harvey Whitney. p. 3-17).

Brase, C.H. & Brase, C.P. 1999. Understandable statistics: concepts and methods. 6th ed. New York : Houghton Mifflin.

Brown, N.J. & Vaughan, D.E. 1998. Angiotensin-Converting Enzyme Inhibitors. *Circulation*, 97:1411-1420.

Carriere, K.C. & Huang, R. 2001. Traditional paradigms in pharmacoeconomics: consideration for cost-effective designs. (*In* Vogenberg, F.R., ed. Introduction to applied Pharmacoeconomics. New York : McGraw-Hill. p. 19-39).

Chen, G.J., Ferrucci, L., Moran, W.P. & Pahor, M. 2005. A cost-minimization analysis of diuretic-based antihypertensive therapy reducing cardiovascular events in older adults with

isolated systolic hypertension. *Cost effectiveness and resource allocation*, 3(2).
<http://www.resource-allocation.com/content/3/1/2> Date of access: 10 Dec. 2011.

Christensen, D.B., Williams, B., Goldberg, H.I., Martin, D.P., Engelberg, L. & Logerfo, J.P. 1997. Assessing compliance to antihypertensive medications using computer-based pharmacy records. *Medical care*, 35(11):1164-1170.

CMS **see** South Africa. Council for Medical Schemes.

Coca, A. 2008. Economic benefits of treating high-risk hypertension with angiotensin II receptor antagonists (blockers). *Clinical drug investigation*, 28(4):211-220.

Cohen, J. 2001. Taking medication: special concerns in older patients.
http://psychcentral.com/library/meds_older.htm Date of access: 22 Feb. 2012.

Cohn, J.N., McInnes, G.T. & Shepard, A.M. 2011. Direct-acting vasodilators. *The journal of clinical hypertension*, 13(9):690-692.

Costa, F.V. 1996. Compliance with antihypertensive treatment. *Clinical and experimental hypertension*, 18(3&4):463-472.

Coyle, D., Rodby, R., Soroka, S., Levin, A., Muirhead, N., De Cotret, P.R., Chen, R. & Palmer, A. 2007. Cost-effectiveness of irbesartan 300mg given early versus late in patients with hypertension and a history of type 2 diabetes and renal disease: a Canadian perspective. *Clinical therapeutics*, 29(7):1508-1523.

Cramer, J.A., Roy, A., Burrell, A., Fairchild, C.J., Fuledore, M.J., Ollendorf, D.A. & Wong, P.K. 2008. Medication compliance and persistence: terminology and definitions. *Value in health*, 11(1):44-47.

Daban, F., Pasarin, M.I., Rodriguez-Sanz, M., Garcia-Altes, A., Villalbi, J.R., Zara, C. & Borrell, C. 2010. Social determinant of prescribed and non-prescribed medicine use. *International journal of equity in health*, 9:12-22.

Da Costa, J.S., Fuchs, S.C., Olinto, M.T.A., Gigante, D.P., Menezes, A.M.B., Macedo, S. & Gehrke, S. 2002. Cost-effectiveness of hypertension treatment: a population-based study. *São Paulo medical journal*, 120(4):100-104.

Dahlöf, D., Sever, P.S., Poulter, N.R., Beevers, D.G., Caulfield, M., Collins, R., Kjeldsen, S.E., Kristinsson, A., McInnes, G.T., Mehlsen, J., Nieminen, M., O'Brien, E. & Östergren, J. 2005. Prevention of cardiovascular events with an antihypertensive regimen of amlodipine adding perindopril as required versus atenolol adding bendroflumethiazide as required, in the Anglo-Scandinavian cardiac outcomes trial-blood pressure lowering arm (ASCOT-BPLA): a multicentre randomised controlled trial. *Lancet*, 366:895-906.

Dalzell M.A. 2003. Hypertension: prevalence and economic complications. *Managed care (Suppl P & T digest)*, 12(8):6-11.

Department of Health ~~see~~ South Africa. Department of Health.

Devlin, N. & Parkin, D. 2004. Does NICE have a cost-effectiveness threshold and what other factors influence its decisions? A binary choice analysis. *Health economics*, 13(5):437-452.

Dezii, C.M. 2000. A retrospective study of persistence with single-pill combination therapy vs. concurrent two-pill therapy in patients with hypertension. *Managed care*, Suppl 9(9):2-6.

Dezii, C.M. 2001. Persistence with drug therapy: a practical approach using administrative claims data. *Managed care*, 2:42-45.

Diderichsen, F. 2004. Health, Nutrition and Population (HNP) discussion paper. Resource allocation for health equity: issues and methods.
<http://pubhealth.ku.dk/upload/application/pdf/f51d6748/Ressource%20Allocation.pdf> Date of access: 21 Feb. 2007.

Drummond, M.F., Aguiar-Ibáñez, R. & Nixon, J. 2006. Economic evaluation. *Singapore medical journal*, 47(6):456-462.

Drummond, M.F., O'brien, B., Stoddart, G.L. & Torrance, G.W. 1999. Methods for the economic evaluation of health care programmes 2nd ed. New York : Oxford University Press.

Drummond, M.F., Sculpher, M.J., Torrance, G.W., O'Brien, B.J. & Stoddart, G.L. 2005. Methods for the economic evaluation of health care programmes. 3rd ed. New York : Oxford University Press.

- Eichler, H.G., Kong, S.X., Gerth, W.C., Mavros, P. & Jönsson, B. 2004. Use of cost-effectiveness analysis in health-care resource allocation decision-making: how are cost-effectiveness thresholds expected to emerge? *Value in health*, 7(5):518-528.
- Elliot, W.J. 2003. The economic impact of hypertension. *The journal of clinical hypertension*, Suppl 2 V(III):3-13.
- Elliot, W.J. 2007. Systemic hypertension. *Current problems in cardiology*, 32:201-259.
- Ellis, S.M. & Steyn, H.S. 2003. Practical significance (effect sizes) versus or in combination with statistical significance (p-values). *Management dynamics*, 12(4):51-53.
- Fenwick, E., Marshall, D.A., Levy, A.R. & Nichol, G. 2006. Using and interpreting cost-effectiveness acceptability curves: an example using data from a trial of management strategies for arterial fibrillation. *BMC Health Services research*, 6:52-59.
- Fodor, J.G. & Tzerovska, R. 2004. Coronary heart disease: is gender important? *Journal of men's health and gender*, 1(1):32-37.
- Forrester, T. 2004. Historic and early life origins of hypertension in Africans. *The journal of nutrition*, 134:211-216.
- Fretheim, A., Aaserud, M. & Oxman, A.D. 2003. The potential savings of using thiazides as first choice antihypertensive drug: cost-minimisation analysis. *BMC Health Services research*, 3(18). <http://www.biomedcentral.com/1472-6963/3/18> Date of access: 5 Apr. 2011.
- Fujikawa, K., Hasebe, N., Kikuchi, K. & Nice-Combi Study Group. 2005. Cost-effectiveness analysis of hypertension treatment: controlled release nifedipine and candesartan low-dose combination therapy in patients with essential hypertension – The Nifedipine and Candesartan Combination (NICE-COMBI) Study. *Hypertension research*, 28:251-591.
- Fujikawa, K., Yui, Y. & Kawai, C. 2003. Cost-minimization analysis in hypertension with coronary artery disease based on Japan Multicenter Investigation for Cardiovascular Disease (JMIC-B) clinical data: Nifedipine retard versus ACE-inhibitor. (In ISPOR First Asia-Pacific Conference, 1-3 September 2003, Kobe, Japan, International Conference Centre, Kobe.) http://www.ispor.org/research_pdfs/2/pdf/files/PCSCD3.pdf Date of access: 8 Sep. 2011.

Gafni, A. 2005. Economic evaluation of health care interventions: the biggest bang for the buck or the bigger bucks for the bang? <http://www.chere.uts.edu.au/pdf/AmiramGafni.pdf> Date of access: 5 Aug. 2008.

Gafni, A. & Birch, S. 1993. Guidelines for the adoption of new technologies: a prescription for uncontrolled growth in expenditures and how to avoid the problem. *Canadian Medical Association journal*, 148(6):913-917.

Gafni, A. & Birch, S. 2006. Incremental cost-effectiveness ratios (ICERs): the silence of the lambda. *Social science & medicine*, 62:2091-2100.

Gandjour, A. & Stock, S. 2007. A national hypertension treatment program in Germany and its estimated impact on costs, life expectancy, and cost-effectiveness. *Health policy*, 83:257-267.

Gaziano, T.A., Steyn, K., Cohen, D.J., Weinstein, M.C. & Opie, L.H. 2005. Cost-effectiveness analysis of hypertension guidelines in South Africa: absolute risk versus blood pressure level. *Circulation*, 112:3569-3576.

Gibbon, C.J., ed. 2005. South African medicines formulary. 6th ed. Cape Town : The South African Medical Association.

Greene, R.S., Escobar Quinones, M. & Edwards, K.L. 2007. Evaluation of thiazide diuretic use as preferred therapy in uncomplicated essential hypertension patients. *Pharmacy practice*, 5(3):130-134.

Grymonpre, R.G., Cheang, M., Fraser, M., Metge, C. & Sitar, D.S. 2006. Validity of a prescription claims database to estimate medication adherence in older persons. *Medical care*, 44(5):471-477.

Hagberg, J.M., Park, J.-J. & Brown, M.D. 2000. The role of exercise training on the treatment of hypertension. *Sports medicine*, 30(3):193-206.

Hanson, G.R., Ventrurelli, P.J. & Fleckenstein, A.E. 2005. Drugs and Society. Jones & Bartlett Publishers.

Hansson, L., Lindholm, L.H., Ekbom, T., Dahlöf, B., Lanke, J., Schersten, B., Wester, P.O., Hedner, T. & De Faire, U., 1999. Randomised trial of old and new antihypertensive drugs in

elderly patients: cardiovascular mortality and morbidity the Swedish Trial in Old Patients with Hypertension-2 study. *Lancet*, 354:1751-1756.

Haycox, A. 2004. Quality assurance in pharmacoeconomic analyses. (In Walley T., Haycox, A. & Boland, A., eds. *Pharmacoeconomics*. London : Churchill Livingstone. p.155-165).

Haycox, A. 2009. What is cost-minimization analysis?

http://www.medicine.ox.ac.uk/bandolier/painres/download/whatis/What_is_cost-min.pdf Date of access: 8 Sep. 2011.

Haycox, A. 2010. What is cost-minimization analysis? (In Arnold, R.J.G, ed.

Pharmacoeconomics from theory to practice. Boca Raton : CRC Press. p. 83-94).

Heidenreich, P.A., Davis, B.R., Cutler, J.A., Furberg, C.D., Lairson, D.R., Shlipak, M.G., Pressel, S.L., Nwachuku, C. & Goldman, L. 2008. Cost-effectiveness of chlortalidone, amlodipine, and lisinopril as first-step treatment for patients with hypertension: an analysis of the Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT). *Journal of general internal medicine*, 23(5):509-516.

Hellriegel, D., Jackson, S.E., Slocum, J., Staude, G., Amos, T., Klopper, H.B., Louw, L. & Oosthuizen, T. Introduction to organizations and the nature of management. (In Hellberg, D., Jackson, S.E., Slocum, J., Staude, G., Amos, T., Klopper, H.B., Louw, L. & Oosthuizen, T. *Management 3rd South African edition*. Cape Town : Oxford University Press Southern Africa. p. 3-20).

Hess, L.M., Raebel, M.A., Conner, D.A. & Malone, D.C. 2006. Measurement of adherence in pharmacy administrative databases: a proposal for standard definitions and preferred measures. *The annals of pharmacotherapy*, 40:1280-1288.

Holm, S.W., Cunningham, L.L., Bensadoun, E. & Madsen, M.J. 2006. Hypertension: Classification, pathophysiology, and management during outpatient sedation and local anesthesia. *Journal of oral maxillofacial surgery*, 64;111-121.

Hughes, D., Lara, A.M. & Mujica-Mota, R. 2004. Approaches to pharmacoeconomic analysis. (In Walley, T., Haycox, A. & Boland, A., eds. *Pharmacoeconomics*. New York : Churchill Livingstone. p. 101-126).

Humphreys, G.S. & Delvin, D.G. 1968. Ineffectiveness of Propranolol in hypertensive Jamaicans. *British medical journal*, 2:601-603.

Hutubessy, R., Chisholm, D., Edejer, T.T. & Who-Choice. 2003. Generalized cost-effectiveness analysis for national-level priority-setting in the health sector. *Cost-effectiveness and resource allocation*, 1:8-20.

Jackson, K.C., Sheng, X., Nelson, R.E., Keskinaslan, A. & Brixner, D.I. 2008. Adherence with multiple-combination antihypertensive pharmacotherapies in a US managed care database. *Clinical therapeutics*, 30(8):1558-1563.

Jin, J., Sklar, G.E., Oh, V.M.S. & Li, S.C. 2008. Factor affecting therapeutic compliance: a review from the patient's perspective. *Therapeutics and clinical risk management*, 4(1):269-286.

Jönsson, B., Hansson, L. & Ståhlhammar, N.O. 2003. Health economics in the Hypertension Optimal Treatment (HOT) study: costs and cost-effectiveness of intensive blood pressure lowering and low-dose aspirin in patients with hypertension. *Journal of internal medicine*, 253:472-480.

Kaplan, N.M. 1999. Angiotensin II receptor antagonists in the treatment of hypertension. *American family physician*, 60(4):1185-1190.

Kirk, J.K. 1999. Angiotensin-II receptor antagonists: their place in therapy. *American family physician*, 59(11):3140-8.

Klabunde, R.E. 2007. Cardiovascular Pharmacology Concepts. Beta-adrenoceptor antagonists (Beta-blockers). <http://www.cvpharmacology.com/cardioinhibitory/beta-blockers.htm> Date of access: 11 Nov. 2007.

Kopp, W. 2005. Pathogenesis and etiology of essential hypertension: role of dietary carbohydrate. *Medical hypotheses*, 64:782-787.

Kozlowski, J., Rossier, J., Hill, G. 1988. Ultimate Environmental Threshold (UET) method in a marine environment (Great Barrier Reef Marine Park in Australia). *Landscape & urban planning*, 15(3):327-336.

- Krigsman, K., Melander, A., Carlsten, A., Ekedahl, A. & Nilson, J.L.G. 2007. Refill non-adherence to repeat prescriptions leads to treatment gaps or to high extra costs. *Pharmaceutical world of science*, 29:19-24.
- Larson, L.N. 2005. Cost determination and analysis. (In Bootman, J.L., Townsend, R.J. & McGhan, W.F., eds. *Principles of pharmacoeconomics*. Cincinnati, OH : Harvey Whitney. p. 47-63).
- Larson, L.N. 2001. US health care system and pharmacoeconomics. (In Vogenberg, F.R., ed. *Introduction to applied pharmacoeconomics*. New York : McGraw-Hill. p. 1-18).
- Laurier, C., Tessier, G., Champagne, F. & Contandriopoulos, AP. 1992. Cost-minimization analysis of Fosinopril (Monopril), a new angiotensin-converting enzyme (ACE) inhibitor for the treatment of mild to moderate hypertension. Université de Montréal, Faculté de Médecine.
- Law, M.R., Wald, N.J., Morris, R. & Jordan, R.E. 2003. Value of low dose combination treatment with blood pressure lowering drugs: analysis of 354 randomised trials. *British medical journal*, 326(7404):1427-1434.
- Levick, J.R. 1995. An introduction to cardiovascular physiology 2nd ed. London : Oxford, Butterworth-Heineman.
- Levinson, D.R. 2006. Generic drug utilization in state Medicaid programs. <http://oig.hhs.gov/oei/reports/oei-05-05-00360.pdf> Date of access: 15 Nov. 2011.
- Li, W., Wallhagen, M.I. & Froelicher, E.S. 2007. Hypertension control, predictors for medication adherence and gender differences in older Chinese immigrants. *Journal of advanced nursing*. 61(3):326-335.
- Lip, G.Y.H. & Chung, N. 2002. Hypertension: patients at risk. London : Excerpta Medica 64p.
- Lopez, J., Meier, J., Cunningham, F. & Siegel, D. 2004. Antihypertensive medication use in the Department of Veterans Affairs: a national analysis of prescribing patterns from 2000 to 2002. *American journal of hypertension*, 19:1095-1099.
- Loth, R. 2012. Financial ratio tutorial. <http://www.investopedia.com/university/ratios/> 10 Apr. 2012.

- Luiz, J. & Wessels, M. 2004. Changes in the provision of health care in South Africa. *South African journal of business management*, 35(3):2-11.
- Luma, G.B. & Spiotta, R.T. 2006. Hypertension in children and adolescents. *American academy of family physicians*, 73:1158-1168.
- Lunet, N. & Barros, H. 2002. Gender differences in the treatment of hypertension: a community based study in Porto. *Revised portal of cardiology*, 21(1):7-19.
- Mancia, G., De Backer, G., Dominiczak, A., Cifkova, R., Fagard, R., Germano, G., Grassi, G., Heagerty, A.M., Kjeldsen, S.E., Laurent, S., Narkiewicz, K., Ruilope, L., Rynkiewicz, A., Schmieder, R.E., Struijker Boudier, H.A.J. & Zanchetti, A. 2007. 2007 Guidelines for the management of arterial hypertension. *European heart journal*, 28:1462-1536.
- Maniadakis, N., Ekman, M., Fragoulakis, V., Papagiannopoulou, V. & Yfantopoulos, J. 2011. Economic evaluation of irbesartan in combination with hydrochlorothiazide in the treatment of hypertension in Greece. *European journal of health economics*, 12:253-261.
- McCombs, J.S. 1998. Pharmacoeconomics: what is it and where is it going? *American journal of hypertension*, 11:112S-119S.
- McInnes, G., Burke, T.A. & Carides, G. 2006. Cost-effectiveness of losartan-based therapy in patients with hypertension and left-ventricular hypertrophy: a UK-based economic evaluation of the Losartan Intervention For Endpoint reduction in hypertension (LIFE) study. *Journal of human hypertension*, 20:51-58.
- McPhee, S.J. & Massie, B.M. 2006. Systemic Hypertension. (In Tierney, L.M., McPhee, S.J. & Papadakis, M.A., eds. Current medical diagnosis and treatment. 45th ed. New York : Lange Medical Books. p.419-445).
- Medicine Usage in South Africa. 2011. Research data [correspondence]. 31 Mar., Potchefstroom.
- Medikredit. 2010. NAPPI® product file layout V5.5.
https://www.medikredit.co.za/attachments/093_NAPPI%20File%20Layout%20v5%2000_External_%20v5%205.pdf Date of access 20 Sep. 2011.
- MRC **see** South Africa. Medical Research Council.

Muennig, P. 2002. Designing and conducting cost-effectiveness analyses in medicine and health care. San Francisco, CA : John Wiley.

MUSA **see** Medicine Usage in South Africa.

Narine, L., Hague, L.K., Walker, J.H., Vicente, C., Schilz, R., Desjardins, O., Einarson, T.R. & Iskedjian, M. 2005. Cost-minimization analysis of treprostinil vs. epoprostenol as an alternate to oral therapy non-responders for the treatment of pulmonary arterial hypertension. *Current medical research and opinions*, 21(12):2007-2016.

National Medicines Information Centre. 2002. An introduction to pharmacoeconomics. Volume 8 Number 5.

Niles R., 2012. Median. <http://www.robertniles.com/stats/median.shtml> Date of access 2 Feb. 2012.

Nordmann, A.J., Krahn, M., Logan, A.G., Naglie, G. & Detsky, A.S. 2003. Cost-effectiveness of ACE inhibitors as first-line antihypertensive therapy. *Pharmacoeconomics*, 21(8):573-585.

Norman, R., Gaziano, T., Laubscher, R., Steyn, K., Bradshaw, D. & South African Comparative Risk Assessment Collaborating Group. 2007. Estimating the burden of disease attributable to high blood pressure in South Africa in 2000. *South African medical journal*, 97(8):692-698.

O'Brien, B.J., Gertsen, K., Willan, A.R. & Faulkner, L.A. 2002. Is there a kink in consumers' threshold value for cost-effectiveness in health care? *Health economics*, 11:175-180.

OED: Oxford English Dictionary. 2011. Threshold. www.oed.com Date of access: 10 Mar. 2011.

OED: Oxford English Dictionary. 2012. Management. <http://oxforddictionaries.com/definition/management?q=management> Date of access: 19 Mar. 2012.

OED: Oxford English Dictionary. 2012. Ratio. www.oed.com Date of access: 30 Mar. 2012.

- Ortmeier, B.G. 1996. Economic outcomes. (*In* Smith, M.C. & Wertheimer, A.I., eds. Social and behavioral aspects of pharmaceutical care. New York : Pharmaceutical Products Press. p.385-401).
- Osei, K. 1999. Insulin resistance and systemic hypertension. *American journal of cardiology*, 84;33J-36J.
- Osterhaus, J.T. & Draugalis, J.R. 1991. Application of pharmacoeconomics for drug therapy decisions. (*In* Bootman, J.L., Townsend, R.J. & McGhan, W.F., eds. Principles of pharmacoeconomics. Cincinnati, OH : Harvey Whitney. p. 135-145).
- Owen, D.K. 1998. Interpretation of cost-effectiveness analyses. *Journal of general internal medicine*, 13:716-717.
- Page, S.P. & Halcox, J.P.J. 2006. Management of hypertension. *Medicine*, 34(8):290-295.
- Panjrath, G.S. & Messerli, F.H. 2006. β -Blockers for primary prevention in hypertension: era bygone? *Progress in cardiovascular disease*, 49(2):76-87.
- Parry, M. L., Carter, T. R. & Hulme, M. 1996. What is a dangerous climate change? *Global environmental change*, 6(1):1-6.
- Pearce, K.A., Furberg, C.D., Psaty, B.M. & Kirk, J. 1998. Cost-minimization and the number needed to treat in uncomplicated hypertension. *American journal of hypertension*, 11:618-629.
- Pestana, J.A.X., Steyn, K., Leiman, A. & Hartzenberg, G.M. 1996. The direct and indirect costs of cardiovascular disease in South Africa in 1991. *South African medical journal*, 86:679-684.
- Porter, R.S. & Kaplan, J.L., eds. 2010. The Merck manual of diagnosis and therapy. 19th ed. <http://www.merck.com/mmpe/print/sec07/ch071/ch071a.html> Date of access: 15 Feb. 2012.
- Pudifin, D.J., Boon, G., Sinxadi, P.Z. & Jamaloodien, K., eds. 2008. Standard treatment guidelines and essential drugs list. Pretoria. : The National Department of Health.
- Rayner, B. 2007. Combination therapy in hypertension. *South African pharmaceutical journal*, 6:30-34.

Rayner, B., Blockman, M., Baines, D. & Trinder, Y. 2007. A survey of hypertensive practices at two community health centres in Cape Town. *South African medical journal*, 97(4):280-284.

Reckelhoff, J.F. 2001. Gender differences in the regulation of blood pressure. *Hypertension*, 37:1199-1208.

Reeder, C.E., Gourley, G.A., Wurtzbacher, J.D. & Reed, P. 2000. The impact of angiotensin-converting enzyme inhibitors on managed care: economic, clinical and humanistic outcomes. *The American journal of managed care*, 6(Suppl):S112-S128.

Richardson, G., Godfrey, L., Gravelle, H. & Watt, I. 2004. Cost-effectiveness of implementing new guidelines for treatment of hypertension in general practice. *British journal of general practice*, 54(10):765-771.

Roe, C.M., McNamara, A.M. & Motheral, B.R. 2002. Gender-and age-related prescription drug use patterns. *Annals of pharmacotherapy*, 36(1):30-39.

Rossiter, D., ed. 2010. South African medicines formulary. 9th ed. Cape Town : The South African Medical Association.

Sacks, F.M., Svetkey, L.P., Vollmer, W.M., Appel, L.J., Bray, G.A., Harsha, D., Obarzanek, E., Conlin, P.R., Miller, E.R., Simons-Morton, D.G., Karanja, N. & Lin, P.H. 2001. Effects of blood pressure of reduced dietary sodium and the dietary approaches to stop hypertension (DASH) diet. *The New England journal of medicine*, 334(1):3-10).

SA **see** South Africa.

SAHS **see** South African Hypertension Society.

SAS Institute Inc. 2005. SAS for Windows 9.1., 2002-2003.

Schultz, M. 2009. Combination therapy for hypertension. *South African pharmaceutical journal*, Sept.:24-28.

Seedat, Y.K. 1980. Trial of atenolol and chlortalidone for hypertension in black South Africans. *British medical journal*, 281:1241-1243, 8 Nov.

Seedat, Y.K., Croasdale, M.A., Milne, F.J., Opie, L.H., Pinkey-Atkinson, V.J., Rayner, B.L. & Veriava, Y. 2006. South African hypertension guideline 2006. *South African medical journal*, 96(4);337-362.

Seedat, Y.K. & Rayner, B.L. 2012. South African hypertension guidelines 2011. *South African medical journal*, 102(1):60-83.

Seedat, Y.K. & Reddy, J. 1971. Propranolol in the South African non-white hypertensive patient. *South African medical journal*: 284-285, 13 Mar.

Serfontein, J.H.P. 1989. Medisyneverbruik in provinsiale hospitale met besondere verwysing na die rol van die apteker in die beheerproses. Potchefstroom : PU vir CHO. (Thesis – D.Pharm).

Simons, R. 2003. Comparative cost effectiveness of angiotensin II receptor blockers in a US managed care setting: Olmesartan medoxomil compared with losartan, valsartan and irbesartan. *PharmacoEconomics*, 21(1):61-74.

Smith, M.D. 2003. Health care cost, quality, and outcomes. ISPOR book of terms. Lawrenceville : ISPOR.

Snyman, J.R. ed. 2004. MIMS monthly index of medical specialities. Pretoria : MIMS.

Snyman, J.R. ed. 2007. MIMS monthly index of medical specialities. Pretoria : MIMS.

Snyman, J.R. ed. 2010. MIMS monthly index of medical specialities. Pretoria : MIMS.

South Africa. Council For Medical Schemes. 2003. Draft therapeutic algorithms for CDL conditions. <http://www.medicalschemes.com> Date of access: 5 Jun. 2004.

South Africa. Council For Medical Schemes. 2003. Final document: Recommendations of the committee on standardisation of data and billing practices. <http://www.medicalschemes.com/publications/ZipPublications/Presentations%20And%20Reports/StandardisationManual.pdf> Date of access: 20 Sep. 2011.

South Africa. Council For Medical Schemes. 2006. Annual report 2005-6. http://www.medicalschemes.com/publications/ZipPublications/Annual%20Reports/CMS_annual_report_2005-6.pdf Date of access: 24 Nov. 2006.

- South Africa. Council For Medical Schemes. 2007. Annual report 2006-7.
<http://www.medicalschemes.com/Publications.aspx> Date of access: 26 Mar. 2008.
- South Africa. Council For Medical Schemes. 2009. Annual report 2008-9.
http://www.medicalschemes.com/files/Annual%20Reports/CMS_A-R_2008-09_20090902.pdf
 Date of access: 11 Jan. 2010.
- South Africa. Department of Health. 2010. National health insurance. Healthcare for all South Africans. <http://www.doh.gov.za> Date of access: 10 Jan. 2012.
- South Africa. Department of Public Service And Administration. 2005. Annual Report 2004/2005. <http://www.dpsa.gov.za/documents/annualreports/annualreport2005.pdf> Date of access: 5 Feb. 2007.
- South Africa. Medical Research Council. Burden of Disease Research Unit. 2007. Frequently asked questions. <http://www.mrc.ac.za//bod/faqcardio.htm> Date of access 28 Jun. 2007.
- South African Hypertension Society. 1995. Guidelines for the management of hypertension at primary care level. *South African medical journal*, 85:1321-1325.
- South African Hypertension Society. 2001. Hypertension clinical guidelines 2000. *South African medical journal*, 91:163-172.
- Spencer, C. & Lip, G. 1999. Antihypertensive drugs. *The pharmaceutical journal*, 263(7061):351-354.
- Staessen, J.A., Wang, J., Bianchi, G. & Birkenhäger, W.H. 2003. Essential hypertension. *Lancet*, 361:1629-1641.
- Stats SA. 2005. Mid-year population estimates, South Africa 1 August 2005. Statistics South Africa, Pretoria; 2005. pp 1-25.
- Stats SA. 2006. Mid-year population estimates, South Africa 1 August 2006. Statistics South Africa, Pretoria; 2006. pp 1-11.
- Stats SA. 2007. Mid-year population estimates, South Africa 3 July 2007. Statistics South Africa, Pretoria; 2007. pp 1-9.

Stats SA. 2008. Mid-year population estimates, South Africa 31 July 2008. Statistics South Africa, Pretoria; 2008. pp 1-22.

Stats SA. 2007. A national poverty line for South Africa.
<http://www.treasury.gov.za/publications/> Date of access: 10 May 2008.

Steyn, H.S. 1999. Praktiese beduidenheid: die gebruik van effekgroottes. Potchefstroom : PU vir CHO.

Steyn, A.G.W., Smit, C.F., Du Toit, S.H.C. & Strasheim, C. 2003. Modern statistics in practice. Pretoria : Van Schaik.

Steyn, K. 2007. Heart disease in South Africa. Media data document.
<http://www.mrc.ac.za/chronic/heartandstroke.pdf> Date of access: 30 Jun. 2009.

Steyn, K., Sliwa, K., Hawken, S., Commerford, P., Onen, C., Damasceno, A., Ounpuu, S. & Yusuf, S. 2005. Risk factors associated with myocardial infarction in Africa: the INTERHEART African study. *Circulation*, 112:3554-3561.

Struwig, V. 2001. Pharmacoeconomics. Potchefstroom : PU vir CHO. (Study guide FPHA 611).

Sung, S.K., Lee, S.G., Lee, K.S., Kim D.S., Kim, K.H. & Kim, K.Y. 2009. First-year treatment adherence among outpatients initiating antihypertensive medication in Korea: results of a retrospective claims review. *Clinical therapeutics*, 31(6):1309-1320.

Sutters, M. 2007. Systemic Hypertension. (In Tierney, L.M., McPhee, S.J. & Papadakis, M.A., eds. Current medical diagnosis and treatment. 46th ed. New York : Lange Medical Books. p.429-460).

Svensson, S., Kjellgren, K.I., Ahlner, J. & Säljö, R. 2000. Reasons for adherence with antihypertensive medication. *International journal of cardiology*, 76:157-163.

Svetkey, L.P., Harsha, D.W., Vollmer, W.M., Stevens, V.J., Obarzanek, E., Elmer, P.J., Lin, P.-H., Champagne, C., Simons-Morton, D.G., Aickin, M., Proschan, M.A. & Appel, L.J. 2003. Premier: a clinical trial of comprehensive lifestyle modification for blood pressure control: rationale, design and baseline characteristics. *Annals of epidemiology*, 13:462-471.

Talheimer, W. & Cook, S. 2002. How to calculate effect sizes from published research: a simplified methodology. http://www.work-learning.com/effect_sizes.htm Date of access: 24 Jan. 2011.

The ALLHAT Officers and coordinators for the ALLHAT collaborative research group. 2002. Major outcomes in high-risk hypertensive patients randomized to angiotensin-converting enzyme inhibitor or calcium channel blocker vs diuretic. The antihypertensive and lipid-lowering treatment to prevent heart attack trial (ALLHAT). *Journal of the American Medical Association*, 288:2981-2997.

The NHS Information Centre. 2011. Prescribed daily doses (PDDs). <http://www.ic.nhs.uk/services/prescribing-support-unit-psu/using-the-service/reference/measure/volume-measures/prescribed-daily-doses-pdds> Date of access: 23 Sep. 2011.

Torrance, G.W., Siegel, J.E. & Luce, B.R. 1996. Framing and designing the cost-effectiveness analysis. (In Gold, M.R., Siegel, J.E., Russell, L.B. & Weinstein, M.C., eds. Cost-effectiveness in health and medicine. New York : Oxford University Press. p. 54-81).

Truter, I. 1995. Drug utilisation research: the future for health care analysis in South Africa. *South African pharmaceutical journal*, 62:338-339.

Ubel, P.A. 2003. What is the price of life and why doesn't it increase at the rate of inflation? *Archives of internal medicine*, 163:1637-1641.

United States Department Of Health And Human Services. 2004. The Seventh Report of the Joint National Committee on prevention, Detection, Evaluation, and Treatment of High Blood Pressure. <http://www.nhlbi.nih.gov/guidelines/hypertension/> Date of access: 12 Jul. 2007.

United States Department Of Health And Human Services. National Woman's Health Information Centre. 2002. Frequently asked questions. Heart and cardiovascular disease. <http://www.WomensHealth.gov> Date of access: 27 Feb. 2007.

Vasan, R.S., Larson, M.G., Leip, E.P., Kannel, W.B. & Levy, D. 2001. Assessment of frequency of progression to hypertension in non-hypertensive participants in the Framingham heart study: a cohort study. *Lancet*, 358:1682-1686.

Vega, C.P. 2009. How effective are ACE inhibitors for hypertension? A best evidence review. <http://www.medscape.com/viewarticle/589195> Date of access: 23 Aug. 2010.

Venter, R. Organizational alignment and strategy implementation through organizational architecture. (In Louw, L. & Venter, P., eds. Strategic management: winning in the Southern African workplace. Cape Town : Oxford Southern Africa. p. 392-451).

Vikrant, S. & Tiwari, S.C. 2001. Essential hypertension: pathogenesis and pathophysiology. *Journal of the Indian Academy of Clinical Medicine*, 2(3);140-161.

Vlasnik J.J., Aliotta, S.L. & Delor, B. 2005. Medication adherence: factors influencing compliance with prescribed medication plans. *The case manager*, 16(2):47-51.

Walley, T. 2004. Pharmacoeconomics and economic evaluation of drug therapies. (In De Souich, P., Orme, M. & Erill, S., eds. The IUPHAR compendium of basic principles for pharmacological research in humans. p. 67-75. http://www.iuphar.org/pdf/hum_67.pdf Date of access: 27 Feb. 2007).

Walley, T. & Strobl, J. (2004) Cost of illness studies. (In: Walley, T., Haycox, A. & Boland, A., eds. Pharmacoeconomics. Edinburgh : Churchill Livingstone. p.203.

Wallinga, J., Heijne, C.J.M., Kretzschmar, M. 2005. A measles epidemic threshold in a highly vaccinated population. *PLoS Med* 2(11):e316.

Weibert R.T. 2000. Hypertension. (In Herfindal, E.T. & Gourley, D.R., eds. Textbook of therapeutics: drug disease management. 7th ed. New York : Lippincott Williams & Wilkens. p. 795-824).

Wertheimer, A.I. & Navarro, R.P. 1999. Glossary of managed care terms. (In Wertheimer, A.I. & Navarro, R.P., eds. Managed care pharmacy principles and practice. New York : Pharmaceutical Products Press. p. 351-387).

Wetzels, G., Nelemans, P., Van Wijk, B., Broers, N., Schouten, J. & Prins, M. 2006. Determinants of poor adherence in hypertensive patients: development and validation of the "Maastricht Utrecht Adherence in Hypertension (MUAH)-questionnaire". *Patient education and counseling*, 64:151-158.

WHO **see** World Health Organization.

Williams, B., Poulter, N.R., Brown, M.J., Davis, M., McInnes, G.T., Potter, J.F., Sever, P.S. & Thom, S.McG. 2004. British Hypertension Society guideline. Guidelines for management of hypertension: report of the fourth working party of the British Hypertension Society, 2004 – BHS IV. *Journal of human hypertension*, 18:139-185.

Wilson, A.E. 1999. De-mystifying pharmacoeconomics. *Drug benefit trends*, 11(5):56-67.

Williams, B., Poulter, N.R., Brown, M.J., Davis, M., Potter, J.F., Sever, P.S. & Thom, S.M. 2004. Guidelines for management of hypertension: report of the fourth working party of the British Hypertension Society, 2004 – BHS IV. *Journal of human hypertension*, 18:139-185.

Wolf-Maier, K., Cooper, R.S., Kramer, H., Banegas, J.R., Giampaoli, S., Joffres, M.R., Poulter, N., Primatesta, P., Stegmayr, B. & Thamm, M. 2004. Hypertension treatment and control in five European countries, Canada and the United States. *Hypertension*, 43:10-17.

Wordnet. 2011. Threshold.

<http://wordnetweb.princeton.edu/perl/webwn?s=threshold&o2=&o0=1&o8=1&o1=1&o7=&o5=&o9=&o6=&o3=&o4=&h=> Date of access: 1 Jul. 2011.

World Health Organization. 1977. The selection of essential drugs. Technical report series 615. Geneva : World Health Organization.

World Health Organization. 2003. Global strategy on diet, physical activity and health. <http://www.who.int> Date of access: 9 May 2007.

World Health Organization. 2003. Introduction to drug utilization research. http://www.whocc.no/filearchive/publications/drug_utilization_research.pdf Date of access 15 Sep. 2011.

World Health Organization, International Society Of Hypertension Writing Group. 2003. 2003 World Health Organization (WHO) / International Society of Hypertension (ISH) statement on management of hypertension. *Journal of hypertension* 21;1983-1992.

World Health Organization. 2006a. Cost-effectiveness thresholds. <http://www.who.int/choice> Date of access 1 Dec. 2006.

World Health Organization. 2006b. CHOosing Interventions that are Cost Effective (WHO-CHOICE). More information on the rationale, activities, and goals of WHO-CHOICE. <http://www.who.int/choice/description/en/> Date of access 10 Jan. 2007.

World Health Organization. 2006c. The atlas of heart disease and stroke. http://www.who.int/cardiovascular_diseases/resources/atlas/en/print.htm Date of access: 3 Feb. 2006.

World Health Organization. 2012. Raised blood pressure. http://www.who.int/gho/ncd/risk_factors/blood_pressure_prevalence_text/en/index.html Date of access: 14 Feb. 2012.

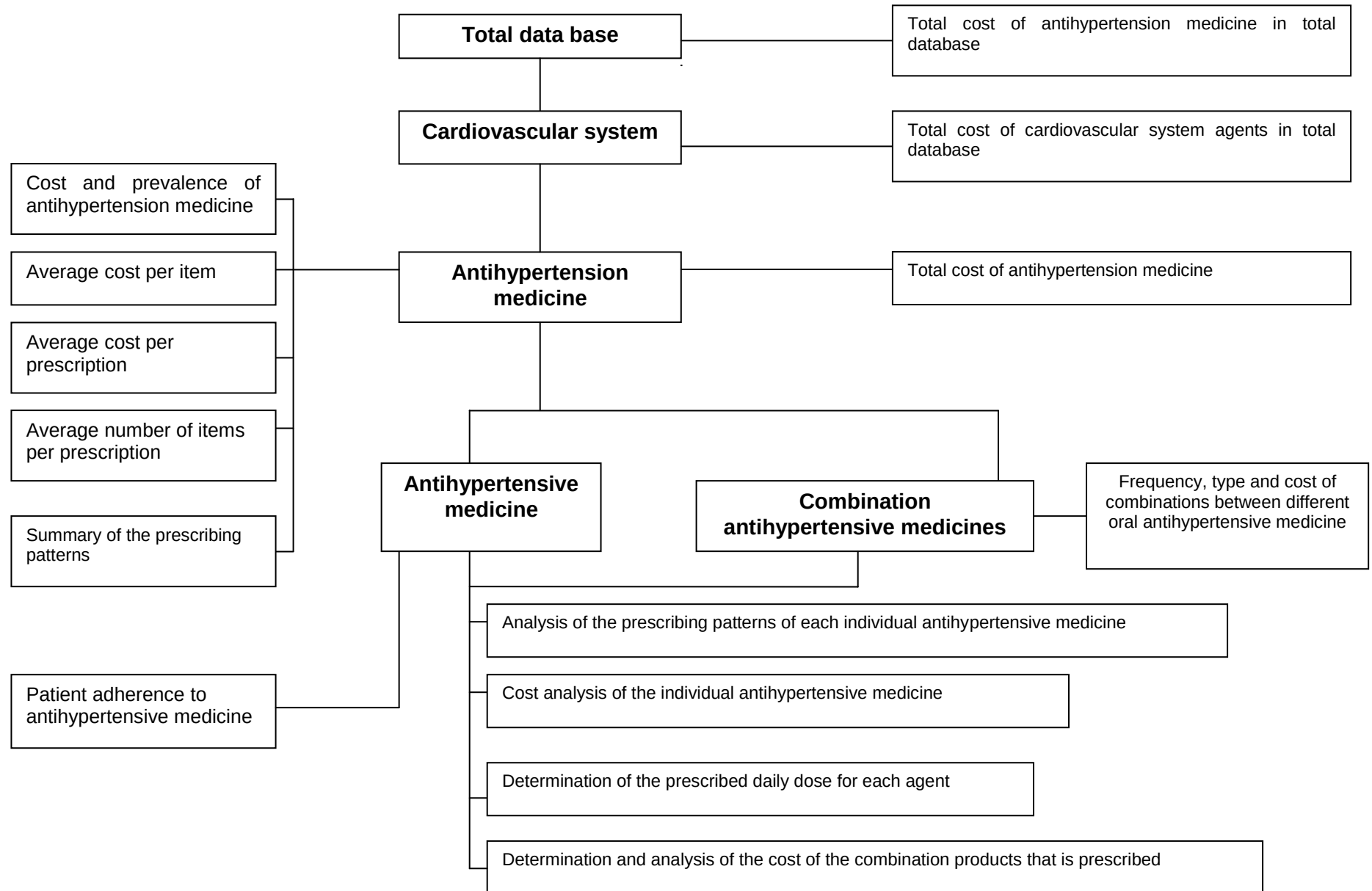
World Health Organization. 2010. Generic drugs. <http://www.who.int/trade/glossary/story034/en/#> Date of access: 8 Nov. 2011.

Yusuf, S., Reddy, S., Ôunpuu, S. & Anand, S. 2001. Global Burden of Cardiovascular Diseases Part I: General considerations, the epidemiologic transition, risk factors, and impact of urbanization. *Circulation*, 104:2746-2753.

Zarbock, S. 2005. Hypertension in children. <http://www.medscape.com/viewarticle/510523> Date of access: 15 Nov. 2011.

Zwart-Van Rijkom, J.E., Leufkens, H.G., Busschbach, J.J., Broekmans, A.W. & Rutten, F.F. 2000. Differences in attitudes, knowledge and use of economic evaluations in decision-making in The Netherlands. The Dutch results from the EUROMET Project. *PharmacoEconomics*, 18(2):149-160.

APPENDIX A



APPENDIX B

Table B1: The MIMS classification (MIMS, 2007:11a-13a).

CENTRAL NERVOUS SYSTEM Central nervous system stimulants Central analeptics Respiratory stimulants Others Sedative Hypnotics Benzodiazepines Barbiturate Others Anxiolytics Benzodiazepines Others Anti-depressants Tricyclic Non-Tricyclic Mono-Amine Oxidase inhibitors Non-selective mono-amine oxidase inhibitors Selective mono-amine oxidase inhibitors Selective serotonin re-uptake inhibitors Serotonin and nor-adrenaline re-uptake inhibitors Lithium Others Anti-psychotics Phenothiazines Butyrophenones Others Anti-epileptics Anti-Parkinson agents Dopaminergics Anticholinergics Others Anti-vertigo and anti-emetic agents Anti-migraine agents Alzheimer's disease
ANAESTHETICS General anaesthetics Inhalation anaesthetics Parenteral anaesthetics Local anaesthetics Surface anaesthetics Muscle relaxants
ANALGESICS

Narcotic analgesics Analgesics and antipyretics Combinations Others
MUSCULO-SKELETAL AGENTS Non-steroidal anti-inflammatory agents COX inhibitors Selective COX2 inhibitors Specific cyclo-oxygenase-2 inhibitor (COXIB) Anti-gout Topical agents Gold Centrally acting muscle relaxants Others Osteoporosis (and other metabolic bone disorders) Bisphosphonates Selective oestrogen receptor modulators Calcitonin Minerals and vitamin
AUTONOMIC Sympathomimetics Sympatholytics Cholinergics Anti-cholinergics Others
AUTACOIDS Anti-histamines Serotonin antagonists NK1 Antagonists
CARDIO-VASCULAR AGENTS Positive inotropic agents Cardiac glycosides Others Anti-arrhythmics Anti-hypertensives (Single agents and combinations including diuretic combinations) Central acting sympathetic nervous system inhibitors Alpha-receptor blockers Beta-receptor blockers Alpha- and beta-receptor blockers Sympathetic nervous blockers Direct-acting vasodilators Calcium channel blockers ACE inhibitors Angiotensin receptor antagonists Others Anti-anginal agents Calcium channel blockers Beta-receptor blockers Organic nitrates

Other vasodilators After-load reducers Peripheral vasodilators Vasoconstrictors Hipolipidaemic agents Fibrates HMG-CoA reductase inhibitors (Statins) Cholesterol absorption inhibitors Others Plasma expanders
BLOOD AND HAEMOPOEITIC Haemostatics Anticoagulants Fibrinolytics Platelet aggregation inhibitors Sclerosing agents Haematinics Others
ALCOHOLISM
RESPIRATORY SYSTEM Coughs and colds Antitussives and expectorants Decongestant, analgesic combinations Decongestants Bronchodilators Sympathomimetics Methylxanthines and combinations Anticholinergics Combinations Mucolytics Anti-asthmatics Glucocorticoids Leukotriene receptor antagonists Chromones Other anti-asthmatics Surfactants Others
EAR, NOSE AND THROAT Topical nasal preparations Antimicrobial and combinations Glucocorticosteroids Chromones Decongestants Antihistamines Mucolytics Others Ear drops and ointments Mouth and throat preparations
GASTRO-INTESTINAL TRACT

Digestants Appetite suppressants Anti-spasmodics Acid reducers Antacids Antacids and combinations Histamine-2 receptor antagonists Proton pump inhibitors Cytoprotective agents Other acid reducers Motility enhancers Laxatives Antidiarrhoeals Liver, gall bladder and bile Suppositories and anal ointments Others
ANTHELMINTICS
DERMATOLOGICALS Anti-bacterial antiseptic agents Anti-parasitics Fungicides Cortico-steroids 14.4.1 Cortico-steroids with anti-infective agents Psoriasis Acne Melanin inhibitors and stimulants Emollients and protectives Others
OPHTHALMICS Anti-infectives Antivirals Corticoids Combinations (anti infectives with corticoids) Decongestants Mydriatics Glaucoma Others
URINARY SYSTEM Diuretics Anti-diuretics Urinary alkalinisers Urinary antiseptics Others
GENITAL SYSTEM Contraceptives Hormonal (including oral) Locally acting Contraceptive devices Vaginal preparations

Oxytocics Uterine antispasmodics Sexual dysfunction Others Erectile dysfunction
ANTI-MICROBIALS Beta-lactams Penicillins Cephalosporins Others Erythromycin and other macrolides Aminoglycosides Tetracyclines Chloramphenicols Sulphonamides and combinations Quinolones Mycobacteria Tuberculostatics Anti-leprotics Other anti-bacterial agents Anti-fungal agents Anti-protozoal agents Anti-viral agents
ENDOCRINE SYSTEM Anti-diabetic agents Insulins Oral agents Anti-hypoglycaemic agents Thyroid Parathyroid and calcitonin Corticosteroids Sex hormones Androgens and anabolic steroids Oestrogens Progestogens Combinations Others Tropic hormones Hormone inhibitors
VITAMINS, TONICS, MINERALS AND ELECTROLYTES Vitamins Vitamin combinations Vitamins with minerals Tonics Minerals and electrolytes
AMINO-ACIDS
SPECIAL FOODS
CYTOSTATICS
Immunological

Immunosuppressants
Immunostimulants
CHELATING AGENTS, ION EXCHANGE PREPARATIONS
BIOLOGICALS
ENZYMES
POISON ANTIDOTES
OTHERS
MEDICAL GASES

APPENDIX C

Table C1: Cost and prevalence of the antihypertensive medicine items according to active ingredient (7.3.1)

Year	Active ingredient	Number of items	Average cost (R)	Total cost (R)	% Prevalence	Cost %	CPI	d-value
2005	Methyldopa	17 955	70.40 ± 55.19	1 263 954.23	77.25	53.57	0.69	0.50
	Moxonidine	5 288	207.15 ± 43.09	1 095 434.62	29.26	46.43	1.59	1.24
	Total	23 243		2 359 388.85				
2006	Methyldopa	18 074	72.04 ± 56.42	1 302 129.13	75.04	51.42	0.69	0.44
	Moxonidine	6 011	204.67 ± 45.91	1 230 261.00	24.96	48.58	1.95	1.31
	Total	24 085		2 532 390.13				
2007	Methyldopa	13 494	76.41 ± 58.32	1 031 031.07	67.64	43.26	0.64	0.44
	Moxonidine	6 457	209.44 ± 49.81	1 352 338.65	32.36	56.74	1.75	1.31
	Total	19 951		2 383 369.72				
2008	Methyldopa	12 795	78.83 ± 56.35	1 008 669.5	66.61	42.34	0.64	0.36
	Moxonidine	6 414	214.13 ± 56.40	1 373 443.39	33.39	57.66	1.73	1.48
	Total	19 209		2 382 112.89				

d-values was calculated comparing the average cost of all antihypertensive medicine items against the average cost per active ingredient. For 2005 the average cost was R109.69 ± R78.34, for 2006 R105.26 ± R75.72, for 2007 it was R109.68 ± R76.00 and for 2008 it was R105.24 ± R73.50.

Table C2: Cost and prevalence of the antihypertensive medicine items according to active ingredient (7.3.2)

Year	Active ingredient	Number of items	Average cost (R)	Total cost	% Prevalence	Cost %	CPI	d-value
2005	Alfuzosin	4950	281.49 ± 59.38	1393368.84	12.83	20.66	1.61	2.19
	Doxazosin	24345	161.78 ± 72.64	3938518.52	63.12	58.39	0.93	0.66
	Prazosin	5929	92.83 ± 69.17	550401.79	22.84	8.16	0.36	0.22
	Terazosin	3346	257.80 ± 100.14	862589.17	57.27	12.79	0.22	1.48
	Total	38570		6744878.32				
2006	Alfuzosin	6452	286.78 ± 52.68	1850326.37	15.57	26.00	1.67	2.40
	Doxazosin	25954	151.18 ± 73.71	3923789.69	62.64	55.12	0.88	0.61
	Prazosin	5842	89.65 ± 66.54	523719.67	14.10	7.36	0.52	0.21
	Terazosin	3184	257.43 ± 99.00	819668.12	7.68	11.52	1.50	1.54
	Total	41432		7117503.85				
2007	Alfuzosin	6454	300.86 ± 69.83	1941762.74	17.07	28.41	1.66	2.52
	Doxazosin	24361	153.95 ± 80.45	3750441.52	64.44	54.87	0.85	0.55
	Prazosin	4420	99.41 ± 79.34	439413.2	11.69	6.43	0.55	0.13
	Terazosin	2569	273.97 ± 109.01	703840.77	6.80	10.30	1.52	1.51
	Total	37804		6835458.23				
2008	Alfuzosin	6174	309.07 ± 79.23	1908203.64	17.46	30.04	1.72	2.57
	Doxazosin	23305	151.04 ± 84.87	3519904.34	65.89	55.41	0.84	0.54
	Prazosin	4060	102.81 ± 83.87	417390.15	11.48	6.57	0.57	0.03
	Terazosin	1831	277.17 ± 111.80	507505.03	5.18	7.99	1.54	1.54
	Total	35370		6353003.16				

d-values was calculated comparing the average cost of all antihypertensive medicine items against the average cost per active ingredient. For 2005 the average cost was R109.69 ± R78.34, for 2006 R105.26 ± R75.72, for 2007 it was R109.68 ± R76.00 and for 2008 it was R105.24 ± R73.50.

Table C3: Cost and prevalence of the antihypertensive medicine items according to active ingredient (7.3.3)

Year	Active ingredient	Number of items	Average cost (R)	Total cost (R)	% Prevalence	Cost %	CPI	d-value
2005	Acebutolol	11 734	170.46 ± 67.49	2 000 148.48	5.03	8.73	1.74	0.78
	Atenolol/Chlortalidone	47 775	77.49 ± 39.60	3 701 896.47	20.48	16.17	0.79	0.41
	Bisoprolol	75 590	75.47 ± 30.12	5 704 930.52	32.40	24.91	0.77	0.44
	Bisoprolol/HTCZ	73 605	117.05 ± 10.34	8 615 400.92	31.55	37.62	1.19	0.09
	Metoprolol	644	230.22 ± 92.47	148 264.14	0.28	0.65	2.35	1.30
	Nadolol	785	214.21 ± 58.00	168 157.58	0.34	0.73	2.18	1.33
	Nadolol/Bendroflumethiazide	684	199.41 ± 55.34	136 398.62	0.29	0.60	2.03	1.15
	Propranolol	6 352	21.22 ± 11.77	134 784.89	2.72	0.59	0.22	1.13
	Propranolol/ Bendroflumethiazide	1	354.40 ± 0.00	354.40	0.0004	0.002	3.61	3.12
	Sotalol	12 074	113.36 ± 68.72	1 368 764.79	5.18	5.98	1.16	0.05
	Timolol/Amiloride	4 063	226.48 ± 53.72	920 196.15	1.74	4.02	2.31	1.49
	Total	233 307		22 899 296.96				
2006	Acebutolol	10 020	162.94 ± 66.15	1 632 675.23	3.91	7.05	1.80	0.76
	Atenolol/Chlortalidone	78	24.92 ± 9.50	1 943.70	0.03	0.01	0.28	1.06
	Bisoprolol	46 468	76.61 ± 37.68	3 559 878.54	18.14	15.37	0.85	0.38
	Bisoprolol/HTCZ	98 441	63.60 ± 28.80	6 260 469.81	38.43	27.04	0.70	0.55
	Metoprolol	78 555	115.83 ± 11.84	9 099 323.69	30.67	39.30	1.28	0.14
	Nadolol	568	230.24 ± 94.22	130 776.15	0.22	0.56	2.55	1.33
	Nadolol/ Bendroflumethiazide	695	201.44 ± 61.22	140 000.47	0.27	0.60	2.23	1.27
	Propranolol	548	186.60 ± 66.72	102 258.94	0.21	0.44	2.06	1.07
	Propranolol/ Bendroflumethiazide	5 254	21.60 ± 11.90	113 510.32	2.05	0.49	0.24	1.10
	Sotalol	12 308	113.07 ± 67.35	1 391 676.34	4.80	6.01	1.25	0.10
	Timolol/Amiloride	3 227	223.61 ± 53.77	721 584.60	1.26	3.12	2.47	1.56
	Total	256 162		23 154 097.79				

Table C3 (cont.): Cost and prevalence of the antihypertensive medicine items according to active ingredient (7.3.3)

Year	Active ingredient	Number of items	Average cost (R)	Total cost (R)	% Prevalence	Cost %	CPI	d-value
2007	Acebutolol	8 177	166.59 ± 75.31	1 362 183.75	3.29	6.09	1.85	0.75
	Atenolol/Chlortalidone	703	20.24 ± 11.07	14 226.56	0.28	0.06	0.23	1.17
	Bisoprolol	38 072	80.80 ± 39.44	3 076 333.90	15.30	13.75	0.90	0.38
	Bisoprolol/HTCZ	111 466	62.70 ± 28.77	6 988 379.63	44.80	31.23	0.70	0.62
	Metoprolol	74 044	119.86 ± 20.11	8 874 664.37	29.76	39.65	1.33	0.13
	Nadolol	479	249.17 ± 125.09	119 350.44	0.19	0.53	2.77	1.12
	Nadolol/ Bendroflumethiazide	221	181.09 ± 67.83	40 021.96	0.09	0.18	2.01	0.94
	Propranolol	46	208.39 ± 76.46	9 586.15	0.02	0.04	2.32	1.29
	Propranolol/ Bendroflumethiazide	2 268	17.91 ± 11.16	40 628.28	0.91	0.18	0.20	1.21
	Sotalol	10 923	115.91 ± 70.34	1 266 083.25	4.39	5.66	1.29	0.08
	Timolol/Amiloride	2 435	241.92 ± 62.05	589 072.92	0.98	2.63	2.69	1.74
	Total	248 834		22 380 531.21				
2008	Acebutolol	6 211	167.45 ± 75.72	1 040 006.42	2.70	5.00	1.85	0.82
	Atenolol/Chlortalidone	422	20.88 ± 8.46	8 810.06	0.18	0.04	0.23	1.15
	Bisoprolol	28 525	88.21 ± 47.96	2 516 216.68	12.39	12.10	0.98	0.23
	Bisoprolol/HTCZ	118 670	63.80 ± 29.36	7 570 875.84	51.56	36.40	0.71	0.56
	Metoprolol	64 404	124.61 ± 20.90	8 025 675.72	27.98	38.59	1.38	0.26
	Nadolol	326	251.64 ± 139.26	82 034.67	0.14	0.39	2.78	1.05
	Nadolol/ Bendroflumethiazide	1	173.66 ± 0.00	173.66	0.0004	0.001	1.92	0.93
	Propranolol	535	14.39 ± 10.76	7 700.14	0.23	0.04	0.16	1.24
	Sotalol	9 336	119.86 ± 72.15	1 119 037.98	4.06	5.38	1.33	0.20
	Timolol/Amiloride	1 730	247.02 ± 65.92	427 338.75	0.75	2.05	2.73	1.93
	Total	230 160		20 797 869.92				

d-values was calculated comparing the average cost of all antihypertensive medicine items against the average cost per active ingredient. For 2005 the average cost was R109.69 ± R78.34, for 2006 R105.26 ± R75.72, for 2007 it was R109.68 ± R76.00 and for 2008 it was R105.24 ± R73.50.

