AVAILABILITY OF PHARMACOECONOMIC DATA AND ITS USE IN THE DEVELOPMENT OF DRUG FORMULARIES IN SOUTH AFRICA

By

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“Nor wild Romance nor Pride allured me here:
Duty and destiny with equal voice Constrained my steps.
I had no other choice…
Something for Africa to do or say_” - Pringle
CONTENTS

ACKNOWLEDGEMENTS............................................................................................................. i

LIST OF CONTENTS.................................................................................................................. vi

LIST OF FIGURES.................................................................................................................. vii

LIST OF TABLES..................................................................................................................... viii

LIST OF ABBREVIATIONS....................................................................................................... ix

LIST OF APPENDICES ........................................................................................................... x

SUMMARY .............................................................................................................................. xi

CHAPTER 1
OVERVIEW ............................................................................................................................. 1

1.1 MOTIVATION FOR THE STUDY................................................................................... 1

1.2 HYPOTHESIS................................................................................................................ 2

1.3 PRIMARY OBJECTIVES OF THE RESEARCH............................................................ 2

1.4 CHAPTER LAYOUT ...................................................................................................... 2

CHAPTER 2
THE ROLE OF PHARMACOECONOMICS IN REDUCING HEALTH CARE EXPENDITURE................................. 4

2.1 ESCALATING COSTS OF HEALTH CARE WORLDWIDE............................................ 4

2.2 THE HEALTH CARE SCENARIO IN SOUTH AFRICA............................................... 8

2.3 ROLE OF HEALTH ECONOMICS AND PHARMACOECONOMICS IN HEALTH CARE ......................................................................................................................... 14

2.3.1 Costs in pharmacoeconomic evaluations ............................................................... 16

2.3.2 Methods of pharmacoeconomic evaluations .......................................................... 17

2.3.2.1 Cost-minimisation analysis .............................................................................. 19

2.3.2.2 Cost-effectiveness analysis ............................................................................. 20

2.3.2.3 Cost-benefit analysis ..................................................................................... 20

2.3.2.4 Cost-utility analysis ...................................................................................... 21

2.4 APPLIED PHARMACOECONOMICS ...................................................................... 22

2.4.1 Evaluating pharmacoeconomic studies ................................................................. 23

2.4.2 Generalisability of pharmacoeconomic studies ...................................................... 30

2.4.3 Use and misuse of pharmacoeconomics in the literature ...................................... 32

2.4.4 National use of pharmacoeconomic data in decision-making ................................ 33

2.4.4.1 Australia ......................................................................................................... 34

2.4.4.2 Canada........................................................................................................... 35
2.4.4.2.1 Clinical factor ................................................................. 36
2.4.4.2.2 Type of drug ................................................................. 37
2.4.4.2.3 Quality factor ................................................................. 37
2.4.4.2.4 Consistency factor .......................................................... 37
2.4.4.2.5 The role of economic analysis ........................................... 37
2.4.4.2.6 Value adjustments .......................................................... 37
2.4.4.3 USA ................................................................................. 38
2.4.4.4 South Africa ................................................................. 40
2.5 FORMULARIES AND THE DEVELOPMENT OF FORMULARIES ............ 42
2.5.1 Types of formularies ............................................................. 42
2.5.1.1 Open formularies ............................................................. 43
2.5.1.2 Closed formularies ........................................................... 43
2.5.1.3 Partially/selectively closed formulary ....................................... 43
2.5.2 The formulary decision-making process .................................. 43
2.5.2.1 Pharmacological and clinical evaluation .................................. 45
2.5.2.2 Pharmacoeconomic evaluation ............................................ 45
2.5.2.3 Development of drug-use criteria ......................................... 46
2.5.2.4 Approval by the PTC ......................................................... 46
2.5.2.5 Administrative and ethical reviews ........................................ 46
2.5.2.6 Drug use monitoring ........................................................ 46
2.5.2.7 Follow-up review by the PTC .............................................. 46
2.6 EVIDENCE BASED MEDICINE ..................................................... 46
2.7 THE USE OF PHARMACOECONOMIC DATA IN THE FORMULARY
DECISION-MAKING PROCESSES INTERNATIONALLY AND IN SOUTH
AFRICA ................................................................................................. 47
2.7.1 Drug formularies and their development in South Africa ................. 49
2.8 CONCLUSION ............................................................................. 51