Table C4: Cost and prevalence of the antihypertensive medicine items according to active ingredient (7.3.4)

Year	Active ingredient	Number of items	Average cost (R)	Total cost (R)	% Prevalence	Cost %	CPI	d-value
2005	Carvedilol	56 001	117.61 ± 54.37	6 586 035.40	99.65	99.21	1.00	0.10
	Labetalol	195	269.82 ± 118.18	52 615.56	0.35	0.79	2.28	1.36
	Total	56 196		6 638 650.96				
2006	Carvedilol	66 521	108.97 ± 49.77	7 248 545.58	99.71	99.25	1.00	0.05
	Labetalol	191	285.63 ± 182.96	54 554.55	0.29	0.75	2.61	0.99
	Total	66 712		7 303 100.13				
2007	Carvedilol	69 800	109.48 ± 47.64	7 641 640.96	99.78	99.35	1.00	0.002
	Labetalol	151	329.63 ± 233.67	497 73.79	0.22	0.65	3.00	0.94
	Total	69 951		7 691 414.75				
2008	Carvedilol	71 472	109.32 ± 46.87	7 813 552.85	99.95	99.85	1.00	0.06
	Labetalol	33	355.23 ± 258.17	11 722.58	0.05	0.15	3.25	0.97
	Total	71 505		7 825 275.43				

d-values was calculated comparing the average cost of all antihypertensive medicine items against the average cost per active ingredient. For 2005 the average cost was R109.69 ± R78.34, for 2006 R105.26 ± R75.72, for 2007 it was R109.68 ± R76.00 and for 2008 it was R105.24 ± R73.50.

Table C5: Cost and prevalence of the antihypertensive medicine items according to active ingredient (7.3.5)

Year	Active ingredient	Number of items	Average cost (R)	Total cost (R)	Prevalence%	Cost %	CPI	d-value
2005	Chlortalidone	452	189.49 ± 68.66	85 647.42	2.42	4.85	2.00	1.02
	Chlortalidone/Reserpine	227	187.13 ± 61.87	42 479.41	1.22	2.41	1.98	0.99
	Dihydroergocristine/Cloppamine	125	189.77 ± 40.69	23 721.46	0.67	1.34	2.00	1.02
	Ergocristine/Cloppamine	7 221	181.07 ± 33.31	1 307 498.29	38.72	74.03	1.91	0.91
	Hydroflumethiazide/Reserpine	1 900	54.23 ± 20.20	103 036.54	10.19	5.83	0.57	0.71
	Reserpine	8 722	23.37 ± 11.10	203 797.52	46.77	11.54	0.25	1.10
	Total	18 647		1 766 180.64				
2006	Chlortalidone	406	181.13 ± 77.69	73 539.61	2.47	5.12	2.07	0.98
	Chlortalidone/Reserpine	2	243.62 ± 21.04	487.24	0.02	0.03	1.55	1.83
	Dihydroergocristine/Cloppamine	11	169.39 ± 5.75	1 863.24	0.07	0.13	1.94	0.85
	Ergocristine/Cloppamine	5 989	181.31 ± 37.34	1 085 890.18	36.41	75.58	2.08	1.00
	Hydroflumethiazide/Reserpine	1 117	53.45 ± 18.10	59 700.45	6.79	4.16	0.61	0.68
	Reserpine	8 924	24.12 ± 10.76	215 222.46	54.25	14.98	0.28	1.07
	Total	16 449		1 436 703.18				
2007	Chlortalidone	274	188.74 ± 100.48	51 714.68	3.00	4.84	1.61	0.79
	Dihydroergocristine/Cloppamine	3	220.91 ± 79.75	662.73	0.03	0.06	1.89	1.39
	Ergocristine/Cloppamine	5 150	185.17 ± 45.75	953 602.66	56.36	89.24	1.58	0.99
	Hydroflumethiazide/Reserpine	27	43.28 ± 14.95	1 168.66	0.30	0.11	0.37	0.87
	Reserpine	3 683	16.69 ± 7.15	61 456.19	40.31	5.75	0.14	1.22
	Total	9 137		1 068 604.92				
2008	Chlortalidone	281	171.03 ± 81.25	48 059.8	3.26	5.43	1.67	0.81
	Ergocristine/Cloppamine	3 776	194.28 ± 50.07	733 588.94	43.79	82.87	1.89	1.21
	Hydroflumethiazide/Reserpine	3	56.05 ± 4.45	168.16	0.03	0.02	0.55	0.67
	Reserpine	4 562	22.68 ± 10.42	103 460.27	52.91	11.69	0.22	1.12

Table C5 (cont.): Cost and prevalence of the antihypertensive medicine items according to active ingredient (7.3.5)

Year	Active ingredient	Number of items	Average cost (R)	Total cost (R)	Prevalence%	Cost %	CPI	d-value
	Total	8 622		885 277.17				

d-values was calculated comparing the average cost of all antihypertensive medicine items against the average cost per active ingredient. For 2005 the average cost was R109.69 ± R78.34, for 2006 R105.26 ± R75.72, for 2007 it was R109.68 ± R76.00 and for 2008 it was R105.24 ± R73.50.

Table C6: Cost and prevalence of the antihypertensive medicine items according to active ingredient (7.3.6)

Year	Active ingredient	Number of items	Average cost (R)	Total Cost (R)	% Prevalence	Cost %	CPI	d-value
2005	Dihydralazine Mesylate	4	36.82 ± 30.82	147.27	0.17	0.07	0.41	0.93
	Hydralazine	1 787	64.52 ± 59.92	115 294.45	76.40	55.16	0.72	0.58
	Minoxidil	546	171.30 ± 104.84	93 527.33	23.34	44.74	1.92	0.59
	Sodium Nitroprusside	2	31.11 ± 43.85	62.21	0.09	0.03	0.35	1.00
	Total	2 339		209 031.26				
2006	Dihydralazine Mesylate	1	63.50 ± 0.00	63.50	0.04	0.03	0.72	0.55
	Hydralazine	2 085	61.72 ± 54.50	128 685.43	77.71	54.46	0.70	0.58
	Minoxidil	597	180.12 ± 112.91	107 531.52	22.25	45.51	2.05	0.66
	Total	2 683		236 280.45				
2007	Hydralazine	1 777	62.62 ± 52.78	111 267.27	75.58	51.62	0.68	0.62
	Minoxidil	574	181.69 ± 113.65	104 290.33	24.42	48.38	1.98	0.63
	Total	2 351		215 557.60				
2008	Hydralazine	1 597	52.49 ± 28.41	83 829.13	77.34	50.84	0.66	0.72
	Minoxidil	468	173.19 ± 104.53	81 053.23	22.66	49.16	2.17	0.65
	Total	2 065		164 882.36				

d-values was calculated comparing the average cost of all antihypertensive medicine items against the average cost per active ingredient. For 2005 the average cost was R109.69 ± R78.34, for 2006 R105.26 ± R75.72, for 2007 it was R109.68 ± R76.00 and for 2008 it was R105.24 ± R73.50.

Table C7: Cost and prevalence of the antihypertensive medicine items according to active ingredient (7.3.7)

Year	Active ingredient	Number of items	Average cost (R)	Total cost (R)	% Prevalence	Cost %	CPI	d-value
2005	Amlpodipine	83 113	139.19 ± 35.88	11 568 491.79	54.38	45.20	0.83	0.38
	Felodipine	27 021	157.27 ± 55.97	4 249 619.79	17.68	16.60	0.94	0.61
	Felodipine/Ramipril	20 986	224.07 ± 48.55	4 702 263.21	13.73	18.37	1.34	1.46
	Isradipine	5 742	230.65 ± 58.18	1 324 400.74	3.76	5.17	1.38	1.54
	Lercanidipine	1 391	149.09 ± 27.73	207 385.78	0.91	0.81	0.89	0.50
	Nifedipine	11 563	269.44 ± 32.12	3 115 541.32	7.57	12.17	1.61	2.04
	Nisoldipine	7	297.73 ± 0.00	2 084.11	0.004	0.01	1.78	2.40
	Verapamil	3 019	140.84 ± 40.39	425 195.58	1.98	1.66	0.84	0.40
	Total	152 842		25 594 982.32				
2006	Amlpodipine	115 532	127.30 ± 34.00	14 706 926.52	60.35	49.74	0.82	0.29
	Felodipine	27 320	145.42 ± 52.72	3 972 867.11	14.27	13.44	0.94	0.53
	Felodipine/Ramipril	21 969	225.65 ± 46.65	4 957 309.63	11.48	16.77	1.46	1.59
	Isradipine	4 803	231.26 ± 59.69	1 110 758.41	2.51	3.76	1.50	1.66
	Lercanidipine	5 161	150.78 ± 34.26	778 160.47	2.70	2.63	0.98	0.60
	Nifedipine	13 502	266.98 ± 28.06	3 604 774.69	7.05	12.19	1.73	2.14
	Verapamil	3 143	139.24 ± 38.70	437 617.06	1.64	1.48	0.90	0.45
	Total	191 430		29 568 413.89				
2007	Amlpodipine	139 584	128.29 ± 40.50	17 907 756.07	70.07	62.00	0.88	0.24
	Felodipine	25 375	146.76 ± 53.66	3 724 115.81	12.74	12.89	1.01	0.49
	Felodipine/Ramipril	19 810	234.80 ± 55.16	4 651 479.93	9.94	16.11	1.62	1.65
	Isradipine	3 749	243.91 ± 68.29	914 427.37	1.88	3.17	1.68	1.77
	Lercanidipine	7 730	161.44 ± 35.73	1 247 933.52	3.88	4.32	1.11	0.68
	Verapamil	2 949	147.85 ± 42.08	436 011.2	1.48	1.51	1.02	0.50
	Total	199 197		28 881 723.9				

Table C7 (cont.): Cost and prevalence of the antihypertensive medicine items according to active ingredient (7.3.7)

Year	Active ingredient	Number of items	Average cost (R)	Total cost (R)	% Prevalence	Cost %	CPI	d-value
2008	Amlpodipine	153 204	114.55 ± 42.27	17 549 586.96	69.88	56.39	0.81	0.13
	Felodipine	22 660	146.24 ± 52.76	3 313 711.93	10.34	10.65	1.03	0.56
	Felodipine/Ramipril	16 287	240.43 ± 56.61	3 915 903.81	7.43	12.58	1.69	1.84
	Isradipine	28 63	259.03 ± 73.33	741 611.43	1.31	2.38	1.82	2.09
	Lercanidipine	8 795	167.54 ± 35.75	1 473 491.8	4.01	4.73	1.18	0.85
	Nifedipine	12 729	290.51 ± 37.86	3 697 963.58	5.81	11.88	2.05	2.52
	Verapamil	2 711	157.82 ± 46.39	427 840.08	1.24	1.37	1.11	0.72
	Total	219 249		31 120 109.59				

d-values was calculated comparing the average cost of all antihypertensive medicine items against the average cost per active ingredient. For 2005 the average cost was R109.69 ± R78.34, for 2006 R105.26 ± R75.72, for 2007 it was R109.68 ± R76.00 and for 2008 it was R105.24 ± R73.50.

Table C8: Cost and prevalence of the antihypertensive medicine items according to active ingredient (7.3.8)

Year	Active ingredient	Number of items	Average cost (R)	Total cost (R)	Prevalence %	Cost %	CPI	d-value
2005	Benazapril	508	172.71 ± 65.39	87 739.04	0.09	0.15	1.69	0.81
	Benazapril/HCTZ	237	234.85 ± 49.12	55 660.17	0.04	0.10	2.30	1.60
	Captopril	35 061	38.94 ± 34.17	1 365 284.86	6.24	2.38	0.38	0.90
	Captopril/HTCZ	5 265	73.21 ± 35.62	385 465.96	0.94	0.67	0.72	0.47
	Cilazapril	2 335	142.67 ± 29.82	333 124.63	0.42	0.58	1.40	0.42
	Cilazapril/HCTZ	1 781	153.81 ± 18.89	273 941.62	0.32	0.48	1.51	0.56
	Enalapril	120 317	56.04 ± 24.04	6 742 149.28	21.42	11.76	0.55	0.68
	Enalapril/HTCZ	60 022	84.13 ± 17.14	5 049 439.60	10.68	8.81	0.82	0.33
	Fosinopril	2 924	183.19 ± 44.04	535 638.82	0.52	0.93	1.80	0.94
	Fosinopril/HTCZ	1 205	206.34 ± 24.06	248 640.90	0.21	0.43	2.02	1.23
	Lisinopril	100 059	65.08 ± 28.19	6 512 145.48	17.81	11.36	0.64	0.57
	Lisinopril/HTCZ	24 221	149.56 ± 53.49	3 622 398.47	4.31	6.32	1.47	0.51
	Moexipril	68	137.48 ± 88.42	9 348.44	0.01	0.02	1.35	0.31
	Perindopril	117 580	131.43 ± 30.42	15 453 790.90	20.93	26.96	1.29	0.28
	Quinapril	14 048	160.88 ± 43.28	2 260 073.83	2.50	3.94	1.58	0.65
	Quinapril/HCTZ	28 207	174.29 ± 37.64	4 916 071.17	5.02	8.58	1.71	0.82
	Ramipril	36 654	192.26 ± 66.31	7 047 210.65	6.52	12.29	1.88	1.05
	Ramipril/HCTZ	1	4.41 ± 0.00	4.41	0.0001	0.000004	0.04	1.34
	Trandolapril	2 878	138.63 ± 30.71	398 971.36	0.51	0.70	1.36	0.37
	Trandolapril/Verapamil	8 458	240.13 ± 37.17	2 030 995.3	1.51	3.54	2.35	1.67
	Total	561 829		57 328 094.89				
2006	Benazapril	438	172.25 ± 68.62	75 445.83	0.07	0.13	1.84	0.88
	Benazapril/HTCZ	198	223.80 ± 15.40	421.57	0.03	0.001	0.02	1.57
	Captopril	35 871	37.24 ± 32.87	1 335 793.50	5.80	2.30	0.40	0.90
	Captopril/HTCZ	5 880	68.86 ± 29.70	404 886.40	0.95	0.70	0.74	0.48

Table C8 (cont.): Cost and prevalence of the antihypertensive medicine items according to active ingredient (7.3.8)

Year	Active ingredient	Number of items	Average cost (R)	Total cost (R)	Prevalence %	Cost %	CPI	d-value
	Cilazapril	1 806	143.88 ± 29.36	259 849.10	0.29	0.45	1.54	0.51
	Cilazapril/HCTZ	1 409	153.23 ± 19.98	215 902.80	0.23	0.37	1.64	0.63
	Enalapril	132 815	54.72 ± 22.59	7 267 976.21	21.46	12.54	0.58	0.67
	Enalapril/HTCZ	67 298	81.53 ± 15.70	5 487 067.29	10.87	9.46	0.87	0.31
	Fosinopril	2 274	182.98 ± 47.71	416 092.85	0.37	0.72	1.95	1.03
	Fosinopril/HTCZ	442	206.69 ± 22.11	91 356.84	0.07	0.16	2.21	1.34
	Lisinopril	110 644	62.22 ± 22.39	6 884 477.82	17.88	11.87	0.66	0.57
	Lisinopril/HTCZ	32 202	92.71 ± 25.45	2 985 322.25	5.20	5.15	0.99	0.17
	Moexipril	38	141.63 ± 116.83	5 381.96	0.01	0.01	1.51	0.48
	Perindopril	143 503	130.88 ± 30.70	18 781 979.91	23.19	32.39	1.40	0.34
	Quinapril	11 990	127.99 ± 44.19	1 534 593.99	1.94	2.66	1.37	0.30
	Quinapril/HTCZ	24 627	155.80 ± 44.19	3 836 906.33	3.98	6.62	1.66	0.67
	Ramipril	33 364	167.35 ± 71.03	5 583 623.28	5.39	9.63	1.79	0.82
	Trandolapril	5 642	133.52 ± 26.05	753 296.84	0.91	1.30	1.43	0.37
	Trandolapril/Verapamil	8 420	239.36 ± 40.24	2 015 423.91	1.36	3.48	2.55	1.77
	Total	618 861		57 979 689.34				
2007	Benazapril	288	169.50 ± 82.38	48 814.68	0.07	0.14	1.99	0.73
	Benazapril/HTCZ	102	222.39 ± 0.62	22 683.56	0.03	0.07	2.62	1.48
	Captopril	18 880	32.83 ± 35.84	619 833.35	4.64	1.79	0.39	1.01
	Captopril/HTCZ	4 106	70.81 ± 31.82	290 748.02	1.01	0.84	0.83	0.51
	Cilazapril	1 324	143.30 ± 43.23	189 733.15	0.33	0.55	1.69	0.44
	Cilazapril/HCTZ	1 170	153.51 ± 25.19	179 606.18	0.29	0.52	1.81	0.58
	Enalapril	110 307	57.49 ± 24.71	6 341 160.04	27.14	18.36	0.68	0.69
	Enalapril/HTCZ	61 935	85.27 ± 16.73	5 281 068.92	15.24	15.29	1.00	0.32
	Fosinopril	1 757	178.95 ± 57.76	314 414.86	0.43	0.91	2.11	0.91

Table C8 (cont.): Cost and prevalence of the antihypertensive medicine items according to active ingredient (7.3.8)

Year	Active ingredient	Number of items	Average cost (R)	Total cost (R)	Prevalence %	Cost %	CPI	d-value
	Fosinopril/HTCZ	247	211.90 ± 30.39	52 340.08	0.06	0.15	2.49	1.35
	Lisinopril	96 124	65.49 ± 24.70	6 294 890.25	23.65	18.22	0.77	0.58
	Lisinopril/HTCZ	35 661	93.99 ± 27.78	3 351 859.91	8.77	9.70	1.11	0.21
	Moexipril	38	118.75 ± 36.45	4 512.52	0.01	0.01	1.40	0.129
	Quinapril	10 626	119.89 ± 34.30	1 273 934.64	2.61	3.69	1.41	0.13
	Quinapril/HTCZ	20 759	136.04 ± 28.63	2 824 052.53	5.11	8.18	1.60	0.35
	Ramipril	30 278	159.20 ± 70.59	4 820 105.9	7.45	13.96	1.87	0.65
	Trandolapril	5 126	137.84 ± 32.18	706 542.23	1.26	2.05	1.62	0.37
	Trandolapril/Verapamil	7 736	248.66 ± 38.88	1 923 603.68	1.90	5.57	2.93	1.83
	Total	406 464		34 539 904.50				
2008	Benazapril	227	168.51 ± 72.25	38 250.99	0.04	0.07	1.76	0.86
	Benazapril/HTCZ	84	255.63 ± 198.29	21 472.65	0.02	0.04	2.67	0.76
	Captopril	21 721	31.73 ± 28.46	689 251.09	4.06	1.34	0.33	1.00
	Captopril/HTCZ	3 576	74.90 ± 31.25	267 830.30	0.67	0.52	0.78	0.41
	Cilazapril	966	149.85 ± 38.80	144 759.22	0.18	0.28	1.57	0.61
	Cilazapril/HCTZ	886	159.91 ± 22.43	141 682.86	0.17	0.28	1.67	0.74
	Enalapril	115 448	59.78 ± 24.14	6 901 624.63	21.56	13.46	0.62	0.62
	Enalapril/HTCZ	64 940	87.57 ± 15.76	5 686 639.58	12.13	11.09	0.91	0.24
	Fosinopril	1 362	180.10 ± 57.86	245 302.62	0.25	0.49	1.88	1.02
	Fosinopril/HTCZ	219	213.60 ± 40.90	46 778.84	0.04	0.09	2.23	1.47
	Lisinopril	97 064	67.14 ± 24.62	6 517 168.6	18.13	12.71	0.70	0.52
	Lisinopril/HTCZ	35 595	96.52 ± 28.01	34 35 587.73	6.65	6.70	1.01	0.12
	Moexipril	13	165.25 ± 19.72	2 148.28	0.002	0.004	1.73	0.82
	Perindopril	127 942	133.68 ± 36.58	17 102 818.21	23.89	33.36	1.40	0.39
	Perindopril/Indapamide	4 051	149.56 ± 15.21	605 852.47	0.76	1.18	1.56	0.60

Table C8 (cont.): Cost and prevalence of the antihypertensive medicine items according to active ingredient (7.3.8)

Year	Active ingredient	Number of items	Average cost (R)	Total cost (R)	Prevalence %	Cost %	CPI	d-value
	Quinapril	9 397	113.21 ± 37.39	1 063 874.46	1.75	2.07	1.18	0.11
	Quinapril/HTCZ	14 227	134.12 ± 29.23	1 908 119.88	2.66	3.72	1.40	0.39
	Ramipril	27 756	155.80 ± 68.18	4 324 379.58	5.18	8.43	1.63	0.69
	Trandolapril	3 868	144.92 ± 33.24	560 565.83	0.72	1.09	1.51	0.54
	Trandolapril/Verapamil	6 157	254.54 ± 40.07	1 567 229.93	1.15	3.06	2.66	2.03
	Total	535 499		51 271 337.75				

d-values was calculated comparing the average cost of all antihypertensive medicine items against the average cost per active ingredient. For 2005 the average cost was R109.69 ± R78.34, for 2006 R105.26 ± R75.72, for 2007 it was R109.68 ± R76.00 and for 2008 it was R105.24 ± R73.50.

Table C9: Cost and prevalence of the antihypertensive medicine items according to active ingredient (7.3.9)

Year	Active ingredient	Number of items	Average cost (R)	Total cost (R)	Prevalence%	Cost %	CPI	d-value
2005	Candesartan cilexetil	32 786	186.29 ± 33.00	6 107 766.43	18.06	16.14	0.89	0.98
	Candesartan cilexetil/HTCZ	25 610	196.61 ± 23.89	5 035 283.04	14.11	13.31	0.94	1.11
	Eprosartan	849	202.32 ± 14.88	171 765.49	0.47	0.45	0.97	1.18
	Irbesartan	15 867	217.73 ± 28.72	3 454 690.21	8.74	9.13	1.04	1.38
	Irbesartan/HTCZ	13 935	217.30 ± 30.02	3 028 015.49	7.68	8.00	1.04	1.37
	Losartan	20 407	223.29 ± 47.58	4 556 604.42	11.24	12.04	1.07	1.45
	Losartan/HTCZ	40 258	219.83 ± 2.34	8 849 673.53	22.18	23.39	1.05	1.41
	Telmisartan	17 453	208.96 ± 28.16	3 647 056.17	9.62	9.64	1.00	1.27
	Telmisartan/HTCZ	14 347	208.04 ± 26.45	2 984 699.68	7.90	7.89	1.00	1.26
	Total	181 511		37 835 554.50				
2006	Candesartan cilexetil	32 162	187.23 ± 42.91	6 021 839.06	13.21	11.81	0.89	1.08
	Candesartan cilexetil/HTCZ	27 021	197.43 ± 26.35	5 334 792.81	11.09	10.47	0.94	1.22
	Eprosartan	1 421	202.05 ± 29.84	287 715.45	0.58	0.56	0.97	1.28
	Irbesartan	16 602	218.95 ± 31.10	3 634 958.60	6.82	7.13	1.05	1.50
	Irbesartan/HTCZ	17 128	216.84 ± 32.70	3 714 100.82	7.03	7.29	1.04	1.47
	Losartan	19 124	222.79 ± 48.33	4 260 629.97	7.85	8.36	1.06	1.55
	Losartan/HTCZ	41 108	219.55 ± 2.65	9 025 067.15	16.88	17.71	1.05	1.51
	Telmisartan	19 188	211.00 ± 30.78	4 048 682.12	7.88	7.94	1.01	1.40
	Telmisartan/HTCZ	16 951	210.22 ± 29.94	3 563 353.86	6.96	6.99	1.00	1.39
	Valsartan	27 432	210.07 ± 29.56	5 762 767.32	11.26	11.31	1.00	1.38
	Valsartan/HTCZ	25 403	209.32 ± 26.62	5 317 296.97	10.43	10.43	1.00	1.37
	Total	243 543		50 971 204.10				
2007	Candesartan cilexetil	29 227	193.49 ± 43.56	5 655 089.39	12.11	11.46	0.95	1.10
	Candesartan cilexetil/HTCZ	26 524	205.69 ± 36.46	5 455 827.61	10.99	11.06	1.00	1.26

Table C9 (cont.): Cost and prevalence of the antihypertensive medicine items according to active ingredient (7.3.9)

Year	Active ingredient	Number of items	Average cost (R)	Total cost (R)	Prevalence%	Cost %	CPI	d-value
	Eprosartan	6 473	177.20 ± 32.15	1 146 983.7	2.68	2.32	0.87	0.89
	Irbesartan	15 235	227.81 ± 43.38	3 470 670.97	6.31	7.03	1.11	1.55
	Irbesartan/HTCZ	17 979	226.71 ± 39.80	4 075 992.80	7.45	8.26	1.11	1.54
	Losartan	16 603	200.27 ± 63.66	3 325 088.73	6.88	6.74	0.98	1.19
	Losartan/HTCZ	38 743	196.37 ± 2.31	7 607 985.05	16.05	15.42	0.96	1.14
	Telmisartan	19 477	214.44 ± 43.36	4 176 571.24	8.07	8.46	1.05	1.38
	Telmisartan /HTCZ	18 463	214.92 ± 39.88	3 968 020.76	7.65	8.04	1.05	1.38
	Valsartan	27 853	199.09 ± 42.60	5 545 331.82	11.54	11.24	0.97	1.18
	Valsartan /HTCZ	24 772	198.66 ± 41.37	4 921 290.17	10.26	9.97	0.97	1.17
	Total	241 349		49 348 852.20				
2008	Candesartan cilexetil	23 727	201.26 ± 44.53	4 775 374.49	10.05	11.19	1.11	1.31
	Candesartan cilexetil/HTCZ	22 513	212.15 ± 38.54	4 776 191.91	9.54	11.19	1.17	1.45
	Eprosartan	14 397	172.07 ± 32.94	2 477 237.88	6.10	5.80	0.95	0.91
	Irbesartan	13 050	231.74 ± 39.23	3 024 167.46	5.53	7.08	1.28	1.72
	Irbesartan/HTCZ	15 711	231.09 ± 37.58	3 630 594.51	6.66	8.50	1.28	1.71
	Losartan	21 933	105.67 ± 30.19	2 317 757.51	9.29	5.43	0.58	0.01
	Losartan/HTCZ	37 920	116.94 ± 0.45	4 434 295.70	16.07	10.39	0.65	0.16
	Telmisartan	17 285	215.53 ± 43.27	3 725 362.64	7.32	8.73	1.19	1.50
	Telmisartan /HTCZ	16 913	215.41 ± 43.81	3 643 188.40	7.17	8.53	1.19	1.50
	Valsartan	26 945	187.23 ± 46.17	5 044 986.61	11.42	11.82	1.04	1.12
	Valsartan /HTCZ	25 635	188.93 ± 41.76	4 843 265.90	10.86	11.34	1.04	1.14
	Total	236 029		42 692 423.01				

d-values was calculated comparing the average cost of all antihypertensive medicine items against the average cost per active ingredient. For 2005 the average cost was R109.69 ± R78.34, for 2006 R105.26 ± R75.72, for 2007 it was R109.68 ± R76.00 and for 2008 it was R105.24 ± R73.50.

Table C10: Cost and prevalence of the antihypertensive medicine items according to active ingredient (7.3.10)

Year	Active ingredient	Number of items	Average cost (R)	Total cost (R)	Prevalence %	Cost %	CPI	d-value
2005	Nebivolol	3 984	160.64 ± 25.26	640 004.85	100	100	1	0.65
2006	Nebivolol	3 903	159.80 ± 26.70	623 692.93	100	100	1	0.72
2007	Nebivolol	3 634	164.78 ± 37.86	598 813.71	100	100	1	0.73
2008	Nebivolol	3 047	169.27 ± 33.50	515 770.47	100	100	1	0.87

d-values was calculated comparing the average cost of all antihypertensive medicine items against the average cost per active ingredient. For 2005 the average cost was R109.69 ± R78.34, for 2006 R105.26 ± R75.72, for 2007 it was R109.68 ± R76.00 and for 2008 it was R105.24 ± R73.50.

Table C11: Cost and prevalence of the antihypertensive medicine items according to active ingredient (16.1)

Year	Active ingredient	Number of items	Average cost (R)	Total cost (R)	Prevalence %	Cost %	CPI	d-values
2005	Acetazolamide	1 839	47.58 ± 39.34	87 501.66	0.30	0.22	0.74	0.79
	Amiloride/HTCZ	129 614	13.89 ± 14.00	1 800 308.20	21.12	4.55	0.22	1.22
	Bumetanide	801	131.75 ± 60.24	105 532.06	0.13	0.27	2.04	0.28
	Bumetanide/KCL	16 887	87.08 ± 32.48	1 470 454.56	2.75	3.724	1.35	0.29
	Chlortalidone	452	189.49 ± 68.66	85 647.42	0.07	0.22	2.94	1.02
	Chlortalidone/Reserpine	227	187.13 ± 61.87	42 479.41	0.049	0.118	2.90	0.99
	Furosemide	87 350	77.86 ± 95.63	6 800 862.79	14.23	17.20	1.21	0.33
	HTCZ	69 198	13.67 ± 8.79	946 014.21	11.28	2.39	0.21	1.23
	HTCZ/Triamterene	6 966	27.60 ± 13.71	192 248.85	1.14	0.49	0.43	1.05
	HTCZ/Valsartan	20 680	210.34 ± 24.07	4 349 821.69	3.37	11.00	3.26	1.28
	Indapamide	147 093	41.69 ± 30.79	6 132 925.58	23.97	15.51	0.65	0.87
	Indapamide/Perindopril	67 854	180.48 ± 20.76	12 246 128.72	11.06	30.961	2.80	0.90
	Piretanide	2 656	113.15 ± 45.45	300 533.65	0.43	0.76	1.76	0.04
	Spironolactone	46 246	58.67 ± 58.22	2 713 470.67	7.54	6.86	0.91	0.65
	Spironolactone/Isobutyl	1 230	117.30 ± 37.60	144 282.20	0.20	0.36	1.82	0.10
	Torazemide	14 600	145.91 ± 50.69	2 130 225.21	2.38	5.39	2.26	0.46

Table C11 (cont.): Cost and prevalence of the antihypertensive medicine items according to active ingredient (16.1)

Year	Active ingredient	Number of items	Average cost (R)	Total cost (R)	Prevalence %	Cost %	CPI	d-values
	Xipamide	6	171.54 ± 7.01	1 029.26	0.001	0.003	2.66	0.79
	Total	613 699		39 549 466.14				
2006	Acetazolamide	1 903	48.40 ± 3.09	9 2105.18	0.28	0.21	0.74	0.75
	Amiloride/HTCZ	131 488	12.97 ± 12.51	1 705 054.80	19.45	3.83	0.20	1.22
	Bumetanide	677	147.59 ± 71.39	99 916.32	0.10	0.221	2.24	0.56
	Bumetanide/KCL	15 297	85.16 ± 33.35	1 302 741.74	2.26	2.93	1.29	0.27
	Chlortalidone	406	181.13 ± 77.69	73 539.61	0.06	0.17	2.75	0.98
	Chlortalidone/Reserpine	2	243.62 ± 21.04	487.24	0.0003	0.001	3.70	1.83
	Furosemide	94 506	78.21 ± 95.39	7 391 269.41	13.98	16.61	1.19	0.28
	HTCZ	76 894	14.11 ± 9.031	1 084 734.57	11.38	2.44	0.21	1.20
	HTCZ/Triamterene	6 512	27.18 ± 13.18	177 013.12	0.96	0.40	0.41	1.03
	HTCZ/Valsartan	25 074	209.52 ± 29.30	5 253 535.72	3.71	11.81	3.18	1.38
	Indapamide	154 868	38.51 ± 29.37	5 963 148.32	22.91	13.40	0.58	0.88
	Indapamide/Perindopril	97 080	163.53 ± 26.46	15 875 322.15	14.36	35.68	2.48	0.77
	Piretanide	2 242	109.66 ± 40.95	245 859.20	0.33	0.55	1.67	0.06
	Spironolactone	52 961	55.63 ± 54.87	2 946 082.39	7.845	6.62	0.84	0.66
	Spironolactone/Isobutyl	1 097	113.53 ± 39.12	124 544.75	0.16	0.28	1.72	0.11
	Torazemide	14 917	144.97 ± 52.60	2 162 551.40	2.21	4.86	2.20	0.52
	Xipamide	2	141.39 ± 35.04	282.78	0.0003	0.0006	2.15	0.48
	Total	675 926		44 498 188.70				
2007	Acetazolamide	1 842	53.95 ± 46.03	99 381.18	0.29	0.22	0.75	0.73
	Amiloride/HTCZ	101 566	11.59 ± 12.52	1 177 074.15	16.24	0.41	0.03	1.23
	Bumetanide	677	155.72 ± 89.74	105 422.93	0.11	0.23	2.17	0.51
	Bumetanide/KCL	13 633	90.70 ± 37.66	1 236 512.95	2.18	2.75	1.26	0.25
	Chlortalidone	274	188.74 ± 100.48	51 714.68	0.04	0.12	2.63	0.79
	Furosemide	89 107	81.00 ± 104.56	7 218 016.58	14.25	16.08	1.13	0.27

Table C11 (cont.): Cost and prevalence of the antihypertensive medicine items according to active ingredient (16.1)

Year	Active ingredient	Number of items	Average cost (R)	Total cost (R)	Prevalence %	Cost %	CPI	d-values
	HTCZ	62 586	13.75 ± 8.38	860 815.54	10.01	1.92	0.19	1.26
	HTCZ/Quinapril	827	92.95 ± 20.70	76 871.98	0.13	0.17	1.30	0.22
	HTCZ/Triamterene	5 503	27.94 ± 13.31	153 733.12	0.88	0.34	0.39	1.08
	HTCZ/Valsartan	27 960	177.81 ± 32.50	4 971 516.10	4.47	11.08	2.48	0.90
	Indapamide	135 605	38.63 ± 30.30	5 238 568.30	21.68	11.67	0.54	0.93
	Indapamide/Perindopril	119 754	156.80 ± 27.99	18 777 007.59	19.14	41.83	2.19	0.62
	Piretanide	1 754	113.95 ± 42.29	199 871.44	0.28	0.46	1.59	0.06
	Spironolactone	51 779	56.67 ± 53.67	2 935 164.77	8.28	6.54	0.79	0.70
	Spironolactone/Isobutyl	902	118.89 ± 42.83	107 240.88	0.14	0.24	1.66	0.12
	Torazemide	11 755	142.64 ± 51.02	1 676 782.28	1.88	3.74	1.99	0.43
	Xipamide	1	166.17 ± 0.00	166.17	0.0002	0.0004	2.32	0.74
	Total	625 525		44 885 860.64				
2008	Acetazolamide	1 604	56.92 ± 45.36	91 293.17	0.26	0.214	0.80	0.66
	Amiloride/HTCZ	100 910	12.91 ± 10.01	1 302 434.10	16.54	3.004	0.18	1.23
	Bumetanide	623	165.97 ± 100.24	103 401.99	0.10	0.24	2.33	0.61
	Bumetanide/KCL	11 544	92.52 ± 37.32	1 068 094.58	1.89	2.46	1.30	0.17
	Chlortalidone	281	171.03 ± 81.25	48 059.80	0.05	0.11	2.40	0.81
	Furosemide	85 458	77.42 ± 110.95	6 616 511.21	14.01	15.25	1.09	0.25
	HTCZ	64 966	15.21 ± 9.15	988 006.27	10.65	2.28	0.21	1.22
	HTCZ/Quinapril	3 467	94.16 ± 23.05	326 465.93	0.57	0.75	1.32	0.15
	HTCZ/Triamterene	4 708	28.10 ± 13.12	132 289.70	0.77	0.30	0.39	1.05
	HTCZ/Valsartan	30 147	168.23 ± 27.36	5 071 756.29	4.94	11.69	2.36	0.86
	Indapamide	126 497	38.79 ± 29.93	4 907 310.43	20.74	11.31	0.55	0.90
	Indapamide/Perindopril	116 186	156.42 ± 27.00	18 173 691.22	19.05	41.87	2.20	0.70
	Piretanide	1 500	114.98 ± 44.58	172 471.56	0.26	0.40	1.62	0.13
	Spironolactone	52 321	56.87 ± 52.71	2 975 302.75	8.58	6.86	0.80	60.65

Table C11 (cont.): Cost and prevalence of the antihypertensive medicine items according to active ingredient (16.1)

Year	Active ingredient	Number of items	Average cost (R)	Total cost (R)	Prevalence %	Cost %	CPI	d-values
	Spironolactone/Isobutyl	718	116.56 ± 42.92	83 689.88	0.12	0.19	1.64	0.15
	Torazemide	9 020	148.49 ± 51.11	1 339 373.70	1.48	3.09	2.09	0.59
	Total	609 950		43 400 152.58				

d-values was calculated comparing the average cost of all antihypertensive medicine items against the average cost per active ingredient. For 2005 the average cost was R109.69 ± R78.34, for 2006 R105.26 ± R75.72, for 2007 it was R109.68 ± R76.00 and for 2008 it was R105.24 ± R73.50

APPENDIX D

Table D1: Number of items according to pharmacological group with indication of drug status

Year	Pharmacological group	Generic indicator	Number of items	Average cost (R)	Total cost (R)	Prevalence percentage	Cost percentage	CPI
2005	Central-acting inhibitors	N	5 351	205.21 ± 46.47	1 098 052.37	23.02	46.54	2.0
		O	712	180.89 ± 102.23	128 796.43	3.06	5.46	1.8
		Y	17 180	65.92 ± 47.11	1 132 540.05	73.91	48.00	0.6
	Alpha-receptor blockers	N	20 389	231.87 ± 70.58	4 727 625.90	52.86	70.09	1.3
		O	4 409	191.50 ± 42.58	844 311.35	11.43	12.52	1.1
		Y	13 772	85.17 ± 56.10	1 172 941.07	35.71	17.39	0.5
	Beta-receptor blockers	N	94 629	120.73 ± 34.61	11 424 478.77	40.35	49.75	1.2
		O	55 958	102.39 ± 61.09	5 729 352.48	23.86	24.95	1.0
		Y	83 951	69.21 ± 39.18	5 809 893.88	35.79	25.30	0.7
	Alpha- and Beta-receptor blockers	N	3 927	168.13 ± 69.06	660 240.91	6.99	9.96	1.4
		O	13 468	158.47 ± 56.27	2 134 227.07	23.97	32.15	1.3
		Y	38 801	99.07 ± 41.10	3 844 182.98	69.05	57.91	0.8
	Sympathetic nervous blockers	N	18 195	92.36 ± 79.59	1 680 533.22	100	100	1.0
	Direct-acting vasodilators	N	552	169.81 ± 105.27	93 736.81	23.60	44.84	1.9
		O	229	195.63 ± 72.08	44 798.36	9.79	21.43	2.2
		Y	1 558	45.25 ± 21.40	70 496.09	66.61	33.73	0.52
	Calcium channel blockers	N	23 619	232.79 ± 58.13	5 498 222.76	17.91	26.32	1.5
		O	66 108	160.25 ± 41.21	10 594 103.24	50.14	50.71	1.0
		Y	42 129	113.95 ± 25.41	4 800 393.11	31.95	22.98	0.7

Table D1 (cont.): Number of items according to pharmacological group with indication of drug status

Year	Pharmacological group	Generic indicator	Number of items	Average cost (R)	Total cost (R)	Prevalence percentage	Cost percentage	CPI
	ACE inhibitors	N	148 824	187.19 ± 45.46	27 857 684.65	22.92	37.54	1.6
		O	114 178	142.37 ± 60.19	16 255 468.88	17.58	21.90	1.2
		Y	386 436	77.89 ± 41.29	30 098 905.12	59.50	40.56	0.7
	Angiotensin-receptor blockers	N	255 199	209.20 ± 31.43	53 386 468.70	100	100	1.0
	Others	N	3 984	160.64 ± 25.26	640 004.85	100	100	1.0
	Diuretics	N	99 387	97.43 ± 78.81	9 683 513.30	18.93	42.27	2.2
		O	34 071	130.58 ± 73.04	4 449 096.95	6.49	19.42	3.0
		Y	391 480	22.42 ± 22.96	8 778 426.07	74.58	38.32	0.5
2006	Central-acting inhibitors	N	6 011	204.67 ± 45.91	1 230 261.00	24.96	48.58	1.91
		O	668	173.87 ± 105.20	116 144.17	2.77	4.59	1.7
		Y	17 406	68.14 ± 49.67	1 185 984.96	72.27	46.83	6.5
	Alpha-receptor blockers	N	12 790	270.99 ± 67.86	3 466 023.46	30.87	48.70	1.6
		O	11 639	187.44 ± 34.92	2 181 595.69	28.09	30.65	1.1
		Y	17 003	86.45 ± 53.91	1 469 884.70	41.04	20.65	0.51
	Beta-receptor blockers	N	89 859	120.56 ± 30.54	10 833 139.02	35.07	46.78	1.31
		O	51 368	98.35 ± 59.67	5 052 217.52	20.05	21.82	1.1
		Y	114 993	63.23 ± 34.72	7 271 494.65	44.88	31.40	0.7
	Alpha- and Beta-receptor blockers	N	191	285.63 ± 182.96	54 554.55	0.29	0.75	2.6
		O	11 691	158.79 ± 60.33	1 856 417.90	17.53	25.43	1.5
		Y	54 807	98.35 ± 39.84	5 390 217.80	82.18	73.83	0.9
	Sympathetic nervous blockers	N	16 043	84.97 ± 78.81	1 363 163.57	100	100	1.0
	Direct-acting vasodilators	N	598	179.92 ± 112.91	107 595.02	22.29	45.54	2.0
		O	229	191.89 ± 65.24	43 943.24	8.54	18.60	2.2
		Y	1 856	45.66 ± 21.54	84 742.19	69.18	35.87	0.5
	Calcium channel blockers	N	27 856	224.67 ± 60.60	6 258 396.51	16.58	25.79	1.6
		O	57 871	152.06 ± 38.55	8 800 087.18	34.45	36.27	1.1
		Y	82 262	111.90 ± 23.98	9 205 285.52	48.97	37.94	0.8

Table D1 (cont.): Number of items according to pharmacological group with indication of drug status

Year	Pharmacological group	Generic indicator	Number of items	Average cost (R)	Total cost (R)	Prevalence percentage	Cost percentage	CPI
	ACE inhibitors	N	61 897	193.80 ± 56.00	11 995 646.91	8.39	15.22	1.8
		O	138 252	147.37 ± 56.31	20 374 754.15	18.74	25.85	1.4
		Y	537 726	86.37 ± 44.03	46 441 076.54	72.87	58.93	0.84
	Angiotensin-receptor blockers	N	233 975	209.26 ± 35.37	48 961 277.78	87.10	87.08	1.0
		O	34 600	209.68 ± 28.23	7 255 049.50	12.88	12.90	1.0
		Y	42	200.30 ± 48.59	8 412.57	0.016	0.015	1.0
	Others	N	5 375	180.66 ± 48.21	971 027.98	100	100	1.0
	Diuretics	N	94 087	96.44 ± 83.10	9 073 873.25	16.99	38.83	2.3
		O	37 930	129.67 ± 70.86	4 918 351.23	6.85	21.05	3.1
		Y	421 754	22.23 ± 22.84	9 376 619.11	76.16	40.12	0.51
2007	Central-acting inhibitors	N	6 457	209.44 ± 49.81	1 352 338.65	32.36	56.74	1.8
		O	302	146.79 ± 98.31	44 330.68	1.51	1.86	1.2
		Y	13 192	74.80 ± 56.06	986 700.39	66.12	41.40	0.6
	Alpha-receptor blockers	N	12 164	286.10 ± 77.43	3 480 082.96	32.18	50.91	1.6
		O	10 226	194.00 ± 40.18	1 983 892.10	27.05	29.02	1.1
		Y	15 414	88.98 ± 58.95	1 371 483.17	40.77	20.06	0.5
	Beta-receptor blockers	N	83 749	122.39 ± 34.09	10 250 090.81	33.66	45.80	1.4
		O	42 542	98.12 ± 63.07	4 174 062.27	17.10	18.65	1.1
		Y	122 527	64.93 ± 36.11	7 955 636.36	49.24	35.55	0.7
	Alpha- and Beta-receptor blockers	N	151	329.63 ± 233.67	49 773.79	0.22	0.65	3.0
		O	8 901	159.78 ± 61.40	1 422 214.33	12.74	18.51	1.5
		Y	60 828	102.16 ± 40.31	6 212 087.68	87.05	80.84	0.9
	Sympathetic nervous blockers	N	8 863	114.73 ± 90.20	1 016 890.24	100	100	1.0
	Direct-acting vasodilators	N	574	181.69 ± 113.65	104 290.33	24.42	48.38	2.0
		O	163	192.46 ± 76.16	31 371.75	6.93	14.55	2.1
		Y	1 614	49.50 ± 24.68	79 895.52	68.65	37.06	0.5
	Calcium channel blockers	N	29 255	231.89 ± 67.53	6 783 987.62	15.52	25.14	1.6

Table D1 (cont.): Number of items according to pharmacological group with indication of drug status

Year	Pharmacological group	Generic indicator	Number of items	Average cost (R)	Total cost (R)	Prevalence percentage	Cost percentage	CPI
	Calcium channel blockers	O	43 242	157.12 ± 43.82	6 793 977.92	22.94	25.17	1. 1
		Y	115 963	115.66 ± 28.18	13 411 994.41	61.53	49.69	0.8
	ACE inhibitors	N	48 278	207.35 ± 61.64	10 010 393.95	6.98	12.97	1.9
		O	100 295	144.38 ± 58.70	14 480 713.12	14.50	18.76	1.3
		Y	543 201	97.03 ± 45.52	52 705 006.07	78.52	68.27	0.9
	Angiotensin-receptor blockers	N	209 940	204.06 ± 46.16	42 840 971.60	77.96	78.87	1.0
		O	43 449	203.16 ± 42.71	8 827 262.14	16.13	16.25	1.0
		Y	15 920	166.59 ± 30.09	2 652 134.60	5.91	4.88	0.8
	Others	N	8 577	206.35 ± 57.30	1 769 844.91	100	100	1.0
	Diuretics	N	62 020	95.93 ± 98.73	5 949 291.55	13.00	28.25	2.2
		O	52 403	133.30 ± 68.73	6 985 465.49	10.99	33.17	3.0
		Y	362 561	22.41 ± 24.15	8 125 707.93	76.01	38.58	0.5
2008	Central-acting inhibitors	N	4 428	212.29 ± 58. 20	940 006.25	23.05	39.46	1.7
		O	1 991	214.72 ± 59.18	427 515.00	10.36	17.95	1.7
		Y	12 790	79.33 ± 56.51	1 014 591.64	66.58	42.59	0.6
	Alpha-receptor blockers	N	10 966	294.08 ± 79.86	3 224 923.82	31.00	50.76	1.6
		O	9 210	199.46 ± 39.91	1 837 044.51	26.04	28.92	1.1
		Y	15 195	84.96 ± 59.55	1 291 041.03	42.96	20.32	0.01
	Beta-receptor blockers	N	73 603	124.82 ± 33.23	9 186 909.27	31.98	44.18	1.4
		O	36 664	102.63 ± 64.55	3 762 900.53	15.93	18.09	1.1
		Y	119 866	65.46 ± 35.79	7 846 725.33	52.09	37.73	0.7
	Alpha- and Beta-receptor blockers	N	33	355.23 ± 258.17	11 722.58	0.05	0.15	3.2
		O	6 863	167.60 ± 64.81	1 150 241.83	9.60	14.71	1.5
		Y	64 576	103.12 ± 39.79	6 659 388.84	90.35	85.14	0.9
	Sympathetic nervous blockers	N	8 341	100.37 ± 92.14	837 217.37	100	100	1.0
	Direct-acting vasodilators	N	468	173.19 ± 104.53	81 053.23	22.66	49.16	2.2
		O	7	222.70 ± 126.77	1 558.88	0.34	0.95	2.8

Table D1 (cont.): Number of items according to pharmacological group with indication of drug status

Year	Pharmacological group	Generic indicator	Number of items	Average cost (R)	Total cost (R)	Prevalence percentage	Cost percentage	CPI
	Calcium channel blockers	Y	1 590	51.74 ± 24.93	82 270.25	77.00	49.90	0.6
		N	27 259	236.72 ± 70.34	6 452 628.21	13.79	24.87	1.8
		O	28 916	157.29 ± 51.16	4 548 241.3	14.62	17.53	1.2
		Y	141 550	105.58 ± 28.65	14 944 841.94	71.59	57.60	0.8
	ACE inhibitors	N	39 913	214.27 ± 61.20	8 552 098.69	5.94	11.61	2.0
		O	67 768	143.43 ± 61.33	9 719 788.93	10.09	13.19	1.3
		Y	563 791	98.30 ± 45.63	55 419 433.27	83.96	75.20	0.9
	Angiotensin-receptor blockers	N	180 315	186.99 ± 54.77	33 717 967.78	67.74	70.56	1.0
		O	36 512	177.29 ± 59.61	6 473 213.76	13.72	13.56	1.0
		Y	49 363	153.51 ± 42.24	7 577 481.81	18.54	15.86	0.9
	Others	N	8 310	213.67 ± 57.24	1 775 593.39	100	100	1.0
	Diuretics	N	54 813	99.50 ± 113.09	5 454 106.02	11.91	27.51	2.3
		O	42 634	134.78 ± 71.14	5 746 197.29	9.27	28.98	3.1
		Y	362 703	23.79 ± 24.61	8 627 935.83	78.82	43.51	0.6

Table D2: Possible cost saving due to generic substitution

Year	Pharmacological group	Generic indicator	Number of items	Average cost (R)	Total cost (R)	Cost saving (R) 100% substitution	Cost savings (R) 45% substitution
2005	Central-acting inhibitors	O	712	180.89 ± 102.23	128 796.43	82 893.37	36 836.98
		Y	17 180	65.92 ± 47.11	1 132 540.05		
	Alpha-receptor blockers	O	4 409	191.50 ± 42.58	844 311.35	468 808.97	210 964.04
		Y	13 772	85.17 ± 56.10	1 172 941.07		
	Beta-receptor blockers	O	55 958	102.39 ± 61.09	5 729 352.48	1 856 686.44	835 508.90
		Y	83 951	69.21 ± 39.18	5 809 893.88		
	Alpha- and Beta-receptor blockers	O	13 468	158.47 ± 56.27	2 134 227.07	799 999.20	359 999.64
		Y	38 801	99.07 ± 41.10	3 844 182.98		

Table D2 (cont.): Possible cost saving due to generic substitution

Year	Pharmacological group	Generic indicator	Number of items	Average cost (R)	Total cost (R)	Cost saving (R) 100% substitution	Cost savings (R) 45% substitution
	Direct-acting vasodilators	O	229	195.63 ± 72.08	44 798.36	34 437.02	15 496.66
		Y	1 558	45.25 ± 21.40	70 496.09		
	Calcium channel blockers	O	66 108	160.25 ± 41.21	10 594 103.24	3 060 800.40	1 377 360.18
		Y	42 129	113.95 ± 25.41	4 800 393.11		
	ACE inhibitors	O	114 178	142.37 ± 60.19	16 255 468.88	7 362 197.44	3 312 988.85
		Y	386 436	77.89 ± 41.29	30 098 905.12		
	Diuretics	O	34 071	130.58 ± 73.04	4 449 096.95	3 685 119.36	1 658 303.71
		Y	391 480	22.42 ± 22.96	8 778 426.07		
	Total cost savings					17 350 942.20	7 807 458.96
2006	Central-acting inhibitors	O	668	173.87 ± 105.20	116 144.17	70 627.64	31 782.44
		Y	17 406	68.14 ± 49.67	1 185 984.96		
	Alpha-receptor blockers	O	11 639	187.44 ± 34.92	2 181 595.69	1 175 422.61	528 940.17
		Y	17 003	86.45 ± 53.91	1 469 884.70		
	Beta-receptor blockers	O	51 368	98.35 ± 59.67	5 052 217.52	1 804 044.16	811 819.87
		Y	114 993	63.23 ± 34.72	7 271 494.65		
	Alpha- and Beta-receptor blockers	O	11 691	158.79 ± 60.33	1 856 417.90	706 604.04	317 971.82
		Y	54 807	98.35 ± 39.84	5 390 217.80		
2006	Direct-acting vasodilators	O	229	191.89 ± 65.24	43 943.24	33 486.67	15 069.00
		Y	1 856	45.66 ± 21.54	84 742.19		
	Calcium channel blockers	O	57 871	152.06 ± 38.55	8 800 087.18	2 324 099.36	1 045 844.71
		Y	82 262	111.90 ± 23.98	9 205 285.52		
	ACE inhibitors	O	138 252	147.37 ± 56.31	20 374 754.15	8 433 372.00	3 795 017.40
		Y	537 726	86.37 ± 44.03	46 441 076.54		
	Angiotensin-receptor blockers	O	34 600	209.68 ± 28.23	725 5049.5	324 548.00	146 046.60
		Y	42	200.30 ± 48.59	8 412.57		
	Diuretics	O	37 930	129.67 ± 70.86	4 918 351.23	4 075 199.20	1 833 839.64
		Y	421 754	22.23 ± 22.84	9 376 619.11		

Table D2 (cont.): Possible cost saving due to generic substitution

Year	Pharmacological group	Generic indicator	Number of items	Average cost (R)	Total cost (R)	Cost saving (R) 100% substitution	Cost savings (R) 45% substitution
	Total cost savings					18 947 403.68	8 526 331.64
2007	Central-acting inhibitors	O	302	146.79 ± 98.31	44 330.68	21 740.98	9 783.44
		Y	13 192	74.80 ± 56.06	986 700.39		
	Alpha-receptor blockers	O	10 226	194.00 ± 40.18	1 983 892.1	1 073 934.52	483 270.53
		Y	15 414	88.98 ± 58.95	1 371 483.17		
	Beta-receptor blockers	O	42 542	98.12 ± 63.07	41 74 062.27	1 411 968.98	635 386.04
		Y	122 527	64.93 ± 36.11	79 55 636.36		
	Alpha- and Beta-receptor blockers	O	8 901	159.78 ± 61.40	14 22 214.33	513 142.65	230 914.19
		Y	60 828	102.13 ± 40.31	6 212 087.68		
	Direct-acting vasodilators	O	163	192.46 ± 76.16	31 371.75	23 302.48	10 486.12
		Y	1 614	49.50 ± 24.68	79 895.52		
	Calcium channel blockers	O	43 242	157.12 ± 43.82	6 793 977.92	1 792 813.32	806 765.99
		Y	115 963	115.66 ± 28.18	13 411 994.41		
	ACE inhibitors	O	100 295	144.38 ± 58.70	14 480 713.12	4 748 968.25	2 137 035.71
		Y	543 201	97.03 ± 45.52	52 705 006.07		
	Angiotensin-receptor blockers	O	43 449	203.16 ± 42.71	8 827 262.14	1 588 929.93	715 018.47
		Y	15 920	166.59 ± 30.09	2 652 134.6		
	Diuretics	O	52 403	133.30 ± 68.73	6 985 465.49	5 810 968.67	2 614 935.90
		Y	362 561	22.41 ± 24.15	8 125 707.93		
	Total cost savings					15 573 800.80	7 643 596.37
2008	Central-acting inhibitors	O	1 991	214.72 ± 59.18	427 515.00	269 561.49	121 302.67
		Y	12 790	79.33 ± 56.51	1 014 591.64		
	Alpha-receptor blockers	O	9 210	199.46 ± 39.91	1 837 044.51	1 054 545.00	474 345.28
		Y	15 195	84.96 ± 59.55	1 291 041.03		
	Beta-receptor blockers	O	36 664	102.63 ± 64.55	3 762 900.53	1 362 800.88	613 260.40
		Y	119 866	65.46 ± 35.79	7 846 725.33		
	Alpha- and Beta-receptor	O	6 863	167.60 ± 64.81	1 150 241.83	442 526.24	199 136.81