CHAPTER 3
RESEARCH METHODOLOGY ........................................................................... 52
3.1 DETERMINING THE AVAILABILITY OF SOUTH AFRICAN
PHARMACOECONOMIC STUDIES ................................................................. 52
3.1.1 Study design ........................................................................... 52
3.1.2 Eligibility criteria ................................................................. 54
3.1.2.1 Inclusion criteria ............................................................... 54
3.1.2.2 Exclusion criteria ............................................................. 54
3.1.3 Search strategy ...................................................................... 54
3.1.3.1 Search terms .................................................................. 54
3.1.3.2 Databases searched .................................................................................. 55
3.1.3.2.1 Nexus database system ........................................................................ 55
3.1.3.2.2 Sabinet Online ....................................................................................... 55
3.1.3.2.3 EBSCOhost ........................................................................................... 55
3.1.3.2.4 Science Direct........................................................................................ 56
3.1.4 Retrieval and further scrutiny of identified studies .......................................... 56
3.1.5 Quality appraisal ............................................................................................. 56
3.1.6 Emerging trends .............................................................................................. 58

3.2 DETERMINING THE USE OF PHARMACOECONOMIC DATA IN
FORMULARY DEVELOPMENT ...................................................................... 58
3.2.1 Research design ............................................................................................. 58
3.2.1.1 Exploratory study ....................................................................................... 58
3.2.1.2 Descriptive study ........................................................................................ 59
3.2.1.3 Cross-sectional survey ............................................................................... 59
3.2.2 Study population ............................................................................................. 60
3.2.2.1 Private health sector ................................................................................... 60
3.2.2.2 Public health sector ................................................................................... 60
3.2.3 Development of a survey instrument .............................................................. 60
3.2.3.1 Composition of the formulary committees.................................................. 61
3.2.3.2 Importance of pharmacoeconomics in the formulary decisions ................ 61
3.2.3.3 Rating of important factors in the formulary decision-making process ...... 61
3.2.4 Testing of the questionnaire ............................................................................ 61
3.2.5 Dissemination of the questionnaire ................................................................. 62
3.2.5.1 Medical scheme administrators .................................................................. 62
3.2.5.2 Managed care organisations ..................................................................... 62
3.2.5.3 Private hospitals ........................................................................................ 62
3.2.5.4 Public sector ............................................................................................... 62
3.2.6 Assessment of the response rate ................................................................... 62
3.2.7 Data analysis ................................................................................................... 63

3.3 DISSEMINATION OF DATA ............................................................................ 63

CHAPTER 4
AVAILABILITY OF SOUTH AFRICAN BASED PHARMACOECONOMIC DATA . 64
4.1 RESULTS OF THE LITERATURE REVIEW ................................................... 64
4.2 APPLICATION OF THE SELECTION CRITERIA........................................... 65
4.2.1 Application of the exclusion criteria............................................................... 65
4.2.2 Included studies ............................................................................................. 65
4.3 EMERGING TRENDS ...................................................................................... 67
4.3.1 Classes of drugs investigated ................................................................. 67
4.3.2 Types of economic evaluations conducted ............................................. 68
4.3.3 Nature of the publications ...................................................................... 68
   4.3.3.1 Journals .......................................................................................... 68
   4.3.3.2 Databases ....................................................................................... 69
   4.3.3.3 Unpublished studies ....................................................................... 69
4.3.4 Influence of sponsorship on the quality of the evaluation ...................... 69

4.4 QUALITY APPRAISAL OF THE INDIVIDUAL STUDIES ......................... 70
   4.4.1 Quality appraisal of the individual studies ........................................... 70
   4.4.2 Assessment of the level of quality adherence of economic evaluations
       conducted in South Africa in comparison with other countries .................. 72
   4.4.3 Quality appraisal of the individual questions for all the included studies . 73
   4.4.4 Comparison of quality amongst the various types of
       pharmacoeconomic evaluations .............................................................. 73
   4.4.5 Comparison of quality scores over a period of time ............................. 75

4.5 CONCLUSION .............................................................................................. 74

CHAPTER 5
USE OF PHARMACOECONOMIC DATA IN THE FORMULARY DECISION

5.1 INTRODUCTION .......................................................................................... 76

5.2 DISSEMINATION OF QUESTIONNAIRES .................................................... 76
   5.2.1 Private health sector ............................................................................ 76
       5.2.1.1 Managed care organisations ............................................................ 77
       5.2.1.2 Medical aid administrators ............................................................ 77
       5.2.1.3 Private hospitals .......................................................................... 77
   5.2.2 Public sector .......................................................................................... 78
       5.2.2.1 Pharmaceutical directorates ........................................................... 78
   5.2.3 Survey response rate ............................................................................ 78

5.3 FORMULARY COMMITTEES AND THEIR ACTIVITIES ............................. 79
   5.3.1 Use of formularies and formulary committees ...................................... 79
   5.3.2 Composition of the formulary committees ......................................... 81
       5.3.2.1 Size of the committees ................................................................. 81
       5.3.2.2 Composition of the committees ..................................................... 82