Table D2 (cont.): Possible cost saving due to generic substitution

Year	Pharmacological group	Generic indicator	Number of items	Average cost (R)	Total cost (R)	Cost saving (R) 100% substitution	Cost savings (R) 45% substitution
	blockers	Y	64 576	103.12 ± 39.79	6 659 388.84		
	Direct-acting vasodilators	O	7	222.70 ± 126.77	1 558.88	1 196.72	538.52
		Y	1 590	51.74 ± 24.93	82 270.25		
	Calcium channel blockers	O	28 916	157.29 ± 51.16	454 8241.3	1 495 246.36	672 860.86
		Y	141 550	105.58 ± 28.65	14 944 841.94		
	ACE inhibitors	O	67 768	143.43 ± 61.33	9 719 788.93	3 058 369.84	1 376 266.43
		Y	563 791	98.30 ± 45.63	5 5419 433.27		
	Angiotensin-receptor blockers	O	36 512	177.29 ± 59.61	6 473 213.76	868 255.36	390 714.91
		Y	49 363	153.51 ± 42.24	7 577 481.81		
	Diuretics	O	42 634	134.78 ± 71.14	5 746 197.29	4 731 947.66	2 129 376.45
		Y	362 703	23.79 ± 24.61	8 627 935.83		
	Total cost savings					13 284 449.55	5 978 002.33

APPENDIX E

Table E1: Number of items per pharmacological group and age group

Year	Pharmacological group	Age group	Number of items	Average cost per item (R)	Total cost (R)	Prevalence %	Cost %	CPI
2005	Central acting inhibitors	AG1	35	92.50 ± 70.95	3 237.55	0.15	0.14	0.91
		AG2	3 938	92.67 ± 73.23	364 951.80	16.94	15.47	0.91
		AG3	19 270	103.33 ± 78.66	1 991 199.50	82.91	84.39	1.02
	Alpha-receptor blockers	AG1	31	112.55 ± 75.29	3 489.05	0.08	0.05	0.64
		AG2	1 971	183.46 ± 101.12	361 606.87	5.11	5.36	1.05
		AG3	36 568	174.46 ± 92.16	6 379 782.40	94.81	94.59	1.00
	Beta-receptor blockers	AG1	292	63.46 ± 42.45	18 520.78	0.12	0.08	0.65
		AG2	19 544	90.74 ± 40.89	1 773 359.91	8.33	7.72	0.93
		AG3	214 702	98.61 ± 49.96	21 171 844.44	91.54	82.20	1.01
	Alpha- and beta-receptor blockers	AG1	36	90.45 ± 29.60	3 256.14	0.06	0.05	0.77
		AG2	3 513	117.53 ± 54.01	412 866.82	6.25	6.22	0.99
		AG3	52 647	118.19 ± 55.54	6 222 528.00	93.68	93.73	1.00
	Sympathetic nervous blockers	AG1	7	83.84 ± 86.81	586.86	0.04	0.03	0.91
		AG2	1 753	45.91 ± 53.86	80 481.01	9.63	4.79	0.50
		AG3	16 435	97.32 ± 80.29	1 599 465.35	90.33	95.18	1.05
	Direct acting vasodilators	AG1	4	69.52 ± 39.32	278.08	0.17	0.13	0.78
		AG2	171	122.05 ± 97.91	20 870.07	7.31	9.98	1.37

Table E1 (cont.): Number of items per pharmacological group and age group

Year	Pharmacological group	Age group	Number of items	Average cost per item (R)	Total cost (R)	Prevalence %	Cost %	CPI
		AG3	2 164	86.82 ± 84.27	187 883.11	92.52	89.88	0.97
	Calcium channel blockers	AG1	142	173.87 ± 56.09	24 689.68	0.11	0.12	1.10
		AG2	9 341	163.08 ± 61.52	1 523 318.82	7.08	7.29	1.03
		AG3	122 373	158.08 ± 56.99	19 344 710.61	92.81	92.59	1.00
	ACE-inhibitors	AG1	744	83.37 ± 57.28	62 025.10	0.11	0.08	0.73
		AG2	62 632	110.07 ± 63.39	6 894 101.93	9.64	9.29	0.96
		AG3	586 062	114.76 ± 65.53	67 255 931.62	90.24	90.63	1.00
	Angiotensin receptor blockers	AG1	95	213.65 ± 80.48	20 297.03	0.04	0.04	1.02
		AG2	21 322	211.24 ± 28.38	4 504 069.54	8.36	8.44	1.01
		AG3	233 782	209.01 ± 31.65	48 862 102.13	91.61	91.53	1.00
	Others	AG2	311	160.76 ± 23.16	49 995.24	7.81	7.81	1.00
		AG3	3 673	160.63 ± 25.43	590 009.61	92.19	92.19	1.00
	Diuretics	AG1	953	61.49 ± 66.71	58 595.51	0.18	0.26	1.41
		AG2	50 367	35.32 ± 57.27	1 778 845.87	9.59	7.76	0.81
		AG3	473 618	44.49 ± 57.27	21 073 594.94	90.22	91.98	1.02
2006	Central acting inhibitors	AG1	27	99.47 ± 79.08	2 685.69	0.11	0.11	0.95
		AG2	4 180	95.18 ± 73.90	397 860.13	17.36	15.71	0.91
		AG3	19 878	107.25 ± 79.63	2 131 844.31	82.53	84.18	1.02
	Alpha-receptor blockers	AG1	80	116.04 ± 109.39	9 282.86	0.19	0.13	0.68
		AG2	2 105	185.70 ± 107.41	390 907.69	5.08	5.49	1.08
		AG3	39 247	171.15 ± 94.32	6 717 313.30	94.73	94.38	1.00
	Beta-receptor blockers	AG1	311	81.30 ± 74.60	25 283.29	0.12	0.11	0.90
		AG2	20 749	87.12 ± 40.34	1 807 664.89	8.10	7.81	0.96
		AG3	235 160	90.68 ± 47.90	21 323 903.01	91.78	92.08	1.00
	Alpha- and beta-receptor blockers	AG1	55	80.25 ± 42.73	4 413.86	0.08	0.06	0.73

Table E1 (cont.): Number of items per pharmacological group and age group

Year	Pharmacological group	Age group	Number of items	Average cost per item (R)	Total cost (R)	Prevalence %	Cost %	CPI
		AG2	4 265	110.86 ± 59.53	472 826.29	6.40	6.48	1.01
		AG3	62 369	109.41 ± 50.93	6 823 950.10	93.52	93.46	1.00
	Sympathetic nervous blockers	AG1	29	33.23 ± 29.40	963.54	0.18	0.07	0.39
		AG2	1 875	39.69 ± 45.73	74 414.75	11.69	5.46	0.47
		AG3	14 139	91.08 ± 80.33	1 287 785.28	88.13	94.47	1.07
	Direct acting vasodilators	AG1	7	141.73 ± 152.37	992.11	0.26	0.42	1.61
		AG2	258	107.97 ± 90.15	27 855.23	9.62	11.79	1.23
		AG3	2 418	85.79 ± 86.13	207 433.11	90.12	87.79	0.97
	Calcium channel blockers	AG1	204	151.26 ± 59.01	30 856.19	0.12	0.13	1.05
		AG2	12 283	148.41 ± 58.52	1 822 883.70	7.31	7.51	1.03
		AG3	155 502	144.11 ± 54.53	22 410 029.23	92.57	92.36	1.00
	ACE-inhibitors	AG1	857	77.67 ± 55.50	66 564.99	0.12	0.08	0.73
		AG2	72 693	105.01 ± 58.92	7 633 619.79	9.85	9.69	0.98
		AG3	664 325	107.04 ± 59.34	71 111 292.82	90.03	90.23	1.00
	Angiotensin receptor blockers	AG1	71	202.51 ± 39.59	14 377.92	0.03	0.03	0.97
		AG2	21 460	209.44 ± 34.48	4 494 541.33	7.99	7.99	1.00
		AG3	247 086	209.30 ± 34.53	51 715 820.60	91.98	91.98	1.00
	Others	AG2	481	194.71 ± 50.05	93 656.70	8.95	9.65	1.08
		AG3	4 894	179.27 ± 47.80	877 371.28	91.05	90.35	0.99
	Diuretics	AG1	1 091	60.61 ± 69.86	61 762.11	0.18	0.26	1.44
		AG2	50 653	33.68 ± 54.07	1 706 225.12	9.15	7.30	0.80
		AG3	502 099	43.02 ± 57.12	21 600 856.36	90.67	92.43	1.02
2007	Central acting inhibitors	AG1	31	131.02 ± 78.40	4 061.64	0.16	0.17	1.10
		AG2	3 251	103.04 ± 80.88	334 997.02	16.29	14.06	0.86
		AG3	16 669	122.64 ± 83.68	2 044 311.06	83.55	85.77	1.03

Table E1 (cont.): Number of items per pharmacological group and age group

Year	Pharmacological group	Age group	Number of items	Average cost per item (R)	Total cost (R)	Prevalence %	Cost %	CPI
	Alpha-receptor blockers	AG1	41	145.82 ± 109.32	5 978.82	0.11	0.09	0.81
		AG2	1 783	198.97 ± 116.85	354 769.68	4.72	5.19	1.10
		AG3	35 980	179.95 ± 103.33	6 474 709.73	95.18	94.72	1.00
	Beta-receptor blockers	AG1	211	86.35 ± 113.34	18 220.35	0.08	0.08	0.96
		AG2	18 351	86.49 ± 43.19	1 587 222.99	7.38	7.09	0.96
		AG3	230 256	90.22 ± 49.17	20 774 346.10	92.54	82.83	1.00
	Alpha- and beta-receptor blockers	AG1	40	100.41 ± 91.58	4 016.37	0.06	0.05	0.91
		AG2	4 129	112.47 ± 70.26	464 377.11	5.91	6.04	1.02
		AG3	65 711	109.81 ± 48.25	7 215 682.32	94.03	93.90	1.00
	Sympathetic nervous blockers	AG1	3	15.37 ± 0.66	46.10	0.03	0.00	0.13
		AG2	530	61.36 ± 81.92	32 522.57	5.98	3.20	0.53
		AG3	8 330	118.17 ± 89.64	984 321.57	93.99	96.80	1.03
	Direct acting vasodilators	AG1	1	41.72 ± 0.00	41.72	0.04	0.02	0.46
		AG2	271	123.33 ± 106.91	33 422.43	11.53	15.51	1.35
		AG3	2 079	87.59 ± 85.26	182 093.45	88.43	84.48	0.96
	Calcium channel blockers	AG1	188	155.11 ± 75.40	29 160.83	0.10	0.11	1.08
		AG2	14 196	140.89 ± 60.77	2 000 127.62	7.53	7.41	0.98
		AG3	174 076	143.39 ± 57.79	24 960 671.50	92.37	92.48	1.00
	ACE-inhibitors	AG1	586	77.74 ± 58.75	45 554.89	0.08	0.06	0.70
		AG2	64 035	109.05 ± 57.07	6 983 064.81	9.26	9.05	0.98
		AG3	627 153	111.88 ± 57.98	70 167 493.44	90.66	90.90	1.00
	Angiotensin receptor blockers	AG1	74	165.16 ± 55.16	12 221.65	0.03	0.02	0.82
		AG2	20 272	197.74 ± 50.46	4 008 503.12	7.53	7.38	0.98
		AG3	248 963	202.04 ± 45.24	50 299 463.60	92.45	92.60	1.00
	Others	AG1	3	255.08 ± 26.88	765.23	0.03	0.04	1.24

Table E1 (cont.): Number of items per pharmacological group and age group

Year	Pharmacological group	Age group	Number of items	Average cost per item (R)	Total cost (R)	Prevalence %	Cost %	CPI
	Diuretics	AG2	709	215.75 ± 59.17	150 841.70	8.27	8.52	1.03
		AG3	7 865	205.75 ± 57.10	1 618 237.98	91.70	91.43	1.00
		AG1	781	69.87 ± 81.58	54 569.77	0.16	0.26	1.58
		AG2	38 003	36.46 ± 65.83	1 385 684.94	7.97	6.5	0.83
		AG3	438 200	44.77 ± 61.27	19 620 210.26	91.87	93.16	1.01
	Central acting inhibitors	AG1	30	149.12 ± 80.20	4 473.63	0.16	0.19	1.20
		AG2	2 887	110.81 ± 82.16	319 907.38	15.03	13.43	0.89
		AG3	16 292	126.30 ± 85.45	2 057 731.88	84.81	86.38	1.02
	Alpha-receptor blockers	AG1	28	168.89 ± 101.39	4 728.89	0.08	0.07	0.94
		AG2	1 403	197.48 ± 121.83	277 070.82	3.97	4.36	1.10
		AG3	33 940	178.88 ± 108.61	6 071 209.65	95.95	95.56	1.00
2008	Beta-receptor blockers	AG1	204	74.41 ± 64.21	15 179.70	0.09	0.07	0.82
		AG2	14 841	87.28 ± 43.60	1 295 303.25	6.42	6.23	0.97
		AG3	215 088	90.60 ± 49.43	19 486 052.18	93.46	93.70	1.00
	Alpha- and beta-receptor blockers	AG1	45	98.53 ± 66.11	4 433.70	0.06	0.06	0.90
		AG2	3 744	107.19 ± 54.38	401 306.41	5.24	5.13	0.98
		AG3	67 683	109.56 ± 47.03	7 415 613.14	94.70	94.81	1.00
	Sympathetic nervous blockers	AG1	5	52.93 ± 78.87	264.63	0.06	0.03	0.53
		AG2	596	47.03 ± 57.61	28 027.22	7.15	3.35	0.47
		AG3	7 740	104.51 ± 93.02	808 925.52	91.80	96.62	1.05
	Direct acting vasodilators	AG2	191	116.29 ± 94.38	22 211.32	9.25	13.47	1.46
		AG3	1 874	76.13 ± 71.93	142 671.04	90.75	86.53	0.95
	Calcium channel blockers	AG1	135	146.81 ± 71.28	19 819.39	0.07	0.08	1.12
		AG2	13 937	126.47 ± 62.71	1 762 662.31	7.05	6.79	0.96
		AG3	183.653	131.57 ± 61.16	24 163 229.75	92.88	93.13	1.00

Table E1 (cont.): Number of items per pharmacological group and age group

Year	Pharmacological group	Age group	Number of items	Average cost per item (R)	Total cost (R)	Prevalence %	Cost %	CPI
	ACE-inhibitors	AG1	431	71.22 ± 51.90	30 696.70	0.06	0.04	0.65
		AG2	57 518	107.15 ± 55.42	6 192 940.31	8.57	8.36	0.98
		AG3	613 523	110.02 ± 56.90	67 497 683.88	91.37	91.60	1.00
	Angiotensin receptor blockers	AG1	45	136.19 ± 67.87	6 128.45	0.02	0.01	0.76
		AG2	18 561	174.36 ± 58.84	3 236 342.24	6.97	6.78	0.97
		AG3	247 584	179.84 ± 54.57	44 526 192.66	93.01	93.21	1.00
	Others	AG1	2	181.06 ± 66.67	362.03	0.02	0.02	0.85
		AG2	563	222.38 ± 66.23	125 201.76	6.77	7.05	1.04
		AG3	7 745	213.04 ± 56.48	1 650 029.60	93.20	92.93	1.00
	Diuretics	AG1	707	74.72 ± 88.75	52 824.89	0.15	0.27	1.73
		AG2	32 606	35.94 ± 66.51	1 171 761.71	7.09	5.91	0.83
		AG3	426 837	43.58 ± 62.22	18 603 652.54	92.76	93.82	1.01

APPENDIX F

Table F1: Number of items with respect to treatment category, generic indicator and age group according to pharmacological group for the year 2005

Pharmacological group	Treatment category	Generic indicator	Age group	Number of items	Average cost (R)	Total cost (R)	Prevalence %	Cost %	CPI
Central-acting inhibitors	TC1	N	1	4	155.80 ± 69.13	623.18	0.02	0.03	1.53
	TC1	N	2	289	199.03 ± 37.02	57 519.21	1.24	2.44	1.96
	TC1	N	3	2 729	204.74 ± 47.23	558 729.71	11.74	23.68	2.02
	TC1	O	1	2	156.23 ± 0.00	312.46	0.01	0.01	1.54
	TC1	O	2	180	170.79 ± 102.73	30 742.54	0.77	1.30	1.68
	TC1	O	3	235	203.68 ± 107.99	47 864.21	1.01	2.03	2.01
	TC1	Y	1	23	62.07 ± 47.55	1 427.65	0.10	0.06	0.61
	TC1	Y	2	2 166	73.50 ± 55.92	159 191.93	9.32	6.75	0.72
	TC1	Y	3	5 785	64.54 ± 47.93	373 362.55	24.89	15.82	0.64
	TC2	N	3	9	227.15 ± 118.30	2 044.36	0.04	0.09	2.24
	TC2	O	2	3	351.61 ± 159.33	1 054.84	0.01	0.04	3.46
	TC2	O	3	1	167.63 ± 0.00	167.63	0.004	0.01	1.65
	TC2	Y	2	7	49.59 ± 24.49	347.12	0.03	0.01	0.49
	TC2	Y	3	55	56.53 ± 38.76	3 109.27	0.24	0.13	0.56
	TC3	N	1	1	190.36 ± 0.00	190.36	0.004	0.01	1.88
	TC3	N	2	137	214.79 ± 60.56	29 426.90	0.59	1.25	2.12

Table F1 (cont.): Number of items with respect to treatment category, generic indicator and age group according to pharmacological group for the year 2005

Pharmacological group	Treatment category	Generic indicator	Age group	Number of items	Average cost (R)	Total cost (R)	Prevalence %	Cost %	CPI
	TC3	N	3	2 182	206.01 ± 44.95	449 518.65	9.39	19.05	2.03
	TC3	O	1	3	191.68 ± 97.67	575.05	0.01	0.02	1.89
	TC3	O	2	47	160.61 ± 120.78	7 548.76	0.20	0.32	1.58
	TC3	O	3	241	168.18 ± 86.22	40 530.94	1.04	1.718	1.66
	TC3	Y	1	2	54.43 ± 21.79	108.85	0.01	0.005	0.54
	TC3	Y	2	1 109	71.34 ± 49.33	79 120.50	4.77	3.35	0.70
	TC3	Y	3	8 033	64.22 ± 43.28	515 872.18	34.56	21.86	0.63
				23 243		2 359 388.85			
Alpha-receptor blockers	TC1	N	1	12	160.63 ± 50.78	1 927.54	0.03	0.03	0.92
	TC1	N	2	895	239.24 ± 95.47	214 122.67	2.32	3.17	1.37
	TC1	N	3	13 603	233.91 ± 70.76	3 181 904.98	35.27	47.18	1.34
	TC1	O	2	148	184.35 ± 49.08	27 284.45	0.38	0.40	1.05
	TC1	O	3	2 794	190.55 ± 39.50	532 402.71	7.24	7.89	1.09
	TC1	Y	1	10	44.43 ± 41.90	444.32	0.03	0.01	0.25
	TC1	Y	2	437	92.44 ± 63.25	40 394.80	1.13	0.60	0.53
	TC1	Y	3	8 117	82.34 ± 53.91	668 390.80	21.04	9.91	0.47
	TC2	N	2	1	184.94 ± 0.00	184.94	0.002	0.003	1.06
	TC2	N	3	99	244.28 ± 82.31	24 184.19	0.26	0.36	1.40
	TC2	O	3	23	191.21 ± 14.63	4 397.88	0.06	0.07	1.09
	TC2	Y	3	40	76.25 ± 53.28	3 050.06	0.10	0.05	0.44
	TC3	N	2	176	216.10 ± 54.35	38 033.44	0.46	0.56	1.24
	TC3	N	3	5 603	226.18 ± 65.03	1 267 268.14	14.53	18.79	1.29
	TC3	O	2	61	203.94 ± 87.96	12 440.37	0.16	0.18	1.17

Table F1 (cont.): Number of items with respect to treatment category, generic indicator and age group according to pharmacological group for the year 2005

Pharmacological group	Treatment category	Generic indicator	Age group	Number of items	Average cost (R)	Total cost (R)	Prevalence %	Cost %	CPI
	TC3	O	3	1 383	193.63 ±44.88	267 785.94	3.59	3.97	1.11
	TC3	Y	1	9	124.13 ± 79.47	1 117.19	0.02	0.02	0.71
	TC3	Y	2	253	115.20 ± 66.58	29 146.20	0.66	0.43	0.66
	TC3	Y	3	4 906	87.73 ± 57.71	430 397.70	12.72	6.38	0.50
				38 570		6 744 878.32			
Beta-receptor blockers	TC1	N	1	55	108.37 ± 31.01	5 960.47	0.02	0.03	1.11
	TC1	N	2	7 832	116.20 ±19.63	910 045.02	3.34	3.96	1.19
	TC1	N	3	68 620	120.31 ± 31.97	8 256 012.37	29.26	35.95	1.23
	TC1	O	1	81	67.55 ± 38.92	5 471.20	0.03	0.02	0.69
	TC1	O	2	2 991	92.67 ± 51.80	277 184.79	1.28	1.21	0.95
	TC1	O	3	36 873	103.62 ± 62.36	3 820 605.48	15.72	16.64	1.06
	TC1	Y	1	136	45.26 ± 30.57	6 155.35	0.06	0.03	0.46
	TC1	Y	2	5 883	59.48 ± 27.66	349 896.84	2.51	1.52	0.61
	TC1	Y	3	57 685	71.90 ± 40.16	4 147 817.53	24.60	18.06	0.73
	TC2	N	2	18	159.52 ±64.37	2 871.30	0.01	0.01	1.63
	TC2	N	3	225	127.19 ± 41.14	28 618.75	0.10	0.12	1.30
	TC2	O	2	8	67.63 ± 27.55	541.07	0.003	0.002	0.69
	TC2	O	3	175	97.89 ± 54.97	17 131.46	0.07	0.07	1.00
	TC2	Y	2	11	56.81 ± 17.17	624.88	0.004	0.003	0.58
	TC2	Y	3	189	72.79 ± 39.15	13 758.03	0.08	0.06	0.74
	TC3	N	1	3	162.25 ± 57.04	486.76	0.001	0.002	1.66
	TC3	N	2	932	121.27 ± 32.57	113 027.16	0.40	0.49	1.24
	TC3	N	3	16 944	124.38 ± 47.50	2 107 456.94	7.22	9.18	1.27

Table F1 (cont.): Number of items with respect to treatment category, generic indicator and age group according to pharmacological group for the year 2005

Pharmacological group	Treatment category	Generic indicator	Age group	Number of items	Average cost (R)	Total cost (R)	Prevalence %	Cost %	CPI
	TC3	O	1	2	61.49 ± 28.98	122.97	0.0008	0.0005	0.63
	TC3	O	2	575	92.86 ± 45.29	53 394.72	0.25	0.23	0.95
	TC3	O	3	15 253	101.94 ± 60.09	1 554 900.79	6.50	6.77	1.04
	TC3	Y	1	15	21.60 ± 18.54	324.03	0.01	0.001	0.22
	TC3	Y	2	1 294	50.83 ± 28.12	65 774.13	0.55	0.29	0.52
	TC3	Y	3	18 738	65.40 ± 38.72	1 225 543.09	7.99	5.34	0.67
				234 538		22 963 725.13			
Alpha- and Beta-receptor blockers	TC1	N	2	97	212.09 ± 123.47	20 573.17	0.17	0.31	1.80
	TC1	N	3	1 355	163.53 ± 75.31	221 582.20	2.41	3.34	1.38
	TC1	O	1	4	97.46 ± 37.36	389.84	0.01	0.01	0.82
	TC1	O	2	477	153.96 ± 50.47	73 438.42	0.85	1.11	1.30
	TC1	O	3	5 731	151.61 ± 53.61	868 904.51	10.20	13.09	1.28
	TC1	Y	1	19	90.56 ± 36.15	1 720.67	0.03	0.03	0.77
	TC1	Y	2	1 486	97.67 ± 34.57	145 132.71	2.64	2.19	0.83
	TC1	Y	3	16 279	97.18 ± 39.40	1 582 003.65	28.97	23.83	0.82
	TC2	N	3	26	179.12 ± 53.74	4 657.03	0.05	0.07	1.52
	TC2	O	2	5	125.17 ± 2.37	625.86	0.01	0.01	1.06
	TC2	O	3	69	156.98 ± 49.75	10 831.45	0.12	0.16	1.33
	TC2	Y	2	12	95.77 ± 21.92	1 149.20	0.02	0.02	0.81
	TC2	Y	3	253	104.42 ± 47.38	26 418.20	0.45	0.40	0.88
	TC3	N	1	1	124.11 ± 0.00	124.11	0.001	0.002	1.05
	TC3	N	2	86	184.41 ± 66.03	15 859.53	0.15	0.24	1.56
	TC3	N	3	2 362	168.27 ± 61.37	397 444.87	4.20	5.99	1.42

Table F1 (cont.): Number of items with respect to treatment category, generic indicator and age group according to pharmacological group for the year 2005

Pharmacological group	Treatment category	Generic indicator	Age group	Number of items	Average cost (R)	Total cost (R)	Prevalence %	Cost %	CPI
	TC3	O	1	2	62.06 ± 0.00	124.12	0.003	0.002	0.53
	TC3	O	2	242	150.15 ± 49.84	36 335.26	0.43	0.55	1.27
	TC3	O	3	6 938	164.83 ± 58.30	1 143 577.61	12.35	17.23	1.40
	TC3	Y	1	10	89.74 ± 0.00	897.40	0.02	0.01	0.76
	TC3	Y	2	1 108	108.08 ± 42.36	119 752.67	1.97	1.80	0.91
	TC3	Y	3	19 634	100.19 ± 42.66	1 967 108.48	34.94	29.63	0.85
				56 196		6 638 650.96			
Sympathetic nervous blockers	TC1	N	1	4	135.74 ± 81.81	542.95	0.02	0.03	1.47
	TC1	N	2	658	73.54 ± 73.44	48 389.44	3.62	2.88	0.80
	TC1	N	3	8 660	125.88 ± 75.77	1 090 145.84	47.60	64.87	1.36
	TC2	N	2	3	13.88 ± 0.73	41.63	0.02	0.002	0.15
	TC2	N	3	73	77.67 ± 88.65	5 670.08	0.40	0.34	0.84
	TC3	N	1	3	14.64 ± 0.58	43.91	0.02	0.003	0.16
	TC3	N	2	1 092	29.35 ± 25.95	32 049.94	6.00	1.91	0.32
	TC3	N	3	7 702	65.39 ± 72.72	503 649.43	42.33	29.97	0.71
				18 195		1 680 533.22			
Direct-acting vasodilators	TC1	N	2	39	181.04 ± 99.81	7 060.67	1.67	3.38	2.03
	TC1	N	3	138	158.56 ± 80.41	21 880.91	5.90	10.47	1.77
	TC1	O	2	6	203.36 ± 151.63	1 220.16	0.26	0.58	2.28
	TC1	O	3	78	179.49 ± 59.42	14 000.02	3.33	6.70	2.01
	TC1	Y	1	1	38.28 ±	38.28	0.04	0.02	0.43
	TC1	Y	2	40	43.39 ± 19.82	1 735.53	1.71	0.83	0.49

Table F1 (cont.): Number of items with respect to treatment category, generic indicator and age group according to pharmacological group for the year 2005

Pharmacological group	Treatment category	Generic indicator	Age group	Number of items	Average cost (R)	Total cost (R)	Prevalence %	Cost %	CPI
	TC1	Y	3	655	40.89 ± 15.38	26 784.25	28.00	12.81	0.46
	TC2	O	3	7	306.92 ± 0.00	2 148.46	0.30	1.03	3.43
	TC2	Y	3	1	62.83 ± 0.00	62.83	0.04	0.03	0.70
	TC3	N	2	48	183.62 ± 74.24	8 813.62	2.05	4.22	2.05
	TC3	N	3	327	71.20 ± 118.15	55 981.61	13.98	26.78	1.92
	TC3	O	2	3	166.16 ± 122.68	498.47	0.13	0.24	1.86
	TC3	O	3	135	199.49 ± 69.94	26 931.25	5.77	12.88	2.23
	TC3	Y	1	3	79.93 ± 40.84	239.80	0.13	0.11	0.89
	TC3	Y	2	35	44.05 ± 15.46	1 541.62	1.50	0.74	0.49
	TC3	Y	3	823	48.72 ± 24.79	40 093.78	35.19	19.18	0.55
				2 339		209 031.26			
Calcium channel blockers	TC1	N	1	9	235.71 ± 43.09	2 121.43	0.01	0.01	1.49
	TC1	N	2	1 284	248.97 ± 52.98	319 680.74	0.97	1.53	1.57
	TC1	N	3	12 649	227.51 ± 56.00	2 877 720.61	9.59	13.77	1.44
	TC1	O	1	88	180.66 ± 53.05	15 898.29	0.07	0.08	1.14
	TC1	O	2	2 863	157.07 ± 37.02	449 698.83	2.17	2.15	0.99
	TC1	O	3	40 368	159.79 ± 40.66	6 450 369.25	30.62	30.87	1.01
	TC1	Y	1	16	104.92 ± 36.92	1 678.69	0.01	0.01	0.66
	TC1	Y	2	2 136	116.40 ± 25.71	248 627.99	1.62	1.19	0.73
	TC1	Y	3	23 856	113.32 ± 25.27	2 703 367.31	18.09	12.94	0.72
	TC2	N	2	18	252.64 ± 9.09	4 547.48	0.01	0.02	1.59
	TC2	N	3	98	236.97 ± 108.98	23 223.18	0.07	0.11	1.50
	TC2	O	2	21	187.30 ± 51.99	3 933.32	0.02	0.02	1.18

Table F1 (cont.): Number of items with respect to treatment category, generic indicator and age group according to pharmacological group for the year 2005

Pharmacological group	Treatment category	Generic indicator	Age group	Number of items	Average cost (R)	Total cost (R)	Prevalence %	Cost %	CPI
	TC2	O	3	196	171.21 ± 49.07	33 556.42	0.15	0.16	1.08
	TC2	Y	2	11	121.82 ± 32.54	1 339.98	0.01	0.01	0.77
	TC2	Y	3	147	119.45 ± 29.14	17 558.97	0.11	0.08	0.75
	TC3	N	1	1	229.64 ± 0.00	229.64	0.001	0.001	1.45
	TC3	N	2	743	246.22 ± 48.64	182 940.21	0.56	0.88	1.55
	TC3	N	3	8 817	236.79 ± 60.84	2 087 759.47	6.69	9.99	1.49
	TC3	O	1	17	171.30 ± 48.01	2 912.03	0.01	0.01	1.08
	TC3	O	2	1 148	158.28 ± 41.84	181 706.41	0.87	0.87	1.00
	TC3	O	3	21 407	161.44 ± 42.49	3 456 028.69	16.24	16.54	1.02
	TC3	Y	1	11	168.15 ± 29.12	1 849.60	0.01	0.01	1.06
	TC3	Y	2	1 117	117.14 ± 24.39	130 843.86	0.85	0.63	0.74
	TC3	Y	3	14 835	114.27 ± 25.51	1 695 126.71	11.25	8.11	0.72
				131 856		20 892 719.11			
ACE inhibitors	TC1	N	1	79	167.51 ± 35.45	13 233.62	0.01	0.02	1.47
	TC1	N	2	11 141	179.85 ± 39.49	2 003 663.72	1.72	2.70	1.57
	TC1	N	3	99 554	184.12 ± 43.55	18 329 751.95	15.33	24.70	1.61
	TC1	O	1	176	95.92 ± 56.75	16 881.12	0.03	0.02	0.84
	TC1	O	2	7 287	146.75 ± 52.96	1 069 385.37	1.12	1.44	1.28
	TC1	O	3	72 273	140.33 ± 56.62	10 141 808.06	11.13	13.67	1.23
	TC1	Y	1	254	69.80 ± 43.85	17 729.07	0.04	0.02	0.61
	TC1	Y	2	24 643	76.80 ± 40.53	1 892 513.49	3.79	2.55	0.67
	TC1	Y	3	196 517	77.47 ± 39.19	15 225 078.84	30.26	20.52	0.68
	TC2	N	2	20	176.56 ± 20.41	3 531.13	0.003	0.005	1.55
	TC2	N	3	416	194.88 ± 38.87	81 070.72	0.06	0.11	1.71

Table F1 (cont.): Number of items with respect to treatment category, generic indicator and age group according to pharmacological group for the year 2005

Pharmacological group	Treatment category	Generic indicator	Age group	Number of items	Average cost (R)	Total cost (R)	Prevalence %	Cost %	CPI
	TC2	O	1	1	96.65 ± 0.00	96.65	0.0001	0.0001	0.85
	TC2	O	2	30	168.91 ± 36.20	5 067.29	0.005	0.01	1.48
	TC2	O	3	361	164.79 ± 57.28	59 490.65	0.06	0.08	1.44
	TC2	Y	2	86	100.98 ± 58.87	8 684.56	0.01	0.01	0.88
	TC2	Y	3	1 031	82.02 ± 39.47	84 563.91	0.16	0.11	0.72
	TC3	N	1	3	115.52 ± 35.87	346.57	0.0005	0.0005	1.01
	TC3	N	2	2 542	192.99 ± 44.04	490 572.46	0.39	0.66	1.69
	TC3	N	3	35 069	197.77 ± 50.70	6 935 514.48	5.40	9.35	1.73
	TC3	O	1	61	97.49 ± 60.84	5 946.89	0.01	0.01	0.85
	TC3	O	2	2 308	153.93 ± 58.18	355 279.50	0.36	0.48	1.35
	TC3	O	3	31 681	145.25 ± 68.80	4 601 513.35	4.88	6.20	1.27
	TC3	Y	1	170	45.83 ± 32.31	7 791.18	0.03	0.01	0.40
	TC3	Y	2	14 575	73.10 ± 43.01	1 065 404.41	2.24	1.44	0.64
	TC3	Y	3	149 160	79.09 ± 43.78	11 797 139.66	22.97	15.90	0.69
				649 438		74 212 058.65			
Angiotensin-receptor blockers	TC1	N	1	80	216.16 ± 86.81	17 292.61	0.03	0.03	1.03
	TC1	N	2	18 170	211.07 ± 26.72	3 835 196.91	7.12	7.18	1.01
	TC1	N	3	171 463	209.12 ± 30.31	35 855 720.28	67.19	67.16	1.00
	TC2	N	2	25	206.68 ± 20.84	5 166.94	0.01	0.01	0.99
	TC2	N	3	769	215.22 ± 47.02	165 502.25	0.30	0.31	1.03
	TC3	N	1	15	200.29 ± 27.12	3 004.42	0.01	0.01	0.96
	TC3	N	2	3 127	212.25 ± 36.58	663 705.69	1.23	1.24	1.01
	TC3	N	3	61 550	208.63 ± 34.89	12 840 879.60	24.12	24.05	1.00

Table F1 (cont.): Number of items with respect to treatment category, generic indicator and age group according to pharmacological group for the year 2005

Pharmacological group	Treatment category	Generic indicator	Age group	Number of items	Average cost (R)	Total cost (R)	Prevalence %	Cost %	CPI
	TC3			255 199		53 386 468.70			
Other	TC1	N	2	213	161.84 ± 27.62	34 472.63	5.35	5.39	1.01
	TC1	N	3	2 257	160.61 ± 24.42	362 503.34	56.65	56.64	1.00
	TC2	N	3	25	134.83 ± 35.75	3 370.70	0.63	0.53	0.84
	TC3	N	2	98	158.39 ± 6.27	15 522.61	2.46	2.43	0.99
	TC3	N	3	1 391	161.13 ± 26.57	224 135.57	34.91	35.02	1.00
				3 984		640 004.85			
Diuretics	TC1	N	1	2	66.05 ± 0.00	132.10	0.0004	0.001	1.51
	TC1	N	2	18	64.80 ± 128.96	1 166.34	0.003	0.01	1.48
	TC1	N	3	533	102.80 ± 60.36	54 795.05	0.10	0.24	2.36
	TC1	O	2	15	197.56 ± 157.65	2 963.47	0.003	0.01	4.53
	TC1	O	3	260	134.11 ± 67.07	34 867.74	0.05	0.15	3.07
	TC1	Y	2	145	20.22 ± 14.76	2 932.13	0.03	0.01	0.46
	TC1	Y	3	2 160	27.53 ± 26.16	59 472.25	0.41	0.26	0.63
	TC2	N	1	121	111.68 ± 72.45	13 513.36	0.02	0.06	2.56
	TC2	N	2	4 665	77.52 ± 77.69	361 620.74	0.89	1.58	1.78
	TC2	N	3	33 552	89.39 ± 64.02	2 999 225.1	6.39	13.09	2.05
	TC2	O	1	94	78.34 ± 51.56	7 363.86	0.02	0.03	1.79
	TC2	O	2	1 274	101.93 ± 74.07	129 860.41	0.24	0.57	2.34
	TC2	O	3	10 015	123.41 ± 71.00	1 235 955.81	1.91	5.39	2.83
	TC2	Y	1	436	40.12 ± 53.29	17 494.11	0.08	0.08	0.92
	TC2	Y	2	19 543	19.36 ± 24.82	378 371.17	3.72	1.65	0.44
	TC2	Y	3	126 672	21.55 ± 23.45	2 729 275.77	24.13	11.91	0.49
	TC3	N	1	84	113.71 ± 79.05	9 551.55	0.02	0.04	2.61

Table F1 (cont.): Number of items with respect to treatment category, generic indicator and age group according to pharmacological group for the year 2005

Pharmacological group	Treatment category	Generic indicator	Age group	Number of items	Average cost (R)	Total cost (R)	Prevalence %	Cost %	CPI
	TC3	N	2	3 954	90.14 ± 108.06	356 424.65	0.75	1.56	2.07
	TC3	N	3	56 458	104.27 ± 83.67	5 887 084.41	10.76	25.70	2.39
	TC3	O	1	54	136.45 ± 62.19	7 368.44	0.01	0.03	3.13
	TC3	O	2	1 042	145.88 ± 111.97	152 009.47	0.20	0.66	3.34
	TC3	O	3	21 317	135.04 ± 70.76	2 878 707.75	4.06	12.56	3.09
	TC3	Y	1	162	19.58 ± 18.01	3 172.09	0.03	0.01	0.45
	TC3	Y	2	19 711	19.96 ± 21.96	393 497.49	3.75	1.72	0.46
	TC3	Y	3	222 651	23.33 ± 22.39	5 194 211.06	42.41	22.67	0.53
				524 938		22 911 036.32			

Table F2: Number of items with respect to treatment category, generic indicator and age group according to pharmacological group for the year 2006

Pharmacological group	Treatment category	Generic indicator	Age group	Number of items	Average cost (R)	Total cost (R)	Prevalence %	Cost %	CPI
Central-acting inhibitors	TC1	N	1	8	193.89 ± 9.97	1 551.09	0.03	0.06	1.84
	TC1	N	2	273	202.47 ± 33.99	55 274.78	1.13	2.18	1.93
	TC1	N	3	2 993	203.22 ± 48.90	608 233.07	12.43	24.02	1.93
	TC1	O	1	2	164.73 ± 118.08	329.45	0.01	0.01	1.57
	TC1	O	2	160	151.42 ± 102.02	24 226.87	0.66	0.96	1.44
	TC1	O	3	203	188.65 ± 106.47	38 296.43	0.84	1.51	1.79
	TC1	Y	1	13	47.96 ± 40.20	623.49	0.05	0.03	0.46

Table F2 (cont.): Number of items with respect to treatment category, generic indicator and age group according to pharmacological group for the year 2006

Pharmacological group	Treatment category	Generic indicator	Age group	Number of items	Average cost (R)	Total cost (R)	Prevalence %	Cost %	CPI
	TC1	Y	2	2 449	79.10 ± 59.38	193 721.17	10.17	7.65	0.75
	TC1	Y	3	5 536	67.57 ± 49.69	374 094.64	22.99	14.77	0.64
	TC2	N	3	16	159.93 ± 54.44	2 558.8	0.066	0.10	1.52
	TC2	O	2	1	147.58 ± 0.00	147.58	0.004	0.01	1.40
	TC2	O	3	1	19.51 ± 0.00	19.51	0.004	8E-04	0.19
	TC2	Y	2	7	100.14 ± 63.16	700.97	0.03	0.03	0.95
	TC2	Y	3	40	64.80 ± 53.67	2 592.16	0.17	0.10	0.62
	TC3	N	2	138	220.38 ± 58.88	30 412.73	0.57	1.20	2.10
	TC3	N	3	2 583	206.05 ± 42.19	532 230.53	10.72	21.02	1.96
	TC3	O	2	70	190.39 ± 132.81	13 327.02	0.29	0.53	1.81
	TC3	O	3	231	172.28 ± 94.09	39 797.31	0.96	1.57	1.64
	TC3	Y	1	4	45.42 ± 29.27	181.66	0.02	0.01	0.43
	TC3	Y	2	1 082	73.98 ± 52.12	80 049.01	4.49	3.16	0.70
	TC3	Y	3	8 275	64.53 ± 45.46	534 021.86	34.36	21.09	0.61
				24 085		2 532 390.10			
Alpha-receptor blockers	TC1	N	1	6	299.97 ± 111.18	1 799.79	0.01	0.03	1.75
	TC1	N	2	714	271.26 ± 89.84	193 677.71	1.72	2.72	1.58
	TC1	N	3	8 751	272.10 ± 67.13	2 381 118.4	21.12	33.45	1.58
	TC1	O	1	8	97.83 ± 0.00	782.64	0.02	0.01	0.57
	TC1	O	2	368	185.00 ± 36.49	68 081.10	0.89	0.96	1.08
	TC1	O	3	7 472	186.99 ± 34.13	1 397 163.90	18.03	19.63	1.09
	TC1	Y	1	45	43.75 ± 27.51	1 968.55	0.11	0.03	0.25
	TC1	Y	2	501	86.45 ± 71.63	43 311.42	1.21	0.61	0.50

Table F2 (cont.): Number of items with respect to treatment category, generic indicator and age group according to pharmacological group for the year 2006

Pharmacological group	Treatment category	Generic indicator	Age group	Number of items	Average cost (R)	Total cost (R)	Prevalence %	Cost %	CPI
	TC1	Y	3	9 847	82.69 ± 49.58	814 243.77	23.77	11.44	0.48
	TC2	N	3	29	278.73 ± 36.96	8 083.06	0.07	0.11	1.62
	TC2	O	2	1	184.94 ±	184.94	0.002	0.003	1.08
	TC2	O	3	40	177.55 ± 17.58	7 102.07	0.10	0.10	1.03
	TC2	Y	3	68	82.91 ± 35.41	5 637.68	0.16	0.08	0.48
	TC3	N	2	81	295.83 ± 114.95	23 962.38	0.20	0.34	1.72
	TC3	N	3	3 209	267.18 ± 62.27	857 382.11	7.75	12.05	1.56
	TC3	O	1	5	360.11 ± 22.65	1 800.57	0.01	0.03	2.10
	TC3	O	2	156	189.96 ± 19.98	29 633.86	0.38	0.42	1.11
	TC3	O	3	3 589	188.59 ± 36.18	676 846.64	8.66	9.51	1.10
	TC3	Y	1	16	183.21 ± 49.82	2 931.31	0.04	0.04	1.07
	TC3	Y	2	284	112.87 ± 77.36	32 056.28	0.69	0.45	0.66
	TC3	Y	3	6 242	91.27 ± 56.74	569 735.69	15.07	8.01	0.53
				41 432		7 117 503.90			
Beta-receptor blockers	TC1	N	1	46	129.96 ± 91.08	5 978.24	0.02	0.03	1.44
	TC1	N	2	7 811	115.70 ± 21.46	903 700.89	3.05	3.90	1.28
	TC1	N	3	65 770	119.97 ± 27.47	7 890 358.30	25.67	34.07	1.33
	TC1	O	1	95	74.19 ± 60.24	7 047.76	0.04	0.03	0.82
	TC1	O	2	3 014	86.70 ± 47.89	261 304.72	1.18	1.13	0.96
	TC1	O	3	34 065	99.73 ± 61.91	3 397 212.30	13.30	14.67	1.10
	TC1	Y	1	133	45.83 ± 24.57	6 095.53	0.05	0.03	0.51
	TC1	Y	2	6 682	57.16 ± 26.91	381 927.54	2.61	1.65	0.63
	TC1	Y	3	77 272	64.93 ± 35.39	5 017 318.30	30.16	21.67	0.72

Table F2 (cont.): Number of items with respect to treatment category, generic indicator and age group according to pharmacological group for the year 2006

Pharmacological group	Treatment category	Generic indicator	Age group	Number of items	Average cost (R)	Total cost (R)	Prevalence %	Cost %	CPI
	TC2	N	1	1	250.06 ± 0.00	250.06	4E-04	0.001	2.77
	TC2	N	2	27	121.85 ± 1.53	3 289.83	0.01	0.01	1.35
	TC2	N	3	196	125.37 ± 43.10	24 572.19	0.08	0.11	1.39
	TC2	O	2	15	76.72 ± 21.65	1 150.75	0.01	0.01	0.85
	TC2	O	3	132	89.49 ± 37.77	1 1812.30	0.05	0.05	0.99
	TC2	Y	2	11	79.04 ± 2.95	869.46	0.004	0.004	0.87
	TC2	Y	3	299	57.86 ± 32.86	17 300.04	0.12	0.08	0.64
	TC3	N	1	8	259.24 ± 110.31	2 073.95	0.003	0.01	2.87
	TC3	N	2	850	122.11 ± 29.06	103 792.08	0.33	0.45	1.35
	TC3	N	3	15 150	125.35 ± 43.21	1 899 123.50	5.91	8.20	1.39
	TC3	O	1	15	197.78 ± 69.16	2 966.66	0.01	0.01	2.19
	TC3	O	2	636	88.68 ± 48.36	56 399.62	0.25	0.24	0.98
	TC3	O	3	13 396	98.11 ± 56.41	1 314 323.40	5.23	5.68	1.09
	TC3	Y	1	13	67.01 ± 29.10	871.09	0.01	0.004	0.74
	TC3	Y	2	1 703	55.92 ± 25.29	95 230.00	0.67	0.41	0.62
	TC3	Y	3	28 880	60.66 ± 34.69	1 751 882.70	11.27	7.57	0.67
				256 220		23 156 851.00			
Alpha- and Beta-receptor blockers	TC1	N	2	12	371.26 ± 173.38	4 455.16	0.02	0.06	3.39
	TC1	N	3	76	271.38 ± 144.92	20 624.53	0.11	0.28	2.48
	TC1	O	1	2	175.27 ± 64.83	350.53	0.003	0.01	1.60
	TC1	O	2	385	143.62 ± 62.93	55 293.53	0.58	0.76	1.31
	TC1	O	3	4 589	154.77 ± 57.76	710 225.16	6.88	9.73	1.41
	TC1	Y	1	26	62.01 ± 16.34	1 612.14	0.04	0.02	0.57

Table F2 (cont.): Number of items with respect to treatment category, generic indicator and age group according to pharmacological group for the year 2006

Pharmacological group	Treatment category	Generic indicator	Age group	Number of items	Average cost (R)	Total cost (R)	Prevalence %	Cost %	CPI
	TC1	Y	2	2 143	98.89 ± 39.42	211 918.94	3.21	2.90	0.90
	TC1	Y	3	22 544	95.91 ± 37.97	2 162 274.30	33.80	29.62	0.88
	TC2	O	2	2	129.42 ± 0.00	258.84	0.003	0.004	1.18
	TC2	O	3	86	143.93 ± 50.54	12 377.99	0.13	0.17	1.31
	TC2	Y	2	14	79.74 ± 33.87	1 116.31	0.02	0.02	0.73
	TC2	Y	3	344	109.54 ± 41.12	37 682.23	0.52	0.52	1.00
	TC3	N	2	7	883.77 ± 282.48	6 186.42	0.01	0.09	8.07
	TC3	N	3	96	242.59 ± 111.92	23 288.44	0.14	0.32	2.22
	TC3	O	1	22	89.03 ± 47.54	1 958.67	0.03	0.03	0.81
	TC3	O	2	236	164.23 ± 57.00	38 759.05	0.35	0.53	1.50
	TC3	O	3	6 369	162.85 ± 61.76	1 037 194.10	9.55	14.21	1.49
	TC3	Y	1	5	98.50 ± 50.45	492.52	0.01	0.01	0.90
	TC3	Y	2	1 466	105.62 ± 39.01	154 838.04	2.20	2.12	0.96
	TC3	Y	3	28 265	99.78 ± 41.20	2 820 283.40	42.38	38.63	0.91
				66 689		7 301 190.30			
Sympathetic nervous blockers	TC1	N	1	22	34.82 ± 33.30	766.02	0.14	0.06	0.41
	TC1	N	2	636	58.89 ± 66.22	37 456.51	3.96	2.75	0.69
	TC1	N	3	7 152	123.73 ± 78.02	884 926.06	44.58	64.92	1.46
	TC2	N	2	7	14.07 ± 0.22	98.46	0.04	0.01	0.17
	TC2	N	3	39	87.28 ± 83.33	3 403.90	0.24	0.25	1.03
	TC3	N	1	7	28.22 ± 10.71	197.52	0.04	0.01	0.33
	TC3	N	2	1 232	29.92 ± 25.15	36 859.78	7.68	2.70	0.35
	TC3	N	3	6 948	57.49 ± 67.85	399 455.32	43.31	29.30	0.68

Table F2 (cont.): Number of items with respect to treatment category, generic indicator and age group according to pharmacological group for the year 2006

Pharmacological group	Treatment category	Generic indicator	Age group	Number of items	Average cost (R)	Total cost (R)	Prevalence %	Cost %	CPI
				16 043		1 363 163.60			
Direct-acting vasodilators	TC1	N	1	2	229.83 ± 184.64	459.66	0.08	0.20	2.61
	TC1	N	2	33	162.91 ± 148.87	5 375.96	1.23	2.28	1.85
	TC1	N	3	150	180.33 ± 128.78	27 049.98	5.59	11.45	2.05
	TC1	O	1	1	364.89 ±	364.89	0.04	0.15	4.14
	TC1	O	2	11	144.52 ± 82.04	1 589.68	0.41	0.67	1.64
	TC1	O	3	78	187.44 ± 48.32	14 620.21	2.91	6.19	2.13
	TC1	Y	1	4	41.89 ± 1.69	167.56	0.15	0.07	0.48
	TC1	Y	2	81	53.39 ± 32.86	4 324.63	3.02	1.83	0.61
	TC1	Y	3	714	42.00 ± 15.02	29 988.39	26.61	12.69	0.48
	TC2	O	3	4	129.08 ± 45.28	516.32	0.15	0.22	1.47
	TC2	Y	3	6	39.71 ± 0.81	238.23	0.22	0.10	0.45
	TC3	N	2	75	169.09 ± 68.39	12 682.02	2.80	5.37	1.92
	TC3	N	3	338	183.51 ± 109.26	62 027.40	12.60	26.25	2.08
	TC3	O	2	6	171.35 ± 91.82	1 028.07	0.22	0.44	1.95
	TC3	O	3	129	200.19 ± 67.99	25 824.07	4.81	10.93	2.27
	TC3	Y	2	52	54.90 ± 24.77	2 854.87	1.94	1.21	0.62
	TC3	Y	3	999	47.22 ± 23.70	47 168.51	37.23	19.96	0.54
				2 683		236 280.45			
Calcium channel blockers	TC1	N	1	5	228.00 ± 105.43	1 140.00	0.003	0.01	1.58
	TC1	N	2	1 450	236.71 ± 55.72	343 231.87	0.86	1.42	1.64
	TC1	N	3	15 086	220.54 ± 60.01	3 327 120.80	8.98	13.71	1.53

Table F2 (cont.): Number of items with respect to treatment category, generic indicator and age group according to pharmacological group for the year 2006

Pharmacological group	Treatment category	Generic indicator	Age group	Number of items	Average cost (R)	Total cost (R)	Prevalence %	Cost %	CPI
	TC1	O	1	105	158.72 ± 47.46	16 665.34	0.06	0.07	1.10
	TC1	O	2	2 450	150.07 ± 37.99	367 671.10	1.46	1.52	1.04
	TC1	O	3	36 104	150.78 ± 37.79	5 443 760.00	21.49	22.44	1.04
	TC1	Y	1	52	113.05 ± 30.02	5 878.79	0.03	0.02	0.78
	TC1	Y	2	4 334	113.91 ± 23.38	493 701.80	2.58	2.04	0.79
	TC1	Y	3	46 739	110.99 ± 23.56	5 187 671.90	27.82	21.38	0.77
	TC2	N	2	8	265.49 ± 11.35	2 123.88	0.01	0.01	1.84
	TC2	N	3	112	218.62 ± 56.51	24 485.94	0.07	0.10	1.51
	TC2	O	2	9	136.62 ± 14.14	1 229.62	0.01	0.01	0.95
	TC2	O	3	181	148.47 ± 30.16	26 873.28	0.11	0.11	1.03
	TC2	Y	2	15	117.84 ± 22.50	1 767.67	0.01	0.01	0.82
	TC2	Y	3	364	112.50 ± 24.97	40 951.69	0.22	0.17	0.78
	TC3	N	2	814	241.43 ± 59.24	196 523.94	0.49	0.81	1.67
	TC3	N	3	10 381	227.70 ± 61.62	2 363 770.10	6.18	9.74	1.58
	TC3	O	1	22	189.20 ± 53.48	4 162.36	0.01	0.02	1.31
	TC3	O	2	1 097	155.59 ± 42.03	170 681.73	0.65	0.70	1.08
	TC3	O	3	17 903	154.67 ± 39.73	2 769 043.80	10.66	11.41	1.07
	TC3	Y	1	20	150.49 ± 97.12	3 009.70	0.01	0.01	1.04
	TC3	Y	2	2 106	116.79 ± 22.49	245 952.09	1.25	1.01	0.81
	TC3	Y	3	28 632	112.68 ± 24.59	3 226 351.90	17.04	13.30	0.78
				167 989		24 263 769.00			
ACE inhibitors	TC1	N	1	24	138.51 ± 62.68	3 324.15	0.003	0.004	1.30
	TC1	N	2	4 337	179.78 ± 65.59	779 704.24	0.59	1.00	1.68
	TC1	N	3	37 960	189.72 ± 54.00	7 201 798.80	5.15	9.14	1.78

Table F2 (cont.): Number of items with respect to treatment category, generic indicator and age group according to pharmacological group for the year 2006

Pharmacological group	Treatment category	Generic indicator	Age group	Number of items	Average cost (R)	Total cost (R)	Prevalence %	Cost %	CPI
	TC1	O	1	179	100.22 ± 62.02	17 939.26	0.02	0.02	0.94
	TC1	O	2	9 747	151.81 ± 49.65	1 479 711.50	1.32	1.88	1.42
	TC1	O	3	92 524	145.79 ± 53.38	13 488 662.00	12.54	17.12	1.36
	TC1	Y	1	387	72.87 ± 47.49	28 199.27	0.05	0.04	0.68
	TC1	Y	2	37 141	89.28 ± 44.98	3 316 035.10	5.03	4.21	0.84
	TC1	Y	3	290 552	87.76 ± 42.82	25 499 277.00	39.38	32.35	0.82
	TC2	N	2	12	239.75 ± 41.84	2 877.00	0.002	0.004	2.24
	TC2	N	3	183	193.77 ± 58.99	35 460.03	0.03	0.05	1.81
	TC2	O	2	44	146.07 ± 39.08	6 426.94	0.01	0.01	1.37
	TC2	O	3	380	152.89 ± 55.96	58 097.84	0.05	0.07	1.43
	TC2	Y	2	96	80.23 ± 45.09	7 702.00	0.01	0.01	0.75
	TC2	Y	3	1 537	95.59 ± 50.69	146 927.91	0.21	0.19	0.90
	TC3	N	2	1 341	202.02 ± 63.05	270 904.40	0.18	0.34	1.89
	TC3	N	3	18 040	205.19 ± 55.06	3 701 578.30	2.45	4.70	1.92
	TC3	O	1	89	111.80 ± 55.85	9 950.26	0.01	0.01	1.05
	TC3	O	2	2 431	150.29 ± 60.59	365 351.36	0.33	0.46	1.41
	TC3	O	3	32 858	150.61 ± 64.88	4 948 614.60	4.45	6.28	1.41
	TC3	Y	1	178	40.18 ± 31.39	7 152.05	0.02	0.01	0.38
	TC3	Y	2	17 544	80.08 ± 45.51	1 404 907.30	2.38	1.78	0.75
	TC3	Y	3	190 291	84.24 ± 45.27	16 030 876.00	25.79	20.34	0.79
				737 875		78 811 478.00			
Angiotensin-receptor blockers	TC1	N	1	45	199.48 ± 46.75	8 976.46	0.02	0.02	0.95
	TC1	N	2	15 508	209.56 ± 35.41	3 249 858.00	5.77	5.78	1.00

Table F2 (cont.): Number of items with respect to treatment category, generic indicator and age group according to pharmacological group for the year 2006

Pharmacological group	Treatment category	Generic indicator	Age group	Number of items	Average cost (R)	Total cost (R)	Prevalence %	Cost %	CPI
	TC1	N	3	156 418	209.22 ± 34.91	32 725 788.00	58.23	58.21	1.00
	TC1	O	1	15	214.79 ± 11.24	3 221.82	0.01	0.01	1.03
	TC1	O	2	2 503	207.67 ± 30.71	519 791.80	0.93	0.92	0.99
	TC1	O	3	23 310	209.79 ± 27.83	4 890 270.00	8.68	8.70	1.00
	TC1	Y	2	9	208.20 ± 9.96	1 873.77	0.003	0.003	0.99
	TC1	Y	3	19	202.95 ± 54.09	3 856.05	0.01	0.01	0.97
	TC2	N	2	50	217.41 ± 18.68	10 870.34	0.02	0.02	1.04
	TC2	N	3	687	205.41 ± 37.30	141 113.54	0.26	0.25	0.98
	TC2	O	3	188	212.93 ± 15.69	40 031.07	0.07	0.07	1.02
	TC3	N	1	11	198.15 ± 29.84	2 179.64	0.004	0.004	0.95
	TC3	N	2	3 014	210.26 ± 34.07	633 712.09	1.12	1.13	1.00
	TC3	N	3	58 242	209.28 ± 36.59	12 188 780.00	21.68	21.68	1.00
	TC3	O	2	372	208.70 ± 22.48	77 637.29	0.14	0.14	1.00
	TC3	O	3	8 212	209.95 ± 28.99	1 724 097.50	3.06	3.07	1.00
	TC3	Y	2	4	199.50 ± 0.00	798.00	0.001	0.001	0.95
	TC3	Y	3	10	188.48 ± 67.69	1 884.75	0.004	0.003	0.90
				268 617		56 224 740.00			
Other	TC1	N	2	367	196.68 ± 51.35	72 182.98	6.83	7.43	1.09
	TC1	N	3	3 251	179.57 ± 49.11	583 785.20	60.48	60.12	0.99
	TC2	N	2	14	170.39 ± 29.31	2 385.44	0.26	0.25	0.94
	TC2	N	3	18	211.06 ± 55.12	3 799.12	0.34	0.39	1.17
	TC3	N	2	100	190.88 ± 46.62	19 088.28	1.86	1.97	1.06
	TC3	N	3	1 625	178.33 ± 44.88	289 786.96	30.23	29.84	0.99
				5 375		971 027.98			

Table F2 (cont.): Number of items with respect to treatment category, generic indicator and age group according to pharmacological group for the year 2006

Pharmacological group	Treatment category	Generic indicator	Age group	Number of items	Average cost (R)	Total cost (R)	Prevalence %	Cost %	CPI
Diuretics	TC1	N	2	33	120.08 ± 73.03	3 962.57	0.01	0.02	2.85
	TC1	N	3	577	122.11 ± 101.04	70 455.14	0.10	0.30	2.89
	TC1	O	2	28	140.74 ± 55.72	3 940.74	0.01	0.02	3.34
	TC1	O	3	420	137.50 ± 59.46	57 748.57	0.08	0.25	3.26
	TC1	Y	2	154	18.91 ± 16.16	2 911.84	0.03	0.01	0.45
	TC1	Y	3	2 365	26.56 ± 26.16	62 812.09	0.43	0.27	0.63
	TC2	N	1	130	92.12 ± 83.61	11 975.29	0.02	0.05	2.18
	TC2	N	2	4 048	67.39 ± 59.94	272 798.32	0.73	1.17	1.60
	TC2	N	3	30 647	86.53 ± 65.28	2 651 974.90	5.53	11.35	2.05
	TC2	O	1	84	89.79 ± 71.08	7 542.25	0.02	0.03	2.13
	TC2	O	2	1 301	98.79 ± 73.99	128 521.59	0.24	0.55	2.34
	TC2	O	3	9 827	124.31 ± 71.86	1 221 545.80	1.78	5.23	2.95
	TC2	Y	1	439	46.48 ± 60.39	20 404.60	0.08	0.09	1.10
	TC2	Y	2	18 524	18.59 ± 24.21	344 316.94	3.35	1.47	0.44
	TC2	Y	3	128 325	21.40 ± 24.62	2 745 665.20	23.17	11.75	0.51
	TC3	N	1	95	121.04 ± 83.36	11 499.16	0.02	0.05	2.87
	TC3	N	2	3 537	89.23 ± 114.49	315 595.79	0.64	1.35	2.11
	TC3	N	3	55 020	104.25 ± 89.46	5 735 612.10	9.94	24.54	2.47
	TC3	O	1	61	108.63 ± 52.38	6 626.28	0.01	0.03	2.57
	TC3	O	2	1 330	141.51 ± 103.11	188 207.02	0.24	0.81	3.35
	TC3	O	3	24 879	132.81 ± 67.74	3 304 219.00	4.49	14.14	3.15
	TC3	Y	1	210	17.69 ± 18.32	3 714.53	0.04	0.02	0.42
	TC3	Y	2	21 698	20.55 ± 21.17	445 970.31	3.92	1.91	0.49
	TC3	Y	3	250 039	23.00 ± 21.67	5 750 823.60	45.15	24.61	0.55

Table F2 (cont.): Number of items with respect to treatment category, generic indicator and age group according to pharmacological group for the year 2006

Pharmacological group	Treatment category	Generic indicator	Age group	Number of items	Average cost (R)	Total cost (R)	Prevalence %	Cost %	CPI
				553 771		23 368 844.00			

Table F3: Number of items with respect to treatment category, generic indicator and age group according to pharmacological group for the year 2007

Pharmacological group	Treatment category	Generic indicator	Age group	Number of items	Average cost (R)	Total cost (R)	Prevalence %	Cost %	CPI
Central-acting inhibitors	TC1	N	1	14	199.72 ± 4.88	2 796.09	0.07	0.12	1.67
	TC1	N	2	377	199.45 ± 41.10	75 193.63	1.89	3.15	1.67
	TC1	N	3	3 331	208.54 ± 53.90	694 651.90	16.70	29.15	1.75
	TC1	O	2	84	132.93 ± 98.73	11 166.04	0.42	0.47	1.11
	TC1	O	3	85	160.74 ± 99.63	13 663.13	0.43	0.57	1.35
	TC1	Y	1	15	78.55 ± 65.95	1 178.29	0.08	0.05	0.66
	TC1	Y	2	1 872	82.15 ± 69.02	153 785.80	9.38	6.45	0.69
	TC1	Y	3	4 296	73.26 ± 52.58	314 743.46	21.53	13.21	0.61
	TC2	N	3	9	210.06 ± 11.07	1 890.53	0.05	0.08	1.76
	TC2	O	2	1	19.86 ± 0.00	19.86	0.01	0.00	0.17
	TC2	Y	2	6	54.21 ± 58.49	325.23	0.03	0.01	0.45
	TC2	Y	3	36	76.17 ± 54.16	2 741.94	0.18	0.12	0.64
	TC3	N	2	158	224.97 ± 53.14	35 545.08	0.79	1.49	1.88
	TC3	N	3	2 568	211.16 ± 44.90	542 261.42	12.87	22.75	1.77
	TC3	O	2	30	170.06 ± 121.93	5 101.81	0.15	0.21	1.42
	TC3	O	3	102	140.98 ± 87.12	14 379.84	0.51	0.60	1.18
	TC3	Y	1	2	43.63 ± 23.73	87.26	0.01	0.00	0.37
	TC3	Y	2	723	74.49 ± 59.12	53 859.57	3.62	2.26	0.62
	TC3	Y	3	6 242	73.69 ± 53.47	459 978.84	31.29	19.30	0.62
				19 951		2 383 369.72			

Table F3 (cont.): Number of items with respect to treatment category, generic indicator and age group according to pharmacological group for the year 2007

Pharmacological group	Treatment category	Generic indicator	Age group	Number of items	Average cost (R)	Total cost (R)	Prevalence %	Cost %	CPI
Alpha-receptor blockers	TC1	N	1	5	182.57 ± 166.76	912.84	0.01	0.01	1.01
	TC1	N	2	652	292.98 ± 106.94	191 021.38	1.72	2.79	1.62
	TC1	N	3	8 296	285.27 ± 78.10	2 366 605.12	21.94	34.62	1.58
	TC1	O	1	1	138.54 ±	138.54	0.00	0.00	0.77
	TC1	O	2	359	185.59 ± 40.74	66 628.21	0.95	0.97	1.03
	TC1	O	3	6 286	193.93 ± 36.91	1 219 025.62	16.63	17.83	1.07
	TC1	Y	1	18	68.09 ± 37.18	1 225.66	0.05	0.02	0.38
	TC1	Y	2	396	97.18 ± 74.78	38 484.78	1.05	0.56	0.54
	TC1	Y	3	9 076	85.51 ± 55.15	776 110.84	24.01	11.35	0.47
	TC2	N	3	46	313.34 ± 58.10	14 413.57	0.12	0.21	1.73
	TC2	O	3	30	195.32 ± 30.90	5 859.45	0.08	0.09	1.08
	TC2	Y	2	1	58.23 ±	58.23	0.00	0.00	0.32
	TC2	Y	3	96	86.34 ± 35.82	8 289.03	0.25	0.12	0.48
	TC3	N	2	53	265.56 ± 52.51	14 074.65	0.14	0.21	1.47
	TC3	N	3	3 112	286.97 ± 67.88	893 055.40	8.23	13.07	1.59
	TC3	O	1	3	380.76 ± 9.32	1 142.28	0.01	0.02	2.11
	TC3	O	2	136	175.24 ± 59.40	23 832.29	0.36	0.35	0.97
	TC3	O	3	3 411	195.62 ± 44.19	667 265.71	9.02	9.76	1.08
	TC3	Y	1	14	182.82 ± 57.41	2 559.50	0.04	0.04	1.01
	TC3	Y	2	186	111.13 ± 97.73	20 670.14	0.49	0.30	0.61
	TC3	Y	3	5 627	93.14 ± 61.58	524 084.99	14.88	7.67	0.52
				37 804		6 835 458.23			

Table F3 (cont.): Number of items with respect to treatment category, generic indicator and age group according to pharmacological group for the year 2007

Pharmacological group	Treatment category	Generic indicator	Age group	Number of items	Average cost (R)	Total cost (R)	Prevalence %	Cost %	CPI
Beta-receptor blockers	TC1	N	1	15	119.64 ± 33.76	1 794.56	0.01	0.01	1.33
	TC1	N	2	6 981	115.47 ± 31.74	806 100.25	2.81	3.60	1.28
	TC1	N	3	61 543	122.12 ± 30.52	7 515 547.56	24.73	33.58	1.36
	TC1	O	1	84	55.62 ± 41.10	4 672.29	0.03	0.02	0.62
	TC1	O	2	2 399	83.45 ± 49.96	200 204.91	0.96	0.89	0.93
	TC1	O	3	28 200	98.48 ± 64.03	2 777 058.96	11.33	12.41	1.09
	TC1	Y	1	74	44.72 ± 36.40	3 309.60	0.03	0.01	0.50
	TC1	Y	2	6 358	58.63 ± 28.84	372 771.91	2.56	1.67	0.65
	TC1	Y	3	82 051	66.35 ± 37.20	5 444 399.67	32.98	24.33	0.74
	TC2	N	2	12	122.31 ± 5.56	1 467.67	0.00	0.01	1.36
	TC2	N	3	131	127.27 ± 25.26	16 672.04	0.05	0.07	1.41
	TC2	O	2	14	48.33 ± 8.64	676.61	0.01	0.00	0.54
	TC2	O	3	193	108.53 ± 76.15	20 946.65	0.08	0.09	1.21
	TC2	Y	2	10	54.50 ± 19.84	544.98	0.00	0.00	0.61
	TC2	Y	3	491	71.82 ± 33.44	35 264.36	0.20	0.16	0.80
	TC3	N	1	9	542.86 ± 101.21	4 885.74	0.00	0.02	6.04
	TC3	N	2	768	119.11 ± 38.32	91 473.10	0.31	0.41	1.32
	TC3	N	3	14 290	126.81 ± 45.39	1 812 149.89	5.74	8.10	1.41
	TC3	O	1	16	183.22 ± 77.01	2 931.54	0.01	0.01	2.04
	TC3	O	2	346	91.20 ± 49.61	31 554.40	0.14	0.14	1.01
	TC3	O	3	11 290	100.62 ± 62.76	1 136 016.91	4.54	5.08	1.12
	TC3	Y	1	13	48.20 ± 20.34	626.62	0.01	0.00	0.54
	TC3	Y	2	1 463	56.34 ± 25.06	82 429.16	0.59	0.37	0.63

Table F3 (cont.): Number of items with respect to treatment category, generic indicator and age group according to pharmacological group for the year 2007

Pharmacological group	Treatment category	Generic indicator	Age group	Number of items	Average cost (R)	Total cost (R)	Prevalence %	Cost %	CPI
	TC3	Y	3	32 067	62.88 ± 34.70	2 016 290.06	12.89	9.01	0.70
				248 818		22 379 789.44			
Alpha- and Beta-receptor blockers	TC1	N	2	28	692.45 ± 256.52	19 388.47	0.04	0.25	6.30
	TC1	N	3	70	199.79 ± 99.19	13 985.40	0.10	0.18	1.82
	TC1	O	1	3	102.73 ± 34.50	308.18	0.00	0.00	0.93
	TC1	O	2	269	138.54 ± 58.65	37 266.22	0.38	0.48	1.26
	TC1	O	3	3 648	151.50 ± 56.38	552 687.36	5.22	7.19	1.38
	TC1	Y	1	11	59.52 ± 31.99	654.73	0.02	0.01	0.54
	TC1	Y	2	2 187	99.58 ± 38.81	217 791.12	3.13	2.83	0.91
	TC1	Y	3	26 606	98.91 ± 38.13	2 631 635.64	38.07	34.25	0.90
	TC2	O	2	3	131.48 ± 6.38	394.43	0.00	0.01	1.20
	TC2	O	3	78	174.46 ± 48.66	13 607.71	0.11	0.18	1.59
	TC2	Y	2	8	108.60 ± 29.74	868.77	0.01	0.01	0.99
	TC2	Y	3	367	107.38 ± 45.99	39 407.19	0.53	0.51	0.98
	TC3	N	3	53	309.43 ± 127.62	16 399.92	0.08	0.21	2.81
	TC3	O	1	14	169.85 ± 119.07	2 377.84	0.02	0.03	1.54
	TC3	O	2	181	182.51 ± 64.19	33 034.24	0.26	0.43	1.66
	TC3	O	3	4 705	166.32 ± 63.94	782 538.35	6.73	10.18	1.51
	TC3	Y	1	12	56.30 ± 43.59	675.62	0.02	0.01	0.51
	TC3	Y	2	1 453	107.11 ± 43.46	155 633.86	2.08	2.03	0.97
	TC3	Y	3	30 184	104.87 ± 41.79	3 165 420.75	43.19	41.19	0.95
				69 880		7 684 075.80			

Table F3 (cont.): Number of items with respect to treatment category, generic indicator and age group according to pharmacological group for the year 2007

Pharmacological group	Treatment category	Generic indicator	Age group	Number of items	Average cost (R)	Total cost (R)	Prevalence %	Cost %	CPI
Sympathetic nervous blockers	TC1	N	1	2	15.18 ± 0.81	30.35	0.02	0.00	0.13
	TC1	N	2	242	100.27 ± 98.04	24 266.19	2.73	2.39	0.87
	TC1	N	3	5 094	147.83 ± 79.10	753 053.60	57.47	74.05	1.29
	TC2	N	2	9	164.79 ± 56.66	1 483.14	0.10	0.15	1.44
	TC2	N	3	14	97.97 ± 141.95	1 371.63	0.16	0.13	0.85
	TC3	N	1	1	15.75 ± 0.00	15.75	0.01	0.00	0.14
	TC3	N	2	279	24.28 ± 36.06	6 773.24	3.15	0.67	0.21
	TC3	N	3	3 222	71.35 ± 84.94	229 896.34	36.35	22.61	0.62
				8 863		1 016 890.24			
Direct-acting vasodilators	TC1	N	2	30	198.52 ± 151.44	5 955.74	1.28	2.76	2.17
	TC1	N	3	177	155.19 ± 116.64	27 468.45	7.53	12.74	1.69
	TC1	O	2	11	180.52 ± 128.85	1 985.71	0.47	0.92	1.97
	TC1	O	3	62	183.33 ± 58.70	11 366.68	2.64	5.27	2.00
	TC1	Y	1	1	41.72 ±	41.72	0.04	0.02	0.46
	TC1	Y	2	79	42.80 ± 18.09	3 381.16	3.36	1.57	0.47
	TC1	Y	3	552	46.59 ± 16.57	25 714.93	23.48	11.93	0.51
	TC2	N	3	6	119.55 ± 1.07	717.31	0.26	0.33	1.30
	TC2	O	3	1	337.98 ±	337.98	0.04	0.16	3.69
	TC2	Y	3	11	49.83 ± 34.79	548.08	0.47	0.25	0.54
	TC3	N	2	91	187.22 ± 94.26	17 036.95	3.87	7.90	2.04
	TC3	N	3	270	196.71 ± 111.14	53 111.88	11.48	24.64	2.15
	TC3	O	2	4	262.06 ± 84.49	1 048.23	0.17	0.49	2.86

Table F3 (cont.): Number of items with respect to treatment category, generic indicator and age group according to pharmacological group for the year 2007

Pharmacological group	Treatment category	Generic indicator	Age group	Number of items	Average cost (R)	Total cost (R)	Prevalence %	Cost %	CPI
	TC3	O	3	85	195.68 ± 76.68	1 6633.15	3.62	7.72	2.13
	TC3	Y	2	56	71.69 ± 1.06	4 014.64	2.38	1.86	0.78
	TC3	Y	3	915	50.49 ± 26.95	46 194.99	38.92	21.43	0.55
				2 351		215 557.60			
Calcium channel blockers	TC1	N	1	6	254.74 ± 35.23	1 528.46	0.00	0.01	1.78
	TC1	N	2	1 400	228.44 ± 75.67	319 813.77	0.74	1.18	1.60
	TC1	N	3	16 040	227.94 ± 65.72	3 656 233.55	8.51	13.55	1.59
	TC1	O	1	63	169.29 ± 42.40	10 665.04	0.03	0.04	1.18
	TC1	O	2	2 021	151.63 ± 48.16	306 440.31	1.07	1.14	1.06
	TC1	O	3	27 010	156.64 ± 43.24	4 230 940.66	14.33	15.68	1.09
	TC1	Y	1	81	109.48 ± 37.88	8 867.71	0.04	0.03	0.76
	TC1	Y	2	6 152	114.12 ± 30.40	702 041.50	3.26	2.60	0.80
	TC1	Y	3	67 444	114.87 ± 27.89	7 747 047.50	35.79	28.70	0.80
	TC2	N	2	10	280.21 ± 17.36	2 802.14	0.01	0.01	1.96
	TC2	N	3	132	210.40 ± 74.92	27 772.37	0.07	0.10	1.47
	TC2	O	2	9	147.73 ± 19.28	1 329.53	0.00	0.00	1.03
	TC2	O	3	104	163.88 ± 26.61	17 043.01	0.06	0.06	1.14
	TC2	Y	2	22	124.63 ± 22.16	2 741.86	0.01	0.01	0.87
	TC2	Y	3	428	121.89 ± 4.47	52 167.53	0.23	0.19	0.85
	TC3	N	1	2	137.56 ± 0.00	275.12	0.00	0.00	0.96
	TC3	N	2	769	250.32 ± 65.42	192 498.94	0.41	0.71	1.75
	TC3	N	3	10 896	237.07 ± 68.53	2 583 063.27	5.78	9.57	1.66
	TC3	O	1	24	186.62 ± 58.68	4 478.77	0.01	0.02	1.30

Table F3 (cont.): Number of items with respect to treatment category, generic indicator and age group according to pharmacological group for the year 2007

Pharmacological group	Treatment category	Generic indicator	Age group	Number of items	Average cost (R)	Total cost (R)	Prevalence %	Cost %	CPI
	TC3	O	2	776	154.40 ± 44.36	119 815.89	0.41	0.44	1.08
	TC3	O	3	13 235	158.92 ± 44.24	2 103 264.71	7.02	7.79	1.11
	TC3	Y	1	12	278.81 ± 165.82	3 345.73	0.01	0.01	1.95
	TC3	Y	2	3 037	116.12 ± 28.28	352 643.68	1.61	1.31	0.81
	TC3	Y	3	38 787	117.13 ± 27.87	4 543 138.90	20.58	16.83	0.82
				188 460		26 989 959.95			
ACE-inhibitors	TC1	N	1	14	164.28 ± 81.01	2 299.89	0.00	0.00	1.47
	TC1	N	2	3 286	186.97 ± 66.18	614 396.60	0.48	0.80	1.68
	TC1	N	3	28 225	204.29 ± 0.94	5 766 144.47	4.08	7.47	1.83
	TC1	O	1	98	113.62 ± 58.79	11 135.17	0.01	0.01	1.02
	TC1	O	2	6 606	142.87 ± 52.01	943 831.34	0.95	1.22	1.28
	TC1	O	3	68 213	143.10 ± 55.06	9 761 039.53	9.86	12.64	1.28
	TC1	Y	1	277	73.70 ± 47.65	20 415.81	0.04	0.03	0.66
	TC1	Y	2	38 002	100.17 ± 47.13	3 806 519.18	5.49	4.93	0.90
	TC1	Y	3	321 687	99.37 ± 44.28	31 966 971.19	46.50	41.41	0.89
	TC2	N	2	7	150.16 ± 30.51	1 051.10	0.00	0.00	1.35
	TC2	N	3	162	213.08 ± 56.73	34 519.16	0.02	0.04	1.91
	TC2	O	2	18	155.65 ± 42.64	2 801.69	0.00	0.00	1.39
	TC2	O	3	275	140.31 ± 50.14	38 585.27	0.04	0.05	1.26
	TC2	Y	1	6	35.66 ± 5.14	213.97	0.00	0.00	0.32
	TC2	Y	2	107	89.46 ± 51.96	9 571.98	0.02	0.01	0.80
	TC2	Y	3	1 572	106.20 ± 48.05	166 944.44	0.23	0.22	0.95
	TC3	N	1	1	243.71 ±	243.71	0.00	0.00	2.18
	TC3	N	2	983	10.15 ± 69.19	206 575.43	0.14	0.27	1.88

Table F3 (cont.): Number of items with respect to treatment category, generic indicator and age group according to pharmacological group for the year 2007

Pharmacological group	Treatment category	Generic indicator	Age group	Number of items	Average cost (R)	Total cost (R)	Prevalence %	Cost %	CPI
	TC3	N	3	15 600	217.00 ± 59.79	3 385 163.59	2.26	4.39	1.94
	TC3	O	1	69	95.44 ± 70.47	6 585.24	0.01	0.01	0.86
	TC3	O	2	1 574	145.42 ± 0.92	228 894.98	0.23	0.30	1.30
	TC3	O	3	23 442	148.79 ± 69.39	3 487 839.90	3.39	4.52	1.33
	TC3	Y	1	121	38.52 ± 35.66	4 661.10	0.02	0.01	0.35
	TC3	Y	2	13 452	86.93 ± 48.52	1 169 422.51	1.94	1.51	0.78
	TC3	Y	3	167 977	92.63 ± 46.70	15 560 285.89	24.28	20.16	0.83
				691 774		77 196 113.14			
	TC1	N	1	33	174.29 ± 54.67	5 751.63	0.01	0.01	0.86
Angiotensin-receptor Blockers	TC1	N	2	13 255	201.21 ± 53.03	2 667 041.05	4.92	4.91	1.00
	TC1	N	3	141 849	203.40 ± 45.47	28 852 032.89	52.67	53.11	1.01
	TC1	O	1	15	187.48 ± 61.34	2 812.21	0.01	0.01	0.93
	TC1	O	2	2 465	196.23 ± 47.03	483 707.36	0.92	0.89	0.97
	TC1	O	3	29 558	203.33 ± 42.08	6 010 172.12	10.98	11.06	1.01
	TC1	Y	1	9	162.93 ± 3.15	1 466.37	0.00	0.00	0.81
	TC1	Y	2	1 373	161.98 ± 33.63	222 398.10	0.51	0.41	0.80
	TC1	Y	3	9 736	167.06 ± 28.94	1 626 539.39	3.62	2.99	0.83
	TC2	N	2	29	208.98 ± 19.10	6 060.43	0.01	0.01	1.04
	TC2	N	3	732	205.68 ± 52.56	150 558.37	0.27	0.28	1.02
	TC2	O	2	4	144.91 ± 59.21	579.63	0.00	0.00	0.72
	TC2	O	3	123	205.69 ± 24.30	25 299.93	0.05	0.05	1.02
	TC2	Y	2	3	146.37 ± 33.46	439.11	0.00	0.00	0.73
	TC2	Y	3	99	170.20 ± 18.55	16 849.67	0.04	0.03	0.84

Table F3 (cont.): Number of items with respect to treatment category, generic indicator and age group according to pharmacological group for the year 2007

Pharmacological group	Treatment category	Generic indicator	Age group	Number of items	Average cost (R)	Total cost (R)	Prevalence %	Cost %	CPI
	TC3	N	1	11	135.37 ± 61.15	1 489.08	0.00	0.00	0.67
	TC3	N	2	2 430	203.14 ± 40.96	493 629.98	0.90	0.91	1.01
	TC3	N	3	51 601	206.67 ± 46.17	10 664 408.17	19.16	19.63	1.02
	TC3	O	1	5	108.09 ± 0.00	540.45	0.00	0.00	0.54
	TC3	O	2	466	201.44 ± 37.00	93 869.72	0.17	0.17	1.00
	TC3	O	3	10 813	204.41 ± 43.53	2 210 280.72	4.02	4.07	1.01
	TC3	Y	1	1	161.88 ± 0.00	161.88	0.00	0.00	0.80
	TC3	Y	2	247	165.09 ± 36.91	40 777.74	0.09	0.08	0.82
	TC3	Y	3	4 452	167.00 ± 31.08	743 502.34	1.65	1.37	0.83
				269 309		54 320 368.34			
Other	TC1	N	1	3	255.08 ± 26.88	765.23	0.03	0.04	1.24
	TC1	N	2	582	214.42 ± 63.00	124 790.46	6.79	7.05	1.04
	TC1	N	3	5 435	206.25 ± 55.88	1 120 992.34	63.37	63.34	1.00
	TC2	N	2	6	302.85 ± 0.00	1 817.10	0.07	0.10	1.47
	TC2	N	3	21	235.61 ± 48.22	4 947.84	0.24	0.28	1.14
	TC3	N	2	121	200.28 ± 29.36	24 234.14	1.41	1.37	0.97
	TC3	N	3	2 409	204.36 ± 59.76	492 297.80	28.09	27.82	0.99
				8 577		1 769 844.91			
Diuretics	TC1	N	2	21	61.25 ± 29.76	1 286.30	0.00	0.01	1.39
	TC1	N	3	380	113.07 ± 119.50	42 967.64	0.08	0.20	2.56
	TC1	O	2	17	233.53 ± 102.28	3 970.07	0.00	0.02	5.29
	TC1	O	3	543	147.53 ± 76.50	80 108.77	0.11	0.38	3.34
	TC1	Y	1	13	71.97 ± 58.94	935.60	0.00	0.00	1.63
	TC1	Y	2	101	17.84 ± 10.11	1 802.07	0.02	0.01	0.40

Table F3 (cont.): Number of items with respect to treatment category, generic indicator and age group according to pharmacological group for the year 2007

Pharmacological group	Treatment category	Generic indicator	Age group	Number of items	Average cost (R)	Total cost (R)	Prevalence %	Cost %	CPI
	TC1	Y	3	2 203	26.69 ± 24.72	58 795.89	0.46	0.28	0.60
	TC2	N	1	75	112.33 ± 100.85	8 424.87	0.02	0.04	2.54
	TC2	N	2	2 699	67.79 ± 63.02	182 973.91	0.57	0.87	1.54
	TC2	N	3	21 251	85.09 ± 66.44	1 808 341.07	4.46	8.59	1.93
	TC2	O	1	71	96.80 ± 67.89	6 873.02	0.01	0.03	2.19
	TC2	O	2	1 634	100.67 ± 77.29	164 502.10	0.34	0.78	2.28
	TC2	O	3	11 924	126.85 ± 73.03	1 512 554.98	2.50	7.18	2.87
	TC2	Y	1	333	54.72 ± 69.01	18 221.59	0.07	0.09	1.24
	TC2	Y	2	13 285	18.25 ± 30.62	242 444.24	2.79	1.15	0.41
	TC2	Y	3	106 780	21.35 ± 26.03	2 280 055.87	22.39	10.83	0.48
	TC3	N	1	19	129.33 ± 160.64	2 457.25	0.00	0.01	2.93
	TC3	N	2	2 053	118.68 ± 174.08	243 652.57	0.43	1.16	2.69
	TC3	N	3	35 522	103.01 ± 109.20	3 659 187.94	7.45	17.37	2.33
	TC3	O	1	113	129.46 ± 86.86	14 628.76	0.02	0.07	2.93
	TC3	O	2	1 636	139.95 ± 81.59	228 956.09	0.34	1.09	3.17
	TC3	O	3	36 465	136.40 ± 65.36	497 3871.7	7.64	23.62	3.09
	TC3	Y	1	157	19.29 ± 18.04	3 028.68	0.03	0.01	0.44
	TC3	Y	2	16 557	19.09 ± 21.40	316 097.59	3.47	1.50	0.43
	TC3	Y	3	223 132	23.32 ± 22.69	5 204 326.40	46.78	24.71	0.53
				476 984		21 060 464.97			

Table F4: Number of items with respect to treatment category, generic indicator and age group according to pharmacological group for the year 2008

Pharmacological group	Treatment category	Generic indicator	Age group	Number of items	Average cost (R)	Total cost (R)	Prevalence %	Cost %	CPI
Central-acting inhibitors	TC1	N	1	11	202.71 ± 5.54	2 229.77	0.06	0.09	1.63
	TC1	N	2	274	203.50 ± 56.78	55 758.74	1.43	2.34	1.64
	TC1	N	3	2 093	212.51 ± 61.62	444 773.87	10.90	18.67	1.71
	TC1	O	1	6	213.71 ± 6.23	1 282.24	0.03	0.05	1.72
	TC1	O	2	131	205.13 ± 53.63	26 872.52	0.68	1.13	1.65
	TC1	O	3	980	213.29 ± 64.90	209 028.47	5.10	8.77	1.72
	TC1	Y	1	12	78.67 ± 69.13	944.02	0.06	0.04	0.63
	TC1	Y	2	1 690	86.90 ± 68.35	146 859.40	8.80	6.17	0.70
	TC1	Y	3	4 417	80.23 ± 55.45	354 382.79	22.99	14.88	0.65
	TC2	N	3	27	221.99 ± 94.87	5 993.76	0.14	0.25	1.79
	TC2	O	3	16	241.12 ± 56.51	3 857.86	0.08	0.16	1.94
	TC2	Y	2	7	99.06 ± 38.02	693.40	0.04	0.03	0.80
	TC2	Y	3	29	54.50 ± 29.72	1 580.64	0.15	0.07	0.44
	TC3	N	2	109	219.97 ± 56.86	23 976.49	0.57	1.01	1.77
	TC3	N	3	1 914	212.79 ± 53.89	407 273.62	9.96	17.10	1.72
	TC3	O	2	51	235.97 ± 63.64	12 034.60	0.27	0.51	1.90
	TC3	O	3	807	216.16 ± 51.91	174 439.31	4.20	7.32	1.74
	TC3	Y	1	1	17.60 ± 0.00	17.60	0.01	0.00	0.14
	TC3	Y	2	625	85.94 ± 67.03	53 712.23	3.25	2.25	0.69
	TC3	Y	3	6 009	75.95 ± 52.02	456 401.56	31.28	19.16	0.61

Table F4 (cont.): Number of items with respect to treatment category, generic indicator and age group according to pharmacological group for the year 2008

Pharmacological group	Treatment category	Generic indicator	Age group	Number of items	Average cost (R)	Total cost (R)	Prevalence %	Cost %	CPI
				19 209		2 382 112.89			
Alpha-receptor blockers	TC1	N	1	2	175.29 ± 113.71	350.57	0.01	0.01	0.98
	TC1	N	2	439	289.85 ± 98.78	127 242.59	1.24	2.00	1.61
	TC1	N	3	7 634	294.86 ± 84.20	2 250 969.11	21.58	35.43	1.64
	TC1	O	1	4	301.79 ± 83.74	1 207.17	0.01	0.02	1.68
	TC1	O	2	238	195.43 ± 43.12	46 512.41	0.67	0.73	1.09
	TC1	O	3	5 624	199.33 ± 37.98	1 121 047.99	15.90	17.65	1.11
	TC1	Y	1	12	75.81 ± 56.55	909.76	0.03	0.01	0.42
	TC1	Y	2	365	110.13 ± 105.86	40 196.53	1.03	0.63	0.61
	TC1	Y	3	8 838	81.03 ± 53.06	716 121.91	24.99	11.27	0.45
	TC2	N	3	38	313.55 ± 66.73	11 915.06	0.11	0.19	1.75
	TC2	O	2	1	356.38 ± 0.00	356.38	0.00	0.01	1.98
	TC2	O	3	41	215.64 ± 58.13	8 841.36	0.12	0.14	1.20
	TC2	Y	3	78	90.17 ± 47.79	7 033.40	0.22	0.11	0.50
	TC3	N	2	86	311.80 ± 89.51	26 814.64	0.24	0.42	1.74
	TC3	N	3	2 767	291.88 ± 61.89	807 631.85	7.82	12.71	1.63
	TC3	O	2	74	205.12 ± 67.40	15 178.84	0.21	0.24	1.14
	TC3	O	3	3 228	199.47 ± 41.45	643 900.36	9.13	10.14	1.11
	TC3	Y	1	10	226.14 ± 10.18	2 261.39	0.03	0.04	1.26
	TC3	Y	2	200	103.85 ± 88.70	20 769.43	0.57	0.33	0.58
	TC3	Y	3	5 692	88.50 ± 62.79	503 748.61	16.09	7.93	0.49
				35 371		6 353 009.36			

Table F4 (cont.): Number of items with respect to treatment category, generic indicator and age group according to pharmacological group for the year 2008

Pharmacological group	Treatment category	Generic indicator	Age group	Number of items	Average cost (R)	Total cost (R)	Prevalence %	Cost %	CPI
Beta-receptor blockers	TC1	N	1	20	88.82 ± 40.07	1 776.34	0.01	0.01	0.98
	TC1	N	2	5 249	117.98 ± 31.10	619 275.00	2.28	2.98	1.31
	TC1	N	3	54 556	124.71 ± 30.48	6 803 610.85	23.71	32.72	1.38
	TC1	O	1	83	64.72 ± 27.43	5 371.56	0.04	0.03	0.72
	TC1	O	2	1 877	86.63 ± 52.89	162 605.73	0.82	0.78	0.96
	TC1	O	3	24 321	103.02 ± 65.68	2 505 585.93	10.57	12.05	1.14
	TC1	Y	1	68	56.82 ± 45.52	3 863.55	0.03	0.02	0.63
	TC1	Y	2	5 233	59.44 ± 27.49	311 068.73	2.27	1.50	0.66
	TC1	Y	3	75 889	65.80 ± 37.07	4 993 598.55	32.98	24.01	0.73
	TC2	N	3	140	121.98 ± 24.47	17 077.18	0.06	0.08	1.35
	TC2	O	2	2	141.68 ± 0.00	283.36	0.00	0.00	1.57
	TC2	O	3	148	93.68 ± 52.27	13 864.06	0.06	0.07	1.04
	TC2	Y	2	7	64.74 ± 27.16	453.21	0.00	0.00	0.72
	TC2	Y	3	518	67.73 ± 34.22	35 085.45	0.23	0.17	0.75
	TC3	N	1	5	236.35 ± 171.39	1 181.76	0.00	0.01	2.62
	TC3	N	2	602	117.97 ± 43.91	71 020.61	0.26	0.34	1.31
	TC3	N	3	13 031	128.38 ± 42.57	1 672 967.53	5.66	8.04	1.42
	TC3	O	1	10	231.29 ± 51.28	2 312.88	0.00	0.01	2.56
	TC3	O	2	377	91.35 ± 52.12	34 438.66	0.16	0.17	1.01
	TC3	O	3	9 846	105.47 ± 63.90	1 038 438.35	4.28	4.99	1.17
	TC3	Y	1	18	37.42 ± 41.85	673.61	0.01	0.00	0.41
	TC3	Y	2	1 494	64.36 ± 30.31	96 157.95	0.65	0.46	0.71
	TC3	Y	3	36 639	65.66 ± 34.23	2 405 824.28	15.92	11.57	0.73

Table F4 (cont.): Number of items with respect to treatment category, generic indicator and age group according to pharmacological group for the year 2008

Pharmacological group	Treatment category	Generic indicator	Age group	Number of items	Average cost (R)	Total cost (R)	Prevalence %	Cost %	CPI
				230 133		20 796 535.13			
Alpha- and beta-receptor blockers	TC1	N	2	3	466.43 ± 151.31	1 399.28	0.00	0.02	4.26
	TC1	N	3	19	302.61 ± 192.56	5 749.63	0.03	0.07	2.77
	TC1	O	1	1	27.95 ± 0.00	27.95	0.00	0.00	0.26
	TC1	O	2	146	167.63 ± 78.29	24 473.95	0.20	0.31	1.53
	TC1	O	3	2 925	162.73 ± 62.62	475 975.91	4.09	6.09	1.49
	TC1	Y	1	13	43.26 ± 50.18	562.36	0.02	0.01	0.40
	TC1	Y	2	2 243	98.69 ± 37.21	221 370.39	3.14	2.83	0.90
	TC1	Y	3	29 231	100.38 ± 38.16	2 934 333.78	40.90	37.52	0.92
	TC2	O	2	3	134.64 ± 1.15	403.93	0.00	0.01	1.23
	TC2	O	3	51	185.71 ± 66.56	9 471.00	0.07	0.12	1.70
	TC2	Y	2	9	129.00 ± 46.19	1 161.00	0.01	0.01	1.18
	TC2	Y	3	369	108.64 ± 38.26	40 089.14	0.52	0.51	0.99
	TC3	N	2	2	1123.22 ± 0.00	2 246.44	0.00	0.03	10.26
	TC3	N	3	9	258.58 ± 91.01	2 327.23	0.01	0.03	2.36
	TC3	O	1	8	156.32 ± 80.19	1 250.52	0.01	0.02	1.43
	TC3	O	2	174	169.53 ± 73.41	29 497.64	0.24	0.38	1.55
	TC3	O	3	3 555	171.35 ± 65.21	609 140.93	4.97	7.79	1.57
	TC3	Y	1	23	112.73 ± 43.19	2 592.87	0.03	0.03	1.03
	TC3	Y	2	1 164	103.74 ± 43.85	120 753.78	1.63	1.54	0.95
	TC3	Y	3	31 524	105.90 ± 41.05	3 338 525.52	44.11	42.68	0.97
				71 472		7 821 353.25			

Table F4 (cont.): Number of items with respect to treatment category, generic indicator and age group according to pharmacological group for the year 2008

Pharmacological group	Treatment category	Generic indicator	Age group	Number of items	Average cost (R)	Total cost (R)	Prevalence %	Cost %	CPI
Sympathetic nervous blockers	TC1	N	1	3	74.44 ± 103.28	223.33	0.04	0.03	0.74
	TC1	N	2	211	64.27 ± 70.47	13 561.91	2.53	1.62	0.64
	TC1	N	3	4 131	139.55 ± 88.26	576 472.27	49.53	68.86	1.39
	TC2	N	3	14	28.16 ± 10.86	394.30	0.17	0.05	0.28
	TC3	N	1	2	20.65 ± 8.82	41.30	0.02	0.00	0.21
	TC3	N	2	385	37.57 ± 46.62	14 465.31	4.62	1.73	0.37
	TC3	N	3	3 595	64.55 ± 81.54	232 058.95	43.10	27.72	0.64
				8 341		837 217.37			
Direct- acting vasodilators	TC1	N	2	21	289.97 ± 103.83	6 089.27	1.02	3.69	3.63
	TC1	N	3	155	175.47 ± 88.30	27 198.29	7.51	16.50	2.20
	TC1	O	2	2	163.85 ± 110.30	327.69	0.10	0.20	2.05
	TC1	O	3	2	167.98 ± 104.43	335.95	0.10	0.20	2.10
	TC1	Y	2	37	46.88 ± 21.18	1 734.65	1.79	1.05	0.59
	TC1	Y	3	609	49.19 ± 20.87	29 957.35	29.49	18.17	0.62
	TC2	N	3	4	332.77 ± 86.35	1 331.07	0.19	0.81	4.17
	TC2	O	3	1	247.46 ± 0.00	247.46	0.05	0.15	3.10
	TC2	Y	2	1	22.00 ± 0.00	22.00	0.05	0.01	0.28
	TC2	Y	3	10	58.14 ± 26.00	581.43	0.48	0.35	0.73
	TC3	N	2	57	139.22 ± 68.40	7 935.44	2.76	4.81	1.74
	TC3	N	3	231	166.66 ± 113.00	38 499.16	11.19	23.35	2.09
	TC3	O	2	1	464.14 ± 0.00	464.14	0.05	0.28	5.81
	TC3	O	3	1	183.64 ± 0.00	183.64	0.05	0.11	2.30

Table F4 (cont.): Number of items with respect to treatment category, generic indicator and age group according to pharmacological group for the year 2008

Pharmacological group	Treatment category	Generic indicator	Age group	Number of items	Average cost (R)	Total cost (R)	Prevalence %	Cost %	CPI
	TC3	Y	2	72	78.31 ± 38.72	5 638.13	3.49	3.42	0.98
	TC3	Y	3	861	51.49 ± 25.00	44 336.69	41.69	26.89	0.64
				2 065		164 882.36			
Calcium channel blockers	TC1	N	1	2	219.84 ± 88.17	439.67	0.00	0.00	1.68
	TC1	N	2	1 061	241.08 ± 71.52	255 785.56	0.54	0.99	1.84
	TC1	N	3	15 317	233.16 ± 68.44	3 571 337.92	7.75	13.76	1.78
	TC1	O	1	33	169.42 ± 73.04	5 590.99	0.02	0.02	1.29
	TC1	O	2	1 176	154.10 ± 54.79	181 224.48	0.59	0.70	1.17
	TC1	O	3	18 376	155.78 ± 50.63	2 862 624.95	9.29	11.03	1.19
	TC1	Y	1	73	115.83 ± 48.06	8 455.67	0.04	0.03	0.88
	TC1	Y	2	7 451	103.43 ± 32.30	770 632.65	3.77	2.97	0.79
	TC1	Y	3	82 676	104.72 ± 28.18	8 657 889.93	41.81	33.37	0.80
	TC2	N	2	2	266.77 ± 0.00	533.54	0.00	0.00	2.03
	TC2	N	3	107	257.68 ± 51.47	27 572.10	0.05	0.11	1.96
	TC2	O	2	6	100.84 ± 43.51	605.02	0.00	0.00	0.77
	TC2	O	3	57	150.72 ± 31.07	8 591.24	0.03	0.03	1.15
	TC2	Y	2	14	97.71 ± 15.44	1 367.96	0.01	0.01	0.74
	TC2	Y	3	527	109.56 ± 24.43	57 736.16	0.27	0.22	0.83
	TC3	N	2	615	256.70 ± 69.08	157 870.49	0.31	0.61	1.96
	TC3	N	3	10 155	240.19 ± 72.83	2 439 088.93	5.14	9.40	1.83
	TC3	O	1	18	203.41 ± 61.44	3 661.39	0.01	0.01	1.55
	TC3	O	2	390	157.48 ± 43.18	61 418.67	0.20	0.24	1.20
	TC3	O	3	8 860	160.78 ± 51.82	1 424 524.56	4.48	5.49	1.23

Table F4 (cont.): Number of items with respect to treatment category, generic indicator and age group according to pharmacological group for the year 2008

Pharmacological group	Treatment category	Generic indicator	Age group	Number of items	Average cost (R)	Total cost (R)	Prevalence %	Cost %	CPI
	TC3	Y	1	9	185.74 ± 113.49	1 671.67	0.00	0.01	1.42
	TC3	Y	2	3 222	103.42 ± 30.78	333 223.94	1.63	1.28	0.79
	TC3	Y	3	47 578	107.48 ± 28.54	5 113 863.96	24.06	19.71	0.82
				197 725		25 945 711.45			
ACE Inhibitors	TC1	N	1	6	189.71 ± 77.79	1 138.28	0.00	0.00	1.73
	TC1	N	2	2 158	199.96 ± 64.99	431 503.68	0.32	0.59	1.82
	TC1	N	3	23 784	210.44 ± 61.73	5 005 087.67	3.54	6.79	1.92
	TC1	O	1	44	120.01 ± 55.72	5 280.46	0.01	0.01	1.09
	TC1	O	2	3 764	143.34 ± 58.14	539 530.20	0.56	0.73	1.31
	TC1	O	3	46 406	141.55 ± 57.04	6 568 598.27	6.91	8.91	1.29
	TC1	Y	1	188	75.48 ± 50.54	14 189.98	0.03	0.02	0.69
	TC1	Y	2	37 338	102.29 ± 46.66	3 819 217.17	5.56	5.18	0.93
	TC1	Y	3	337 891	101.54 ± 44.43	34 309 135.18	50.32	46.56	0.93
	TC2	N	3	118	216.60 ± 70.50	25 558.26	0.02	0.03	1.97
	TC2	O	2	7	136.70 ± 16.82	956.89	0.00	0.00	1.25
	TC2	O	3	111	140.89 ± 60.99	15 638.69	0.02	0.02	1.28
	TC2	Y	2	80	96.63 ± 56.42	7 730.21	0.01	0.01	0.88
	TC2	Y	3	1 614	106.25 ± 47.89	171 493.19	0.24	0.23	0.97
	TC3	N	1	1	112.37 ± 0.00	112.37	0.00	0.00	1.02
	TC3	N	2	688	212.57 ± 61.43	146 245.44	0.10	0.20	1.94
	TC3	N	3	13 158	223.62 ± 58.23	2 942 452.99	1.96	3.99	2.04
	TC3	O	1	46	71.37 ± 51.01	3 282.79	0.01	0.00	0.65
	TC3	O	2	845	146.02 ± 63.34	123 390.36	0.13	0.17	1.33
	TC3	O	3	16 545	148.87 ± 72.20	2 463 111.27	2.46	3.34	1.36

Table F4 (cont.): Number of items with respect to treatment category, generic indicator and age group according to pharmacological group for the year 2008

Pharmacological group	Treatment category	Generic indicator	Age group	Number of items	Average cost (R)	Total cost (R)	Prevalence %	Cost %	CPI
	TC3	Y	1	146	45.84 ± 27.73	6 692.82	0.02	0.01	0.42
	TC3	Y	2	12 638	86.59 ± 47.61	1 094 366.36	1.88	1.49	0.79
	TC3	Y	3	173 896	91.99 ± 46.69	15 996 608.36	25.90	21.71	0.84
				671 472		73 691 320.89			
Angiotensin-receptor blockers	TC1	N	1	21	156.39 ± 62.23	3 284.18	0.01	0.01	0.87
	TC1	N	2	10 177	185.48 ± 56.49	1 887 594.49	3.82	3.95	1.03
	TC1	N	3	124 061	185.20 ± 55.08	22 975 869.27	46.61	48.10	1.03
	TC1	O	1	3	210.91 ± 0.62	632.73	0.00	0.00	1.18
	TC1	O	2	1 769	163.99 ± 67.69	290 091.79	0.66	0.61	0.91
	TC1	O	3	23 714	180.40 ± 58.36	4 277 904.68	8.91	8.96	1.01
	TC1	Y	1	3	140.64 ± 36.79	421.91	0.00	0.00	0.78
	TC1	Y	2	3 453	148.02 ± 46.30	511 107.09	1.30	1.07	0.82
	TC1	Y	3	29 898	155.98 ± 39.84	4 663 365.71	11.23	9.76	0.87
	TC2	N	2	30	187.16 ± 21.84	5 614.73	0.01	0.01	1.04
	TC2	N	3	459	192.75 ± 54.80	88 471.46	0.17	0.19	1.07
	TC2	O	3	76	149.63 ± 56.37	11 371.50	0.03	0.02	0.83
	TC2	Y	2	1	90.74 ± 0.00	90.74	0.00	0.00	0.51
	TC2	Y	3	181	146.06 ± 41.85	26 436.02	0.07	0.06	0.81
	TC3	N	1	8	143.83 ± 69.44	1 150.66	0.00	0.00	0.80
	TC3	N	2	1 855	191.71 ± 63.56	355 620.90	0.70	0.74	1.07
	TC3	N	3	43 704	192.21 ± 52.72	8 400 362.09	16.42	17.59	1.07
	TC3	O	1	9	53.01 ± 0.00	477.09	0.00	0.00	0.30
	TC3	O	2	348	159.65 ± 58.78	55 559.00	0.13	0.12	0.89

Table F4 (cont.): Number of items with respect to treatment category, generic indicator and age group according to pharmacological group for the year 2008

Pharmacological group	Treatment category	Generic indicator	Age group	Number of items	Average cost (R)	Total cost (R)	Prevalence %	Cost %	CPI
	TC3	O	3	10 593	173.43± 60.25	1 837 176.97	3.98	3.85	0.97
	TC3	Y	1	1	161.88 ± 0.00	161.88	0.00	0.00	0.90
	TC3	Y	2	928	140.80 ± 46.98	130 663.50	0.35	0.27	0.78
	TC3	Y	3	14 898	150.71 ±45.08	2 245 234.96	5.60	4.70	0.84
				266 190		47 768 663.35			
Other	TC1	N	1	2	181.02 ± 66.67	362.03	0.02	0.02	0.85
	TC1	N	2	446	222.02 ± 69.10	99 021.87	5.37	5.58	1.04
	TC1	N	3	5 414	214.10 ± 55.15	1 159 164.15	65.15	65.28	1.00
	TC2	N	3	28	253.14 ± 77.59	7 087.98	0.34	0.40	1.18
	TC3	N	2	117	223.76 ± 54.19	26 179.89	1.41	1.47	1.05
	TC3	N	3	2 303	210.06 ± 58.97	483 777.47	27.71	27.25	0.98
				8 310		1 775 593.39			
Diuretics	TC1	N	2	13	144.46 ± 219.71	1 878.04	0.00	0.01	3.35
	TC1	N	3	320	159.05 ± 256.59	50 897.26	0.07	0.26	3.69
	TC1	O	2	23	140.41 ± 44.80	3 229.42	0.00	0.02	3.26
	TC1	O	3	394	144.92 ± 58.11	57 096.60	0.09	0.29	3.36
	TC1	Y	2	127	29.99 ± 24.35	3 808.87	0.03	0.02	0.70
	TC1	Y	3	2 042	27.59 ± 33.82	56 347.47	0.44	0.28	0.64
	TC2	N	1	40	86.92 ± 78.92	3 476.83	0.01	0.02	2.02
	TC2	N	2	1 917	67.56 ± 84.03	129 508.54	0.42	0.65	1.57
	TC2	N	3	18 343	87.39 ± 84.66	1 603 069.21	3.99	8.08	2.03
	TC2	O	1	63	102.55 ± 61.46	6 460.58	0.01	0.03	2.38
	TC2	O	2	966	95.64 ± 72.38	92 390.00	0.21	0.47	2.22
	TC2	O	3	9 432	125.08 ± 74.39	1 179 795.91	2.05	5.95	2.90

Table F4 (cont.): Number of items with respect to treatment category, generic indicator and age group according to pharmacological group for the year 2008

Pharmacological group	Treatment category	Generic indicator	Age group	Number of items	Average cost (R)	Total cost (R)	Prevalence %	Cost %	CPI
	TC2	Y	1	284	72.40 ± 94.02	20 561.08	0.06	0.10	1.68
	TC2	Y	2	11 874	22.51± 33.51	267 263.58	2.58	1.35	0.52
	TC2	Y	3	104 192	22.64 ±25.33	2 359 074.78	22.64	11.90	0.53
	TC3	N	1	10	149.34 ±72.27	1 493.43	0.00	0.01	3.47
	TC3	N	2	1 619	116.98 ± 179.37	189 382.80	0.35	0.96	2.71
	TC3	N	3	32 551	106.74 ± 120.69	3 474 399.91	7.07	17.52	2.48
	TC3	O	1	64	201.05 ± 97.12	12 867.00	0.01	0.06	4.67
	TC3	O	2	1 063	153.39 ± 116.41	163 057.52	0.23	0.82	3.56
	TC3	O	3	30 629	138.15 ± 67.23	4 231 300.26	6.66	21.34	3.21
	TC3	Y	1	246	32.38 ± 38.72	7 965.97	0.05	0.04	0.75
	TC3	Y	2	15 004	21.41 ± 24.22	321 242.94	3.26	1.62	0.50
	TC3	Y	3	228 934	24.42 ± 23.31	5 591 671.14	49.75	28.20	0.57
				460 150		19 828 239.14			

APPENDIX G

Table G1: Number of antihypertensive medicine items according to gender and pharmacological classification

Year	Pharmacological group	Gender	Number of items	Average cost (R)	Total cost (R)	Prevalence %	Cost %	CPI
2005	Central acting inhibitors	F	16 501	98.92 ± 78.14	1 632 306.45	70.99	69.18	0.97
		M	6 742	107.84 ± 76.80	727 082.40	29.01	30.82	1.06
	Alpha-receptor blockers	F	9 580	144.33 ± 80.70	1 382 636.42	24.84	20.50	0.83
		M	28 990	184.97 ± 94.14	5 362 241.90	75.16	79.50	1.06
	Beta-receptor blockers	F	143 744	98.63 ± 49.45	14 177 380.41	61.29	61.74	1.01
		M	90 657	96.77 ± 49.08	8 773 325.78	38.65	38.21	0.99
		U	137	95.03 ± 63.79	13 018.94	0.06	0.06	0.97
	Alpha- and Beta-receptor blockers	F	26 543	116.58 ± 53.61	3 094 293.49	47.23	46.61	0.99
		M	29 645	119.54 ± 57.00	3 543 802.67	52.75	53.38	1.01
		U	8	69.35 ± 0.00	554.80	0.01	0.01	0.59
	Sympathetic nervous blockers	F	11 300	101.80 ± 80.55	1 150 371.06	62.10	68.45	1.10
		M	6 883	76.99 ± 75.53	529 950.22	37.83	31.53	0.83
		U	12	17.66 ± 1.01	211.94	0.07	0.01	0.19
	Direct acting vasodilators	F	1 158	78.61 ± 68.16	91 029.51	49.51	43.55	0.88
		M	1 181	99.92 ± 98.95	118 001.75	50.49	56.45	1.12
	Calcium channel blockers	F	72 782	155.60 ± 56.02	11 324 903.95	55.20	54.21	0.98
		M	59 021	161.94 ± 58.73	9 558 098.25	44.76	45.75	1.02

Table G1 (cont.): Number of antihypertensive medicine items according to gender and pharmacological classification

Year	Pharmacological group	Gender	Number of items	Average cost (R)	Total cost (R)	Prevalence %	Cost %	CPI
	ACE-inhibitors	U	53	183.34 ± 53.54	9 716.91	0.04	0.05	1.16
		F	343 175	113.38 ± 64.44	38 907 929.69	52.84	52.43	0.99
		M	305 872	115.32 ± 66.32	35 272 369.17	47.10	47.53	1.01
		U	391	81.23 ± 54.67	31 759.79	0.06	0.04	0.71
	Angiotensin receptor blockers	F	143 563	208.70 ± 31.59	29 961 525.64	56.26	56.12	1.00
		M	111 539	209.84 ± 31.22	23 405 745.69	43.71	43.84	1.00
		U	97	197.91 ± 14.63	19 197.37	0.04	0.04	0.95
	Other	F	2 367	161.37 ± 29.20	381 963.61	59.41	59.68	1.00
		M	1 617	159.58 ± 17.94	258 041.24	40.59	40.32	0.99
	Diuretics	F	344 265	42.13 ± 53.07	14 502 530.28	65.58	63.30	0.97
		M	180 322	46.56 ± 64.58	8 395 297.59	34.35	36.64	1.07
		U	351	37.63 ± 93.22	13 208.45	0.07	0.06	0.86
2006	Central acting inhibitors	F	16 958	102.37 ± 78.93	1 736 015.32	70.41	68.55	0.97
		M	7 126	111.73 ± 78.08	796 184.45	29.59	31.44	1.06
		U	1	190.36 ± 0.00	190.36	0.00	0.01	1.81
	Alpha-receptor blockers	F	9 859	139.64 ± 81.21	1 376 736.35	23.80	19.34	0.81
		M	31 572	181.83 ± 96.94	5 740 733.95	76.20	80.66	1.06
		U	1	33.55 ± 0.00	33.55	0.00	0.00	0.20
	Beta-receptor blockers	F	155 120	91.53 ± 47.00	14 197 979.08	60.54	61.31	1.01
		M	100 980	88.61 ± 47.88	8 947 647.00	39.41	38.64	0.98
		U	120	93.54 ± 68.11	11 225.11	0.05	0.05	1.04
	Alpha- and Beta-receptor blockers	F	32 019	107.20 ± 49.51	3 432 330.54	48.01	47.01	0.98
		M	34 647	111.62 ± 53.24	3 867 231.61	51.95	52.97	1.02
		U	23	70.79 ± 15.50	1 628.10	0.03	0.02	0.65

Table G1 (cont.): Number of antihypertensive medicine items according to gender and pharmacological classification

Year	Pharmacological group	Gender	Number of items	Average cost (R)	Total cost (R)	Prevalence %	Cost %	CPI
	Sympathetic nervous blockers	F	9 429	96.68 ± 82.12	911 577.95	58.77	66.87	1.14
		M	6 612	68.29 ± 70.54	451 550.88	41.21	33.13	0.80
		U	2	17.37 ± 0.00	34.74	0.01	0.00	0.20
	Direct acting vasodilators	F	1 296	77.28 ± 77.35	100 150.78	48.30	42.39	0.88
		M	1 387	98.15 ± 94.03	136 129.67	51.70	57.61	1.11
	Calcium channel blockers	F	92 688	141.62 ± 53.38	13 126 453.26	55.18	54.10	0.98
		M	75 255	147.89 ± 56.41	11 129 386.96	44.80	45.87	1.02
		U	46	172.37 ± 54.81	7 928.99	0.03	0.03	1.19
	ACE-inhibitors	F	385 027	105.90 ± 58.26	40 774 661.98	52.18	51.74	0.99
		M	352 530	107.81 ± 60.43	3 8007 111.51	47.78	48.23	1.01
		U	318	93.41 ± 45.89	29 704.11	0.04	0.04	0.87
	Angiotensin receptor blockers	F	152 051	208.85 ± 35.01	31 756 308.83	56.61	56.48	1.00
	Angiotensin receptor blockers	M	116 498	209.91 ± 33.90	24 454 483.41	43.37	43.49	1.00
		U	68	205.11 ± 10.69	13 947.61	0.03	0.02	0.98
	Other	F	2 986	177.37 ± 46.69	529 637.17	55.55	54.54	0.98
		M	2 389	184.76 ± 49.74	441 390.81	44.45	45.46	1.02
	Diuretics	F	359 742	40.64 ± 52.87	14 619 161.13	64.96	62.56	0.96
		M	193 777	45.09 ± 63.70	8 738 225.43	34.99	37.39	1.07
		U	252	45.46 ± 64.11	11 457.03	0.05	0.05	1.08
2007	Central acting inhibitors	F	14 172	113.92 ± 83.22	1 614 517.02	71.03	67.74	0.95
		M	5 779	133.04 ± 82.74	768 852.70	28.97	32.26	1.11
	Alpha-receptor blockers	F	9 014	148.17 ± 88.61	1 335 626.42	23.84	19.54	0.82
		M	28 790	191.03 ± 106.45	5 499 831.81	76.16	80.46	1.06

Table G1 (cont.): Number of antihypertensive medicine items according to gender and pharmacological classification

Year	Pharmacological group	Gender	Number of items	Average cost (R)	Total cost (R)	Prevalence %	Cost %	CPI
	Beta-receptor blockers	F	149 231	92.18 ± 48.38	13 756 249.93	59.98	61.47	1.02
		M	99 577	86.59 ± 49.37	8 622 351.12	40.02	38.53	0.96
		U	10	118.84 ± 21.29	1 188.39	0.00	0.01	1.32
	Alpha- and Beta-receptor blockers	F	33 904	107.82 ± 46.80	3 655 384.72	48.52	47.57	0.98
		M	35 976	111.98 ± 52.50	4 028 691.08	51.48	52.43	1.02
	Sympathetic nervous blockers	F	5 751	121.04 ± 90.49	696 086.36	64.89	68.45	1.05
		M	3 112	103.09 ± 88.52	320 803.88	35.11	31.55	0.90
	Direct acting vasodilators	F	1 251	80.98 ± 82.48	101 308.37	53.21	47.00	0.88
		M	1 100	103.86 ± 93.90	114 249.23	46.79	53.00	1.13
	Calcium channel blockers	F	104 199	141.00 ± 56.66	14 692 082.69	55.29	54.44	0.98
		M	84 261	145.95 ± 59.61	12 297 877.26	44.71	45.56	1.02
	ACE-inhibitors	F	362 345	110.66 ± 56.77	40 095 837.37	52.38	51.94	0.99
		M	329 408	112.62 ± 59.13	37 097 967.45	47.62	48.06	1.01
		U	21	109.92 ± 51.26	2 308.32	0.00	0.00	0.99
	Angiotensin receptor blockers	F	152 816	202.25 ± 44.34	30 907 275.01	56.74	56.90	1.00
		M	116 482	200.98 ± 47.37	23 410 843.76	43.25	43.10	1.00
		U	11	204.51 ± 8.23	2 249.57	0.00	0.00	1.01
	Others	F	4 308	203.40 ± 53.69	876 256.34	50.23	49.51	0.99
		M	4 269	209.32 ± 60.58	893 588.57	49.77	50.49	1.01
	Diuretics	F	315 432	42.02 ± 55.82	13 255 975.56	66.13	62.94	0.95
		M	161 536	48.31 ± 71.70	7 803 638.06	33.87	37.05	1.09
		U	16	53.21 ± 34.79	851.35	0.00	0.00	1.21
2008	Central acting inhibitors	F	13 215	120.01 ± 85.25	1 585 920.46	68.80	66.58	0.97
		M	5 994	132.83 ± 84.23	796 192.43	31.20	33.42	1.07

Table G1 (cont.): Number of antihypertensive medicine items according to gender and pharmacological classification

Year	Pharmacological group	Gender	Number of items	Average cost (R)	Total cost (R)	Prevalence %	Cost %	CPI
	Alpha-receptor blockers	F	8 275	147.94 ± 89.53	1 224 198.25	23.39	19.27	0.82
		M	27 096	189.28 ± 112.80	5 128 811.11	76.61	80.73	1.05
	Beta-receptor blockers	F	136 084	93.43 ± 48.88	12 714 855.52	59.13	61.14	1.03
		M	94 049	85.93 ± 49.07	8 081 679.61	40.87	38.86	0.95
	Alpha- and Beta-receptor blockers	F	34 891	107.63 ± 45.47	3 755 254.02	48.82	48.01	0.98
		M	36 581	111.15 ± 49.22	4 066 099.23	51.18	51.99	1.02
	Sympathetic nervous blockers	F	5 072	109.19 ± 94.63	553 819.66	60.81	66.15	1.09
		M	3 269	86.69 ± 86.38	283 397.71	39.19	33.85	0.86
	Direct acting vasodilators	F	1 045	63.63 ± 51.17	66 489.54	50.61	40.33	0.80
		M	1 020	96.46 ± 90.64	98 392.82	49.39	59.67	1.21
	Calcium channel blockers	F	108 177	129.74 ± 60.02	14 034 807.6	54.71	54.09	0.99
		M	89 548	133.01 ± 62.74	11 910 903.85	45.29	45.91	1.01
	ACE-inhibitors	F	345 868	109.49 ± 56.01	37 870 247.68	51.51	51.39	1.00
		M	325 604	110.01 ± 57.59	35 821 073.21	48.49	48.61	1.00
	Angiotensin receptor blockers	F	151 705	180.35 ± 53.34	27 360 407.14	56.99	57.28	1.01
		M	114 485	178.26 ± 56.90	20 408 256.21	43.01	42.72	0.99
	Others	F	4 079	209.74 ± 56.96	855 537.37	49.09	48.18	0.98
		M	4 231	217.46 ± 57.25	920 056.02	50.91	51.82	1.02
	Diuretics	F	297 690	41.49 ± 56.52	12 350 657.39	64.69	62.29	0.96
		M	162 460	46.03 ± 72.39	7 477 581.75	35.31	37.71	1.07

APPENDIX H

Table H1: Number of items with respect to treatment category, generic indicator and gender according to pharmacological group for the year 2005

Pharmacological group	Treatment category	Generic indicator	Gender	Number of items	Average cost (R)	Total cost (R)	Prevalence %	Cost %	CPI
Central acting inhibitors	TC1	N	F	1 864	204.65 ± 53.32	381 469.55	8.02	16.17	2.02
	TC1	N	M	1 158	203.28 ± 32.40	235 402.55	4.98	9.98	2.00
	TC1	O	F	326	196.14 ± 110.78	63 940.16	1.40	2.71	1.93
	TC1	O	M	91	164.60 ± 86.36	14 979.05	0.39	0.63	1.62
	TC1	Y	F	5 885	68.82 ± 51.26	404 988.36	25.32	17.16	0.68
	TC1	Y	M	2 089	61.75 ± 47.41	128 993.77	8.99	5.47	0.61
	TC2	N	F	9	227.15 ± 118.30	2 044.36	0.04	0.09	2.24
	TC2	O	F	4	305.62 ± 159.33	1 222.47	0.02	0.05	3.01
	TC2	Y	F	39	52.80 ± 41.88	2 059.12	0.17	0.09	0.52
	TC2	Y	M	23	60.75 ± 28.17	1 397.27	0.10	0.06	0.60
	TC3	N	F	1 457	208.94 ± 52.72	304 431.62	6.27	12.90	2.06
	TC3	N	M	863	202.44 ± 31.31	174 704.29	3.71	7.40	1.99
	TC3	O	F	250	169.74 ± 90.34	42 435.62	1.08	1.80	1.67
	TC3	O	M	41	151.69 ± 104.28	6 219.13	0.18	0.26	1.49
	TC3	Y	F	6 667	64.45 ± 44.52	429 715.19	28.68	18.21	0.63
	TC3	Y	M	2 477	66.77 ± 42.98	165 386.34	10.66	7.01	0.66
Alpha-receptor blockers	TC1	N	F	1 885	204.90 ± 46.21	386 243.05	4.89	5.73	1.17

Table H1 (cont.): Number of items with respect to treatment category, generic indicator and gender according to pharmacological group for the year 2005

Pharmacological group	Treatment category	Generic indicator	Gender	Number of items	Average cost (R)	Total cost (R)	Prevalence %	Cost %	CPI
	TC1	N	M	12 625	238.55 ± 74.72	3 011 712.14	32.73	44.65	1.36
	TC1	O	F	662	191.65 ± 49.46	126 871.82	1.72	1.88	1.10
	TC1	O	M	2 280	189.83 ± 36.88	432 815.34	5.91	6.42	1.09
	TC1	Y	F	2 648	90.04 ± 60.39	238 438.45	6.87	3.54	0.51
	TC1	Y	M	5 916	79.58 ± 51.27	470 791.47	15.34	6.98	0.46
	TC2	N	F	8	198.71 ± 38.94	1 589.66	0.02	0.02	1.14
	TC2	N	M	92	247.60 ± 83.82	22 779.47	0.24	0.34	1.42
	TC2	O	F	6	184.04 ± 1.40	1 104.22	0.02	0.02	1.05
	TC2	O	M	17	193.74 ± 16.36	3 293.66	0.04	0.05	1.11
	TC2	Y	F	13	61.05 ± 32.52	793.68	0.03	0.01	0.35
	TC2	Y	M	27	83.57 ± 60.00	2 256.38	0.07	0.03	0.48
	TC3	N	F	1 474	210.76 ± 62.63	310 656.36	3.82	4.61	1.21
	TC3	N	M	4 305	231.04 ± 64.67	994 645.22	11.16	14.75	1.32
	TC3	O	F	549	195.53 ± 52.56	107 344.47	1.42	1.59	1.12
	TC3	O	M	895	193.16 ± 44.09	172 881.84	2.32	2.56	1.10
	TC3	Y	F	2 335	89.76 ± 60.51	209 594.71	6.05	3.11	0.51
	TC3	Y	M	2 833	88.62 ± 56.83	251 066.38	7.35	3.72	0.51
Beta-receptor blockers	TC1	N	F	45 975	119.33 ± 28.04	5 485 985.25	19.60	23.89	1.22
	TC1	N	M	30 494	120.67 ± 34.78	3 679 833.92	13.00	16.02	1.23
	TC1	N	U	38	163.12 ± 70.84	6 198.69	0.02	0.03	1.67
	TC1	O	F	20 385	108.36 ± 64.44	2 208 962.66	8.69	9.62	1.11
	TC1	O	M	19 539	96.86 ± 58.11	1 892 640.08	8.33	8.24	0.99
	TC1	O	U	21	78.99 ± 13.71	1 658.73	0.01	0.01	0.81
	TC1	Y	M	23 959	69.09 ± 37.10	1 655 320.19	10.22	7.21	0.71

Table H1 (cont.): Number of items with respect to treatment category, generic indicator and gender according to pharmacological group for the year 2005

Pharmacological group	Treatment category	Generic indicator	Gender	Number of items	Average cost (R)	Total cost (R)	Prevalence %	Cost %	CPI
	TC1	Y	U	46	60.57 ± 40.95	2 786.16	0.02	0.01	0.62
	TC2	N	F	164	128.61 ± 46.01	21 091.66	0.07	0.09	1.31
	TC2	N	M	79	131.63 ± 39.47	10 398.39	0.03	0.05	1.34
	TC2	O	F	114	101.12 ± 64.05	11 528.08	0.05	0.05	1.03
	TC2	O	M	69	89.05 ± 31.67	6 144.45	0.03	0.03	0.91
	TC2	Y	F	129	73.71 ± 42.01	9 508.43	0.06	0.04	0.75
	TC2	Y	M	71	68.65 ± 30.87	4 874.48	0.03	0.02	0.70
	TC3	N	F	12 789	125.48 ± 46.38	1 604 810.80	5.45	6.99	1.28
	TC3	N	M	5 086	121.05 ± 47.88	615 654.60	2.17	2.68	1.24
	TC3	N	U	4	126.37 ± 6.55	505.46	0.00	0.00	1.29
	TC3	O	F	10 488	102.59 ± 60.31	1 076 008.79	4.47	4.69	1.05
	TC3	O	M	5 334	99.67 ± 58.26	531 665.52	2.27	2.32	1.02
	TC3	O	U	8	93.02 ± 35.51	744.17	0.00	0.00	0.95
	TC3	Y	F	14 001	65.26 ± 40.40	913 721.37	5.97	3.98	0.67
	TC3	Y	M	6 026	62.53 ± 32.87	376 794.15	2.57	1.64	0.64
	TC3	Y	U	20	56.29 ± 22.12	1 125.73	0.01	0.00	0.57
Alpha- and Beta-receptor blockers	TC1	N	F	568	163.11 ± 76.83	92 644.22	1.01	1.40	1.38
	TC1	N	M	884	169.13 ± 82.42	149 511.15	1.57	2.25	1.43
	TC1	O	F	2 840	148.80 ± 51.27	422 597.27	5.05	6.37	1.26
	TC1	O	M	3 372	154.25 ± 54.98	520 135.50	6.00	7.83	1.31
	TC1	Y	F	7 733	95.55 ± 36.82	738 878.98	13.76	11.13	0.81
	TC1	Y	M	10 051	98.50 ± 40.57	989 978.05	17.89	14.91	0.83
	TC2	N	F	13	208.23 ± 44.91	2 707.02	0.02	0.04	1.76

Table H1 (cont.): Number of items with respect to treatment category, generic indicator and gender according to pharmacological group for the year 2005

Pharmacological group	Treatment category	Generic indicator	Gender	Number of items	Average cost (R)	Total cost (R)	Prevalence %	Cost %	CPI
	TC2	N	M	13	150.00 ± 46.50	1 950.01	0.02	0.03	1.27
	TC2	O	F	39	167.36 ± 48.44	6 527.02	0.07	0.10	1.42
	TC2	O	M	35	140.87 ± 45.68	4 930.29	0.06	0.07	1.19
	TC2	Y	F	102	120.25 ± 53.70	12 265.52	0.18	0.18	1.02
	TC2	Y	M	163	93.88 ± 38.24	15 301.88	0.29	0.23	0.79
	TC3	N	F	1 170	165.78 ± 58.20	193 960.54	2.08	2.92	1.40
	TC3	N	M	1 279	171.59 ± 64.44	219 467.97	2.28	3.31	1.45
	TC3	O	F	3 849	159.05 ± 57.39	612 193.77	6.85	9.22	1.35
	TC3	O	M	3 333	170.37 ± 58.35	567 843.22	5.93	8.55	1.44
	TC3	Y	F	10 229	98.99 ± 41.01	1 012 519.15	18.20	15.25	0.84
	TC3	Y	M	10 515	102.20 ± 44.19	1 074 684.60	18.71	16.19	0.87
	TC3	Y	U	8	69.35 ± 0.00	554.80	0.01	0.01	0.59
Sympathetic nervous blockers	TC1	N	F	6 023	127.05 ± 75.21	765 226.71	33.10	45.53	1.38
	TC1	N	M	3 299	113.32 ± 78.80	373 851.52	18.13	22.25	1.23
	TC2	N	F	50	84.29 ± 81.11	4 214.46	0.27	0.25	0.91
	TC2	N	M	26	57.59 ± 98.58	1 497.25	0.14	0.09	0.62
	TC3	N	F	5 227	72.88 ± 76.63	380 929.89	28.73	22.67	0.79
	TC3	N	M	3 558	43.45 ± 53.46	154 601.45	19.55	9.20	0.47
	TC3	N	U	12	17.66 ± 1.01	211.94	0.07	0.01	0.19
Direct-acting vasodilators	TC1	N	F	56	122.13 ± 71.93	6 839.18	2.39	3.27	1.37
	TC1	N	M	121	182.66 ± 84.40	22 102.40	5.17	10.57	2.04
	TC1	O	F	54	209.58 ± 62.59	11 317.34	2.31	5.41	2.35
	TC1	O	M	30	130.09 ± 45.69	3 902.84	1.28	1.87	1.46

Table H1 (cont.): Number of items with respect to treatment category, generic indicator and gender according to pharmacological group for the year 2005

Pharmacological group	Treatment category	Generic indicator	Gender	Number of items	Average cost (R)	Total cost (R)	Prevalence %	Cost %	CPI
	TC1	Y	F	329	43.58 ± 15.21	14 337.02	14.07	6.86	0.49
	TC1	Y	M	367	38.75 ± 15.71	14 221.04	15.69	6.80	0.43
	TC2	O	F	7	306.92 ± 0.00	2 148.46	0.30	1.03	3.43
	TC2	Y	F	1	62.83 ± 0.00	62.83	0.04	0.03	0.70
	TC3	N	F	107	114.54 ± 44.64	12 255.96	4.57	5.86	1.28
	TC3	N	M	268	196.04 ± 123.87	52 539.27	11.46	25.13	2.19
	TC3	O	F	101	197.41 ± 71.66	19 938.83	4.32	9.54	2.21
	TC3	O	M	37	202.46 ± 69.66	7 490.89	1.58	3.58	2.27
	TC3	Y	F	503	47.97 ± 22.12	24 129.89	21.50	11.54	0.54
	TC3	Y	M	358	49.57 ± 27.71	17 745.31	15.31	8.49	0.55
Calcium channel blockers	TC1	N	F	7 348	221.26 ± 54.20	1 625 829.26	5.57	7.78	1.40
	TC1	N	M	6 594	238.66 ± 56.68	1 573 693.52	5.00	7.53	1.51
	TC1	O	F	22 306	156.61 ± 39.77	3 493 334.56	16.92	16.72	0.99
	TC1	O	M	20 974	162.87 ± 40.96	3 415 943.21	15.91	16.35	1.03
	TC1	O	U	39	171.50 ± 44.45	6 688.60	0.03	0.03	1.08
	TC1	Y	F	12 796	111.30 ± 25.26	1 424 236.21	9.70	6.82	0.70
	TC1	Y	M	13 209	115.76 ± 25.20	1 529 099.16	10.02	7.32	0.73
	TC1	Y	U	3	112.87 ± 11.01	338.62	0.00	0.00	0.71
	TC2	N	F	97	239.55 ± 108.52	23 236.68	0.07	0.11	1.51
	TC2	N	M	19	238.63 ± 38.41	4 533.98	0.01	0.02	1.51
	TC2	O	F	163	163.92 ± 47.66	26 719.69	0.12	0.13	1.03
	TC2	O	M	54	199.45 ± 45.44	10 770.05	0.04	0.05	1.26
	TC2	Y	F	79	119.45 ± 34.48	9 436.36	0.06	0.05	0.75
	TC2	Y	M	79	119.78 ± 23.17	9 462.59	0.06	0.05	0.76

Table H1 (cont.): Number of items with respect to treatment category, generic indicator and gender according to pharmacological group for the year 2005

Pharmacological group	Treatment category	Generic indicator	Gender	Number of items	Average cost (R)	Total cost (R)	Prevalence %	Cost %	CPI
	TC3	N	F	5 888	230.85 ± 59.98	1 359 260.69	4.47	6.51	1.46
	TC3	N	M	3 663	248.19 ± 58.63	909 118.13	2.78	4.35	1.57
	TC3	N	U	10	255.05 ± 0.00	2 550.50	0.01	0.01	1.61
	TC3	O	F	14 032	158.56 ± 42.35	2 224 871.53	10.64	10.65	1.00
	TC3	O	M	8 540	165.78 ± 42.28	1 415 775.60	6.48	6.78	1.05
	TC3	Y	F	10 073	12.97 ± 24.44	1 137 978.97	7.64	5.45	0.71
	TC3	Y	M	5 889	117.12 ± 26.98	689 702.01	4.47	3.30	0.74
	TC3	Y	U	1	139.19 ± 0.00	139.19	0.00	0.00	0.88
ACE inhibitors	TC1	N	F	57 673	180.17 ± 42.45	10 390 703.36	8.88	14.00	1.58
	TC1	N	M	53 063	187.50 ± 43.64	9 949 295.39	8.17	13.41	1.64
	TC1	N	U	38	175.01 ± 21.46	6 650.54	0.01	0.01	1.53
	TC1	O	F	39 921	137.66 ± 54.37	5 495 377.84	6.15	7.40	1.20
	TC1	O	M	39 772	144.01 ± 58.12	5 727 647.35	6.12	7.72	1.26
	TC1	O	U	43	117.43 ± 48.38	5 049.36	0.01	0.01	1.03
	TC1	Y	F	105 165	76.24 ± 37.76	8 017 354.80	16.19	10.80	0.67
	TC1	Y	M	116 127	78.46 ± 40.71	9 111 666.53	17.88	12.28	0.69
	TC1	Y	U	122	51.64 ± 27.78	6 300.07	0.02	0.01	0.45
	TC2	N	F	230	193.07 ± 39.25	44 406.13	0.04	0.06	1.69
	TC2	N	M	206	195.12 ± 37.48	40 195.72	0.03	0.05	1.71
	TC2	O	F	201	165.73 ± 56.84	33 311.19	0.03	0.04	1.45
	TC2	O	M	191	164.10 ± 55.16	31 343.40	0.03	0.04	1.44
	TC2	Y	F	631	79.05 ± 40.95	49 878.25	0.10	0.07	0.69
	TC2	Y	M	481	89.94 ± 41.33	43 261.13	0.07	0.06	0.79
	TC2	Y	U	5	21.82 ± 2.67	109.09	0.00	0.00	0.19

Table H1 (cont.): Number of items with respect to treatment category, generic indicator and gender according to pharmacological group for the year 2005

Pharmacological group	Treatment category	Generic indicator	Gender	Number of items	Average cost (R)	Total cost (R)	Prevalence %	Cost %	CPI
	TC3	N	F	22 990	195.23 ± 51.05	4 488 295.28	3.54	6.05	1.71
	TC3	N	M	14 609	200.96 ± 48.87	2 935 836.86	2.25	3.96	1.76
	TC3	N	U	15	153.42 ± 24.17	2 301.37	0.00	0.00	1.34
	TC3	O	F	20 917	141.88 ± 65.62	2 967 643.36	3.22	4.00	1.24
	TC3	O	M	13 111	151.96 ± 71.67	1 992 326.70	2.02	2.68	1.33
	TC3	O	U	22	125.89 ± 51.22	2 769.68	0.00	0.00	1.10
	TC3	Y	F	95 447	77.75 ± 43.49	7 420 959.48	14.70	10.00	0.68
	TC3	Y	M	68 312	79.65 ± 44.09	5 440 796.09	10.52	7.33	0.70
	TC3	Y	U	146	58.76 ± 35.50	8 579.68	0.02	0.01	0.51
Angiotensin-receptor blockers	TC1	N	F	101 312	208.86 ± 30.54	21 160 185.75	39.70	39.64	1.00
	TC1	N	M	88 323	209.83 ± 29.45	18 532 545.79	34.61	34.71	1.00
	TC1	N	U	78	198.44 ± 11.74	15 478.26	0.03	0.03	0.95
	TC2	N	F	520	218.09 ± 52.98	113 406.09	0.20	0.21	1.04
	TC2	N	M	274	208.99 ± 29.56	57 263.10	0.11	0.11	1.00
	TC3	N	F	41 731	208.19 ± 33.66	8 687 933.80	16.35	16.27	1.00
	TC3	N	M	22 942	209.92 ± 37.26	4 815 936.80	8.99	9.02	1.00
	TC3	N	U	19	195.74 ± 23.34	3 719.11	0.01	0.01	0.94
Other	TC1	N	F	1 315	159.36 ± 30.88	209 553.34	33.01	32.74	0.99
	TC1	N	M	1 155	162.27 ± 14.69	187 422.63	28.99	29.28	1.01
	TC2	N	F	9	158.86 ± 0.00	1 429.74	0.23	0.22	0.99
	TC2	N	M	16	121.31 ± 38.78	1 940.96	0.40	0.30	0.76
	TC3	N	F	1 043	163.93 ± 26.86	170 980.53	26.18	26.72	1.02
	TC3	N	M	446	153.99 ± 21.35	68 677.65	11.19	10.73	0.96

Table H1 (cont.): Number of items with respect to treatment category, generic indicator and gender according to pharmacological group for the year 2005

Pharmacological group	Treatment category	Generic indicator	Gender	Number of items	Average cost (R)	Total cost (R)	Prevalence %	Cost %	CPI
Diuretics	TC1	N	F	374	93.88 ± 59.20	35 109.46	0.07	0.15	2.15
	TC1	N	M	179	117.23 ± 70.12	20 984.03	0.03	0.09	2.69
	TC1	O	F	152	136.60 ± 82.23	20 762.89	0.03	0.09	3.13
	TC1	O	M	123	138.77 ± 67.06	17 068.32	0.02	0.07	3.18
	TC1	Y	F	1 262	26.52 ± 29.91	33 462.45	0.24	0.15	0.61
	TC1	Y	M	1 039	27.78 ± 19.30	28 861.86	0.20	0.13	0.64
	TC1	Y	U	4	20.02 ± 2.00	80.07	0.00	0.00	0.46
	TC2	N	F	29 025	87.54 ± 60.21	2 540 737.24	5.53	11.09	2.01
	TC2	N	M	9 291	89.57 ± 81.35	832 159.94	1.77	3.63	2.05
	TC2	N	U	22	66.46 ± 97.13	1 462.02	0.00	0.01	1.52
	TC2	O	F	7 850	120.03 ± 67.94	942 252.41	1.50	4.11	2.75
	TC2	O	M	3 530	122.00 ± 79.25	430 657.65	0.67	1.88	2.80
	TC2	O	U	3	90.01 ± 40.35	270.02	0.00	0.00	2.06
	TC2	Y	F	106 842	20.64 ± 22.35	2 205 343.52	20.35	9.63	0.47
	TC2	Y	M	39 706	23.11 ± 27.29	917 776.97	7.56	4.01	0.53
	TC2	Y	U	103	19.62 ± 18.50	2 020.56	0.02	0.01	0.45
	TC3	N	F	38 295	98.41 ± 73.70	3 768 779.86	7.30	16.45	2.25
	TC3	N	M	22 173	111.79 ± 101.87	2 478 610.51	4.22	10.82	2.56
	TC3	N	U	28	202.51 ± 252.64	5 670.24	0.01	0.02	4.64
	TC3	O	F	13 002	129.30 ± 64.63	1 681 133.75	2.48	7.34	2.96
	TC3	O	M	9 406	144.16 ± 82.83	1 356 005.62	1.79	5.92	3.30
	TC3	O	U	5	189.26 ± 95.00	946.29	0.00	0.00	4.34
	TC3	Y	F	147 463	22.21 ± 21.90	3 274 948.70	28.09	14.29	0.51
	TC3	Y	M	94 875	24.38 ± 23.04	2 313 172.69	18.07	10.10	0.56

Table H1 (cont.): Number of items with respect to treatment category, generic indicator and gender according to pharmacological group for the year 2005

Pharmacological group	Treatment category	Generic indicator	Gender	Number of items	Average cost (R)	Total cost (R)	Prevalence %	Cost %	CPI
	TC3	Y	U	186	14.83 ± 8.08	2 759.25	0.04	0.01	0.34

Table H2: Number of items with respect to treatment category, generic indicator and gender according to pharmacological group for the year 2006

Pharmacological group	Treatment category	Generic indicator	Gender	Number of items	Average cost (R)	Total cost (R)	Prevalence %	Cost %	CPI
Central acting inhibitors	TC1	N	F	1 926	204.91 ± 52.70	394 657.67	8.00	15.58	1.95
	TC1	N	M	1 347	200.60 ± 39.59	270 210.91	5.59	10.67	1.91
	TC1	N	U	1	190.36 ± 0.0	190.36	0.00	0.01	1.81
	TC1	O	F	292	178.46 ± 111.10	52 110.10	1.21	2.06	1.70
	TC1	O	M	73	147.16 ± 77.63	10 742.65	0.30	0.42	1.40
	TC1	Y	F	5 766	71.53 ± 53.78	412 444.76	23.94	16.29	0.68
	TC1	Y	M	2 232	69.89 ± 51.31	155 994.54	9.27	6.16	0.66
	TC2	N	F	11	190.36 ± 0.00	2 093.96	0.05	0.08	1.81
	TC2	N	M	5	92.97 ± 54.44	464.84	0.02	0.02	0.88
	TC2	O	F	2	83.55 ± 90.56	167.09	0.01	0.01	0.79
	TC2	Y	F	26	53.24 ± 39.55	1 384.22	0.11	0.05	0.51
	TC2	Y	M	21	90.90 ± 66.38	1 908.91	0.09	0.08	0.86
	TC3	N	F	1 816	207.81 ± 44.86	377 384.18	7.54	14.90	1.98
	TC3	N	M	905	204.71 ± 39.92	185 259.08	3.76	7.32	1.95
	TC3	O	F	258	183.85 ± 99.13	47 433.29	1.07	1.87	1.75
	TC3	O	M	43	132.35 ± 124.14	5 691.04	0.18	0.22	1.26
	TC3	Y	F	6 861	65.35 ± 46.64	448 340.05	28.49	17.70	0.62

Table H2 (cont.): Number of items with respect to treatment category, generic indicator and gender according to pharmacological group for the year 2006

Pharmacological group	Treatment category	Generic indicator	Gender	Number of items	Average cost (R)	Total cost (R)	Prevalence %	Cost %	CPI
	TC3	Y	M	2 500	66.36 ± 45.62	165 912.48	10.38	6.55	0.63
Alpha-receptor blockers	TC1	N	F	591	253.03 ± 65.13	149 538.89	1.43	2.10	1.47
	TC1	N	M	8 880	273.32 ± 69.20	2 427 057.02	21.43	34.10	1.59
	TC1	O	F	1 663	185.34 ± 36.49	308 222.82	4.01	4.33	1.08
	TC1	O	M	6 185	187.20 ± 33.74	1 157 804.79	14.93	16.27	1.09
	TC1	Y	F	2 985	90.80 ± 60.03	271 047.55	7.20	3.81	0.53
	TC1	Y	M	7 407	79.44 ± 46.25	588 442.64	17.88	8.27	0.46
	TC1	Y	U	1	33.55 ± 0.00	33.55	0.00	0.00	0.20
	TC2	N	F	4	239.14 ± 7.49	956.54	0.01	0.01	1.39
	TC2	N	M	25	285.06 ± 35.83	7 126.52	0.06	0.10	1.66
	TC2	O	F	4	184.12 ± 0.95	736.48	0.01	0.01	1.07
	TC2	O	M	37	177.04 ± 18.20	6 550.53	0.09	0.09	1.03
	TC2	Y	F	35	76.91 ± 23.13	2 691.99	0.08	0.04	0.45
	TC2	Y	M	33	89.26 ± 44.45	2 945.69	0.08	0.04	0.52
	TC3	N	F	455	266.66 ± 70.34	121 328.17	1.10	1.70	1.55
	TC3	N	M	2 835	268.08 ± 63.18	760 016.32	6.84	10.68	1.56
	TC3	O	F	1 395	191.10 ± 35.47	266 577.96	3.37	3.75	1.11
	TC3	O	M	2 355	187.56 ± 36.54	441 703.11	5.68	6.21	1.09
	TC3	Y	F	2 727	93.74 ± 61.68	255 635.95	6.58	3.59	0.55
	TC3	Y	M	3 815	91.50 ± 55.39	349 087.33	9.21	4.90	0.53
Beta-receptor blockers	TC1	N	F	45 276	118.68 ± 24.67	5 373 553.44	17.67	23.21	1.31
	TC1	N	M	28 323	120.80 ± 30.21	3 421 432.49	11.05	14.78	1.34
	TC1	N	U	28	180.41 ± 75.10	5 051.48	0.01	0.02	2.00
	TC1	O	F	18 228	104.18 ± 63.82	1 899 055.53	7.11	8.20	1.15

Table H2 (cont.): Number of items with respect to treatment category, generic indicator and gender according to pharmacological group for the year 2006

Pharmacological group	Treatment category	Generic indicator	Gender	Number of items	Average cost (R)	Total cost (R)	Prevalence %	Cost %	CPI
	TC1	O	M	18 924	93.27 ± 57.68	1 765 088.23	7.39	7.62	1.03
	TC1	O	U	22	64.59 ± 21.58	1 420.99	0.01	0.01	0.71
	TC1	Y	F	49 862	65.65 ± 36.07	3 273 297.87	19.46	14.14	0.73
	TC1	Y	M	34 189	62.30 ± 32.87	2 130 103.92	13.34	9.20	0.69
	TC1	Y	U	36	53.88 ± 40.69	1 939.56	0.01	0.01	0.60
	TC2	N	F	131	128.76 ± 44.56	16 867.38	0.05	0.07	1.42
	TC2	N	M	90	121.06 ± 36.21	10 895.08	0.04	0.05	1.34
	TC2	N	U	3	116.54 ± 0.00	349.62	0.00	0.00	1.29
	TC2	O	F	105	81.44 ± 31.71	8 550.97	0.04	0.04	0.90
	TC2	O	M	42	105.05 ± 42.58	4 412.08	0.02	0.02	1.16
	TC2	Y	F	175	60.69 ± 37.13	10 620.40	0.07	0.05	0.67
	TC2	Y	M	134	54.74 ± 21.23	7 335.46	0.05	0.03	0.61
	TC3	N	F	11 621	125.59 ± 42.04	1 459 471.43	4.54	6.30	1.39
	TC3	N	M	4 386	124.35 ± 44.53	545 401.56	1.71	2.36	1.38
	TC3	N	U	1	116.54 ± 0.00	116.54	0.00	0.00	1.29
	TC3	O	F	9 183	98.30 ± 55.63	902 728.36	3.58	3.90	1.09
	TC3	O	M	4 860	96.82 ± 57.28	470 546.68	1.90	2.03	1.07
	TC3	O	U	4	103.67 ± 49.54	414.68	0.00	0.00	1.15
	TC3	Y	F	20 539	61.05 ± 33.73	1 253 833.70	8.02	5.41	0.68
	TC3	Y	M	10 032	59.05 ± 35.30	592 431.50	3.92	2.56	0.65
	TC3	Y	U	25	68.74 ± 15.71	1 718.60	0.01	0.01	0.76
Alpha- and beta-receptor blockers	TC1	N	F	55	285.42 ± 166.35	15 697.91	0.08	0.22	2.61
	TC1	N	M	33	284.30 ± 126.84	9 381.78	0.05	0.13	2.60

Table H2 (cont.): Number of items with respect to treatment category, generic indicator and gender according to pharmacological group for the year 2006

Pharmacological group	Treatment category	Generic indicator	Gender	Number of items	Average cost (R)	Total cost (R)	Prevalence %	Cost %	CPI
	TC1	O	F	2 149	149.33 ± 55.56	320 913.22	3.22	4.40	1.36
	TC1	O	M	2 827	157.40 ± 59.99	444 956.00	4.24	6.09	1.44
	TC1	Y	F	11 174	94.10 ± 36.05	1 051 514.77	16.76	14.40	0.86
	TC1	Y	M	13 527	97.84 ± 39.65	1 323 470.12	20.28	18.13	0.89
	TC1	Y	U	12	68.37 ± 1.02	820.44	0.02	0.01	0.62
	TC2	O	F	44	156.17 ± 47.46	6 871.35	0.07	0.09	1.43
	TC2	O	M	44	131.03 ± 49.83	5 765.48	0.07	0.08	1.20
	TC2	Y	F	179	104.18 ± 40.41	18 647.78	0.27	0.26	0.95
	TC2	Y	M	179	112.57 ± 41.73	20 150.76	0.27	0.28	1.03
	TC3	N	F	92	241.02 ± 114.10	22 173.40	0.14	0.30	2.20
	TC3	N	M	11	663.77 ± 375.57	7 301.46	0.02	0.10	6.06
	TC3	O	F	3 149	157.93 ± 60.31	497 328.66	4.72	6.81	1.44
	TC3	O	M	3 478	166.93 ± 62.62	580 583.19	5.22	7.95	1.52
	TC3	Y	F	15 177	98.78 ± 40.10	1 499 183.45	22.76	20.53	0.90
	TC3	Y	M	14 548	101.43 ± 42.11	1 475 622.82	21.81	20.21	0.93
	TC3	Y	U	11	73.42 ± 22.64	807.66	0.02	0.01	0.67
Sympathetic nervous blockers	TC1	N	F	4 933	123.01 ± 78.80	606 813.83	30.75	44.52	1.45
	TC1	N	M	2 877	109.95 ± 79.13	316 334.76	17.93	23.21	1.29
	TC2	N	F	18	84.87 ± 83.22	1 527.69	0.11	0.11	1.00
	TC2	N	M	28	70.52 ± 80.67	1 974.47	0.17	0.14	0.83
	TC3	N	F	4 478	67.72 ± 75.72	303 236.43	27.91	22.25	0.80
	TC3	N	M	3 707	35.94 ± 39.70	133 241.45	23.11	9.75	0.42
	TC3	N	U	2	17.37 ± 0.00	37.74	0.01	0.00	0.20
Direct-acting vasodilators	TC1	N	F	69	167.16 ± 184.93	11 533.94	2.57	4.88	1.90

Table H2 (cont.): Number of items with respect to treatment category, generic indicator and gender according to pharmacological group for the year 2006

Pharmacological group	Treatment category	Generic indicator	Gender	Number of items	Average cost (R)	Total cost (R)	Prevalence %	Cost %	CPI
	TC1	N	M	116	184.07 ± 87.99	21 351.66	4.32	9.04	2.09
	TC1	O	F	70	189.31 ± 58.62	13 251.58	2.61	5.61	2.15
	TC1	O	M	20	166.16 ± 52.54	3 323.20	0.75	1.41	1.89
	TC1	Y	F	354	47.36 ± 17.70	16 766.59	13.19	7.10	0.54
	TC1	Y	M	445	39.81 ± 17.44	17 713.99	16.59	7.50	0.45
	TC2	O	F	4	129.08 ± 45.28	516.23	0.15	0.22	1.47
	TC2	Y	F	6	39.71 ± 0.81	238.23	0.22	0.10	0.45
	TC3	N	F	90	137.53 ± 66.58	12 377.90	3.35	5.24	1.56
	TC3	N	M	323	192.98 ± 108.22	62 331.52	12.04	26.38	2.19
	TC3	O	F	83	197.87 ± 81.62	16 423.59	3.09	6.95	2.25
	TC3	O	M	52	20.55 ± 42.47	10 428.55	1.94	4.41	2.28
	TC3	Y	F	620	46.84 ± 20.04	29 042.63	23.11	12.29	0.53
	TC3	Y	M	431	48.68 ± 28.34	20 980.75	16.06	8.88	0.55
Calcium channel blockers	TC1	N	F	8 829	213.54 ± 58.76	1 885 364.17	5.26	7.77	1.48
	TC1	N	M	7 707	231.66 ± 59.57	1 785 401.96	4.59	7.36	1.60
	TC1	N	U	5	145.31 ± 5.00	726.54	0.00	0.00	1.01
	TC1	O	F	19 700	147.56 ± 36.85	2 907 024.21	11.73	11.98	1.02
	TC1	O	M	18 936	154.07 ± 38.57	2 917 531.32	11.27	12.02	1.07
	TC1	O	U	23	153.95 ± 21.64	3 540.89	0.01	0.01	1.07
	TC1	Y	F	25 684	109.02 ± 22.56	2 800 010.26	15.29	11.54	0.75
	TC1	Y	M	25 436	113.49 ± 24.34	2 886 741.40	15.14	11.90	0.79
	TC1	Y	U	5	100.16 ± 0.00	500.80	0.00	0.00	0.69
	TC2	N	F	80	223.33 ± 57.76	17 866.01	0.05	0.07	1.55
	TC2	N	M	40	218.60 ± 52.53	8 743.81	0.02	0.04	1.51

Table H2 (cont.): Number of items with respect to treatment category, generic indicator and gender according to pharmacological group for the year 2006

Pharmacological group	Treatment category	Generic indicator	Gender	Number of items	Average cost (R)	Total cost (R)	Prevalence %	Cost %	CPI
	TC2	O	F	146	146.37 ± 30.40	21 369.64	0.09	0.09	1.01
	TC2	O	M	44	153.03 ± 26.87	6 733.26	0.03	0.03	1.06
	TC2	Y	F	276	109.54 ± 24.76	30 231.70	0.16	0.12	0.76
	TC2	Y	M	103	121.24 ± 23.23	12 487.66	0.06	0.05	0.84
	TC3	N	F	6 894	220.64 ± 62.36	1 521 088.31	4.10	6.27	1.53
	TC3	N	M	4 289	241.58 ± 58.01	1 036 145.11	2.55	4.27	1.67
	TC3	N	U	12	255.05 ± 0.00	3 060.60	0.01	0.01	1.77
	TC3	O	F	11 901	151.98 ± 40.04	1 808 704.85	7.08	7.45	1.05
	TC3	O	M	7 121	159.41 ± 39.21	1 135 183.01	4.24	4.68	1.10
	TC3	Y	F	19 178	111.31 ± 23.85	2 134 794.11	11.42	8.80	0.77
	TC3	Y	M	11 579	115.76 ± 25.55	1 340 419.43	6.89	5.52	0.80
	TC3	Y	U	1	100.16 ± 0.00	100.16	0.00	0.00	0.69
ACE inhibitors	TC1	N	F	21 530	182.97 ± 54.26	3 939 410.53	2.92	5.00	1.71
	TC1	N	M	20 785	194.58 ± 55.95	4 044 403.62	2.82	5.13	1.82
	TC1	N	U	6	168.84 ± 22.84	1 013.05	0.00	0.00	1.58
	TC1	O	F	50 712	143.84 ± 51.14	7 294 545.67	6.87	9.26	1.35
	TC1	O	M	51 674	148.69 ± 54.88	7 683 217.14	7.00	9.75	1.39
	TC1	O	U	64	133.60 ± 53.17	8 550.32	0.01	0.01	1.25
	TC1	Y	F	158 251	88.01 ± 42.62	13 928 069.62	21.45	17.67	0.82
	TC1	Y	M	169 734	87.83 ± 43.52	14 908 471.90	23.00	18.92	0.82
	TC1	Y	U	95	73.37 ± 31.36	6 970.20	0.01	0.01	0.69
	TC2	N	F	118	194.46 ± 65.42	22 946.72	0.02	0.03	1.82
	TC2	N	M	77	199.87 ± 47.89	15 390.31	0.01	0.02	1.87
	TC2	O	F	260	149.30 ± 53.47	38 818.11	0.04	0.05	1.40

Table H2 (cont.): Number of items with respect to treatment category, generic indicator and gender according to pharmacological group for the year 2006

Pharmacological group	Treatment category	Generic indicator	Gender	Number of items	Average cost (R)	Total cost (R)	Prevalence %	Cost %	CPI
	TC2	O	M	164	156.75 ± 55.85	25 706.67	0.02	0.03	1.47
	TC2	Y	F	842	95.23 ± 50.76	80 185.76	0.11	0.10	0.89
	TC2	Y	M	787	94.46 ± 50.12	74 336.25	0.11	0.09	0.88
	TC2	Y	U	4	26.98 ± 26.63	107.90	0.00	0.00	0.25
	TC3	N	F	11 666	202.28 ± 56.17	2 359 849.93	1.58	2.99	1.89
	TC3	N	M	7 714	209.02 ± 54.63	1 612 399.62	1.05	2.05	1.96
	TC3	N	U	1	233.13 ± 0.00	233.13	0.00	0.00	2.18
	TC3	O	F	20 713	145.81 ± 62.48	3 020 124.07	2.81	3.83	1.37
	TC3	O	M	14 661	157.12 ± 66.91	2 303 579.81	1.99	2.92	1.47
	TC3	O	U	4	53.09 ± 1.86	212.36	0.00	0.00	0.50
	TC3	Y	F	120 935	83.44 ± 45.19	10 090 711.57	16.39	12.80	0.78
	TC3	Y	M	86 934	84.43 ± 45.49	7 339 606.19	11.78	9.31	0.79
	TC3	Y	U	144	87.62 ± 34.28	12 617.15	0.02	0.02	0.82
Angiotensin-receptor blockers	TC1	N	F	91 529	208.67 ± 35.96	19 099 162.03	34.07	33.97	1.00
	TC1	N	M	80 379	209.91 ± 33.78	16 872 487.95	29.92	30.01	1.00
	TC1	N	U	63	205.91 ± 9.72	12 972.11	0.02	0.02	0.98
	TC1	O	F	14 140	209.09 ± 27.79	2 956 494.84	5.26	5.26	1.00
	TC1	O	M	11 685	210.20 ± 28.52	2 456 166.06	4.35	4.37	1.00
	TC1	O	U	3	207.59 ± 7.00	622.76	0.00	0.00	0.99
	TC1	Y	F	23	208.39 ± 36.24	4 793.01	0.01	0.01	1.00
	TC1	Y	M	5	187.36 ± 75.69	936.81	0.00	0.00	0.90
	TC2	N	F	450	207.50 ± 33.73	93 373.27	0.17	0.17	0.99
	TC2	N	M	287	204.22 ± 40.34	58 610.61	0.11	0.10	0.98
	TC2	O	F	120	211.83 ± 16.00	25 419.98	0.04	0.05	1.01

Table H2 (cont.): Number of items with respect to treatment category, generic indicator and gender according to pharmacological group for the year 2006

Pharmacological group	Treatment category	Generic indicator	Gender	Number of items	Average cost (R)	Total cost (R)	Prevalence %	Cost %	CPI
	TC2	O	M	68	214.87 ± 15.05	14 611.09	0.03	0.03	1.03
	TC3	N	F	40 143	209.20 ± 36.33	8 397 761.42	14.94	14.94	1.00
	TC3	N	M	21 122	209.57 ± 36.75	4 426 557.65	7.86	7.87	1.00
	TC3	N	U	2	176.37 ± 0.00	352.74	0.00	0.00	0.84
	TC3	O	F	5 634	208.91 ± 24.93	1 177 020.53	2.10	2.09	1.00
	TC3	O	M	2 950	211.77 ± 34.80	624 714.24	1.10	1.11	1.01
	TC3	Y	F	12	190.31 ± 61.38	2 283.75	0.00	0.00	0.91
	TC3	Y	M	2	199.50 ± 0.00	399.00	0.00	0.00	0.95
Others	TC1	N	F	1 802	177.40 ± 49.37	319 681.31	33.53	32.92	0.98
	TC1	N	M	1 816	185.18 ± 49.55	336 286.87	33.79	34.63	1.03
	TC2	N	F	23	165.03 ± 16.30	3 795.77	0.43	0.39	0.91
	TC2	N	M	9	265.42 ± 24.53	2 388.79	0.17	0.25	1.47
	TC3	N	F	1 161	177.57 ± 42.63	206 160.09	21.60	21.23	0.98
	TC3	N	M	564	182.12 ± 49.61	102 715.15	10.49	10.58	1.01
Diuretics	TC1	N	F	347	121.36 ± 103.82	42 111.13	0.06	0.18	2.88
	TC1	N	M	263	122.84 ± 94.13	32 306.58	0.05	0.14	2.91
	TC1	O	F	247	134.70 ± 61.73	33 270.81	0.04	0.14	3.19
	TC1	O	M	201	141.39 ± 55.82	28 418.50	0.04	0.12	3.35
	TC1	Y	F	1 383	23.54 ± 25.34	32 549.47	0.25	0.14	0.56
	TC1	Y	M	1 136	29.20 ± 25.85	33 174.46	0.21	0.14	0.69
	TC2	N	F	26 539	83.59 ± 55.81	2 218 454.09	4.79	9.49	1.98
	TC2	N	M	8 273	86.70 ± 88.37	717 258.97	1.49	3.07	2.05
	TC2	N	U	13	79.65 ± 61.31	1 035.41	0.00	0.00	1.89
	TC2	O	F	7 905	120.16 ± 71.15	949 835.02	1.43	4.06	2.85

Table H2 (cont.): Number of items with respect to treatment category, generic indicator and gender according to pharmacological group for the year 2006

Pharmacological group	Treatment category	Generic indicator	Gender	Number of items	Average cost (R)	Total cost (R)	Prevalence %	Cost %	CPI
	TC2	O	M	3 303	123.33 ± 75.99	407 361.20	0.60	1.74	2.92
	TC2	O	U	4	103.35 ± 32.12	413.38	0.00	0.00	2.45
	TC2	Y	F	106 964	20.35 ± 22.78	2 176 256.02	19.32	9.31	0.48
	TC2	Y	M	40 256	23.17 ± 29.44	932 706.73	7.27	3.99	0.55
	TC2	Y	U	68	20.94 ± 7.75	1 423.98	0.01	0.01	0.50
	TC3	N	F	37 125	98.29 ± 81.65	3 648 917.13	6.70	15.61	2.33
	TC3	N	M	21 504	112.17 ± 105.17	2 412 145.19	3.88	10.32	2.66
	TC3	N	U	23	71.51 ± 49.88	1 644.75	0.00	0.01	1.69
	TC3	O	F	15 028	127.58 ± 64.39	1 917 300.29	2.71	8.20	3.02
	TC3	O	M	11 225	140.53 ± 76.07	1 577 489.91	2.03	6.75	3.33
	TC3	O	U	17	250.71 ± 44.97	4 262.12	0.00	0.02	5.94
	TC3	Y	F	164 204	21.93 ± 20.60	3 600 467.17	29.65	15.41	0.52
	TC3	Y	M	107 616	24.14 ± 23.09	2 597 363.89	19.43	11.11	0.57
	TC3	Y	U	127	21.08 ± 11.08	2 677.39	0.02	0.01	0.50

Table H3: Number of items with respect to treatment category, generic indicator and gender according to pharmacological group for the year 2007

Pharmacological group	Treatment category	Generic indicator	Gender	Number of items	Average cost (R)	Total cost (R)	Prevalence %	Cost %	CPI
Central acting inhibitors	TC1	N	F	2268	210.61 ± 55.40	477662.69	11.37	20.04	1.76
	TC1	N	M	1454	202.87 ± 47.85	294978.93	7.29	12.38	1.70
	TC1	O	F	139	147.87 ± 101.15	20553.81	0.70	0.86	1.24

Table H3 (cont.): Number of items with respect to treatment category, generic indicator and gender according to pharmacological group for the year 2007

Pharmacological group	Treatment category	Generic indicator	Gender	Number of items	Average cost (R)	Total cost (R)	Prevalence %	Cost %	CPI
	TC1	O	M	30	142.51 ± 95.20	4275.36	0.15	0.18	1.19
	TC1	Y	F	4612	76.38 ± 59.17	352281.1	23.12	14.78	0.64
	TC1	Y	M	1571	74.75 ± 55.29	117426.45	7.87	4.93	0.63
	TC2	N	M	9	210.06 ± 11.07	1890.53	0.05	0.08	1.76
	TC2	O	M	1	19.86 ±	19.86	0.01	0.00	0.17
	TC2	Y	F	42	73.03 ± 54.60	3067.17	0.21	0.13	0.61
	TC3	N	F	1709	212.71 ± 49.52	363524.11	8.57	15.25	1.78
	TC3	N	M	1017	210.70 ± 37.85	214282.39	5.10	8.99	1.76
	TC3	O	F	102	151.79 ± 97.80	15482.6	0.51	0.65	1.27
	TC3	O	M	30	133.30 ± 91.60	3999.05	0.15	0.17	1.12
	TC3	Y	F	5300	72.07 ± 51.97	381945.54	26.57	16.03	0.60
	TC3	Y	M	1667	79.17 ± 59.99	131980.13	8.36	5.54	0.66
Alpha-receptor blockers	TC1	N	F	625	264.97 ± 66.89	165604.87	1.65	2.42	1.47
	TC1	N	M	8328	287.34 ± 81.39	2392934.47	22.03	35.01	1.59
	TC1	O	F	1449	194.10 ± 43.06	281254.88	3.83	4.11	1.07
	TC1	O	M	5197	193.29 ± 35.37	1004537.49	13.75	14.70	1.07
	TC1	Y	F	2685	95.19 ± 67.31	255575.19	7.10	3.74	0.53
	TC1	Y	M	6805	82.33 ± 50.59	560246.09	18.00	8.20	0.46
	TC2	N	M	46	313.34 ± 58.10	14413.57	0.12	0.21	1.73
	TC2	O	F	18	202.90 ± 0.44	3652.16	0.05	0.05	1.12
	TC2	O	M	12	183.94 ± 47.77	2207.29	0.03	0.03	1.02
	TC2	Y	F	43	94.67 ± 31.00	4071.01	0.11	0.06	0.52
	TC2	Y	M	54	79.19 ± 38.01	4276.25	0.14	0.06	0.44
	TC3	N	F	512	279.10 ± 66.45	142900.82	1.35	2.09	1.54

Table H3 (cont.): Number of items with respect to treatment category, generic indicator and gender according to pharmacological group for the year 2007

Pharmacological group	Treatment category	Generic indicator	Gender	Number of items	Average cost (R)	Total cost (R)	Prevalence %	Cost %	CPI
	TC3	N	M	2653	288.06 ± 67.86	764229.23	7.02	11.18	1.59
	TC3	O	F	1233	198.83 ± 40.45	245152.94	3.26	3.59	1.10
	TC3	O	M	2317	192.96 ± 47.61	447087.34	6.13	6.54	1.07
	TC3	Y	F	2449	96.94 ± 67.48	237414.55	6.48	3.47	0.54
	TC3	Y	M	3378	91.74 ± 59.92	309900.08	8.94	4.53	0.51
Beta-receptor blockers	TC1	N	F	42524	121.69 ± 28.70	5174815.57	17.09	23.12	1.35
	TC1	N	M	26015	121.03 ± 33.73	3148626.8	10.46	14.07	1.35
	TC1	O	F	15110	102.12 ± 64.66	1543097.39	6.07	6.90	1.14
	TC1	O	M	15571	92.39 ± 61.30	1438674.81	6.26	6.43	1.03
	TC1	O	U	2	81.98 ± 0.00	163.96	0.00	0.00	0.91
	TC1	Y	F	50501	67.86 ± 37.88	3427222.74	20.30	15.31	0.75
	TC1	Y	M	37982	63.01 ± 34.93	2393258.44	15.26	10.69	0.70
	TC2	N	F	96	127.12 ± 16.84	12203.36	0.04	0.05	1.41
	TC2	N	M	47	126.31 ± 35.08	5936.35	0.02	0.03	1.40
	TC2	O	F	155	110.47 ± 79.24	17122.59	0.06	0.08	1.23
	TC2	O	M	52	86.55 ± 58.14	4500.67	0.02	0.02	0.96
	TC2	Y	F	318	67.58 ± 25.56	21489.22	0.13	0.10	0.75
	TC2	Y	M	183	78.25 ± 42.85	14320.12	0.07	0.06	0.87
	TC3	N	F	11046	127.11 ± 42.84	1404071.17	4.44	6.27	1.41
	TC3	N	M	4021	125.45 ± 54.58	504437.56	1.62	2.25	1.39
	TC3	O	F	7514	100.93 ± 62.23	758356.4	3.02	3.39	1.12
	TC3	O	M	4130	99.55 ± 63.10	411122.02	1.66	1.84	1.11
	TC3	O	U	8	128.05 ± 9.87	1024.43	0.00	0.00	1.42
	TC3	Y	F	21967	63.64 ± 35.30	1397871.49	8.83	6.25	0.71

Table H3 (cont.): Number of items with respect to treatment category, generic indicator and gender according to pharmacological group for the year 2007

Pharmacological group	Treatment category	Generic indicator	Gender	Number of items	Average cost (R)	Total cost (R)	Prevalence %	Cost %	CPI
	TC3	Y	M	11576	60.60 ± 32.40	701474.35	4.65	3.13	0.67
Alpha- and Beta-receptor blockers	TC1	N	F	45	189.13 ± 144.27	8510.96	0.06	0.11	1.72
	TC1	N	M	53	469.11 ± 293.72	24862.91	0.08	0.32	4.27
	TC1	O	F	1654	146.49 ± 52.08	242287.41	2.37	3.15	1.33
	TC1	O	M	2266	153.56 ± 59.56	347974.35	3.24	4.53	1.40
	TC1	Y	F	13458	98.26 ± 36.48	1322427.01	19.26	17.21	0.89
	TC1	Y	M	15346	99.55 ± 39.61	1527654.48	21.96	19.88	0.91
	TC2	O	F	38	188.23 ± 53.78	7152.59	0.05	0.09	1.71
	TC2	O	M	43	159.29 ± 38.97	6849.55	0.06	0.09	1.45
	TC2	Y	F	183	111.49 ± 45.39	20402.63	0.26	0.27	1.01
	TC2	Y	M	192	103.51 ± 45.72	19873.33	0.27	0.26	0.94
	TC3	N	F	53	309.43 ± 127.62	16399.92	0.08	0.21	2.81
	TC3	O	F	2235	161.39 ± 65.18	360701.71	3.20	4.69	1.47
	TC3	O	M	2665	171.58 ± 63.04	457248.72	3.81	5.95	1.56
	TC3	Y	F	16238	103.31 ± 40.76	1677502.49	23.24	21.83	0.94
	TC3	Y	M	15411	106.69 ± 42.97	1644227.74	22.05	21.40	0.97
Sympathetic nervous blockers	TC1	N	F	3388	150.15 ± 80.47	508720.66	38.23	50.03	1.31
	TC1	N	M	1950	137.76 ± 80.47	268629.48	22.00	26.42	1.20
	TC2	N	F	16	98.06 ± 135.74	1569.01	0.18	0.15	0.85
	TC2	N	M	7	183.68 ± 0.00	1285.76	0.08	0.13	1.60
	TC3	N	F	2347	79.16 ± 87.30	185796.69	26.48	18.27	0.69
	TC3	N	M	1155	44.06 ± 68.02	50888.64	13.03	5.00	0.38
Direct-acting vasodilators	TC1	N	F	93	150.38 ± 164.18	13985.17	3.96	6.49	1.64

Table H3 (cont.): Number of items with respect to treatment category, generic indicator and gender according to pharmacological group for the year 2007

Pharmacological group	Treatment category	Generic indicator	Gender	Number of items	Average cost (R)	Total cost (R)	Prevalence %	Cost %	CPI
	TC1	N	M	114	170.52 ± 73.28	19439.02	4.85	9.02	1.86
	TC1	O	F	63	184.93 ± 77.05	11650.67	2.68	5.40	2.02
	TC1	O	M	10	170.17 ± 26.54	1701.72	0.43	0.79	1.86
	TC1	Y	F	346	49.89 ± 18.27	17261.48	14.72	8.01	0.54
	TC1	Y	M	286	41.53 ± 13.48	11876.33	12.17	5.51	0.45
	TC2	N	F	6	119.55 ± 1.07	717.31	0.26	0.33	1.30
	TC2	O	F	1	337.98 ± 0.00	337.98	0.04	0.16	3.69
	TC2	Y	F	3	80.71 ± 25.50	242.13	0.13	0.11	0.88
	TC2	Y	M	8	38.24 ± 31.33	305.95	0.34	0.14	0.42
	TC3	N	F	89	187.44 ± 110.60	16681.85	3.79	7.74	2.04
	TC3	N	M	272	196.57 ± 106.02	53466.98	11.57	24.80	2.14
	TC3	O	F	56	191.35 ± 75.84	10715.85	2.38	4.97	2.09
	TC3	O	M	33	211.08 ± 80.55	6965.53	1.40	3.23	2.30
	TC3	Y	F	594	50.03 ± 24.25	29715.93	25.27	13.79	0.55
	TC3	Y	M	377	54.36 ± 33.71	20493.7	16.04	9.51	0.59
Calcium channel blockers									
	TC1	N	F	9230	220.61 ± 65.48	2036207.79	4.90	7.54	1.54
	TC1	N	M	8216	236.29 ± 66.79	1941367.99	4.36	7.19	1.65
	TC1	O	F	14857	153.34 ± 42.61	2278135.2	7.88	8.44	1.07
	TC1	O	M	14237	159.44 ± 44.44	2269910.81	7.55	8.41	1.11
	TC1	Y	F	37142	112.81 ± 27.01	4189980.68	19.71	15.52	0.79
	TC1	Y	M	36535	116.82 ± 29.06	4267976.03	19.39	15.81	0.82
	TC2	N	F	117	207.60 ± 77.06	24288.91	0.06	0.09	1.45
	TC2	N	M	25	251.42 ± 47.89	6285.6	0.01	0.02	1.76

Table H3 (cont.): Number of items with respect to treatment category, generic indicator and gender according to pharmacological group for the year 2007

Pharmacological group	Treatment category	Generic indicator	Gender	Number of items	Average cost (R)	Total cost (R)	Prevalence %	Cost %	CPI
	TC2	O	F	66	161.56 ± 24.14	10662.94	0.04	0.04	1.13
	TC2	O	M	47	164.03 ± 29.51	7709.6	0.02	0.03	1.15
	TC2	Y	F	305	120.46 ± 34.34	36741.17	0.16	0.14	0.84
	TC2	Y	M	145	125.30 ± 33.02	18168.22	0.08	0.07	0.87
	TC3	N	F	7107	231.98 ± 69.72	1648708.55	3.77	6.11	1.62
	TC3	N	M	4560	247.18 ± 65.27	1127128.78	2.42	4.18	1.73
	TC3	O	F	8787	157.04 ± 44.39	1379873.25	4.66	5.11	1.10
	TC3	O	M	5248	161.53 ± 44.00	847686.12	2.78	3.14	1.13
	TC3	Y	F	26588	116.12 ± 27.02	3087484.2	14.11	11.44	0.81
	TC3	Y	M	15248	118.81 ± 29.97	1811644.11	8.09	6.71	0.83
ACE inhibitors	TC1	N	F	15112	197.55 ± 60.05	2985342.56	2.18	3.87	1.77
	TC1	N	M	16412	207.00 ± 62.93	3397241.54	2.37	4.40	1.85
	TC1	N	U	1	256.86 ± 0.00	256.86	0.00	0.00	2.30
	TC1	O	F	36949	141.79 ± 52.29	5238906.62	5.34	6.79	1.27
	TC1	O	M	37965	144.26 ± 57.14	5476663.5	5.49	7.09	1.29
	TC1	O	U	3	145.31 ± 58.51	435.92	0.00	0.00	1.30
	TC1	Y	F	176114	100.05 ± 44.35	17620361.45	25.46	22.83	0.90
	TC1	Y	M	183843	98.85 ± 44.84	18172946.23	26.58	23.54	0.89
	TC1	Y	U	9	66.50 ± 11.30	598.5	0.00	0.00	0.60
	TC2	N	F	92	206.90 ± 63.77	19034.35	0.01	0.02	1.85
	TC2	N	M	77	214.75 ± 48.34	16535.91	0.01	0.02	1.92
	TC2	O	F	174	131.11 ± 45.69	22813.16	0.03	0.03	1.17
	TC2	O	M	119	156.08 ± 51.96	18573.8	0.02	0.02	1.40
	TC2	Y	F	1047	104.17 ± 41.77	109069.77	0.15	0.14	0.93

Table H3 (cont.): Number of items with respect to treatment category, generic indicator and gender according to pharmacological group for the year 2007

Pharmacological group	Treatment category	Generic indicator	Gender	Number of items	Average cost (R)	Total cost (R)	Prevalence %	Cost %	CPI
	TC2	Y	M	638	106.05 ± 58.02	67660.62	0.09	0.09	0.95
	TC3	N	F	9706	215.08 ± 59.51	2087543.62	1.40	2.70	1.93
	TC3	N	M	6878	218.73 ± 61.60	1504439.11	0.99	1.95	1.96
	TC3	O	F	14547	144.21 ± 64.32	2097821.99	2.10	2.72	1.29
	TC3	O	M	10538	154.25 ± 74.48	1625498.13	1.52	2.11	1.38
	TC3	Y	F	108604	91.29 ± 46.55	9914943.85	15.70	12.84	0.82
	TC3	Y	M	72938	93.48 ± 47.34	6818408.61	10.54	8.83	0.84
	TC3	Y	U	8	127.13 ± 0.00	1017.04	0.00	0.00	1.14
Angiotensin-receptor blockers	TC1	N	F	82963	203.41 ± 44.83	16875255.8	30.81	31.07	1.01
	TC1	N	M	72171	202.98 ± 47.66	14648949.73	26.80	26.97	1.01
	TC1	N	U	3	206.68 ± 0.00	620.04	0.00	0.00	1.02
	TC1	O	F	17519	203.73 ± 41.34	3569097.83	6.51	6.57	1.01
	TC1	O	M	14519	201.64 ± 43.91	2927593.86	5.39	5.39	1.00
	TC1	Y	F	5787	166.83 ± 27.66	965459.64	2.15	1.78	0.83
	TC1	Y	M	5331	166.00 ± 31.56	884944.22	1.98	1.63	0.82
	TC2	N	F	520	210.03 ± 55.00	109214.02	0.19	0.20	1.04
	TC2	N	M	241	196.70 ± 42.34	47404.78	0.09	0.09	0.98
	TC2	O	F	88	202.67 ± 27.71	17835.2	0.03	0.03	1.00
	TC2	O	M	39	206.27 ± 27.97	8044.36	0.01	0.01	1.02
	TC2	Y	F	66	170.98 ± 23.24	11284.72	0.02	0.02	0.85
	TC2	Y	M	36	166.78 ± 7.78	6004.06	0.01	0.01	0.83
	TC3	N	F	35315	207.03 ± 44.99	7311232.07	13.11	13.46	1.03
	TC3	N	M	18719	205.50 ± 47.74	3846665.63	6.95	7.08	1.02
	TC3	N	U	8	203.69 ± 9.70	1629.53	0.00	0.00	1.01

Table H3 (cont.): Number of items with respect to treatment category, generic indicator and gender according to pharmacological group for the year 2007

Pharmacological group	Treatment category	Generic indicator	Gender	Number of items	Average cost (R)	Total cost (R)	Prevalence %	Cost %	CPI
	TC3	O	F	7439	205.19 ± 39.28	1526432.99	2.76	2.81	1.02
	TC3	O	M	3845	202.41 ± 50.18	778257.9	1.43	1.43	1.00
	TC3	Y	F	3119	167.19 ± 28.23	521462.74	1.16	0.96	0.83
	TC3	Y	M	1581	166.34 ± 36.89	262979.22	0.59	0.48	0.82
Others	TC1	N	F	2671	204.14 ± 52.35	545267.56	31.14	30.81	0.99
	TC1	N	M	3349	209.40 ± 59.76	701280.47	39.05	39.62	1.01
	TC2	N	F	20	273.25 ± 33.07	5465.09	0.23	0.31	1.32
	TC2	N	M	7	185.69 ± 34.33	1299.85	0.08	0.07	0.90
	TC3	N	F	1617	201.31 ± 55.46	325523.69	18.85	18.39	0.98
	TC3	N	M	913	209.21 ± 63.67	191008.25	10.64	10.79	1.01
Diuretics	TC1	N	F	208	107.17 ± 128.83	22291.58	0.04	0.11	2.43
	TC1	N	M	187	114.74 ± 104.67	21456.14	0.04	0.10	2.60
	TC1	N	U	6	84.37 ± 0.00	506.22	0.00	0.00	1.91
	TC1	O	F	299	151.66 ± 82.93	45345.03	0.06	0.22	3.43
	TC1	O	M	261	148.41 ± 73.64	38733.81	0.05	0.18	3.36
	TC1	Y	F	1353	24.80 ± 24.01	33553.19	0.28	0.16	0.56
	TC1	Y	M	964	29.03 ± 25.84	27980.37	0.20	0.13	0.66
	TC2	N	F	18774	82.89 ± 59.06	1556268.33	3.94	7.39	1.88
	TC2	N	M	5251	84.45 ± 87.90	443471.52	1.10	2.11	1.91
	TC2	O	F	9685	122.88 ± 72.40	1190115.21	2.03	5.65	2.78
	TC2	O	M	3943	125.21 ± 77.92	493695.69	0.83	2.34	2.84
	TC2	O	U	1	119.20 ± 0.00	119.2	0.00	0.00	2.70
	TC2	Y	F	89993	20.48 ± 4.39	1843042.67	18.87	8.75	0.46
	TC2	Y	M	30403	22.95 ± 33.05	697665.58	6.37	3.31	0.52

Table H3 (cont.): Number of items with respect to treatment category, generic indicator and gender according to pharmacological group for the year 2007

Pharmacological group	Treatment category	Generic indicator	Gender	Number of items	Average cost (R)	Total cost (R)	Prevalence %	Cost %	CPI
	TC2	Y	U	2	6.73 ± 0.23	13.45	0.00	0.00	0.15
	TC3	N	F	24968	94.22 ± 93.19	2352404.3	5.23	11.17	2.13
	TC3	N	M	12626	122.99 ± 144.32	1552893.46	2.65	7.37	2.79
	TC3	O	F	21894	131.55 ± 59.51	2880148.45	4.59	13.68	2.98
	TC3	O	M	16320	143.22 ± 73.72	2337308.1	3.42	11.10	3.24
	TC3	Y	F	148258	22.48 ± 21.91	3332806.8	31.08	15.82	0.51
	TC3	Y	M	91581	23.92 ± 23.71	2190433.39	19.20	10.40	0.54
	TC3	Y	U	7	30.35 ± 0.33	212.48	0.00	0.00	0.69

Table H4: Number of items with respect to treatment category, generic indicator and gender according to pharmacological group for the year 2008

Pharmacological group	Treatment category	Generic indicator	Gender	Number of items	Average cost (R)	Total cost (R)	Prevalence %	Cost %	CPI
Central acting inhibitors	TC1	N	F	1464	217.20 ± 61.71	317981.38	7.62	13.35	1.75
	TC1	N	M	914	202.17 ± 58.69	184781	4.76	7.76	1.63
	TC1	O	F	678	215.71 ± 67.15	146253.76	3.53	6.14	1.74
	TC1	O	M	439	207.13 ± 57.21	90929.47	2.29	3.82	1.67
	TC1	Y	F	4395	82.98 ± 61.01	364684.41	22.88	15.31	0.67
	TC1	Y	M	1724	79.76 ± 54.98	137501.8	8.97	5.77	0.64
	TC2	N	F	15	260.66 ± 91.66	3909.83	0.08	0.16	2.10
	TC2	N	M	12	173.66 ± 77.42	2083.93	0.06	0.09	1.40
	TC2	O	F	9	256.00 ± 73.23	2304.04	0.05	0.10	2.06

Table H4 (cont.): Number of items with respect to treatment category, generic indicator and gender according to pharmacological group for the year 2008

Pharmacological group	Treatment category	Generic indicator	Gender	Number of items	Average cost (R)	Total cost (R)	Prevalence %	Cost %	CPI
	TC2	O	M	7	221.97 ± 8.63	1553.82	0.04	0.07	1.79
	TC2	Y	F	30	61.80 ± 38.30	1853.86	0.16	0.08	0.50
	TC2	Y	M	6	70.03 ± 18.49	420.18	0.03	0.02	0.56
	TC3	N	F	1266	211.63 ± 58.22	267918.98	6.59	11.25	1.71
	TC3	N	M	757	215.76 ± 46.21	163331.13	3.94	6.86	1.74
	TC3	O	F	527	221.38 ± 46.44	116669.68	2.74	4.90	1.79
	TC3	O	M	331	210.89 ± 61.21	69804.23	1.72	2.93	1.70
	TC3	Y	F	4831	75.42 ± 52.18	364344.52	25.15	15.30	0.61
	TC3	Y	M	1804	80.81 ± 57.35	145786.87	9.39	6.12	0.65
Alpha-receptor blockers	TC1	N	F	614	276.98 ± 50.56	170068.16	1.74	2.68	1.54
	TC1	N	M	7461	296.01 ± 87.15	2208494.11	21.09	34.76	1.65
	TC1	O	F	1244	200.70 ± 34.55	249667.16	3.52	3.93	1.12
	TC1	O	M	4622	198.85 ± 39.28	919100.41	13.07	14.47	1.11
	TC1	Y	F	2332	91.93 ± 63.70	214369.67	6.59	3.37	0.51
	TC1	Y	M	6883	78.87 ± 53.28	542858.53	19.46	8.54	0.44
	TC2	N	M	38	313.55 ± 66.73	11915.06	0.11	0.19	1.75
	TC2	O	F	19	234.39 ± 89.80	4453.37	0.05	0.07	1.30
	TC2	O	M	23	206.28 ± 7.09	4744.37	0.07	0.07	1.15
	TC2	Y	F	44	88.94 ± 44.44	3913.16	0.12	0.06	0.50
	TC2	Y	M	34	91.77 ± 52.45	3120.24	0.10	0.05	0.51
	TC3	N	F	436	282.99 ± 53.79	123382.38	1.23	1.94	1.58
	TC3	N	M	2417	294.19 ± 64.35	711064.11	6.83	11.19	1.64
	TC3	O	F	1170	202.03 ± 36.12	236371.05	3.31	3.72	1.12
	TC3	O	M	2132	198.27 ± 45.14	422708.15	6.03	6.65	1.10

Table H4 (cont.): Number of items with respect to treatment category, generic indicator and gender according to pharmacological group for the year 2008

Pharmacological group	Treatment category	Generic indicator	Gender	Number of items	Average cost (R)	Total cost (R)	Prevalence %	Cost %	CPI
	TC3	Y	F	2416	91.88 ± 66.03	221973.3	6.83	3.49	0.51
	TC3	Y	M	3486	87.44 ± 62.66	304806.13	9.86	4.80	0.49
Beta-receptor blockers	TC1	N	F	37372	124.81 ± 28.50	4664430.92	16.24	22.43	1.38
	TC1	N	M	22453	122.93 ± 33.78	2760231.27	9.76	13.27	1.36
	TC1	O	F	12885	107.56 ± 66.47	1385962.67	5.60	6.66	1.19
	TC1	O	M	13396	96.12 ± 62.92	1287600.55	5.82	6.19	1.06
	TC1	Y	F	44257	68.26 ± 39.23	3021094.57	19.23	14.53	0.76
	TC1	Y	M	36933	61.93 ± 32.77	2287436.26	16.05	11.00	0.69
	TC2	N	F	100	127.87 ± 20.09	12787.44	0.04	0.06	1.42
	TC2	N	M	40	107.24 ± 28.26	4289.74	0.02	0.02	1.19
	TC2	O	F	92	104.27 ± 58.44	9592.66	0.04	0.05	1.15
	TC2	O	M	58	78.53 ± 35.51	4554.76	0.03	0.02	0.87
	TC2	Y	F	363	72.08 ± 36.93	26166.42	0.16	0.13	0.80
	TC2	Y	M	162	57.85 ± 24.12	9372.24	0.07	0.05	0.64
	TC3	N	F	9662	129.16 ± 37.22	1247954.18	4.20	6.00	1.43
	TC3	N	M	3976	125.05 ± 53.97	497215.72	1.73	2.39	1.38
	TC3	O	F	6330	106.69 ± 62.88	675329.72	2.75	3.25	1.18
	TC3	O	M	3903	102.45 ± 64.84	399860.17	1.70	1.92	1.13
	TC3	Y	F	25023	66.80 ± 35.57	1671536.94	10.87	8.04	0.74
	TC3	Y	M	13128	63.31 ± 30.97	831118.9	5.70	4.00	0.70
Alpha- and Beta-receptor blockers	TC1	N	F	13	338.75 ± 238.47	4403.77	0.02	0.06	3.10
	TC1	N	M	9	305.02 ± 108.56	2745.14	0.01	0.04	2.79
	TC1	O	F	1294	160.48 ± 58.55	207665.36	1.81	2.66	1.47

Table H4 (cont.): Number of items with respect to treatment category, generic indicator and gender according to pharmacological group for the year 2008

Pharmacological group	Treatment category	Generic indicator	Gender	Number of items	Average cost (R)	Total cost (R)	Prevalence %	Cost %	CPI
	TC1	O	M	1778	164.69 ± 66.80	292812.45	2.49	3.74	1.50
	TC1	Y	F	14680	98.80 ± 37.22	1450454.14	20.54	18.54	0.90
	TC1	Y	M	16807	101.49 ± 38.85	1705812.39	23.52	21.81	0.93
	TC2	O	F	34	183.44 ± 72.43	6237.02	0.05	0.08	1.68
	TC2	O	M	20	181.90 ± 54.17	3637.91	0.03	0.05	1.66
	TC2	Y	F	171	112.45 ± 38.23	19228.91	0.24	0.25	1.03
	TC2	Y	M	207	106.38 ± 38.64	22021.23	0.29	0.28	0.97
	TC3	N	F	8	261.68 ± 96.79	2093.42	0.01	0.03	2.39
	TC3	N	M	3	826.75 ± 513.50	2480.25	0.00	0.03	7.55
	TC3	O	F	1700	165.54 ± 62.12	281412.97	2.38	3.60	1.51
	TC3	O	M	2037	175.98 ± 68.08	358476.12	2.85	4.58	1.61
	TC3	Y	F	16991	104.98 ± 40.59	1783758.43	23.77	22.81	0.96
	TC3	Y	M	15720	106.75 ± 41.75	1678113.74	21.99	21.46	0.98
Sympathetic nervous blockers	TC1	N	F	2706	142.13 ± 88.63	384593.61	32.44	45.94	1.42
	TC1	N	M	1639	125.48 ± 88.59	205663.9	19.65	24.57	1.25
	TC2	N	F	5	21.21 ± 11.06	106.07	0.06	0.01	0.21
	TC2	N	M	9	32.03 ± 9.13	288.23	0.11	0.03	0.32
	TC3	N	F	2361	71.63 ± 86.99	169119.98	28.31	20.20	0.71
	TC3	N	M	1621	47.78 ± 63.74	77445.58	19.43	9.25	0.48
Direct-acting vasodilators	TC1	N	F	48	192.64 ± 88.80	9246.52	2.32	5.61	2.41
	TC1	N	M	128	187.82 ± 100.69	24041.04	6.20	14.58	2.35
	TC1	O	F	3	140.60 ± 87.76	421.8	0.15	0.26	1.76
	TC1	O	M	1	241.84 ± 0.00	241.84	0.05	0.15	3.03
	TC1	Y	F	330	49.31 ± 20.52	16270.91	15.98	9.87	0.62

Table H4 (cont.): Number of items with respect to treatment category, generic indicator and gender according to pharmacological group for the year 2008

Pharmacological group	Treatment category	Generic indicator	Gender	Number of items	Average cost (R)	Total cost (R)	Prevalence %	Cost %	CPI
	TC1	Y	M	316	48.80 ± 21.27	15421.09	15.30	9.35	0.61
	TC2	N	M	4	332.77 ± 86.35	1331.07	0.19	0.81	4.17
	TC2	O	F	1	247.46 ± 0.00	247.46	0.05	0.15	3.10
	TC2	Y	F	6	49.60 ± 17.35	297.58	0.29	0.18	0.62
	TC2	Y	M	5	61.17 ± 36.74	305.85	0.24	0.19	0.77
	TC3	N	F	85	120.55 ± 73.58	10246.53	4.12	6.21	1.51
	TC3	N	M	203	178.27 ± 112.99	36188.07	9.83	21.95	2.23
	TC3	O	F	2	323.89 ± 198.34	647.78	0.10	0.39	4.06
	TC3	Y	F	570	51.07 ± 22.72	29110.96	27.60	17.66	0.64
	TC3	Y	M	363	57.48 ± 32.77	20863.86	17.58	12.65	0.72
Calcium channel blockers	TC1	N	F	8682	226.04 ± 67.36	1962448.31	4.39	7.56	1.72
	TC1	N	M	7698	242.29 ± 69.10	1865114.84	3.89	7.19	1.85
	TC1	O	F	9822	153.43 ± 50.24	1507014.59	4.97	5.81	1.17
	TC1	O	M	9763	157.99 ± 51.54	1542425.83	4.94	5.94	1.20
	TC1	Y	F	45313	103.48 ± 8.07	4688773.52	22.92	18.07	0.79
	TC1	Y	M	44887	105.78 ± 29.01	4748204.73	22.70	18.30	0.81
	TC2	N	F	65	266.43 ± 52.13	17318.04	0.03	0.07	2.03
	TC2	N	M	44	245.17 ± 47.06	10787.6	0.02	0.04	1.87
	TC2	O	F	44	145.84 ± 38.83	6417.15	0.02	0.02	1.11
	TC2	O	M	19	146.27 ± 26.05	2779.11	0.01	0.01	1.11
	TC2	Y	F	364	110.22 ± 21.77	40119.37	0.18	0.15	0.84
	TC2	Y	M	177	107.26 ± 28.78	18984.75	0.09	0.07	0.82
	TC3	N	F	6560	233.77 ± 72.34	1533512.63	3.32	5.91	1.78
	TC3	N	M	4210	252.60 ± 71.83	1063446.79	2.13	4.10	1.92

Table H4 (cont.): Number of items with respect to treatment category, generic indicator and gender according to pharmacological group for the year 2008

Pharmacological group	Treatment category	Generic indicator	Gender	Number of items	Average cost (R)	Total cost (R)	Prevalence %	Cost %	CPI
	TC3	O	F	5920	160.11 ± 54.33	947851.61	2.99	3.65	1.22
	TC3	O	M	3348	161.81 ± 46.18	541753.01	1.69	2.09	1.23
	TC3	Y	F	31407	106.07 ± 28.18	3331352.38	15.88	12.84	0.81
	TC3	Y	M	19402	109.13 ± 29.56	2117407.19	9.81	8.16	0.83
ACE-Inhibitors	TC1	N	F	12505	203.66 ± 62.48	2546709.66	1.86	3.46	1.86
	TC1	N	M	13443	215.06 ± 61.18	2891019.97	2.00	3.92	1.96
	TC1	O	F	24453	141.14 ± 53.92	3451247.53	3.64	4.68	1.29
	TC1	O	M	25761	142.16 ± 60.01	3662161.4	3.84	4.97	1.30
	TC1	Y	F	181958	102.49 ± 44.41	18648132.72	27.10	25.31	0.93
	TC1	Y	M	193459	100.77 ± 44.89	19494409.61	28.81	26.45	0.92
	TC2	N	F	65	224.02 ± 84.99	14561.04	0.01	0.02	2.04
	TC2	N	M	53	207.49 ± 46.28	10997.22	0.01	0.01	1.89
	TC2	O	F	73	147.92 ± 65.71	10797.84	0.01	0.01	1.35
	TC2	O	M	45	128.84 ± 45.23	5797.74	0.01	0.01	1.17
	TC2	Y	F	1017	110.23 ± 50.64	112101.74	0.15	0.15	1.00
	TC2	Y	M	677	99.15 ± 43.90	67121.66	0.10	0.09	0.90
	TC3	N	F	8116	222.09 ± 58.39	1802464.69	1.21	2.45	2.02
	TC3	N	M	5731	224.45 ± 58.50	1286346.11	0.85	1.75	2.05
	TC3	O	F	10193	142.48 ± 67.40	1452266.48	1.52	1.97	1.30
	TC3	O	M	7243	157.05 ± 76.90	1137517.94	1.08	1.54	1.43
	TC3	Y	F	107488	91.47 ± 46.76	9831965.98	16.01	13.34	0.83
	TC3	Y	M	79192	91.75 ± 46.81	7265701.56	11.79	9.86	0.84
Angiotensin receptor blockers	TC1	N	F	73096	184.87 ± 53.76	13513379.75	27.46	28.29	1.03
	TC1	N	M	61163	185.62 ± 56.84	11353368.19	22.98	23.77	1.03

Table H4 (cont.): Number of items with respect to treatment category, generic indicator and gender according to pharmacological group for the year 2008

Pharmacological group	Treatment category	Generic indicator	Gender	Number of items	Average cost (R)	Total cost (R)	Prevalence %	Cost %	CPI
	TC1	O	F	13360	183.88 ± 56.91	2456591.28	5.02	5.14	1.02
	TC1	O	M	12126	174.17 ± 61.22	2112037.92	4.56	4.42	0.97
	TC1	Y	F	17362	157.93 ± 38.41	2742054.35	6.52	5.74	0.88
	TC1	Y	M	15992	152.13 ± 42.69	2432840.36	6.01	5.09	0.85
	TC2	N	F	316	192.32 ± 44.65	60773.49	0.12	0.13	1.07
	TC2	N	M	173	192.56 ± 66.58	33312.7	0.06	0.07	1.07
	TC2	O	F	55	143.79 ± 55.54	7908.41	0.02	0.02	0.80
	TC2	O	M	21	164.91 ± 56.98	3463.09	0.01	0.01	0.92
	TC2	Y	F	121	149.59 ± 40.97	18100.01	0.05	0.04	0.83
	TC2	Y	M	61	138.14 ± 43.12	8426.75	0.02	0.02	0.77
	TC3	N	F	29750	191.89 ± 52.38	5708635.44	11.18	11.95	1.07
	TC3	N	M	15817	192.74 ± 54.74	3048498.21	5.94	6.38	1.07
	TC3	O	F	7181	175.93± 59.24	1263344.06	2.70	2.64	0.98
	TC3	O	M	3769	167.12 ± 61.93	629869	1.42	1.32	0.93
	TC3	Y	F	10464	151.91 ± 44.17	1589620.35	3.93	3.33	0.85
	TC3	Y	M	5363	146.64 ± 47.11	786439.99	2.01	1.65	0.82
Others	TC1	N	F	2500	211.67 ± 53.32	529172.72	30.08	29.80	0.99
	TC1	N	M	3362	216.95 ± 58.43	729375.33	40.46	41.08	1.02
	TC2	N	F	17	217.15 ± 81.41	3691.58	0.20	0.21	1.02
	TC2	N	M	11	308.76 ± 6.79	3396.4	0.13	0.19	1.45
	TC3	N	F	1562	206.58 ± 61.97	322673.07	18.80	18.17	0.97
	TC3	N	M	858	218.28± 51.76	187284.29	10.32	10.55	1.02
Diuretics	TC1	N	F	232	150.56 ± 249.70	34929.76	0.05	0.18	3.49
	TC1	N	M	101	176.69 ± 267.08	17845.54	0.02	0.09	4.10

Table H4 (cont.): Number of items with respect to treatment category, generic indicator and gender according to pharmacological group for the year 2008

Pharmacological group	Treatment category	Generic indicator	Gender	Number of items	Average cost (R)	Total cost (R)	Prevalence %	Cost %	CPI
	TC1	O	F	225	138.07 ± 49.71	31065.6	0.05	0.16	3.20
	TC1	O	M	192	152.40 ± 64.60	29260.42	0.04	0.15	3.54
	TC1	Y	F	1256	23.79 ± 19.90	29877.59	0.27	0.15	0.55
	TC1	Y	M	913	33.16 ± 45.23	30278.75	0.20	0.15	0.77
	TC2	N	F	15885	85.22 ± 78.49	1353760.53	3.45	6.83	1.98
	TC2	N	M	4415	86.59 ± 104.33	382294.05	0.96	1.93	2.01
	TC2	O	F	7439	121.83 ± 74.58	906265.85	1.62	4.57	2.83
	TC2	O	M	3022	123.22 ± 74.77	372380.64	0.66	1.88	2.86
	TC2	Y	F	84035	22.13 ± 25.96	1859938.67	18.26	9.38	0.51
	TC2	Y	M	32315	24.35 ± 28.70	786960.77	7.02	3.97	0.57
	TC3	N	F	22336	97.18 ± 94.60	2170561.34	4.85	10.95	2.26
	TC3	N	M	11844	126.20 ± 164.38	1494714.8	2.57	7.54	2.93
	TC3	O	F	18283	134.29 ± 63.98	2455173.92	3.97	12.38	3.12
	TC3	O	M	13473	144.89 ± 76.19	1952050.86	2.93	9.84	3.36
	TC3	Y	F	147999	23.71 ± 22.73	3509084.13	32.16	17.70	0.55
	TC3	Y	M	96185	25.07 ± 24.38	2411795.92	20.90	12.16	0.58

APPENDIX I

Table I1: Prescribed daily dosages of top 10 single prescribed active ingredients according to age group for 2005

Rank	AG	Generic indicator	Active ingredient with PDD in mg	Number of Rx	Average cost per Rx (R)	Total cost per Rx (R)
1	1	Y	Perindopril 4	58	123.45 ± 27.88	7 160.11
2	1	Y	Spironolactone 100	58	167.57 ± 18.24	9 719.27
3	1	Y	Amiloride/HCTZ 5/50	53	8.82 ± 7.62	467.72
4	1	Y	Amiloride/HCTZ 75/750	42	6.11 ± 2.20	256.65
5	1	Y	Indapamide 2.5	40	24.86 ± 9.89	994.55
6	1	O	Amlodipine 10	37	215.76 ± 34.89	7 983.20
7	1	Y	Enalapril 10	35	41.36 ± 12.17	1 447.46
8	1	O	Bisoprolol 2.5	33	40.53 ± 4.89	1 337.43
9	1	N	Indapamide/Perindopril 1.25/4	31	179.87 ± 4.34	5 575.95
10	1	Y	Indapamide 37.5	30	22.31 ± 10.40	669.43
1	2	Y	Amiloride/HCTZ 5/50	6 879	11.69 ± 9.45	80 391.77
2	2	Y	Perindopril 4	5 022	129.62 ± 10.31	650 949.73
3	2	Y	Indapamide 2.5	4 957	22.08 ± 9.37	109 457.00
4	2	N	Indapamide/Perindopril 1.25/4	3 792	181.20 ± 11.22	687 113.59
5	2	N	Bisoprolol/HCTZ 5/6.25	3 035	117.11 ± 8.16	355 431.61
6	2	Y	Enalapril/HCTZ 20/12.5	3 023	78.37 ± 4.97	236 902.06
7	2	Y	Enalapril 10	2 851	40.20 ± 7.25	114 606.66
8	2	Y	Enalapril 20	2 278	68.07 ± 10.69	155 073.75
9	2	Y	Lisinopril 10	2 244	50.10 ± 5.95	112 431.04
10	2	Y	Lisinopril 20	1 969	77.74 ± 10.55	153 073.66

Table I1 (cont.): Prescribed daily dosages of top 10 single prescribed active ingredients according to age group for 2005

Rank	AG	Generic indicator	Active ingredient with PDD in mg	Number of Rx	Average cost per Rx (R)	Total cost per Rx (R)
1	3	Y	Amiloride/HCTZ 5/50	42 677	10.52 ± 8.40	449 116.66
2	3	Y	Indapamide 2.5	41 682	23.67 ± 8.87	986 581.67
3	3	Y	Perindopril 4	35 731	130.00 ± 10.65	4 645 016.66
4	3	Y	Enalapril/HCTZ 20/12.5	29 519	78.08 ± 5.41	2 304 817.42
5	3	N	Indapamide/Perindopril 1.25/4	25 991	182.15 ± 16.28	4 734 264.91
6	3	Y	Enalapril 10	20 726	39.84 ± 7.20	825 747.30
7	3	N	Indapamide 1.5	20 046	85.67 ± 5.66	1 717 436.39
8	3	Y	Enalapril 20	19 903	69.05 ± 11.04	1 374 250.99
9	3	N	Bisoprolol/HCTZ 5/6.25	19 029	117.40 ± 9.97	2 234 055.16
10	3	Y	Lisinopril 10	18 937	50.10 ± 6.52	948 705.44

Table I2: Prescribed daily dosages of top 10 single prescribed active ingredients according to age group for 2006

Rank	AG	Generic indicator	Active ingredient with PDD in mg	Number of Rx	Average cost per Rx (R)	Total cost per Rx(R)
1	1	Y	Amiloride/HCTZ 5/50	109	16.17 ± 10.64	1 763.06
2	1	Y	Perindopril 4	72	124.20 ± 26.18	8 942.36
3	1	Y	Spironolactone 100	69	174.56 ± 14.57	12 044.89
4	1	O	Amlodipine 5	40	134.31 ± 3.47	5 372.55
5	1	O	Bisoprolol 5	35	58.65 ± 24.29	2 052.58
6	1	O	Bisoprolol 2.5	31	41.58 ± 9.41	1 288.98
7	1	Y	Enalapril 10	29	36.27 ± 3.91	1 051.75
8	1	Y	Indapamide 2.5	28	18.59 ± 9.83	520.41
9	1	Y	Indapamide / Perindopril 4/1.25	24	139.65 ± 43.37	3 351.48
10	1	Y	Bisoprolol5	23	50.68 ± 15.61	1 165.73
1	2	Y	Perindopril 4	6 976	128.89 ± 16.04	899 153.99
2	2	Y	Amiloride/HCTZ 5/50	6 730	11.20 ± 9.06	75 390.93
3	2	Y	Indapamide2.5	5 164	21.30 ± 9.22	109 992.41
4	2	Y	Indapamide / Perindopril 4/1.25	4 797	148.23 ± 19.63	711 049.64

Table I2 (cont.): Prescribed daily dosages of top 10 single prescribed active ingredients according to age group for 2006

Rank	AG	Generic indicator	Active ingredient with PDD in mg	Number of Rx	Average cost per Rx (R)	Total cost per Rx(R)
5	2	Y	Enalapril /HCTZ 20/12.5	3 788	77.58 ±7.44	293 884.04
6	2	N	Bisoprolol /HCTZ 5/6.25	3 318	115.49 ±12.24	383 189.55
7	2	O	Indapamide / Perindopril 1.25/4	3 309	179.15 ± 26.38	592 822.41
8	2	Y	Enalapril 10	3 211	39.70 ± 8.19	127 475.80
9	2	Y	Enalapril 20	2 721	67.52 ± 11.10	183 730.49
10	2	Y	Lisinopril 10	2 419	49.48 ± 8.54	119 681.74
1	3	Y	Perindopril 4	47 832	129.57 ± 13.45	6 197 604.47
2	3	Y	Indapamide 2.5	44 356	23.00 ± 9.04	1 020 260.62
3	3	Y	Amiloride /HCTZ 5/50	42 793	10.07 ± 8.07	430 896.98
4	3	Y	Enalapril /HCTZ 20/12.5	35 310	77.62 ± 6.56	2 740 607.02
5	3	Y	Indapamide / Perindopril 4/1.25	29 229	149.81 ± 12.81	4 378 738.02
6	3	Y	Enalapril 20	24 696	67.33 ± 9.01	1 662 688.94
7	3	Y	Enalapril 10	23 640	39.32 ± 7.28	929 556.47
8	3	O	Indapamide / Perindopril 1.25/4	22 507	181.64 ± 17.96	4 088 072.16
9	3	Y	Lisinopril 10	21 166	49.73 ± 7.43	1 052 535.53
10	3	N	Bisoprolol /HCTZ 5/6.25	20 795	115.97 ± 10.64	2 411 670.44

Table I3: Prescribed daily dosages of top 10 single prescribed active ingredients according to age group for 2007

Rank	AG	Generic indicator	Active ingredient with PDD in mg	Number of Rx	Average cost per Rx (R)	Total cost per Rx (R)
1	1	Y	Spironolactone 100	69	176.17 ± 24.19	12 155.72
2	1	Y	Amlodipine 5	51	100.59 ± 15.43	5 130.21
3	1	Y	Amiloride/HCTZ 5/50	45	5.83 ± 2.45	262.19
4	1	Y	Enalapril 10	43	42.30 ± 4.48	1 818.99
5	1	Y	Perindopril 4	41	125.17 ± 32.02	5 132.10
6	1	O	Bisoprolol 2.5	34	41.59 ± 7.98	1 414.00
7	1	Y	Indapamide/Perindopril 4/1.25	31	146.91 ± 17.90	4 554.36
8	1	O	Amlodipine 5	28	138.44 ± 9.61	3 876.25

Table I3 (cont.): Prescribed daily dosages of top 10 single prescribed active ingredients according to age group for 2007

Rank	AG	Generic indicator	Active ingredient with PDD in mg	Number of Rx	Average cost per Rx (R)	Total cost per Rx (R)
9	1	Y	Spironolactone 25	28	28.53 ± 9.42	798.83
10	1	Y	Bisoprolol 5	25	50.62 ± 11.01	1 265.49
1	2	Y	Perindopril 4	7 282	124.82 ± 27.11	908 974.25
2	2	Y	Indapamide/Perindopril 4/1.25	7 263	146.10 ± 28.17	1 061 159.75
3	2	Y	Amloride/HCTZ 5/50	4 253	7.55 ± 4.92	32 095.26
4	2	Y	Indapamide 2.5	3 621	19.60 ± 9.69	70 985.70
5	2	Y	Enalapril/HCTZ 20/12.5	3 128	80.77 ± 11.24	252 632.99
6	2	N	Bisoprolol/HCTZ 5/6.25	2 852	116.04 ± 23.37	330 949.39
7	2	Y	Enalapril 10	2 234	39.22 ± 8.75	87 626.66
8	2	Y	Enalapril 20	2 092	70.91 ± 12.03	148 351.13
9	2	Y	Lisinopril 20	1 989	78.62 ± 17.86	156 385.03
10	2	Y	Lisinopril 10	1 926	49.90 ± 12.21	96 102.90
1	3	Y	Perindopril 4	51 143	129.99 ± 17.02	6 647 919.90
2	3	Y	Indapamide/Perindopril 4/1.25	50 619	150.89 ± 18.59	7 637 795.21
3	3	Y	Indapamide 2.5	38 785	23.46 ± 9.81	910 011.13
4	3	Y	Amloride/HCTZ 5/50	33 889	8.90 ± 5.38	301 588.61
5	3	Y	Enalapril/HCTZ 20/12.5	32 066	82.50 ± 10.37	2 645 512.73
6	3	Y	Enalapril 20	20 735	71.55 ± 11.30	1 483 599.91
7	3	N	Bisoprolol/HCTZ 5/6.25	19 871	119.53 ± 19.51	2 375 214.14
8	3	Y	Enalapril 10	19 643	41.07 ± 7.70	806 681.51
9	3	Y	Lisinopril 20	18 122	82.18 ± 15.51	1 489 187.65
10	3	Y	Lisinopril 10	17 905	52.01 ± 10.05	931 261.03

Table I4: Prescribed daily dosages of top 10 single prescribed active ingredients according to age group for 2008

Rank	AG	Generic indicator	Active ingredient	Prescribed daily dose in mg	Number of prescriptions	Average cost per prescription (R)	Total cost per prescription (R)
1	1	Y	Spironolactone	100	83	173.98 ± 32.49	14 440.44
2	1	Y	Amiloride/HCTZ	5/50	49	8.25 ± 6.81	404.19
3	1	Y	Amlodipine	5	33	94.69 ± 19.14	3 124.88
4	1	Y	Perindopril	4	33	137.05 ± 17.78	4 522.71
5	1	O	Bisoprolol	2.5	27	45.60 ± 3.74	1 231.32
6	1	Y	Amlodipine	10	26	154.95 ± 43.86	4 028.67
7	1	Y	Enalapril	10	26	43.54 ± 3.98	1 132.12
8	1	O	Bisoprolol	5	25	67.19 ± 20.66	1 679.84
9	1	Y	Furosemide	20	20	17.25 ± 9.96	344.97
10	1	Y	Bisoprolol	5	19	50.43 ± 11.46	958.25
1	2	Y	Indapamide/Perindopril	4/1.25	7 537	147.73 ± 27.88	1 113 456.89
2	2	Y	Perindopril	4	6 146	125.50 ± 28.10	771 297.09
3	2	Y	Amiloride/HCTZ	5/50	4 093	12.46 ± 9.49	50 989.88
4	2	Y	Enalapril/HCTZ	20/12.5	3 713	84.45 ± 10.03	313 545.06
5	2	Y	Indapamide	2.5	3 339	23.31 ± 10.82	77 841.25
6	2	Y	Enalapril	20	2 235	73.09 ± 13.32	163 353.53
7	2	Y	Enalapril	10	2 181	42.94 ± 9.57	93 655.81
8	2	N	Bisoprolol /HCTZ	5/6.25	2 049	118.78 ± 29.61	243 383.13
9	2	Y	Lisinopril	10	1 846	50.81 ± 13.67	93 786.12
10	2	Y	Lisinopril	20	1 663	80.41 ± 19.24	133 714.34
1	3	Y	Indapamide/Perindopril	4/1.25	56 805	152.87 ± 18.84	8 683 732.63
2	3	Y	Perindopril	4	47 176	130.62 ± 20.24	6 162 087.75
3	3	Y	Indapamide	2.5	37 041	24.87 ± 10.01	921 164.54
4	3	Y	Amiloride/HCTZ	5/50	34 376	11.25 ± 7.87	386 690.51
5	3	Y	Enalapril /HCTZ	20/12.5	34 309	85.43 ± 10.46	2 931 153.71

Table I4 (cont.): Prescribed daily dosages of top 10 single prescribed active ingredients according to age group for 2008

Rank	AG	Generic indicator	Active ingredient	Prescribed daily dose in mg	Number of prescriptions	Average cost per prescription (R)	Total cost per prescription (R)
6	3	Y	Enalapril	20	22 213	73.89 ± 10.96	1 641 345.99
7	3	Y	Amlodipine	5	20 480	91.89 ± 19.32	1 881 870.36
8	3	Y	Enalapril	10	20 189	43.18 ± 8.80	871 697.35
9	3	Y	Bisoprolol	5	18 464	51.78 ± 10.00	956 084.44
10	3	Y	Lisinopril	20	18 417	83.52 ± 15.37	1 538 161.37

Table I5: Prescribed daily dosages of top 10 double prescribed active ingredients according to age group for 2005

Rank	AG	GI 1	GI 2	Active ingredient 1	Active ingredient 2	PDD 1	PDD 2	Number of observations	Average cost per prescription (R)	Total cost per prescription (R)
1	1	Y	N	Captopril	Furosemide	25	20	17	117.29 ± 25.58	1 994.01
2	1	O	O	Amlodipine	Perindopril	5	4	13	282.13 ± 11.83	3 667.70
3	1	Y	N	Captopril	Furosemide	12.5	20	11	93.53 ± 0.00	1 028.83
4	1	Y	Y	Carvedilol	Lisinopril	12.5	10	10	121.20 ± 0.00	1 212.00
5	1	Y	Y	Captopril	Sotalol	37.5	120	8	96.61 ± 0.00	772.88
6	1	O	N	Captopril	Furosemide	375	300	7	240.45 ± 21.04	1 683.13
7	1	O	Y	Furosemide	Spironolactone	40	50	7	172.42 ± 0.00	1 206.94
8	1	Y	Y	Amiloride/HCTZ	Propranolol	2.5/25	80	7	24.21 ± 2.56	169.46
9	1	Y	Y	Amiloride/HCTZ	Bisoprolol	2.5/25	2.5	6	26.27 ± 0.00	157.62
10	1	Y	Y	Captopril	Spironolactone	37.5	25	6	45.86 ± 0.00	275.16
1	2	Y	Y	Indapamide	Perindopril	2.5	4	749	149.34 ± 9.86	111 854.70
2	2	Y	Y	Amiloride/HCTZ	Captopril	5/50	50	456	52.21 ± 21.01	23 808.71
3	2	Y	N	Amiloride/HCTZ	Reserpine	5/50	0.25	410	51.42 ± 20.99	21 082.89
4	2	Y	Y	Amiloride/HCTZ	Perindopril	5/50	4	320	139.21 ± 9.51	44 548.17
5	2	Y	Y	Captopril	Indapamide	50	2.5	289	61.15 ± 21.45	17 671.42
6	2	Y	Y	Amiloride/HCTZ	Enalapril	5/50	10	280	49.65 ± 12.29	13 901.82
7	2	Y	Y	Enalapril	Indapamide	20	2.5	279	92.93 ± 15.12	25 927.79

Table I5 (cont.): Prescribed daily dosages of top 10 double prescribed active ingredients according to age group for 2005

Rank	AG	GI 1	GI 2	Active ingredient 1	Active ingredient 2	PDD 1	PDD 2	Number of observations	Average cost per prescription (R)	Total cost per prescription (R)
8	2	Y	Y	Enalapril	HCTZ	20	12.5	262	77.86 ± 14.36	20 399.62
9	2	Y	Y	Indapamide	Lisinopril	2.5	20	252	98.50 ± 13.87	24 822.10
10	2	Y	Y	Enalapril	Indapamide	10	2.5	246	58.74 ± 12.32	14 450.45
1	3	Y	Y	Indapamide	Perindopril	2.5	4	6 281	150.90 ± 14.66	947 794.15
2	3	Y	Y	HCTZ	Lisinopril	12.5	20	2 540	85.01 ± 15.03	215 919.93
3	3	Y	Y	Indapamide	Lisinopril	2.5	20	2 494	100.75 ± 15.14	251 261.48
4	3	Y	Y	Amloride/HCTZ	Captopril	5/50	50	2 348	52.61 ± 21.15	123 535.76
5	3	Y	Y	Enalapril	HCTZ	20	12.5	2 191	76.83 ± 14.99	168 339.60
6	3	Y	Y	HCTZ	Lisinopril	25	20	2 086	93.27 ± 15.93	194 564.28
7	3	Y	Y	Enalapril	Indapamide	20	2.5	2 039	92.52 ± 16.04	188 639.60
8	3	Y	Y	Enalapril	HCTZ	20	25	1 857	85.22 ± 15.06	158 258.61
9	3	Y	Y	Amloride/HCTZ	Perindopril	5/50	4	1 823	140.03 ± 11.04	255 270.50
10	3	Y	Y	Amloride/HCTZ	Enalapril	5/50	20	1 609	80.56 ± 15.35	129 618.47

Table I6: Prescribed daily dosages of top 10 double prescribed active ingredients according to age group for 2006

Rank	AG	GI 1	GI 2	Active ingredient 1	Active ingredient 2	PDD 1	PDD 2	Number of observations	Average cost per observation (R)	Total cost per prescription(R)
1	1	O	O	Amlodipine	Perindopril	5	4	22	275.37 ± 1.36	6 058.21
2	1	Y	Y	Furosemide	Spironolactone	40	25	10	56.76 ± 0.01	567.60
3	1	O	O	Indapamide/Perindopril	Lisinopril	1.25/4	10	9	252.98 ± 0.00	2 276.82
4	1	Y	N	Captopril	Furosemide	25	20	9	92.08 ± 10.34	828.68
5	1	Y	Y	Amlodipine	Carvedilol	10	12.5	9	193.13 ± 1.03	1 738.19
6	1	Y	Y	Amlodipine	Lisinopril	5	10	9	153.90 ± 2.08	1 385.14
7	1	Y	Y	Bisoprolol	Perindopril	5	2	9	117.00 ± 3.91	1 053.01
8	1	Y	Y	Carvedilol	Lisinopril	12.5	10	9	119.38 ± 47.85	1 074.39
9	1	O	Y	Amlodipine	Enalapril	10	10	8	210.72 ± 0.37	1 685.76

Table I6 (cont.): Prescribed daily dosages of top 10 double prescribed active ingredients according to age group for 2006

Rank	AG	GI 1	GI 2	Active ingredient 1	Active ingredient 2	PDD 1	PDD 2	Number of observations	Average cost per observation (R)	Total cost per prescription(R)
10	1	Y	Y	Captopril	HCTZ	50	25	8	69.94 ± 0.00	559.52
1	2	Y	Y	Indapamide	Perindopril	2.5	4	848	151.03 ± 13.33	128 073.17
2	2	Y	N	Amiloride/HCTZ	Reserpine	5/50	0.25	529	52.38 ± 17.24	27 709.39
3	2	Y	Y	HCTZ	Perindopril	25	4	395	146.27 ± 11.94	57 775.02
4	2	Y	Y	Amiloride/HCTZ	Captopril	5/50	50	383	54.22 ± 18.92	20 768.10
5	2	Y	Y	Amiloride/HCTZ	Perindopril	5/50	4	330	139.53 ± 6.79	46 046.21
6	2	Y	Y	Amiloride/HCTZ	Enalapril	5/50	20	320	83.36 ± 15.67	26 675.26
7	2	Y	Y	Enalapril	Indapamide	20	2.5	318	90.23 ± 14.62	28 694.06
8	2	Y	Y	Enalapril	Indapamide	10	2.5	302	58.36 ± 11.20	17 624.19
9	2	Y	Y	Indapamide	Lisinopril	2.5	20	280	96.49 ± 15.09	27 018.26
10	2	Y	Y	Enalapril	HCTZ	20	12.5	264	84.87 ± 16.26	22 405.29
1	3	Y	Y	Indapamide	Perindopril	2.5	4	6 795	152.21 ± 12.75	1 034 265.68
2	3	Y	Y	Indapamide	Lisinopril	2.5	20	3 001	97.41 ± 15.61	292 315.17
3	3	Y	Y	Enalapril	Indapamide	20	2.5	2 671	89.41 ± 13.73	238 801.03
4	3	Y	Y	HCTZ	Lisinopril	25	20	2 337	92.35 ± 16.55	215 829.94
5	3	Y	Y	HCTZ	Lisinopril	12.5	20	2 317	85.27 ± 15.50	197 566.19
6	3	Y	Y	Enalapril	HCTZ	20	25	2 299	84.17 ± 14.81	193 497.98
7	3	Y	Y	Amiloride/HCTZ	Perindopril	5/50	4	2 245	139.83 ± 9.06	313 907.29
8	3	Y	Y	Amiloride/HCTZ	Captopril	5/50	50	2 213	52.05 ± 19.43	115 190.32
9	3	Y	Y	HCTZ	Perindopril	25	4	1 999	145.43 ± 16.25	290 718.27
10	3	Y	Y	Indapamide	Lisinopril	2.5	10	1 969	71.90 ± 15.40	141 570.24

Table I7: Prescribed daily dosages of top 10 double prescribed active ingredients according to age group for 2007

Rank	AG	GI 1	GI 2	Active ingredient 1	Active ingredient 2	PDD 1	PDD 2	Number of observations	Average cost per observation (R)	Total cost per prescription(R)
1	1	O	O	Amlodipine	Perindopril	5	4	17	290.12 ± 6.61	4 932.10
2	1	O	Y	Furosemide	Spironolactone	20	25	8	119.55 ± 2.11	956.36
3	1	Y	Y	Furosemide	Spironolactone	40	25	8	51.16 ± 4.36	409.30
4	1	Y	Y	Amiloride/HCTZ	Captopril	2.5/25	6.25	7	0.00 ± 0.00	0.00
5	1	O	Y	Amlodipine	Enalapril	10	10	6	235.11 ± 3.26	1 410.65
6	1	Y	Y	HCTZ	Spironolactone	12.5	50	6	56.30 ± 27.58	337.80
7	1	O	O	Captopril	Furosemide	250	21.4	5	227.94 ± 0.00	1 139.70
8	1	O	O	Captopril	Spironolactone	3.3	8.3	4	45.92 ± 0.00	183.68
9	1	Y	Y	Captopril	Furosemide	25	16	4	19.76 ± 5.35	79.03
10	1	Y	Y	Carvedilol	Lisinopril	12.5	10	4	118.90 ± 79.45	475.60
1	2	Y	Y	Indapamide	Perindopril	2.5	4	595	150.27 ± 18.71	89 412.27
2	2	Y	Y	Amlodipine	Indapamide/ Perindopril	5	1.25/4	435	240.69 ± 55.47	104 700.36
3	2	Y	Y	HCTZ	Perindopril	25	4	323	146.12 ± 10.54	47 197.97
4	2	Y	Y	Amlodipine	Indapamide/ Perindopril	10	1.25/4	313	286.40 ± 46.64	89 642.11
5	2	Y	Y	Amlodipine	Perindopril	5	4	246	223.25 ± 40.30	54 920.43
6	2	Y	Y	Enalapril	Indapamide	20	2.5	246	90.85 ± 11.90	22 348.72
7	2	Y	Y	Amlodipine	Indapamide	5	2.5	240	119.17 ± 22.70	28 601.38
8	2	Y	Y	Amiloride/HCTZ	Perindopril	5/50	4	217	138.74 ± 10.92	30 106.82
9	2	Y	Y	Enalapril	Indapamide	10	2.5	216	55.25 ± 10.93	11 933.47
10	2	Y	Y	Indapamide	Lisinopril	2.5	20	210	97.89 ± 18.15	20 556.59
1	3	Y	Y	Indapamide	Perindopril	2.5	4	5 324	153.07 ± 16.84	814 942.48
2	3	Y	Y	Amlodipine	Indapamide/ Perindopril	5	1.25/4	3 326	254.68 ± 23.96	847 061.00
3	3	Y	Y	Indapamide	Lisinopril	2.5	20	2 767	103.73 ± 17.24	287 022.36
4	3	Y	Y	Enalapril	Indapamide	20	2.5	2 130	91.69 ± 17.06	195 306.35
5	3	Y	Y	Bisoprolol	Indapamide/ Perindopril	5	1.25/4	2 102	202.97 ± 14.90	426 653.21
6	3	Y	Y	Amiloride/HCTZ	Perindopril	5/50	4	1 991	139.54 ± 16.26	277 821.55

Table I7 (cont.): Prescribed daily dosages of top 10 double prescribed active ingredients according to age group for 2007

Rank	AG	GI 1	GI 2	Active ingredient 1	Active ingredient 2	PDD 1	PDD 2	Number of observations	Average cost per observation (R)	Total cost per prescription(R)
7	3	Y	Y	HCTZ	Perindopril	25	4	1 989	146.25 ± 21.04	290 884.83
8	3	Y	Y	Amlodipine	Indapamide/ Perindopril	10	1.25/4	1 876	295.06 ± 20.37	553 524.82
9	3	Y	Y	Amlodipine	Enalapril/HCTZ	5	20/12.5	1 839	185.20 ± 21.45	340 576.19
10	3	Y	Y	Amlodipine	Perindopril	5	4	1 823	234.47 ± 18.19	427 447.50

Table I8: Prescribed daily dosages of top 10 double prescribed active ingredients according to age group for 2008

Rank	AG	GI 1	GI 2	Active ingredient 1	Active ingredient 2	PDD 1	PDD 2	Number of observations	Average cost per observation (R)	Total cost per prescription (R)
1	1	Y	Y	Furosemide	Lisinopril	40	10	13	90.92 ± 2.16	1 181.90
2	1	O	Y	Amlodipine	Spironolactone	5	25	9	177.22 ± 3.55	1 594.94
3	1	Y	Y	Carvedilol	Lisinopril	12.5	10	9	53.48 ± 80.24	481.29
4	1	O	Y	Enalapril	Spironolactone	1.25	13.39	7	39.04 ± 0.52	273.28
5	1	Y	Y	Ramipril	Spironolactone	9.375	26.79	7	108.01 ± 3.46	756.09
6	1	Y	Y	Amiloride/HCTZ	Captopril	2.5/25	6.25	6	0.00 ± 0.00	0.00
7	1	Y	Y	Enalapril	HCTZ	20	25	6	108.34 ± 1.72	650.04
8	1	Y	Y	HCTZ	Spironolactone	12.5	50	6	48.14 ± 37.43	288.84
9	1	O	O	Amlodipine	Perindopril	10	4	5	352.50 ± 7.75	1 762.51
10	1	Y	Y	Amiloride/HCTZ	Lisinopril	5/50	10	5	54.00 ± 1.83	269.98
1	2	Y	Y	Amlodipine	Indapamide/Perindopril	5	1.25/4	582	234.52 ± 49.16	136 491.26
2	2	Y	Y	Amlodipine	Indapamide/Perindopril	10	1.25/4	451	270.07 ± 52.62	121 800.65
3	2	Y	Y	Indapamide	Perindopril	2.5	4	364	153.50 ± 16.39	55 874.16
4	2	Y	Y	Amiloride/HCTZ	Enalapril	5/50	10	338	68.84 ± 16.92	23 266.26
5	2	Y	Y	Amlodipine	Indapamide	5	2.5	254	110.14 ± 24.57	27 976.37
6	2	Y	Y	Enalapril	Indapamide	20	2.5	239	100.06 ± 15.08	23 915.18
7	2	Y	Y	Enalapril	Indapamide	10	2.5	222	66.46 ± 21.93	14 753.61
8	2	Y	Y	Amiloride/HCTZ	Enalapril	5/50	20	219	89.26 ± 13.32	19 547.55
9	2	Y	Y	HCTZ	Perindopril	25	4	194	147.30 ± 14.99	28 576.02

Table I8 (cont.): Prescribed daily dosages of top 10 double prescribed active ingredients according to age group for 2008

Rank	AG	GI 1	GI 2	Active ingredient 1	Active ingredient 2	PDD 1	PDD 2	Number of observations	Average cost per observation (R)	Total cost per prescription (R)
10	2	Y	Y	Amlodipine	Perindopril	5	4	191	221.94 ± 14.86	42 390.99
1	3	Y	Y	Amlodipine	Indapamide/Perindopril	5	1.25/4	4 469	245.32 ± 29.41	1 096 322.83
2	3	Y	Y	Indapamide	Perindopril	2.5	4	3 909	154.68 ± 17.16	604 651.51
3	3	Y	Y	Enalapril	Indapamide	20	2.5	3 138	98.93 ± 16.17	310 435.29
4	3	Y	Y	Indapamide	Lisinopril	2.5	20	2 950	105.24 ± 18.58	310 458.16
5	3	Y	Y	Bisoprolol	Indapamide/Perindopril	5	1.25/4	2 477	206.42 ± 16.96	511 306.15
6	3	Y	Y	Amlodipine	Enalapril /HCTZ	5	20/12.5	2 451	177.84 ± 21.97	435 874.55
7	3	Y	Y	Amlodipine	Indapamide/Perindopril	10	1.25/4	2 447	282.40 ± 26.85	691 038.90
8	3	Y	Y	Amiloride/HCTZ	Enalapril	5/50	20	2 213	89.99 ± 14.59	199 151.90
9	3	Y	Y	Amiloride/HCTZ	Enalapril	5/50	10	2 090	59.25 ± 16.59	123 823.29
10	3	Y	Y	Amlodipine	Perindopril	5	4	2 073	222.66 ± 24.42	461 575.32

Table I9: Prescribed daily dosages of top 10 observations of prescriptions with three active ingredients according to age group for 2005

Rank	AG	GI 1	GI 2	GI 3	Active ingredient 1 with PDD in mg	Active ingredient 2 with PDD in mg	Active ingredient 3 with PDD in mg	Number of Rx	Average cost per Rx (R)	Total cost per Rx (R)
1	1	Y	Y	Y	Amlodipine 10	Enalapril 20	HCTZ 12.5	8	263.12 ± 0.01	2 104.94
2	1	O	O	O	Enalapril 4.67	Furosemide 40	Spironolactone 25	5	242.31 ± 0.01	1 211.57
3	1	O	O	Y	Amlodipine 10	Indapamide/Perindopril 1.25/4	Perindopril 4	4	545.27 ± 0	2 181.08
4	1	O	Y	Y	Amlodipine 10	Doxazosin 0.5	HCTZ 12.5	3	293.51 ± 0	880.53
5	1	N	Y	Y	Bumetanide 1	Captopril 19.17	Spironolactone 50	2	179.88 ± 2.47	359.76
6	1	O	O	Y	Acebutolol 400	Amlodipine 5	Enalapril/HCTZ 20/12.5	2	429.84 ± 0	859.68
7	1	O	Y	Y	Amlodipine 5	Doxazosin 4	HCTZ 12.5	2	344.14 ± 0	688.28
8	1	Y	N	Y	Enalapril 5	Furosemide 33.33	Spironolactone 25	2	244.76 ± 0	489.52
9	1	Y	O	O	Amiloride/HCTZ 5/50	Felodipine 10	Furosemide 40	2	313.24 ± 77.44	626.48
10	1	Y	Y	Y	Enalapril 25.5	Furosemide 20	Spironolactone 12.5	2	57.76 ± 0	115.52
1	2	Y	Y	N	Amiloride/HCTZ 5/50	Perindopril 4	Reserpine 0.25	22	152.13 ± 0.51	3 346.88
2	2	Y	Y	N	Amiloride/HCTZ 2.5/25	Propranolol 80	Reserpine 0.25	20	75.45 ± 31.51	1 509.00

Table I9 (cont.): Prescribed daily dosages of top 10 observations of prescriptions with three active ingredients according to age group for 2005

Rank	AG	GI 1	GI 2	GI 3	Active ingredient 1 with PDD in mg	Active ingredient 2 with PDD in mg	Active ingredient 3 with PDD in mg	Number of Rx	Average cost per Rx (R)	Total cost per Rx (R)
3	2	Y	Y	Y	Amloride/HCTZ 5/50	Captopril 100	Methyldopa 750	20	158.37 ± 5.77	3 167.38
4	2	Y	Y	Y	Amlodipine 10	Atenolol/Chlortalidone 50/12.5	Enalapril 20	20	268.33 ± 13.82	5 366.64
5	2	Y	Y	Y	Amloride/HCTZ 2.5/25	Captopril 50	Propranolol 80	19	91.11 ± 27.96	1 731.16
6	2	Y	Y	Y	Doxazosin 1	Enalapril 20	HCTZ 25	19	187.35 ± 3.39	3 559.67
7	2	Y	Y	Y	Amlodipine 5	Indapamide 2.5	Perindopril 4	18	257.12 ± 15.88	4 628.09
8	2	Y	Y	Y	Amlodipine 10	Indapamide 2.5	Perindopril 4	16	299.85 ± 14.88	4 797.56
9	2	Y	Y	Y	Carvedilol 25	Felodipine 5	Perindopril 4	16	336.33 ± 5.50	5 381.26
10	2	N	N	N	Losartan/HCTZ 50/12.5	Nebivolol 5	Nifedipine 60	14	765.91 ± 33.71	10 722.74
1	3	Y	Y	Y	Carvedilol 25	Indapamide 2.5	Perindopril 4	201	246.32 ± 17.26	49 510.28
2	3	Y	Y	Y	Amlodipine 5	Indapamide 2.5	Perindopril 4	154	253.41 ± 13.50	39 025.63
3	3	Y	Y	Y	Furosemide 40	Perindopril 4	Spironolactone 25	132	189.97 ± 17.60	25 076.35
4	3	Y	Y	Y	Carvedilol 25	Furosemide 40	Perindopril 4	113	266.52 ± 26.84	30 116.94
5	3	Y	Y	Y	Carvedilol 12.5	Furosemide 40	Spironolactone 25	84	121.06 ± 20.46	10 169.33
6	3	Y	Y	Y	Carvedilol 12.5	Furosemide 40	Perindopril 4	74	227.55 ± 19.64	16 838.56
7	3	Y	Y	Y	Felodipine 5	HCTZ 12.5	Lisinopril 20	74	185.29 ± 25.40	13 711.34
8	3	Y	Y	Y	Bisoprolol 5	Indapamide 2.5	Perindopril 4	72	210.19 ± 18.14	15 134.01
9	3	Y	Y	Y	Carvedilol 25	Perindopril 4	Spironolactone 25	72	277.25 ± 29.10	19 961.83
10	3	O	Y	Y	Amlodipine 5	HCTZ 12.5	Lisinopril 20	67	217.56 ± 24.53	14 576.65

Table I10: Prescribed daily dosages of top 10 observations of prescriptions with three active ingredients according to age group for 2006

Rank	AG	GI1	GI 2	GI 3	Active ingredient 1 with PDD in mg	Active ingredient 2 with PDD in mg	Active ingredient 3 with PDD in mg	Number of RX	Average cost per RX (R)	Total cost per Rx (R)
1	1	O	Y	Y	Amlodipine 10	Doxazosin 4	HCTZ 12.5	12	447.15 ± 0.00	5 365.80
2	1	Y	Y	Y	Captopril 12.5	HCTZ 12.5	Spironolactone 12.5	10	35.27 ± 0.01	352.68
3	1	O	O	Y	Carvedilol 3.125	Ramipril 1.25	Triamterene/HCTZ 12.5/25	9	158.18 ± 0.34	1 423.59
4	1	N	O	O	Bumetanide 1	Furosemide 40	Spironolactone 100	6	373.49 ± 69.34	2 240.96

Table I10 (cont.): Prescribed daily dosages of top 10 observations of prescriptions with three active ingredients according to age group for 2006

Rank	AG	GI1	GI 2	GI 3	Active ingredient 1 with PDD in mg	Active ingredient 2 with PDD in mg	Active ingredient 3 with PDD in mg	Number of RX	Average cost per RX (R)	Total cost per Rx (R)
5	1	O	N	Y	Enalapril 4.67	Furosemide 40	Spironolactone 25	6	231.79 ± 1.04	1 390.71
6	1	O	Y	Y	Amlodipine 5	Prazosin 2	Ramipril 2.5	6	315.60 ± 25.52	1 893.62
7	1	Y	Y	Y	Captopril 25	Furosemide 40	Spironolactone 25	5	14.12 ± 0.04	70.60
8	1	O	O	Y	Carvedilol 6.70	Ramipril 1.25	Triamterene/HCTZ 26.8/53.6	4	220.54 ± 0.00	882.16
9	1	N	O	Y	Furosemide 60	Sotalol 160	Spironolactone 25	3	425.08 ± 0.00	1 275.24
10	1	O	Y	O	Amlodipine 10	Captopril 25	Furosemide 80	3	409.25 ± 0.00	1 227.75
1	2	Y	Y	Y	Amlodipine 5	Indapamide 2.5	Perindopril 4	39	249.60 ± 6.88	9 734.56
2	2	Y	Y	Y	Carvedilol 25	Indapamide 2.5	Perindopril 4	23	255.56 ± 16.21	5 877.91
3	2	Y	Y	Y	Amlodipine 5	Enalapril 20	Indapamide 2.5	22	182.77 ± 6.56	4 020.91
4	2	Y	Y	Y	Amlodipine 10	Bisoprolol 10	Enalapril /HCTZ 20/12.5	21	302.91 ± 22.40	6 361.17
5	2	Y	Y	Y	Amlodipine 5	Enalapril 20	HCTZ 12.5	18	179.92 ± 10.75	3 238.52
6	2	Y	Y	Y	Carvedilol 25	Felodipine 5	Perindopril 4	18	323.62 ± 0.00	5 825.16
7	2	Y	Y	Y	Amiloride/HCTZ 5/50	Amlodipine 5	Captopril 50	17	128.37 ± 0.37	2 182.32
8	2	Y	Y	Y	Amlodipine 5	Bisoprolol 5	Perindopril 4	17	282.85 ± 16.03	4 808.40
9	2	Y	N	N	Enalapril 10	HCTZ 50	Reserpine 0.25	16	76.73 ± 28.00	1 227.60
10	2	Y	Y	Y	Amiloride/HCTZ 5/50	Amlodipine 5	Perindopril 4	16	237.44 ± 0.00	3 799.04
1	3	Y	Y	Y	Amlodipine 5	Indapamide 12.5	Perindopril 4	400	255.14 ± 12.45	102 056.02
2	3	Y	Y	Y	Furosemide 40	Perindopril 4	Spironolactone 25	240	181.59 ± 19.67	43 582.48
3	3	Y	Y	Y	Carvedilol 25	Indapamide 2.5	Perindopril 4	203	248.72 ± 25.21	50 489.67
4	3	Y	Y	Y	Bisoprolol 5	Indapamide 2.5	Perindopril 4	173	208.86 ± 24.72	36 131.98
5	3	Y	Y	Y	Amlodipine 10	Indapamide 2.5	Perindopril 4	169	294.94 ± 10.91	49 844.12
6	3	Y	Y	Y	Carvedilol 25	Furosemide 40	Perindopril 4	128	264.06 ± 24.98	33 799.49
7	3	Y	Y	Y	Amlodipine 5	HCTZ 12.5	Lisinopril 20	107	186.22 ± 12.53	19 925.20
8	3	O	Y	Y	Amlodipine 5	Indapamide 2.5	Perindopril 5	96	288.07 ± 11.51	27 655.18
9	3	Y	Y	Y	Carvedilol 12.5	Furosemide 40	Perindopril 4	96	231.42 ± 35.39	22 215.98
10	3	Y	Y	Y	Carvedilol 25	Perindopril 4	Spironolactone 25	92	272.74 ± 25.34	25 092.51

Table I11: Prescribed daily dosages of top 10 observations of prescriptions with three active ingredients according to age group for 2007

Rank	AG	GI1	GI2	GI 3	Active ingredient 1 with PDD in mg	Active ingredient 2 with PDD in mg	Active ingredient 3 with PDD in mg	Number of RX	Average cost per TX (R)	Total cost per Rx (R)
1	1	O	Y	Y	Amlodipine 10	Doxazosin 4	HCTZ 12.5	11	466.38 ± 3.23	5 130.18
2	1	Y	O	Y	Enalapril 5	Furosemide 20	Spironolactone 25	8	146.22 ± 0.57	1 169.76
3	1	O	Y	Y	Furosemide 60	Sotalol 58.67	Spironolactone 25	7	276.70 ± 28.91	1 936.89
4	1	O	O	Y	Carvedilol 12.5	Ramipril 2.5	Spironolactone 50	5	545.64 ± 0.00	2 728.20
5	1	Y	Y	Y	Captopril 12.5	HCTZ 12.5	Spironolactone 12.5	5	32.94 ± 5.74	164.69
6	1	O	O	O	Carvedilol 12.5	Ramipril 2.5	Spironolactone 50	4	509.54 ± 339.69	2 038.15
7	1	Y	Y	Y	Amlodipine 10	Enalapril 20	Triamterene/HCTZ 25/12.5	2	282.22 ± 0.40	564.44
8	1	Y	Y	Y	Enalapril 10	HCTZ 12.5	Spironolactone 100	2	187.47 ± 0.00	374.94
9	1	N	N	N	Indapamide 1.5	Telmisartan 40	Trandolapril/Verapamil 180/2	1	451.34 ±	451.34
10	1	N	Y	Y	Furosemide 33.33	Perindopril 2	Spironolactone 25	1	297.19 ±	297.19
1	2	Y	Y	Y	Amlodipine 10	Bisoprolol 10	Indapamide/Perindopril 1.25/4	41	375.32 ± 7.34	15 387.97
2	2	Y	Y	Y	Amlodipine 5	Indapamide 2.5	Perindopril4	40	240.96 ± 15.50	9 638.53
3	2	Y	Y	Y	Amlodipine 5	Enalapril 20	HCTZ 12.5	37	191.08 ± 17.26	7 070.08
4	2	Y	Y	Y	Amlodipine 10	Bisoprolol 5	Indapamide/Perindopril 1.25/4	32	349.29 ± 11.28	11 177.20
5	2	Y	N	N	Captopril 300	Indapamide 1.5	Lercanidipine 10	30	235.59 ± 5.26	7 067.70
6	2	Y	Y	Y	Amlodipine 10	Carvedilol 25	Indapamide/Perindopril 1.25/4	30	387.11 ± 22.07	11 613.23
7	2	Y	Y	Y	Amlodipine 5	Indapamide 2.5	Lisinopril 20	24	202.00 ± 9.40	4 847.97
8	2	Y	N	N	Furosemide 40	Irbesartan/HTCZ 300/12.5	Nifedipine 60	22	534.01 ± 35.02	11 748.22
9	2	Y	N	N	Amlodipine 5	Candesartan 16	Indapamide 1.5	18	359.80 ± 26.94	6 476.44
10	2	Y	Y	Y	Carvedilol 50	Furosemide 40	Spironolactone 25	18	203.99 ± 8.57	3 671.86
1	3	Y	Y	Y	Amlodipine 5	Indapamide 20.5	Perindopril 4	433	253.57 ±24.91	109 796.20
2	3	Y	Y	Y	Furosemide 40	Perindopril 4	Spironolactone 25	238	183.29 ± 19.14	43 621.92
3	3	Y	Y	Y	Amlodipine 5	Bisoprolol 5	Indapamide/Perindopril 1.25/4	202	307.98 ± 22.04	62 212.82
4	3	Y	Y	Y	Bisoprolol 5	Indapamide 20.5	Perindopril 4	162	209.41 ± 34.53	33 924.69
5	3	Y	Y	Y	Carvedilol 25	Perindopril4	Spironolactone 25	135	283.99 ± 20.75	38 339.25
6	3	Y	Y	Y	Amlodipine 5	Enalapril 20	Indapamide 2.5	130	193.72 ± 11.62	25 183.14
7	3	O	Y	Y	Furosemide 40	Perindopril 4	Spironolactone 25	123	288.31 ±67.41	35 461.78
8	3	Y	Y	Y	Amlodipine 10	Bisoprolol 5	Indapamide/Perindopril 1.25/4	123	339.60 ± 14.66	41 771.04
9	3	Y	Y	Y	Amlodipine 10	Bisoprolol 10	Indapamide/Perindopril 1.25/4	123	368.13 ± 37.32	45 280.27

Table I11 (cont.): Prescribed daily dosages of top 10 observations of prescriptions with three active ingredients according to age group for 2007

Rank	AG	GI1	GI2	GI 3	Active ingredient 1 with PDD in mg	Active ingredient 2 with PDD in mg	Active ingredient 3 with PDD in mg	Number of RX	Average cost per TX (R)	Total cost per Rx (R)
10	3	Y	Y	Y	Carvedilol 25	Furosemide 40	Perindopril 4	122	260.95 ± 60.07	31 835.48

Table I12: Prescribed daily dosages of top 10 observations of prescriptions with three active ingredients according to age group for 2008

Rank	AG	GI 1	GI 2	GI 3	Active ingredient 1with PDD in mg	Active ingredient 2 with PDD in mg	Active ingredient 3 with PDD in mg	Number of Rx	Average cost per RX (R)	Total cost per Rx (R)
1	1	Y	Y	Y	Enalapril 10	HCTZ 12.5	Spironolactone 100	9	197.35 ± 3.87	1 776.15
2	1	O	O	Y	Furosemide 80	Sotalol 160	Spironolactone 25	7	613.50 ± 12.10	4 294.48
3	1	O	O	Y	Carvedilol 12.5	Ramipril 2.5	Spironolactone 50	5	333.37 ± 137.68	1 666.86
4	1	O	O	O	Enalapril 10	Furosemide 60	Spironolactone 50	4	479.80 ± 6.96	1 919.20
5	1	Y	Y	N	Amlodipine 30	Furosemide 40	Metoprolol 200	4	780.26 ± 11.93	3 121.02
6	1	Y	Y	Y	Amloride/HCTZ 5/50	Captopril 12.5	Propranolol 10	4	89.05 ± 0.00	356.20
7	1	Y	O	Y	Enalapril 5	Furosemide 20	Spironolactone 25	3	128.16 ± 30.37	384.47
8	1	Y	O	Y	Enalapril 10	Furosemide 60	Spironolactone 50	3	362.25 ± 0.00	1 086.75
9	1	O	O	Y	Carvedilol 6.25	Ramipril 2.5	Spironolactone 50	2	291.53 ± 128.48	583.06
10	1	O	Y	Y	Furosemide 60	Sotalol 160	Spironolactone 25	2	406.62 ± 6.32	813.24
1	2	Y	Y	Y	Amlodipine 10	Bisoprolol 5	Indapamide /Perindopril 1.25/4	61	332.78 ± 18.36	20 299.81
2	2	Y	Y	Y	Amlodipine 10	Bisoprolol 10	Indapamide /Perindopril 1.25/4	34	379.09 ± 11.84	12 888.96
3	2	Y	Y	Y	Amlodipine 5	Bisoprolol 5	Indapamide /Perindopril 1.25/4	31	294.55 ± 22.02	9 130.90
4	2	Y	Y	Y	Amlodipine 5	Indapamide 2.5	Perindopril 4	30	237.37 ± 29.37	7 121.00
5	2	Y	Y	Y	Amloride/HCTZ 5/50	Amlodipine 10	Lisinopril 20	27	204.97 ± 19.95	5 534.10
6	2	Y	Y	Y	Amlodipine 5	Indapamide 2.5	Lisinopril 20	24	178.12 ± 17.79	4 274.84
7	2	Y	N	N	Amlodipine 5	Candesartan 16	Indapamide 1.5	23	354.91 ± 32.62	8 163.01
8	2	Y	Y	N	Carvedilol 25	Indapamide/Perindopril 1.25/4	Nifedipine 60	23	534.75 ± 31.68	12 299.31
9	2	Y	Y	Y	Amlodipine 10	Enalapril 10	Indapamide 2.5	23	206.48 ± 12.70	4 749.14
10	2	Y	Y	Y	Amlodipine 5	Enalapril 20	Indapamide 2.5	22	168.25 ± 16.89	3 701.53
1	3	Y	Y	Y	Amlodipine 5	Indapamide 2.5	Perindopril 4	342	238.51 ± 26.98	81 570.93
2	3	Y	Y	Y	Amlodipine 5	Bisoprolol 5	Indapamide /Perindopril 1.25/4	281	297.05 ± 23.44	83 472.25
3	3	Y	Y	Y	Amlodipine 5	Enalapril 20	Indapamide 2.5	233	176.80 ± 23.91	41 195.36
4	3	Y	Y	Y	Furosemide 40	Perindopril 4	Spironolactone 25	211	184.76 ± 21.99	38 984.59

Table I12 (cont.): Prescribed daily dosages of top 10 observations of prescriptions with three active ingredients according to age group for 2008

Rank	AG	GI 1	GI 2	GI 3	Active ingredient 1 with PDD in mg	Active ingredient 2 with PDD in mg	Active ingredient 3 with PDD in mg	Number of Rx	Average cost per RX (R)	Total cost per Rx (R)
5	3	Y	Y	Y	Amlodipine 5	Indapamide 2.5	Lisinopril 20	196	195.06 ± 24.04	38 231.02
6	3	Y	Y	Y	Amlodipine 10	Bisoprolol 5	Indapamide /Perindopril 1.25/4	183	329.72 ± 32.30	60338.08
7	3	Y	Y	Y	Amlodipine 5	HCTZ 12.5	Lisinopril 20	176	186.41 ± 25.15	32808.26
8	3	Y	Y	Y	Amlodipine 5	HCTZ 25	Lisinopril 20	176	190.32 ± 27.59	33495.99
9	3	Y	Y	Y	Amlodipine 10	Enalapril 20	Indapamide 2.5	152	219.72 ± 21.14	33397.34
10	3	Y	Y	Y	Amlodipine 5	Carvedilol 25	Indapamide /Perindopril 1.25/4	143	353.37 ± 30.37	50531.94

Table I13: Prescribed daily dosages of top 10 observations of prescriptions with four active ingredients according to age group for 2005

Rank	AG	Active ingredient 1 with PDD in mg	Active ingredient 2 with PDD in mg	Active ingredient 3 with PDD in mg	Active ingredient 4 with PDD in mg	Number of RX	Average cost per RX (R)	Total cost per Rx (R)
1	1	Enalapril 5	Furosemide 33.3	HCTZ 12.5	Spironolactone 25	6	331.52 ± 0.00	1 989.12
2	1	Bumetanide 1	Captopril 37.5	Furosemide 120	Spironolactone 50	2	271.22 ± 0.00	542.44
3	1	Captopril 53.6	Carvedilol 6.7	Ramipril 2.7	Triamterene/HCTZ 28.81/53.6	1	239.28 ± 0.00	239.28
4	1	Captopril 150	Furosemide 80	Hydralazine 60	Methyldopa 750	1	751.39 ± 0.00	751.39
1	2	Doxazosin 8	Indapamide 2.5	Nifedipine 60	Perindopril 8	16	774.65 ± 0.00	12 394.40
2	2	Bisoprolol /HCTZ 10/6.25	Felodipine /Ramipril 5/5	Furosemide 80	Methyldopa 500	13	730.46 ± 0.00	9 495.98
3	2	HCTZ 12.5	Minoxidil 10	Quinapril 40	Spironolactone 50	12	492.16 ± 21.83	5 905.86
4	2	Carvedilol 25	Enalapril 20	Furosemide 240	Spironolactone 100	12	1 266.08 ± 55.23	15 192.93
5	2	Candesartan 8	Carvedilol 12.5	Furosemide 40	Spironolactone 50	11	332.05 ± 0.00	3 652.55
6	2	Carvedilol 12.5	Furosemide 160	Irbesartan 150	Spironolactone 25	10	822.44 ± 0.00	8 224.41
7	2	Carvedilol 25	Furosemide 160	Ramipril 5	Spironolactone 25	10	841.60 ± 8.04	8 416.02
8	2	Carvedilol 50	Furosemide 60	Perindopril 4	Spironolactone 25	10	369.00 ± 0.00	3 690.00
9	2	Amlodipine 10	Bisoprolol 5	Doxazosin 4	Valsartan/HCTZ 160/12.5	9	655.81 ± 9.18	5 902.30
10	2	Furosemide 40	Methyldopa 1000	Perindopril 4	Prazosin 10	9	608.10 ± 0.00	5 472.90
1	3	Carvedilol 25	Furosemide 40	Lisinopril 5	Spironolactone 25	27	214.60 ± 15.26	5 794.30
2	3	Carvedilol 25	Furosemide 40	Perindopril 2	Spironolactone 25	27	235.72 ± 23.52	6 364.55
3	3	Captopril 50	Enalapril 10	HCTZ 50	Reserpine 0.25	24	139.46 ± 37.64	3 346.94
4	3	Amiloride /HCTZ 5/50	Captopril 50	Propranolol 80	Reserpine 0.5	22	122.36 ± 41.53	2 691.98

Table I13 (cont.): Prescribed daily dosages of top 10 observations of prescriptions with four active ingredients according to age group for 2005

Rank	AG	Active ingredient 1 with PDD in mg	Active ingredient 2 with PDD in mg	Active ingredient 3 with PDD in mg	Active ingredient 4 with PDD in mg	Number of RX	Average cost per RX (R)	Total cost per Rx (R)
5	3	Carvedilol 25	Indapamide /Perindopril 1.25/4	Spironolactone 25	Toraseamide 10	20	444.47 ± 0.00	8 889.40
6	3	Captopril 150	HCTZ 50	Hydralazine 50	Methyldopa 1500	20	237.93 ± 23.98	4 758.52
7	3	Carvedilol 50	Furosemide 80	Lisinopril 20	Spironolactone 25	18	329.41 ± 5.68	5 929.41
8	3	Carvedilol 12.5	Furosemide40	Perindopril 4	Spironolactone 50	16	372.30 ± 0.01	5 956.81
9	3	Amiloride /HCTZ 5/50	Bisoprolol 5	Indapamide 2.5	Perindopril 4	16	212.74 ± 13.36	3 403.80
10	3	Candesartan 16	Indapamide 1.5	Nadolol 80	Spironolactone 25	15	529.84 ± 0.00	7 947.60

Table I14: Prescribed daily dosages of top 10 observations of prescriptions with four active ingredients according to age group for 2006

Rank	AG	Active ingredient 1 with PDD in mg	Active ingredient 2 with PDD in mg	Active ingredient 3 with PDD in mg	Active ingredient 4 with PDD in mg	Number of Rx	Average cost per Rx (R)	Total cost (R)
1	1	Captopril 25	Furosemide 60	Sotalol 160	Spironolactone 25	3	585.44 ± 0.00	1 756.32
2	1	Amlodipine 5	Losartan 50	Ramipril 5	Spironolactone 50	2	615.30 ± 0.00	1 230.60
3	1	Enalapril 10	Enalapril 20	Hydralazine 100	Verapamil 480	2	450.74 ± 50.25	901.48
4	1	Carvedilol 3.125	Furosemide 40	Ramipril 2.5	Spironolactone 25	1	284.20 ± 0.00	284.20
5	1	Amlodipine 2.5	Amlodipine 2.5	Metoprolol 100	Spironolactone 25	1	366.72 ± 0.00	366.72
6	1	Carvedilol 50	Furosemide 20	Perindopril 4	Spironolactone 12.5	1	465.85 ± 0.00	465.85
7	1	Captopril 25	Furosemide 60	Sotalol 160	Spironolactone 25	1	455.68 ± 0.00	455.68
8	1	Carvedilol 12.5	Felodipine 10	Furosemide 80	Perindopril4	1	371.67 ± 0.00	371.67
9	1	Carvedilol 12.5	Furosemide 40	Perindopril 4	Spironolactone 25	1	244.77 ± 0.00	244.77
1	2	Amlodipine 10	Carvedilol 50	Indapamide 2.5	Perindopril 4	14	452.92 ± 2.42	6 340.89
2	2	Carvedilol 12.5	Furosemide 40	Perindopril 4	Spironolactone 25	13	367.70 ± 17.62	4 780.06
3	2	Carvedilol 25	Enalapril 20	Furosemide 240	Spironolactone 100	13	1 255.22 ± 22.05	16 317.86
4	2	Bisoprolol/HCTZ 6.25/10	Felodipine/Ramipril 5/5	Furosemide 80	Methyldopa 500	12	730.46 ±0.00	8 765.52
5	2	HCTZ 25	Minoxidil 10	Quinapril 40	Spironolactone 25	12	413.66 ± 0.00	4 963.92
6	2	Amiloride/HCTZ 5/50	Carvedilol 25	Furosemide 40	Perindopril 4	12	350.97 ± 3.03	4 211.64
7	2	Carvedilol 12.5	Furosemide 40	Perindopril 4	Spironolactone 25	12	250.61 ± 6.37	3 007.37
8	2	Amlodipine 10	Bisoprolol 5	Indapamide 2.5	Perindopril 4	11	365.11 ± 3.76	4 016.19
9	2	Amlodipine 10	Bisoprolol 10	Indapamide 2.5	Perindopril 4	11	360.80 ±4.53	3 968.84
10	2	Carvedilol 12.5	Enalapril 10	Furosemide 40	Spironolactone 25	10	139.54 ± 33.37	1 395.44

Table I14 (cont.): Prescribed daily dosages of top 10 observations of prescriptions with four active ingredients according to age group for 2006

Rank	AG	Active ingredient 1 with PDD in mg	Active ingredient 2 with PDD in mg	Active ingredient 3 with PDD in mg	Active ingredient 4 with PDD in mg	Number of Rx	Average cost per Rx (R)	Total cost (R)
1	3	Carvedilol 25	Furosemide 40	Perindopril 4	Spironolactone 25	35	288.57 ± 27.20	10 099.98
2	3	Carvedilol 12.5	Furosemide 40	Perindopril 4	Spironolactone 25	34	248.12 ± 18.86	8 435.96
3	3	Carvedilol 12.5	Furosemide 40	Perindopril 4	Spironolactone 25	30	370.22 ± 17.85	11 106.62
4	3	Carvedilol 25	Furosemide 80	Perindopril 4	Spironolactone 25	30	321.60 ± 29.75	9 647.99
5	3	Indapamide 1.5	Irbesartan 140	Methyldopa 500	Trandolapril/Verapamil 180/2	26	566.25 ± 0.00	14 722.50
6	3	Carvedilol 25	Furosemide 40	Perindopril 2	Spironolactone 25	25	231.10 ± 21.45	5 777.49
7	3	Carvedilol 25	Furosemide 40	Perindopril 4	Spironolactone 12.5	24	480.91 ± 0.00	11 541.84
8	3	Doxazosin 4	Indapamide 2.5	Losartan/HCTZ 50/12.5	Spironolactone 25	22	362.52 ± 5.00	7 975.52
9	3	Carvedilol 50	Furosemide 40	Lisinopril 20	Spironolactone 25	21	326.47 ± 18.80	6 855.94
10	3	Carvedilol 12.5	Furosemide 40	Perindopril 2	Spironolactone 25	21	185.41 ± 5.21	3 893.51

Table I15: Prescribed daily dosages of top 10 observations of prescriptions with four active ingredients according to age group for 2007

Rank	AG	Active ingredient 1 with PDD in mg	Active ingredient 2 with PDD in mg	Active ingredient 3 with PDD in mg	Active ingredient 4 with PDD in mg	Number of Rx	Average cost per Rx (R)	Total cost (R)
1	1	Captopril 25	Furosemide 60	Sotalol 160	Spironolactone 25	6	631.55 ± 79.87	3 789.27
2	1	Captopril 25	Furosemide 60	Sotalol 160	Spironolactone 25	2	611.89 ± 0.00	1 223.78
3	1	Captopril 12.5	Enalapril 5	HCTZ 12.5	Spironolactone 12.5	2	54.11 ± 0.00	108.22
4	1	Captopril 25	Furosemide 60	Sotalol 160	Spironolactone 25	1	546.81 ± 0.00	546.81
5	1	Enalapril 5	Enalapril 10	HCTZ 12.5	Spironolactone 50	1	246.09 ± 0.00	246.09
1	2	Ergocristine/Clophamine 0.5/5	Losartan/HCTZ 100/25	Moxonidine 0.4	Nifedipine 60	18	174.02 ± 4.05	3 132.42
2	2	Furosemide 80	Minoxidil 10	Nifedipine 60	Perindopril 8	12	402.61 ± 16.37	4 831.32
3	2	Bisoprolol/HCTZ 10/6.25	Felodipine/Ramipril 5/5	Furosemide 80	Methyldopa 500	12	1 286.59 ± 172.39	15 439.07
4	2	Bisoprolol/HCTZ 5/6.25	Furosemide 240	Nifedipine 60	Perindopril 4	11	822.11 ± 45.24	9 043.20
5	2	Bisoprolol/HCTZ 5/6.25	Candesartan 8	Doxazosin 4	Nifedipine 60	11	468.24 ± 38.70	5 150.63
6	2	Bisoprolol/HCTZ 5/6.25	Felodipine/Ramipril 5/5	Furosemide 40	Furosemide 80	11	362.00 ± 10.88	3 981.99
7	2	Bisoprolol/HCTZ 10/6.25	Bisoprolol/HCTZ 5/6.25	Ramipril 2.5	Telmisartan 80	10	490.16 ± 4.21	4 901.56
8	2	Indapamide 1.5	Losartan 50	Spironolactone 50	Trandolapril/Verapamil 180/2	10	680.02 ± 0.01	6 800.16
9	2	Bisoprolol 2.5	Bumetanide/KCL 0.5/537	Perindopril 4	Spironolactone 25	10	455.84 ± 18.41	4 558.43
10	2	Bisoprolol 1.25	Irbesartan 300	Perindopril 4	Spironolactone 25	10	343.24 ± 5.17	3 432.40

Table I15 (cont.): Prescribed daily dosages of top 10 observations of prescriptions with four active ingredients according to age group for 2007

Rank	AG	Active ingredient 1 with PDD in mg	Active ingredient 2 with PDD in mg	Active ingredient 3 with PDD in mg	Active ingredient 4 with PDD in mg	Number of Rx	Average cost per Rx (R)	Total cost (R)
1	3	Alfuzosin 10	Ergocristine/Clopramine 0.5/5	Lercanidipine 20	Losartan/HCTZ 100/25	65	268.44 ± 32.05	17 448.87
2	3	Amlodipine 100	Losartan/HCTZ 180/25	Telmisartan 80	Trandolapril/Verapamil 10/2	47	233.79 ± 25.98	10 987.90
3	3	Bisoprolol/HCTZ 10/6.25	Bumetanide /KCL 0.5/375	Moexipril 15	Nifedipine 60	40	315.32 ± 20.86	12 612.75
4	3	Bisoprolol/HCTZ 10/6.25	Doxazosin 8	Nifedipine 60	Perindopril 10	37	393.53 ± 25.48	14 560.69
5	3	Bisoprolol/HCTZ 5/6.25	Felodipine/Ramipril 5/6.25	Moxonidine 0.2	Trandolapril/Verapamil 180/2	34	317.57 ± 24.54	10 797.37
6	3	Bisoprolol/HCTZ 5/12.5	Indapamide 1.5	Trandolapril/Verapamil 180/2	Valsartan/HCTZ	31	219.83 ± 44.79	6 814.88
7	3	Bisoprolol/HCTZ 10/6.25	Nifedipine 60	Perindopril 10	Valsartan/HCTZ 160/12.5	26	391.36 ± 21.66	10 175.24
8	3	Doxazosin 8	Indapamide 1.5	Moxonidine 0.4	Trandolapril/Verapamil 180/2	25	377.59 ±15.69	9 439.66
9	3	Doxazosin 8	Moxonidine 0.37	Nifedipine 60	Valsartan/HCTZ 160/12.5	25	379.68 ± 36.60	9 492.04
10	3	Doxazosin 8	Moxonidine 0.4	Nifedipine 60	Valsartan/HCTZ 160/12.5	24	346.23 ± 59.27	8 309.42

Table I16: Prescribed daily dosages of top 10 observations of prescriptions with four active ingredients according to age group for 2008

Rank	AG	Active ingredient 1 with PDD in mg	Active ingredient 2 with PDD in mg	Active ingredient 3 with PDD in mg	Active ingredient 4 with PDD in mg	Number of Rx	Average cost per Rx (R)	Total cost (R)
1	1	Carvedilol 25	Lercanidipine 10	Lisinopril/HCTZ 20/12.5	Moxonidine 0.4	1	577.59 ± 0.00	577.59
2	1	Captopril 25	Furosemide 60	Sotalol 160	Spironolactone 25	2	546.82 ± 0.00	1 093.64
3	1	Carvedilol 50	Furosemide 80	Perindopril 4	Spironolactone 50	2	587.57 ± 0.00	1 175.14
4	1	Bisoprolol 5	Enalapril 5	Furosemide 20	Spironolactone 25	1	159.48 ± 0.00	159.48
5	1	Bisoprolol 5	Enalapril 5	Furosemide 40	Spironolactone 25	8	220.66 ± 69.43	1 765.29
6	1	Carvedilol 50	Furosemide 40	Perindopril 4	Spironolactone 25	1	376.86 ± 0.00	376.86
7	1	Carvedilol 50	Furosemide 80	Perindopril 4	Spironolactone 50	3	420.83 ± 9.375	1 262.49
8	1	Bisoprolol 2.5	Furosemide 40	Perindopril 2	Spironolactone 50	1	169.95 ± 0.00	169.95
1	2	Carvedilol 25	Furosemide 160	Lisinopril 10	Spironolactone 50	14	312.71 ± 12.99	4 377.98
2	2	Bisoprolol/HCTZ 10/6.25	Felodipine/Ramipril 5/12	Furosemide 80	Methyldopa 500	12	510.10 ± 20.79	6 121.18
3	2	Bisoprolol 10	Bumetanide/KCL 1/1146	Furosemide 80	Losartan/HCTZ 100/12	12	422.24 ± 12.50	5 066.86
4	2	Amlodipine 10	Indapamide 2.5	Methyldopa 1000	Valsartan/HCTZ 160/25	12	564.21 ± 14.67	6 770.48
5	2	Candesartan 16	Indapamide 2.5	Spironolactone 50	Trandolapril/Verapamil 180/2	11	622.06 ± 12.57	6 842.63
6	2	Amlodipine 10	Bisoprolol/HCTZ 10/6.25	Doxazosin 4	Telmisartan 80	11	748.44 ± 21.20	8 232.86

Table I16 (cont.): Prescribed daily dosages of top 10 observations of prescriptions with four active ingredients according to age group for 2008

Rank	AG	Active ingredient 1 with PDD in mg	Active ingredient 2 with PDD in mg	Active ingredient 3 with PDD in mg	Active ingredient 4 with PDD in mg	Number of Rx	Average cost per Rx (R)	Total cost (R)
7	2	Carvedilol 25	Enalapril 10	Furosemide 40	Spironolactone 25	11	173.55 ± 2.42	1 909.10
8	2	Amlodipine 10	Bisoprolol 10	Doxazosin 8	Indapamide/Perindopril 1.25/4	10	591.42 ± 6.75	5 914.15
9	2	Amlodipine 5	Bisoprolol 5	Indapamide 2.5	Indapamide Perindopril 1.25/4	10	332.38 ± 9.27	3 323.84
10	2	Carvedilol 12.5	Enalapril 10	Furosemide 4	Spironolactone 50	10	256.75 ± 7.23	2 567.45
1	3	Carvedilol 12.5	Furosemide 40	Perindopril 4	Spironolactone 25	68	268.61 ± 31.59	18 265.36
2	3	Carvedilol 25	Furosemide 40	Perindopril 4	Spironolactone 25	67	307.83 ± 19.23	20 624.58
3	3	Carvedilol 12.5	Furosemide 40	Perindopril 4	Spironolactone 25	63	380.56 ± 40.03	23 975.20
4	3	Carvedilol 25	Furosemide 80	Perindopril 4	Spironolactone 25	38	309.30 ± 19.33	11 753.44
5	3	Carvedilol 25	Enalapril 20	Furosemide 40	Spironolactone 25	36	259.26 ± 23.12	9 333.42
6	3	Carvedilol 6.25	Furosemide 80	Lisinopril 20	Spironolactone 25	28	205.21 ± 29.81	5 745.77
7	3	Amlodipine 10	Furosemide 80	Lisinopril 20	Spironolactone 25	27	311.98 ± 20.20	8 423.51
8	3	Carvedilol 6.25	Furosemide 40	Perindopril 4	Spironolactone 25	26	241.17 ± 25.30	6 270.32
9	3	Amlodipine 5	Furosemide 40	Indapamide/Perindopril 1.25/4	Spironolactone 25	25	296.81 ± 8.42	7 420.33
10	3	Bisoprolol 5	Furosemide 40	Perindopril 4	Spironolactone 25	25	250.30 ± 13.93	6 257.43

Table I17: Prescribed daily dosages of top 10 observations of prescriptions with five active ingredients according to age group for 2005

Rank	AG	Active ingredient 1 with PDD in mg	Active ingredient 2 with PDD in mg	Active ingredient 3 with PDD in mg	Active ingredient 4 with PDD in mg	Active ingredient 5 with PDD in mg	Number of Rx	Average cost per Rx (R)	Total cost (R)
1	2	Amlodipine 10	Carvedilol 12.5	Doxazosin 1	Indapamide 2.5	Perindopril 4	7	425.57 ± 31.22	2 979.00
2	2	Amlodipine 10	Doxazosin 8	Furosemide 80	Minoxidil 5	Perindopril 4	6	854.69 ± 2.62	5 128.13
3	2	Amlodipine 10	Bisoprolol 10	Furosemide 40	Indapamide 2.5	Valsartan/HCTZ 160/12.5	6	547.99 ± 0.00	3 287.94
4	2	Carvedilol 50	Furosemide 80	HCTZ 25	Lisinopril 20	Telmisartan 80	5	795.10 ± 33.77	3 975.51
5	2	Bisoprolol 5	Furosemide 500	HCTZ 25	Irbesartan 300	Spironolactone 25	4	1 158.60 ± 0.00	4 634.40
6	2	Carvedilol 25	Furosemide 40	Nifedipine 60	Perindopril 4	Prazosin 2.5	4	678.40 ± 0.00	2 713.60

Table I17 (cont.): Prescribed daily dosages of top 10 observations of prescriptions with five active ingredients according to age group for 2005

Rank	AG	Active ingredient 1 with PDD in mg	Active ingredient 2 with PDD in mg	Active ingredient 3 with PDD in mg	Active ingredient 4 with PDD in mg	Active ingredient 5 with PDD in mg	Number of Rx	Average cost per Rx (R)	Total cost (R)
7	2	Amlodipine 10	Prazosin 2	Prazosin 10	Spironolactone 50	Valsartan /HCTZ 160/12.5	4	708.66 ± 0.00	2 834.64
8	2	Amlodipine 10	Doxazosin 8	Furosemide 40	Minoxidil 5	Perindopril 4	3	768.88 ± 0.00	2 306.64
9	2	Carvedilol 12.5	Carvedilol 25	Furosemide 40	Perindopril 4	Spironolactone 25	3	473.81 ± 0.00	1 421.43
10	2	Amlodipine 10	Bisoprolol 10	Furosemide 40	Indapamide 2.5	Valsartan /HCTZ 160/12.5	2	464.05 ± 0.00	928.10
1	3	Amlodipine 10	Carvedilol 50	Furosemide 20	Perindopril 4	Spironolactone 50	14	646.39 ± 48.11	9 049.49
2	3	Alfuzosin 10	Bisoprolol/HCTZ 0.5/6.25	Ergocristine /Clopamide.5/5	Felodipine 5	Lisinopril 20	13	749.10 ± 0.00	9 738.30
3	3	Amlodipine 5	Carvedilol 25	Furosemide 40	Spironolactone 25	Valsartan 160	13	432.75 ± 9.03	5 625.70
4	3	Amlodipine 10	Carvedilol 12.5	Carvedilol 25	Torasemide 5	Valsartan 160	12	774.18 ± 10.72	9 290.18
5	3	Amlodipine 5	Carvedilol 6.25	Furosemide 40	Spironolactone 25	Valsartan /HCTZ 160/12.5	12	464.63 ± 10.26	5 575.59
6	3	Amlodipine 10	Carvedilol 50	Doxazosin 4	Indapamide 2.5	Perindopril 4	12	507.45 ± 14.40	6 089.34
7	3	Bisoprolol /HCTZ 10/6.25	Prazosin 5	Sotalol 160	Spironolactone 100	Valsartan /HCTZ80/6.25	11	583.24 ± 0.00	6 415.64
8	3	Carvedilol 50	Felodipine 5	Furosemide 20	Perindopril 4	Spironolactone 25	11	680.06 ± 21.92	7 480.68
9	3	Atenolol/Chlortalidone 100/25	Candesartan 16	Methyldopa 1000	Reserpine 0.25	Spironolactone 25	11	513.16 ± 122.82	5 644.77
10	3	Acebutolol 200	Acebutolol 400	Amiloride/HCTZ 5/50	Amlodipine 5	Lisinopril 20	10	582.67 ± 15.11	5 826.74

Table I18: Prescribed daily dosages of top 10 observations of prescriptions with five active ingredients according to age group for 2006

Rank	AG	Active ingredient 1 with PDD in mg	Active ingredient 2 with PDD in mg	Active ingredient 3 with PDD in mg	Active ingredient 4 with PDD in mg	Active ingredient 5 with PDD in mg	Number of Rx	Average cost per Rx (R)	Total cost (R)
1	1	Enalapril 10	Enalapril 20	Hydralazine 100	Telmisartan/HCTZ 80/12.5	Verapamil 480	1	655.03 ± .00	655.03
1	2	Candesartan 8	Carvedilol 12.5	Furosemide 160	HCTZ 50	Spironolactone 50	9	853.62 ± 0.00	7 682.59
2	2	Candesartan 16	Carvedilol 25	Furosemide 40	HCTZ 12.5	Spironolactone 50	8	494.87 ± 0.01	3 958.98
3	2	Bisoprolol/HCTZ 5/6.25	Felodipine 10	Furosemide 160	Lisinopril 20	Telmisartan 80	6	569.34 ± 0.00	3 416.04
4	2	Indapamide/Perindopril 1.25/4	Irbesartan 300	Nifedipine 60	Spironolactone 25	Torasemide 10	5	1 010.79 ± 160.92	5 053.97
5	2	Amlodipine 10	Doxazosin 8	Furosemide 80	Minoxidil 5	Perindopril 4	5	542.35 ± 62.74	2 711.76
6	2	Acetazolamide 500	Bisoprolol 5	Moxonidine 0.37	Ramipril 10	Torasemide 10	4	741.23 ± 0.00	2 964.92
7	2	Amiloride/HCTZ 5/50	Amlodipine 10	Carvedilol 25	Furosemide 80	Minoxidil 10	4	424.92 ± 0.00	1 699.68
8	2	Amlodipine 10	Carvedilol 12.5	Indapamide 2.5	Moxonidine 0.4	Perindopril 4	3	778.39 ± 0.00	2 335.17
9	2	Amlodipine 10	Captopril 75	Doxazosin 4	Furosemide 20	Methyldopa 500	3	188.12 ± 0.00	564.36
10	2	Bisoprolol 5	Bisoprolol 5	Indapamide 2.5	Indapamide/Perindopril 1.25/4	Perindopril 4	3	552.83 ± 69.34	1 658.48
1	3	Bisoprolol /HCTZ 10/100	Lercanidipine 10	Losartan/HCTZ 6.25/25	Nebivolol 5	Torasemide 2.5	16	634.14 ± 0.00	10 146.24
2	3	Alfuzosin 10	Bisoprolol/HCTZ 5/6.25	Ergocristine/Clopamide 0.5/5	Felodipine/Ramipril 5/5	Lisinopril 20	15	731.27 ± 11.60	10 969.11
3	3	Bumetanide/KCL 1/1146	Candesartan 16	Felodipine/Ramipril 5/5	Furosemide 80	Methyldopa 1000	15	625.96 ± 0.00	9 389.40
4	3	Bumetanide/KCL 0.5/573	Candesartan /HCTZ 16/12.5	Furosemide 20	Moxonidine 0.4	Spironolactone 12.5	13	340.77 ± 0.01	4 429.96
5	3	Bumetanide/KCL 1/1146	Felodipine/Ramipril 5/5	Irbesartan 300	Ramipril 5	Torasemide 10	12	800.48 ± 26.80	9 605.73
6	3	Furosemide 40	Losartan 50	Nifedipine 60	Prazosin 4	Spironolactone 25	12	541.08 ± 6.49	6 492.96
7	3	Bisoprolol/HCTZ	Candesartan 16	Doxazosin 1	Moxonidine 0.4	Verapamil 240	12	904.70 ± 0.00	10 856.40

Table I18 (cont.): Prescribed daily dosages of top 10 observations of prescriptions with five active ingredients according to age group for 2006

Rank	AG	Active ingredient 1 with PDD in mg	Active ingredient 2 with PDD in mg	Active ingredient 3 with PDD in mg	Active ingredient 4 with PDD in mg	Active ingredient 5 with PDD in mg	Number of Rx	Average cost per Rx (R)	Total cost (R)
		5/6.25							
8	3	Bumetanide/KCL 0.5/573	Candesartan/HCTZ 16/12.5	Doxazosin 4	Moxonidine 0.3	Quinapril 10	12	591.78 ± 5.30	7 101.39
9	3	Bumetanide/KCL 0.5/573	Candesartan/HCTZ 16/12.5	Doxazosin 4	Moxonidine 0.3	Quinapril 10	12	563.36 ± 31.45	6 760.30
10	3	Candesartan 8	Candesartan/HCTZ 16/12.5	Carvedilol 50	Lercanidipine 10	Prazosin 3	11	1 068.88 ± 0.00	11 757.68

Table I19: Prescribed daily dosages of top 10 observations of prescriptions with five active ingredients according to age group for 2007

Rank	AG	Active ingredient 1 with PDD in mg	Active ingredient 2 with PDD in mg	Active ingredient 3 with PDD in mg	Active ingredient 4 with PDD in mg	Active ingredient 5 with PDD in mg	Number of Rx	Average cost per Rx (R)	Total cost (R)
1	1	Enalapril 10	Enalapril 20	Hydralazine 100	Telmisartan/HCTZ 80/12.5	Verapamil 480	1	625.52 ± 0.00	625.52
1	2	Ergocristine/Clopamide 0.5/5	Losartan/HCTZ 100/25	Moxonidine 0.4	Nifedipine 60	Spironolactone 25	14	1 045.15 ± 61.85	14 632.16
2	2	Bisoprolol 2.5	Irbesartan 300	Perindopril 8	Perindopril 4	Spironolactone 25	11	934.75 ± 18.94	10 282.22
3	2	Bisoprolol 2.5	Furosemide 40	Nifedipine 60	Spironolactone 25	Valsartan/HCTZ 160/12.5	8	393.95 ± 30.97	3 151.58
4	2	Candesartan 8	Carvedilol 12.5	Furosemide 160	HCTZ 50	Spironolactone 50	8	399.12 ± 2.75	3 192.98
5	2	Amlodipine 10	Doxazosin 8	Furosemide 80	Minoxidil 5	Perindopril 4	6	590.22 ± 76.13	3 541.29
6	2	Amlodipine 10	Captopril 75	Doxazosin 8	Furosemide 20	Methyldopa 500	6	487.12 ± 54.65	2 922.71
7	2	Amlodipine 10	Captopril 75	Doxazosin 4	Furosemide 20	Methyldopa 500	6	189.16 ± 3.16	1 134.95
8	2	Bisoprolol 2.5	HCTZ 25	Ramipril 5	Spironolactone 50	Toraseamide 13.3	5	459.18 ± 0.00	2 295.90
9	2	Carvedilol 25	Doxazosin 8	Furosemide 120	Moxonidine 0.2	Perindopril 8	5	468.83 ± 0.00	2 344.15
10	2	Amlodipine 5	Eprosartan 600	Furosemide 40	Prazosin 6	Trandolapril 2	4	669.27 ± 16.79	2 677.06
1	3	Bisoprolol /HCTZ 2.5/6.25	Bisoprolol /HCTZ 5/6.25	Indapamide 1.5	Trandolapril/Verapamil180/2	Valsartan /HCTZ 160/12.5	18	670.33 ± 24.11	12 065.92
2	3	Bisoprolol /HCTZ 5/6.25	Doxazosin 8	Minoxidil 5	Moxonidine 0.4	Trandolapril/Verapamil 180/2	14	346.95 ± 0.01	4 857.36

Table I19 (cont.): Prescribed daily dosages of top 10 observations of prescriptions with five active ingredients according to age group for 2007

Rank	AG	Active ingredient 1 with PDD in mg	Active ingredient 2 with PDD in mg	Active ingredient 3 with PDD in mg	Active ingredient 4 with PDD in mg	Active ingredient 5 with PDD in mg	Number of Rx	Average cost per Rx (R)	Total cost (R)
3	3	Bisoprolol /HCTZ 10/6.25	Felodipine/Ramipril 5/5	Furosemide 60	Losartan/HCTZ 50/12.5	Moxonidine 0.2	14	413.30 ± 7.59	5 786.18
4	3	Bisoprolol /HCTZ 10/6.25	Lercanidipine 10	Losartan/HCTZ 100/25	Nebivolol 5	Toraseamide 2.5	13	767.53 ± 5.21	9 977.91
5	3	Bisoprolol /HCTZ 5/6.25	Doxazosin 8	Irbesartan/HCTZ 300/12.5	Lercanidipine 10	Spironolactone 25	12	1 076.16 ± 70.95	12 913.97
6	3	Bumetanide/KCL 5/1146	Candesartan 16	Felodipine/Ramipril 5/5	Furosemide 80	Methyldopa 1000	12	831.01 ± 214.84	9 972.10
7	3	Lercanidipine 10	Losartan/HCTZ 100/25	Nebivolol 5	Spironolactone 50	Toraseamide 10	12	1 033.17 ± 12.86	12 398.08
8	3	Bisoprolol /HCTZ 10/6.25	Doxazosin 8	Felodipine/Ramipril 5/6.25	Methyldopa 1000	Moxonidine 0.4	12	657.55 ± 3.62	7 890.55
9	3	Bisoprolol /HCTZ 5/6.25	Doxazosin 8	Irbesartan/HCTZ 300/12.5	Spironolactone 25	Telmisartan 37.33	12	752.82 ± 31.05	9 033.87
10	3	Acebutolol 200	Candesartan 16	Doxazosin 8	Nifedipine 60	Piretanide 3	12	624.83 ± 10.03	7 497.98

Table I20: Prescribed daily dosages of top 10 observations of prescriptions with five active ingredients according to age group for 2008

Rank	AG	Active ingredient 1 with PDD in mg	Active ingredient 2 with PDD in mg	Active ingredient 3 with PDD in mg	Active ingredient 4 with PDD in mg	Active ingredient 5 with PDD in mg	Number of Rx	Average cost per Rx (R)	Total cost (R)
1	2	Amlodipine 10	Doxazosin 8	Furosemide 80	Minoxidil 5	Perindopril 4	11	968.07 ± 23.33	10648.74
2	2	Candesartan 8	Carvedilol 12.5	Furosemide 160	HCTZ 50	Spironolactone 50	8	1091.73 ± 40.38	8733.82
3	2	Bumetanide 2	Carvedilol 50	HCTZ 25	Ramipril 10	Spironolactone 12.5	6	698.22 ± 96.58	4189.32
4	2	Bumetanide 2	Carvedilol 50	HCTZ 25	Ramipril 10	Spironolactone 12.5	5	728.65 ± 0.00	3643.25
5	2	Amlodipine/HCTZ 10/20	Hydralazine 75	Methyldopa 1000	Perindopril 8	Telmisartan 80	4	952.36 ± 23.39	3809.42
6	2	Amlodipine 10	Doxazosin 8	Moxonidine 0.2	Nebivolol 0.2	Valsartan/HCTZ 160/12.5	4	644.77 ± 60.01	2579.06

Table I20 (cont.): Prescribed daily dosages of top 10 observations of prescriptions with five active ingredients according to age group for 2008

Rank	AG	Active ingredient 1 with PDD in mg	Active ingredient 2 with PDD in mg	Active ingredient 3 with PDD in mg	Active ingredient 4 with PDD in mg	Active ingredient 5 with PDD in mg	Number of Rx	Average cost per Rx (R)	Total cost (R)
7	2	Ergocristine/Clopamide 0.5/5	Losartan/HCTZ 100/25	Moxonidine 0.4	Nifedipine 60	Spironolactone 25	3	860.44 ± 0.00	2581.32
8	2	Ergocristine/Clopamide 0.5/5	Losartan/HCTZ 100/25	Moxonidine 0.4	Nifedipine 60	Spironolactone 25	3	863.90 ± 0.43	2591.71
9	2	Amlodipine 10	Doxazosin 8	Moxonidine 0.2	Nebivolol 5	Valsartan/HCTZ 160/12.5	3	906.87 ± 159.81	2720.6
10	2	Carvedilol 12.5	Carvedilol 25	Furosemide 120	Perindopril 4	Spironolactone 25	3	971.84 ± 17.21	2915.51
1	3	Carvedilol 50	Doxazosin 1	Enalapril 10	Furosemide 40	Spironolactone 25	16	340.34 ± 6.01	5445.46
2	3	Amlodipine 10	Bisoprolol 5	Doxazosin 4	Indapamide/Perindopril 4/1.25	Spironolactone 25	15	570.69 ± 12.68	8560.39
3	3	Amlodipine 5	Bisoprolol/HCTZ 10/6.25	HCTZ 25	Prazosin 6	Ramipril 10	14	532.10 ± 29.01	7449.39
4	3	Bisoprolol/HCTZ 5/6.25	Doxazosin 8	Irbesartan/HCTZ 300/12.5	Lercanidipine 10	Spironolactone 25	13	841.98 ± 23.62	10945.8
5	3	Amiloride/HCTZ 5/50	Furosemide 40	Hydralazine 25	Nifedipine 60	Reserpine 0.25	13	358.79 ± 9.75	4664.24
6	3	Amlodipine 5	Carvedilol 12.5	Carvedilol 25	Indapamide 1.5	Lisinopril 20	13	350.61 ± 35.31	4557.93
7	3	Amlodipine 10	Bisoprolol 5	Doxazosin 8	Indapamide 2.5	Ramipril 10	12	836.43 ± 225.47	10037.1
8	3	Amlodipine 10	Bisoprolol 10	Doxazosin 4	Irbesartan 300	Quinapril/HCTZ 20/12.5	12	1072.44 ± 27.12	12869.33
9	3	Doxazosin 4	Felodipine/Ramipril 5/5	Minoxidil 5	Reserpine 0.25	Spironolactone 25	12	567.59 ± 14.21	6811.1
10	3	Carvedilol 25	Doxazosin 8	Lercanidipine 10	Lisinopril/HCTZ 20/12.5	Spironolactone 25	12	672.49 ± 13.98	8069.86

Table I21: Prescribed daily dosages of top 10 observations of prescriptions with six active ingredients according to age group for 2005

Rank	AG	Active ingredient 1 with PDD in mg	Active ingredient 2 with PDD in mg	Active ingredient 3 with PDD in mg	Active ingredient 4 with PDD in mg	Active ingredient 5 with PDD in mg	Active ingredient 6 with PDD in mg	Number of Rx	Average cost per Rx (R)	Total cost (R)
1	3	Amiloride/HCTZ 5/50	Atenolol/Chlortalidone 100/25	Doxazosin 2	Enalapril 40	Furosemide 40	Methyldopa 250	15	331.34 ± 27.73	4 970.10
2	3	Candesartan 16	Carvedilol 25	Doxazosin 8	Toraseamide 10	Toraseamide 5	Triamterene/HCTZ 25/50	8	914.44 ± 30.53	7 315.49
3	3	Amlodipine 10	Carvedilol 12.5	Doxazosin 2	Enalapril 20	Enalapril 10	Furosemide 80	7	861.72 ± 89.70	6 032.06
4	3	Amiloride/HCTZ 5/50	Bumetanide/KCl 0.5/573	Furosemide 20	Furosemi de 40	Methyldopa 750	Ramipril 1.25	7	473.88 ± 11.58	3 317.14
5	3	Carvedilol 12.5	Carvedilol 25	Furosemide 40	Perindopril 4	Spirolactone 25	Valsartan/HCTZ 160/12.5	6	1 056.21 ± 0.01	6 337.28
6	3	Amlodipine 10	Bisoprolol 10	Doxazosin 8	Furosemide 40	Methyldopa 1000	Valsartan/HCTZ 160/12.5	6	858.30 ± 3.97	5 149.81
7	3	Furosemide 40	Losartan/HCTZ 100/25	Moxonidine 0.3	Nifedipine 60	Sotalol 160	Spirolactone 75	4	1 148.02 ± 98.15	4 592.07
8	3	Bisoprolol 10	Bisoprolol/HCTZ 5/6.25	Indapamide 1.5	Methyldopa 1000	Nifedipine 56	Telmisartan 74.67	4	936.75 ± 0.00	3 747.00
9	3	Amlodipine 10	Bisoprolol 10	Eprosartan 560	Irbesartan/HCTZ 280/11.67	Prazosin 10	Toraseamide 10	4	1 055.81 ± 16.29	4 223.22
10	3	Amlodipine 5	Bisoprolol 10	Furosemide 120	Irbesartan 280	Methyldopa 1000	Spirolactone 50	4	731.77 ± 121.99	2 927..06

Table I22: Prescribed daily dosages of top 10 observations of prescriptions with six active ingredients according to age group for 2006

Rank	AG	Active ingredient 1 with PDD in mg	Active ingredient 2 with PDD in mg	Active ingredient 3 with PDD in mg	Active ingredient 4 with PDD in mg	Active ingredient 5 with PDD in mg	Active ingredient 6 with PDD in mg	Number of Rx	Average cost (R)	Total cost (R)
1	2	Bisoprolol 10	Furosemide 40	Hydralazine 100	Losartan/HCTZ 100/25	Methyldopa 500	Nifedipine 60	6	918.52 ± 0.00	5 511.12
2	2	Amlodipine 10	Bisoprolol 10	Candesartan 8	Furosemide 80	Furosemide 40	Methyldopa 500	4	843.41 ± 5.62	3 373.64
3	2	Candesartan 16	Carvedilol 25	Furosemide 80	Furosemide40	HCTZ 12.5	Spirolactone 50	3	898.25 ± 2.96	2 694.75

Table I22 (cont.): Prescribed daily dosages of top 10 observations of prescriptions with six active ingredients according to age group for 2006

Rank	AG	Active ingredient 1 with PDD in mg	Active ingredient 2 with PDD in mg	Active ingredient 3 with PDD in mg	Active ingredient 4 with PDD in mg	Active ingredient 5 with PDD in mg	Active ingredient 6 with PDD in mg	Number of Rx	Average cost (R)	Total cost (R)
4	2	Bisoprolol 10	Furosemide 40	Moxonidine 0.4	Nifedipine 60	Perindopril 10	Prazosin 6	1	923.08 ± 0.00	923.08
1	3	Bisoprolol 1.25	Bumetanide/KCl 0.5/573	Doxazosin 8	Indapamide 1.25	Spironolactone 25	Valsartan 149.3	9	523.91 ± 26.16	4 715.23
2	3	Bumetanide 1	Candesartan/HCTZ 16/12.5	Carvedilol 25	Doxazosin 1	Doxazosin 4	Felodipine 5	8	712.48 ± 6.65	5 699.8
3	3	Bumetanide/KCl 0.5/573	Candesartan/HCTZ 16/12.5	Carvedilol 25	Doxazosin 1	Doxazosin 4	Felodipine 5	8	849.62 ± 7.55	6 796.96
4	3	Doxazosin 8	Enalapril 20	HCTZ 25	Minoxidil 15	Moxonidine 0.4	Valsartan 160	7	586.70 ± 0.00	4 106.9
5	3	Candesartan 16	Carvedilol 25	Doxazosin 8	Torsemide 10	Torsemide 5	Triamterene/HCTZ 25/50	7	1064.14 ± 13.54	7 449.01
6	3	Doxazosin 8	Enalapril 20	Minoxidil 10	Moxonidine 0.4	Spironolactone 50	Valsartan 160	6	512.82 ± 0.01	3 076.89
7	3	Doxazosin 8	Enalapril 20	Minoxidil 10	Moxonidine 0.4	Spironolactone 50	Valsartan 160	6	422.95 ± 3.25	2 537.69
8	3	Doxazosin 8	Enalapril 20	Minoxidil 15	Moxonidine 0.4	Spironolactone 50	Valsartan 160	5	936.75 ± 0.00	4 683.75
9	3	Doxazosin 8	Hydralazine 200	Indapamide 1.	Irbesartan 150	Methyldopa 1500	Perindopril 8	5	822.65 ± 0.00	4 113.25
10	3	Candesartan 16	Carvedilol 25	Doxazosin 8	Furosemide 160	Furosemide 160	Lercanidipine 20	5	929.96 ± 0.00	4 649.80

Table I23: Prescribed daily dosages of top 10 observations of prescriptions with six active ingredients according to age group for 2007

Rank	AG	Active ingredient 1 with PDD in mg	Active ingredient 2 with PDD in mg	Active ingredient 3 with PDD in mg	Active ingredient 4 with PDD in mg	Active ingredient 5 with PDD in mg	Col6 Active ingredient 6 with PDD in mg	Number of Rx	Average cost per Rx (R)	Total cost (R)
1	2	Carvedilol 25	Doxazosin 4	Furosemide 120	Lercanidipine 10	Perindopril 4	Spironolactone 25	7	653.20 ± 0.00	4 572.40
2	2	Bisoprolol 10	Furosemide 40	Hydralazine 300	Losartan/HCTZ 100/25	Methyldopa 500	Nifedipine 60	5	817.24 ± 32.86	4 086.22
3	2	Bisoprolol 10	Furosemide 20	Hydralazine 300	Losartan/HCTZ 100/25	Methyldopa 500	Nifedipine 60	4	779.20 ± 37.57	3 116.81
4	2	Amlodipine 10	Carvedilol 41.67	Methyldopa 1000	Moxonidine 0.4	Perindopril 10	Spironolactone 50	2	856.81 ± 0.00	1 713.62
5	2	Bisoprolol 10	Furosemide 40	Hydralazine 100	Losartan/HCTZ 100/25	Methyldopa 500	Nifedipine 60	1	937.06 ± 0.00	937.06

Table I23 (cont.): Prescribed daily dosages of top 10 observations of prescriptions with six active ingredients according to age group for 2007

Rank	AG	Active ingredient 1 with PDD in mg	Active ingredient 2 with PDD in mg	Active ingredient 3 with PDD in mg	Active ingredient 4 with PDD in mg	Active ingredient 5 with PDD in mg	Col6 Active ingredient 6 with PDD in mg	Number of Rx	Average cost per Rx (R)	Total cost (R)
6	2	Bisoprolol 5	Furosemide 40	Nifedipine 60	Prazosin 2	Spironolactone 25	Valsartan/HCTZ 160/12.5	1	660.38 ± 0.00	660.38
7	2	Amlodipine 10	Carvedilol 25	Carvedilol 25	Furosemide 40	Lisinopril 20	Spironolactone 25	1	555.48 ± 0.00	555.48
1	3	Bisoprolol/HCTZ 2.5/6.25	Candesartan/HCTZ 16/12.5	Carvedilol 25	Felodipine 5	Furosemide 40	Lisinopril/HCTZ 10/12.5	11	642.76 ± 12.86	7 070.41
2	3	Bumetanide 1	Candesartan/HCTZ 16/12.5	Carvedilol 25	Doxazosin 1	Doxazosin 4	Felodipine5	11	418.04 ± 5.06	4 598.49
3	3	Bisoprolol/HCTZ 5/6.25	Doxazosin 4	Felodipine/Ramipril 5/5	Furosemide10	Methyldopa 500	Spironolactone 16.67	11	476.56 ± 19.66	5 242.13
4	3	Bisoprolol/HCTZ 5/6.25	Doxazosin 4	Felodipine/Ramipril 5/5	Furosemide 10	Methyldopa 500	Spironolactone 5	9	757.89 ± 26.84	6 821.00
5	3	Bisoprolol/HCTZ 5/6.25	Doxazosin 4	Felodipine/Ramipril 5/5	Furosemide 10	Methyldopa 500	Spironolactone 75	9	512.17 ± 0.01	4 609.50
6	3	Doxazosin 8	Enalapril 20	Minoxidil 10	Moxonidine 0.4	Spironolactone 25	Valsartan 160	7	1158.70 ± 40.43	8 110.88
7	3	Doxazosin 8	Enalapril 20	Minoxidil 10	Moxonidine 0.4	Spironolactone 37.5	Valsartan 160	6	1089.37 ± 19.21	6 536.19
8	3	Doxazosin 8	Enalapril 20	Minoxidil 10	Moxonidine 0.4	Spironolactone 50	Valsartan 160	6	777.06 ± 47.85	4 662.38
9	3	Doxazosin 240	Enalapril 600	Minoxidil 300	Moxonidine 0.4	Spironolactone 1120	Valsartan 4800	6	884.96 ± 0.26	5 309.74
10	3	Alfuzosin 10	Bisoprolol 10	Candesartan/HCTZ 16/12.5	Indapamide 2.5	Lercanidipine 40	Methyldopa 500	6	475.88 ± 19.84	2 855.27

Table I24: Prescribed daily dosages of top 10 observations of prescriptions with six active ingredients according to age group for 2008

Rank	AG	Active ingredient 1 with PDD in mg	Active ingredient 2 with PDD in mg	Active ingredient 3 with PDD in mg	Active ingredient 4 with PDD in mg	Active ingredient 5 with PDD in mg	Active ingredient 6 with PDD in mg	Number of Rx	Average cost per Rx (R)	Total cost (R)
1	2	Bisoprolol 10	Furosemide 20	Hydralazine 300	Losartan/HCTZ 100/25	Methyldopa 500	Nifedipine 60	8	753.09 ± 15.88	6024.72
2	2	Amlodipine 10	Bisoprolol 5	Doxazosin 8	Irbesartan 300	Methyldopa 1500	Spironolactone 50	2	1 030.87 ± 52.32	2061.73
3	2	Carvedilol 25	Doxazosin 8	Furosemide 80	Furosemide 40	Moxonidine 0.4	Nifedipine 60	2	1 242.33 ± 0.00	2484.66
4	2	Amlodipine 10	Carvedilol 50	Enalapril 20	Furosemide 40	Methyldopa 500	Spironolactone 100	2	647.14 ± 2.60	1294.27
5	2	Carvedilol 50	Doxazosin 8	Hydralazine 50	Irbesartan 300	Nifedipine 60	Toraseamide 10	1	1 178.31 ± 0.00	1178.31
6	2	Carvedilol 50	Doxazosin 8	Hydralazine 100	Irbesartan 300	Nifedipine 60	Toraseamide 10	1	1 230.77 ± 0.00	1230.77
7	2	Amlodipine 10	Bisoprolol 5	Doxazosin 8	Irbesartan 300	Methyldopa 1500	Spironolactone 50	1	708.86 ± 0.00	708.86
1	3	Bisoprolol/HCTZ 2.5/6.25	Doxazosin 8	Minoxidil 10	Nifedipine 60	Quinapril 40	Spironolactone 50	14	386.92 ± 11.00	5416.88
2	3	Bisoprolol/HCTZ 2.5/6.25	Doxazosin 8	Minoxidil 10	Nifedipine 60	Quinapril 40	Spironolactone 50	11	662.21 ± 13.91	7284.31
3	3	Alfuzosin 10	Carvedilol 6.25	Perindopril 4	Spironolactone 25	Toraseamide 10	Toraseamide 5	8	1 032.93 ± 216.99	8263.41
4	3	Bisoprolol/HCTZ 10/6.25	Carvedilol 12.5 #	Indapamide 1.5	Moxonidine 0.2	Nifedipine 60	Perindopril 4	8	1 508.66 ± 6.77	12069.28
5	3	Doxazosin 8	Enalapril 20	Minoxidil 10	Moxonidine 0.4	Spironolactone 37.5	Valsartan 160	8	456.95 ± 13.81	3655.61
6	3	Doxazosin 8	Enalapril 20	Minoxidil 10	Moxonidine 0.4	Spironolactone 37.5	Valsartan 160	8	524.15 ± 9.34	4193.23
7	3	Alfuzosin 10	Amlodipine 5	Candesartan 16	Furosemide 40	Indapamide 2.5	Sotalol 320	7	657.60 ± 7.92	4603.20
8	3	Candesartan/HCTZ 16/12.5	Carvedilol 25	Doxazosin 4	Methyldopa 500	Nifedipine 60	Spironolactone 25	6	1 083.90 ± 69.98	6503.37
9	3	Amlodipine/HCTZ 10/10	Carvedilol 50	Doxazosin 1	Furosemide 40	Perindopril 10	Spironolactone 12.5	6	715.49 ± 15.82	4292.94

Table I24 (cont.): Prescribed daily dosages of top 10 observations of prescriptions with six active ingredients according to age group for 2008

Rank	AG	Active ingredient 1 with PDD in mg	Active ingredient 2 with PDD in mg	Active ingredient 3 with PDD in mg	Active ingredient 4 with PDD in mg	Active ingredient 5 with PDD in mg	Active ingredient 6 with PDD in mg	Number of Rx	Average cost per Rx (R)	Total cost (R)
10	3	Bisoprolol/HCTZ 10/6.25	Prazosin 1	Prazosin 5	Sotalol 160	Spironolactone 100	Valsartan/HCTZ 80/6.25	6	762.48 ± 33.51	4574.89

Table I25: Prescribed daily dosages of top 10 observations of prescriptions with seven active ingredients according to age group for 2005

Rank	AG	Active ingredient 1 with PDD in mg	Active ingredient 2 with PDD in mg	Active ingredient 3 with PDD in mg	Active ingredient 4 with PDD in mg	Active ingredient 5 with PDD in mg	Active ingredient 6 with PDD in mg	Active ingredient 7 with PDD in mg	Number of Rx	Average cost per Rx (R)	Total cost (R)
1	3	Atenolol/ Chlortalidone 250/62.5	Doxazosin 4	Enalapril 42.86	Enalapril 20	HCTZ 93.75	Methyldopa 1500	Perindopril 8	4	751.01	3 004.04
2	3	Acebutolol 400	Amlodipine 10	Bisoprolol 5	Bumetanide 1	Doxazosin 8	Nifedipine 60	Valsartan 160	1	1 363.23	1 363.23
3	3	Carvedilol 12.5	Carvedilol 50	Felodipine/Ramipril 5/5	Furosemide 61.33	Indapamide 2.5	Ramipril 5	Spironolactone 44.17	1	1 112.73	1 112.73
4	3	Alfuzosin 5	Amlodipine 10	Bisoprolol 10	Doxazosin 8	Furosemide 40	Methyldopa 1000	Valsartan/HCTZ 160/12.5	1	1 013.11	1 013.11
5	3	Bisoprolol 5	Doxazosin 8	Isradipine 5	Methyldopa 1500	Methyldopa 1500	Torsemide 10	Valsartan 160	1	1 473.66	1 473.66

Table I26: Prescribed daily dosages of top 10 observations of prescriptions with seven active ingredients according to age group for 2006

Rank	AG	Active ingredient 1 with PDD in mg	Active ingredient 2 with PDD in mg	Active ingredient 3 with PDD in mg	Active ingredient 4 with PDD in mg	Active ingredient 5 with PDD in mg	Active ingredient 6 with PDD in mg	Active ingredient 7 with PDD in mg	Number of Rx	Average cost per Rx (R)	Total cost (R)
1	3	Atenolol/Chlortalidone 250/62.5	Doxazosin 4	Enalapril 42.86	Enalapril 20	HCTZ 93.75	Methyldopa 1500	Perindopril 8	6	751.01	4 506.06
2	3	Amlodipine 10	Bisoprolol 5	Enalapril 20	Furosemide 80	Irbesartan 300	Methyldopa 1500	Nifedipine 60	3	1 155.69	3 467.07
3	3	Bisoprolol 5	Enalapril 40	Furosemide 160	Minoxidil 15	Nifedipine 60	Spironolactone 200	Telmisartan/HCTZ 80/12.5	2	1 630.29	3 260.58
4	3	Acebutolol 400	Amlodipine 10	Bisoprolol 5	Doxazosin 8	Isradipine 5	Losartan/HCTZ 20/25	Torsemide 10	1	1 360.76	1 360.76

Table I26 (cont.): Prescribed daily dosages of top 10 observations of prescriptions with seven active ingredients according to age group for 2006

Rank	AG	Active ingredient 1 with PDD in mg	Active ingredient 2 with PDD in mg	Active ingredient 3 with PDD in mg	Active ingredient 4 with PDD in mg	Active ingredient 5 with PDD in mg	Active ingredient 6 with PDD in mg	Active ingredient 7 with PDD in mg	Number of Rx	Average cost per Rx (R)	Total cost (R)
5	3	Acebutolol 400	Amlodipine 10	Bisoprolol 5	Doxazosin 8	Losartan/HCTZ 100/25	Spironolactone 100	Torsemide 10	1	1 346.68	1 346.68
6	3	Doxazosin 8	Furosemide 80	Hydralazine 200	Indapamide 1.5	Irbesartan 150	Methyldopa 1500	Perindopril 8	1	1 127.67	1 127.67
7	3	Bisoprolol 10	Doxazosin 8	Doxazosin 0.8	Indapamide 1.5	Methyldopa 233.33	Methyldopa 1000	Perindopril 4	1	933.52	933.52
8	3	Bisoprolol 10	Candesartan 16	Captopril 75	Furosemide 40	Lercanidipine 10	Moxonidine 0.4	Spironolactone 25	1	864.24	864.24
9	3	Carvedilol 25	Carvedilol 25	Furosemide 40	Perindopril 4	Perindopril 4	Spironolactone 25	Spironolactone 25	1	840.03	840.03
10	3	Amlodipine 10	Amlodipine 10	Bisoprolol 2.5	Bisoprolol 2.5	Indapamide 2.5	Indapamide/Perindopril 4/1.25	Perindopril 4	1	643.41	643.41

Table I27: Prescribed daily dosages of top 10 observations of prescriptions with seven active ingredients according to age group for 2007

Rank	AG	Active ingredient 1 with PDD in mg	Active ingredient 2 with PDD in mg	Active ingredient 3 with PDD in mg	Active ingredient 4 with PDD in mg	Active ingredient 5 with PDD in mg	Active ingredient 6 with PDD in mg	Active ingredient 7 with PDD in mg	Number of Rx	Average cost per Rx (R)	Total cost (R)
1	2	Carvedilol 25	Doxazosin 8	Furosemide 80	Furosemide 40	Moxonidine 0.4	Nifedipine 60	Perindopril 8	1	1473.77 ±	1473.77
1	3	Bisoprolol 10	Bisoprolol/HCTZ 10/12.5	Candesartan 16	Hydralazine 10	Indapamide 2.5	Methyldopa 500	Valsartan/HCTZ 160/12.5	11	1188.63 ± 48.21	13074.90
2	3	Bisoprolol 5	Enalapril 40	Furosemide 80	Minoxidil 10	Nifedipine 60 ^s	Spironolactone 100	Telmisartan/HCTZ 80/12.5	2	1083.79 ±	2167.58
3	3	Bisoprolol 5	Enalapril 40	Furosemide 160	Minoxidil 15	Nifedipine 60	Spironolactone 200	Telmisartan/HCTZ 80/12.5	1	804.69	804.69
4	3	Carvedilol 12.5	Eprosartan 160	Furosemide 40 [*]	Moxonidine 0.4	Spironolactone 50	Trandolapril/Verapamil 180/2	Valsartan/HCTZ 160/12.5	1	1281.93	1281.93
5	3	Bisoprolol 5	Enalapril 20	Furosemide 40	Minoxidil 15	Spironolactone 50	Spironolactone 25	Telmisartan 80	1	1683.43	1683.43

Table I27(cont.): Prescribed daily dosages of top 10 observations of prescriptions with seven active ingredients according to age group for 2007

Rank	AG	Active ingredient 1 with PDD in mg	Active ingredient 2 with PDD in mg	Active ingredient 3 with PDD in mg	Active ingredient 4 with PDD in mg	Active ingredient 5 with PDD in mg	Active ingredient 6 with PDD in mg	Active ingredient 7 with PDD in mg	Number of Rx	Average cost per Rx (R)	Total cost (R)
6	3	Amlodipine 10	Carvedilol 6.25	Doxazosin 4	HCTZ 12.5	Perindopril 4	Spironolactone 25	Torasemide 10	1	873.28	873.28
7	3	Amlodipine 10	Carvedilol 6.25	Doxazosin 4	HCTZ 25	Perindopril 4	Spironolactone 25 [#]	Torasemide 10	1	763.06	763.06
8	3	Carvedilol 12.5	Carvedilol 12.5	Furosemide 40	Lisinopril 10	Lisinopril 10	Spironolactone 12.5	Spironolactone 12.5	1	763.06	763.06
9	3	Amlodipine 10	Bisoprolol 5	Enalapril 20	Furosemide 80	Irbesartan 300	Methyldopa 1500	Nifedipine 60	1	523.40	523.40
10	3	Amlodipine 10	Carvedilol 50	Eprosartan 160	HCTZ 25	Lisinopril 20	Nebivolol 5	Ramipril 10	1	858.74	858.74

Table I28: Prescribed daily dosages of top 10 observations of prescriptions with seven active ingredients according to age group for 2008

Rank	AG	Active ingredient 1 with PDD in mg	Active ingredient 2 with PDD in mg	Active ingredient 3 with PDD in mg	Active ingredient 4 with PDD in mg	Active ingredient 5 with PDD in mg	Active ingredient 6 with PDD in mg	Active ingredient 7 with PDD in mg	Number of Rx	Average cost per Rx (R)	Total cost (R)
1	2	Amlodipine 20	Bisoprolol 10	Bisoprolol 10	Hydralazine 150	Methyldopa 1500	Perindopril 4	Prazosin 15	1	1211.45	1211.45
1	3	Bisoprolol 10	Furosemide 160	Minoxidil 15	Moxonidine 0.4	Nifedipine 60	Prazosin 6	Telmisartan/HCTZ 80/12.5	2	1908.64	3817.28
2	3	Bisoprolol 10	Furosemide 160	Minoxidil 15	Moxonidine 0.4	Nifedipine 60	Spironolactone 50	Telmisartan/HCTZ 80/12.5	2	742.29	1484.58
3	3	Bisoprolol 10	Furosemide 160	Minoxidil 20	Moxonidine 0.4	Nifedipine 60	Spironolactone 50	Telmisartan/HCTZ 80/12.5	1	1816.5	1816.5
4	3	Amlodipine 10	Candesartan 8	Doxazosin 4	Furosemide 40	Indapamide 1.5	Minoxidil 5	Perindopril 8	1	1726.43	1726.43
5	3	Amlodipine 5	Amlodipine 10	Carvedilol 20	HCTZ 25	Moxonidine 0.4	Perindopril 8	Prazosin 15	1	772.05	772.05
6	3	Amlodipine 5	Amlodipine 10	Carvedilol 25	HCTZ 25	Moxonidine 0.4	Perindopril 8	Prazosin 15	1	1133.67	1133.67
7	3	Amiloride/HCTZ 5/50	Amlodipine 10	Bisoprolol 10	Doxazosin 4	Eprosartan 160	Moxonidine 0.2	Spironolactone 50	1	1067.62	1067.62

Table I27(cont.): Prescribed daily dosages of top 10 observations of prescriptions with seven active ingredients according to age group for 2007

Rank	AG	Active ingredient 1 with PDD in mg	Active ingredient 2 with PDD in mg	Active ingredient 3 with PDD in mg	Active ingredient 4 with PDD in mg	Active ingredient 5 with PDD in mg	Active ingredient 6 with PDD in mg	Active ingredient 7 with PDD in mg	Number of Rx	Average cost per Rx (R)	Total cost (R)
8	3	Amlodipine 10	Carvedilol 50	Eprosartan 160	HCTZ 12.5	Lisinopril 20	Nebivolol 5	Ramipril 10	1	847.83	847.83
9	3	Amiloride/HCTZ 5/50	Amlodipine 10	Bisoprolol 10	Doxazosin 4	Eprosartan 160	Moxonidine 0.2	Spironolactone 50	1	738.31	738.31
10	3	Amlodipine 5	Carvedilol 12.5	Carvedilol 25	Doxazosin 4	Furosemide 40	Indapamide/Perindopril 4/1.25	Spironolactone 50	1	582.04	582.04

Table I29: Prescribed daily dosages of the only prescription with eight active ingredients according to age group for 2005

Rank	AG	Active ingredient 1 with PDD in mg	Active ingredient 2 with PDD in mg	Active ingredient 3 with PDD in mg	Active ingredient 4 with PDD in mg	Active ingredient 5 with PDD in mg	Active ingredient 6 with PDD in mg	Active ingredient 7 with PDD in mg	Active ingredient 8 with PDD in mg	Average cost per Rx (R)	Total cost (R)
1	3	Amiloride/HCTZ 5/50	Bisoprolol 5	Bumetanide 1	Doxazosin 8	Methyldopa 1500	Methyldopa 1500	Nifedipine 60	Valsartan 160	1 143.77 ± 0.00	1 143.00

Table I30: Prescribed daily dosages of the two eight-item prescriptions according to age group for 2006

Rank	AG	Active ingredient 1 with PDD in mg	Active ingredient 2 with PDD in mg	Active ingredient 3 with PDD in mg	Active ingredient 4 with PDD in mg	Active ingredient 5 with PDD in mg	Active ingredient 6 with PDD in mg	Active ingredient 7 with PDD in mg	Active ingredient 8 with PDD in mg	Number of Rx	Average cost (R)	Total cost (R)
1	3	Carvedilol 50	Furosemide 40	Hydralazine 75	Indapamide 2.5	Lisinopril 40	Losartan/HCTZ 100/25	Moxonidine 0.4	Spironolactone 25	2	1 150.76	1 150.76
2	3	Amlodipine 10	Amlodipine 10	Bisoprolol 10	Bisoprolol 10	Candesartan/HCTZ 16/12.5	Furosemide 20	Moxonidine 0.3	Spironolactone 25	1	1043.26	

Table I31: Prescribed daily dosages of the three eight-item prescriptions according to age group for 2008

Rank	AG	Active ingredient 1 with PDD in mg	Active ingredient 2 with PDD in mg	Active ingredient 3 with PDD in mg	Active ingredient 4 with PDD in mg	Active ingredient 5 with PDD in mg	Active ingredient 6 with PDD in mg	Active ingredient 7 with PDD in mg	Active ingredient 8 with PDD in mg	Number of Rx	Average cost (R)	Total cost (R)
1	2	Carvedilol 25	Carvedilol 25	Doxazosin 8	Furosemide 120	Furosemide 120	Furosemide 40	Nifedipine 60	Perindopril 4	1	1 236.32	1 236.32
1	3	Amlodipine/HC TZ 10/10	Amlodipine 5	Bisoprolol 5	Bisoprolol 10	Bumetanide/KCI 0.5/573	Eprosartan 160	Torasemide 10	Torasemide 5	3	951.06	2853.18
2	3	Bisoprolol 10	Furosemide 160	Minoxidil 15	Moxonidine 0.4	Nifedipine 60	Prazosin 6	Spirolactone 50	Telmisartan/HC TZ 80/12.5	2	1 960.14	3 920.28

APPENDIX J

Table J1: Threshold estimation for the central acting inhibitors per province (for 2008)

Province	Number of items	Total cost (R)	Total cost for medical aid market (R)	Number of estimated high income households	Treatment cost per household (R)	VAT (R)	Cost minus VAT (R)	Logistics fee (R)	Threshold (R)
Eastern Cape	1 984	192 805.66	339 337.96	182 062	1.86	0.23	1.63	0.41	1.23
Free State	1 224	157 829.18	277 779.36	121 235	2.29	0.28	2.01	0.50	1.51
Gauteng	8 477	1 132 224.15	1 992 714.50	308 325	6.46	0.79	5.67	1.41	4.26
KwaZulu-Natal	2 717	334 789.17	589 228.94	282 421	2.09	0.26	1.83	0.45	1.38
Limpopo	574	60 810.78	107 026.97	136 293	0.79	0.10	0.69	0.17	0.52
Mpumalanga	920	89 464.59	157 457.68	145 358	1.08	0.13	0.95	0.24	0.71
North West	1 252	172 276.13	303 205.99	97 786	3.10	0.38	2.72	0.67	2.05
Northern Cape	827	75 899.19	133 582.57	45 153	2.96	0.36	2.60	0.64	1.95
Western Cape	2 040	27 5551.2	484 970.11	395 355	1.23	0.15	1.08	0.27	0.81
Not indicated	68	4 309.82	7 585.28	2 183 945	0.00	0.00	0.00	0.00	0.00
Total for 7.3.1	20 083	2 495 959.87	4 392 889.37	2 183 945	2.01	0.25	1.76	0.44	1.33

Table J2: Threshold estimation for the alpha-receptor blockers per province (for 2008)

Province	Number of items	Total cost (R)	Total cost for medical aid market (R)	Number of estimated high income households	Treatment cost per household (R)	VAT (R)	Cost minus VAT	Logistics fee (R)	Threshold (R)
Eastern Cape	2 239	299 076.40	526 374.46	182 062	2.89	0.36	2.54	0.63	1.91
Free State	1 778	334 374.56	588 499.23	121 235	4.85	0.60	4.26	1.06	3.20
Gauteng	16 503	3 265 154.51	5 746 671.94	308 325	18.64	2.29	16.35	4.06	12.29
KwaZulu-Natal	6 343	1 027 257.91	1 807 973.92	282 421	6.40	0.79	5.62	1.39	4.22
Limpopo	1 490	258 261.68	454 540.56	136 293	3.34	0.41	2.93	0.73	2.20
Mpumalanga	1 307	216 310.53	380 706.53	145 358	2.62	0.32	2.30	0.57	1.73
North West	1 602	283 224.66	498 475.40	97 786	5.10	0.63	4.47	1.11	3.36
Northern Cape	436	90 691.34	159 616.76	45 153	3.53	0.43	3.10	0.77	2.33
Western Cape	5 904	1 029 596.53	1 812 089.89	395 355	4.58	0.56	4.02	1.00	3.02
Not indicated	55	9 331.58	16 423.58	2 183 945	0.01	0.00	0.01	0.00	0.00
Total	37 657	6 813 279.70	11 991 372.27	2 183 945	5.49	0.67	4.82	1.20	3.62

Table J3: Threshold estimation for the beta-receptor blockers per province (for 2008)

Province	Number of items	Total cost (R)	Total cost for medical aid market (R)	Number of estimated high income households	Treatment cost per household (R)	VAT (R)	Cost minus VAT (R)	Logistics fee (R)	Threshold (R)
Eastern Cape	15 430	1 243 901.59	2 189 266.80	182 062	12.02	1.48	10.55	2.62	7.93
Free State	10 579	1 027 386.87	1 808 200.89	121 235	14.91	1.83	13.08	3.25	9.84
Gauteng	99 726	9 364 480.22	1 6481 485.19	308 325	53.45	6.56	46.89	11.63	35.26
KwaZulu-Natal	41 352	3 584 443.57	6 308 620.68	282 421	22.34	2.74	19.59	4.86	14.73
Limpopo	6 581	608 305.59	1 070 617.84	136 293	7.86	0.96	6.89	1.71	5.18
Mpumalanga	10 690	976 190.79	1 718 095.79	145 358	11.82	1.45	10.37	2.57	7.80
North West	14 510	1 363 413.63	2 399 607.99	97 786	24.54	3.01	21.53	5.34	16.18
Northern Cape	2 892	275 854.49	485 503.90	45 153	10.75	1.32	9.43	2.34	7.09
Western Cape	42 199	3 602 517.53	6 340 430.85	395 355	16.04	1.97	14.07	3.49	10.58
Not indicated	233	21 888.11	38 523.07	2 183 945	0.02	0.00	0.02	0.00	0.01
Total 7.3.3	244 192	22 068 382.39	38840353.01	2 183 945	17.78	2	16	4	11.73

Table J4: Threshold estimation for alpha- and beta-receptor blockers per province (for 2008)

Province	Number of items	Total cost (R)	Total cost for medical aid market (R)	Number of estimated high income households	Treatment cost per household (R)	VAT (R)	Cost minus VAT (R)	Logistics fee (R)	Threshold (R)
Eastern Cape	4 521	483 850.61	851 577.07	182 062	4.68	0.57	4.10	1.02	3.08
Free State	3 879	422 700.7	743 953.23	121 235	6.14	0.75	5.38	1.34	4.05
Gauteng	33 779	3 802 557.69	6 692 501.53	308 325	21.71	2.67	19.04	4.72	14.32
KwaZulu-Natal	10 154	1 024 351.14	1 802 858.01	282 421	6.38	0.78	5.60	1.39	4.21
Limpopo	2 131	235 472.29	414 431.23	136 293	3.04	0.37	2.67	0.66	2.01
Mpumalanga	2 701	272 808.13	480 142.31	145 358	3.30	0.41	2.90	0.72	2.18
North West	3 066	332 825.91	585 773.60	97 786	5.99	0.74	5.25	1.30	3.95
Northern Cape	1 340	144 717.18	254 702.24	45 153	5.64	0.69	4.95	1.23	3.72
Western Cape	14 240	1 591 939.47	2 801 813.47	395 355	7.09	0.87	6.22	1.54	4.67
Not indicated	95	8 586.06	15 111.47	2 183 945	0.01	0.00	0.01	0.00	0.00
Total for 7.3.4	75 906	8 319 809.18	14 642 864.16	2 183 945	6.70	0.82	5.88	1.46	4.42

Table J5: Threshold estimation for sympathetic nervous blockers per province (for 2008)

Province	Number of items	Total cost (R)	Total cost for medical aid market (R)	Number of estimated high income households	Treatment cost per household (R)	VAT (R)	Cost minus VAT (R)	Logistics fee (R)	Threshold (R)
Eastern Cape	913	87 871.92	154 654.58	178 492	0.87	0.11	0.76	0.19	0.57
Free State	772	40 558.17	71 382.38	118 858	0.60	0.07	0.53	0.13	0.40
Gauteng	2 942	408 756.24	719 410.98	807 752	0.89	0.11	0.78	0.19	0.59
KwaZulu-Natal	971	77 864.17	137 040.94	276 883	0.49	0.06	0.43	0.11	0.33
Limpopo	224	20 954.81	36 880.47	133 621	0.28	0.03	0.24	0.06	0.18
Mpumalanga	669	36 762.51	64 702.02	142 508	0.45	0.06	0.40	0.10	0.30
North West	679	100 119.76	176 210.78	95 869	1.84	0.23	1.61	0.40	1.21
Northern Cape	715	31 007.65	54 573.46	44 268	1.23	0.15	1.08	0.27	0.81
Western Cape	742	77 150.76	135 785.34	387 603	0.35	0.04	0.31	0.08	0.23
Total for 7.3.5	8 627	881 045.99	1 550 640.94	2 183 945	0.71	0.62	0.09	0.47	0.07

Table J6: Threshold estimation for direct acting vasodilators per province (for 2008)

Province	Number of items	Total cost (R)	Total cost for medical aid market (R)	Number of high income households	Treatment cost per household (R)	VAT (R)	Cost minus VAT (R)	Logistics fee (R)	Threshold (R)
Eastern Cape	334	21 475.04	37 796.07	182 062	0.21	0.03	0.18	0.05	0.14
Free State	95	5 764.93	10 146.28	121 235	0.08	0.01	0.07	0.02	0.06
Gauteng	844	68 861.41	121 196.08	308 325	0.39	0.05	0.34	0.09	0.26
KwaZulu-Natal	197	14 552.94	25 613.17	282 421	0.09	0.01	0.08	0.02	0.06
Limpopo	19	495.83	872.66	136 293	0.01	0.00	0.01	0.00	0.00
Mpumalanga	43	2 669.61	4 698.51	145 358	0.03	0.00	0.03	0.01	0.02
North West	182	18 333.90	32 267.66	97 786	0.33	0.04	0.29	0.07	0.22
Northern Cape	24	2 212.46	3 893.93	45 153	0.09	0.01	0.08	0.02	0.06
Western Cape	419	36 791.60	64 753.22	395 355	0.16	0.02	0.14	0.04	0.11
Not indicated	0	0.00	0.00	2 183 945	0.00	0.00	0.00	0.00	0.00
Total for 7.3.6	2 157	171 157.72	301 237.59	2 183 945	0.14	0.02	0.12	0.03	0.09

Table J7: Threshold estimation for calcium channel blockers per province (for 2008)

Province	Number of items	Total cost (R)	Total cost for medical aid market (R)	Number of estimated high income households	Treatment cost per household (R)	VAT (R)	Cost minus VAT (R)	Logistics fee (R)	Threshold (R)t
Eastern Cape	17 122	2 092 245.30	3 682 351.73	182 062	20.23	2.48	17.74	4.40	13.34
Free State	7 881	1 154 092.05	2 031 202.01	121 235	16.75	2.06	14.70	3.65	11.05
Gauteng	86 761	11 817 642.07	20 799 050.04	308 325	67.46	8.28	59.17	14.68	44.49
KwaZulu-Natal	34 306	4 289 990.31	7 550 382.95	282 421	26.73	3.28	23.45	5.82	17.63
Limpopo	6 527	904 112.55	1 591 238.09	136 293	11.68	1.43	10.24	2.54	7.70
Mpumalanga	8 051	1 018 110.45	1 791 874.39	145 358	12.33	1.51	10.81	2.68	8.13
North West	10 200	1 413 694.79	2 488 102.83	97 786	25.44	3.12	22.32	5.54	16.78
Northern Cape	2 082	301 697.27	530 987.20	45 153	11.76	1.44	10.32	2.56	7.76
Western Cape	35 518	4 379 875.20	7 708 580.35	395 355	19.50	2.39	17.10	4.24	12.86
Not indicated	190	23 174.50	40 787.12	2 183 945	0.02	0.00	0.02	0.00	0.01
Total for 7.3.7	208 638	27 394 634.49	48 214 556.70	2 183 945	22.08	2.71	19.37	4.81	14.56

Table J8: Threshold estimation for ACE-inhibitors per province (for 2008)

Province	Number of items	Total cost (R)	Total cost for medical aid market (R)	Number of estimated high income households	Treatment cost per household (R)	VAT (R)	Cost minus VAT (R)	Logistics fee (R)	Threshold (R)
Eastern Cape	56 429	5 960 844.46	10 491 086.25	182 062	57.62	7.08	50.55	12.54	38.01
Free State	35 843	3 541 846.99	6 233 650.70	121 235	51.42	6.31	45.10	11.19	33.91
Gauteng	283 145	32 895 477.72	57 896 040.79	308 325	187.78	23.06	164.72	40.87	123.85
KwaZulu-Natal	102 472	10 264 387.80	18 065 322.53	282 421	63.97	7.86	56.11	13.92	42.19
Limpopo	24 316	2 672 789.95	4 704 110.31	136 293	34.51	4.24	30.28	7.51	22.76
Mpumalanga	32 787	3 502 572.30	6 164 527.25	145 358	42.41	5.21	37.20	9.23	27.97
North West	32 400	3 579 015.88	6 299 067.95	97 786	64.42	7.91	56.51	14.02	42.49
Northern Cape	14 542	1 277 290.34	2 248 031.00	45 153	49.79	6.11	43.67	10.84	32.84
Western Cape	122 694	13 878 895.45	24 426 855.99	395 355	61.78	7.59	54.20	13.45	40.75
Not indicated	630	69 770.98	122 796.92	2 183 945	0.06	0.01	0.05	0.01	0.04
Total for 7.3.8	705 258	7 7642 891.87	136 651 489.69	2 183 945	62.57	7.68	54.89	13.62	41.27

Table J9: Threshold estimation for angiotensin receptor blocker per province (for 2008)

Province	Number of items	Total cost (R)	Total cost for medical aid market (R)	Number of estimated high income households	Treatment cost per household (R)	VAT (R)	Cost minus VAT (R)	Logistics fee (R)	Threshold (R)
Eastern Cape	15 718	3 188 586.36	5 611 911.99	182 062	30.82	3.79	27.04	6.71	20.33
Free State	18 246	3 728 363.37	6 561 919.53	121 235	54.13	6.65	47.48	11.78	35.70
Gauteng	122 109	25 793 964.07	45 397 376.76	308 325	147.24	18.08	129.16	32.05	97.11
KwaZulu-Natal	33 006	7 034 385.10	12 380 517.78	282 421	43.84	5.38	38.45	9.54	28.91
Limpopo	7 117	1 477 969.98	2 601 227.16	136 293	19.09	2.34	16.74	4.15	12.59
Mpumalanga	9 020	1 893 649.12	3 332 822.45	145 358	22.93	2.82	20.11	4.99	15.12
North West	14 459	3 024 464.74	5 323 057.94	97 786	54.44	6.69	47.75	11.85	35.90
Northern Cape	3 856	796 377.37	1 401 624.17	45 153	31.04	3.81	27.23	6.76	20.47
Western Cape	47 072	9 705 373.37	17 081 457.13	2 183 945	7.82	0.96	6.86	1.70	5.16
Not indicated	559	95 288.83	167 708.34	395 355	0.42	0.05	0.37	0.09	0.28
Total for 7.3.9	271 162	56 738 422.31	99 859 623.27	2 183 945	45.72	5.62	40.11	9.95	30.16

Table J10: Threshold estimation for antihypertensive medicine items listed as “Others” per province (for 2008)

Province	Number of items	Total cost (R)	Total cost for medical aid market (R)	Number of estimated high income households	Treatment cost per household (R)	VAT (R)	Cost minus VAT (R)	Logistics fee (R)	Threshold (R)
Eastern Cape	413	88 541.58	155 833.18	182 062	0.86	0.11	0.75	0.19	0.56
Free State	301	67 463.19	118 735.21	121 235	0.98	0.12	0.86	0.21	0.65
Gauteng	4 437	978 986.40	1 723 016.06	308 325	5.59	0.69	4.90	1.22	3.69
KwaZulu-Natal	1 266	245 944.93	432 863.08	282 421	1.53	0.19	1.34	0.33	1.01
Limpopo	201	37 696.89	66 346.53	136 293	0.49	0.06	0.43	0.11	0.32
Mpumalanga	263	55 840.87	98 279.93	145 358	0.68	0.08	0.59	0.15	0.45
North West	228	51 386.70	90 440.59	97 786	0.92	0.11	0.81	0.20	0.61
Northern Cape	39	8 055.73	14 178.08	45 153	0.31	0.04	0.28	0.07	0.21
Western Cape	1 619	344 608.68	606 511.28	395 355	1.53	0.19	1.35	0.33	1.01
Not indicated	2	476.85	839.26	2 183 945	0.00	0.00	0.00	0.00	0.00
Total for 7.3.10	8 769	1 879 001.82	3 307 043.20	2 183 945	1.51	0.19	1.33	0.33	1.00

Table J11: Threshold estimation for diuretics per province (for 2008)

Province	Number of items	Total cost (R)	Total cost for medical aid market (R)	Number of estimated high income households	Treatment cost per household (R)	VAT (R)	Cost minus VAT (R)	Logistics fee (R)	Threshold (R)
Eastern Cape	38 868	1 153 300.06	2 029 808.11	182 062	11.15	1.37	9.78	1.13	8.65
Free State	25 682	1 138 263.55	2 003 343.85	121 235	16.52	2.03	14.50	1.67	12.83
Gauteng	178 425	9 162 324.72	16 125 691.51	308 325	52.30	6.42	45.88	5.28	40.60
KwaZulu-Natal	75 675	3 098 214.40	5 452 857.34	282 421	19.31	2.37	16.94	1.95	14.99
Limpopo	18 380	654 580.42	1 152 061.54	136 293	8.45	1.04	7.41	0.85	6.56
Mpumalanga	21 461	842 448.69	1 482 709.69	145 358	10.20	1.25	8.95	1.03	7.92
North West	25 119	983 573.23	1 731 088.88	97 786	17.70	2.17	15.53	1.79	13.74
Northern Cape	11 790	360 374.92	634 259.86	45 153	14.05	1.73	12.32	1.42	10.90
Western Cape	81 389	3 238 718.10	5 700 143.86	395 355	14.42	0.50	3.54	0.41	3.13
Not indicated	467	17 473.69	30 753.69	2 183 945	0.01	0.00	0.01	0.00	0.01
Total for 16.1	477 256	20 649 271.78	36 342 718.33	2 183 945	16.64	2.04	14.60	1.68	12.92