5.4 TRAINING IN PHARMACOECONOMICS .................................................. 84

5.5 FORMULARY PROCESS ............................................................................. 85
   5.5.1 Formulary reviews undertaken in the past year ................................. 85
   5.5.2 Use of analytical tools and software programmes in formulary development. 87
# LIST OF FIGURES

2.1 Health care expenditure of OECD countries as a percentage of the GDPs ............ 5  
2.2 Drivers of health care inflation in South Africa .................................................... 11  
2.3 When to conduct a Pharmacoeconomic evaluation .............................................. 18  
2.4 Steps in conducting a cost-benefit analysis ....................................................... 21  
2.5 Flowchart of the formulary decision-making process .......................................... 45  
3.1 Basic steps for the application of the inclusion or exclusion of the 
    identified economic evaluation studies ............................................................ 53  
3.2 Summary of steps for the research design and method .................................... 59  
4.1 Summary of the results of a literature search ................................................... 64  
5.1 Use of formularies and formulary committees ..................................................... 80  
5.2 Composition of the committee members in terms of professional backgrounds ......................................................... 82  
5.3 Evaluation of the training credentials of the decision-makers ............................. 84  
5.4 Participants scoring of factors considered in formulary decision-making 
    processes ........................................................................................................... 92  
5.5 Scoring of factors that may be considered in formulary decisions-making 
    processes ........................................................................................................... 92  
5.6 Importance of Pharmacoeconomic data in the formulary process ...................... 93  
5.7 Types of Pharmacoeconomic evaluation used in the formulary process ............. 95  
5.8 Common sources of Pharmacoeconomic data ...................................................... 97  
5.9 Transferability and generalisability of Pharmacoeconomic data ......................... 98  
5.10 Performance of sensitivity analysis on the data prior to use ................................ 98
### LIST OF TABLES

2.1 SADC health care spending ................................................................. 8
2.2 Types of costs and consequences ....................................................... 17
2.3 Types of Pharmacoeconomic studies .................................................. 19
2.4 Criteria in guidelines for Pharmacoeconomic evaluations ................. 24
2.5 Checklist for quality appraisal ............................................................. 29
2.6 Criteria for improving generalisability of studies from multi centre clinical trials .... 32
2.7 Standard definitions of methods of conducting economic analyses .......... 33
2.8 Manufacturer’s formulary submission checklist ..................................... 39
3.1 Checklist for quality appraisal ............................................................. 57
4.1 Description of selected studies ............................................................ 66
4.2 Summary of the type of drugs investigated by class .............................. 67
4.3 Frequency of included studies by type of analysis ................................. 68
4.4 Summary of the results of the quality appraisal ..................................... 71
4.5 Comparison of quality appraisal between South Africa and other countries .... 72
4.6 Summary of the quality appraisal of the individual questions for all included studies ................................................................. 74
4.7 Summary of the relationship between various economic analyses to the quality score ................................................................. 74
5.1 Summary of the dissemination of questionnaires and organisation responses ................................................................. 79
5.2 Summary of the number of members who contribute to the formulary committees ................................................................. 81
5.3 Description of professionals who form part of the committees referred to as “other”................................................................. 83
5.4 Summary of training in Pharmacoeconomics by means of continuing education ................................................................. 85
5.5 Number of formulary reviews conducted per year .................................. 86
5.6 Factors that are considered important in the formulary-decision making process ................................................................. 89
5.7 The extent to which PE data is used in the formulary processes .............. 94
LIST OF ABBREVIATIONS

AMCP  Academy of Managed Care Pharmacy
AGM   Annual General Meeting
CBA   Cost-Benefit Analysis
CEA   Cost-Effectiveness Analysis
CMA   Cost-Minimisation Analysis
COI   Cost of Illness
CT    Computed Tomography
CUA   Cost-Utility Analysis
DOH   Department of Health
DQTC  Drug Quality and Therapeutics Committee
DUR   Drug Utilisation Review
EBM   Evidence Based Medicine
EDL   Essential Drugs List
FDA   Food and Drug Administration
GDP   Gross Domestic Product
GEMS  Government Employees Medical Scheme
HASA  Hospitals Association of South Africa
HEU   Health Economics Unit
ICER  Incremental Cost Effectiveness Ratio
ISPOR International Society for Pharmacoeconomics and Outcomes Research
MAUT  Multi Attribute Utility Theory
MBA   Master of Business Administration
MCO   Managed Care Organisation
MRI   Magnetic Resonance Imaging
MSA   Medical Scheme Administration
NDP   National Drug Policy
OECD  Organisation for Economic Cooperation and Development
OTC   Over the Counter
PBS   Pharmaceutical Benefit Scheme
PBPA  Pharmaceutical Benefit Pricing Authority
PBSAC Pharmaceutical Benefit Scheme Advisory Committee
PCMA  Pharmaceutical Care Management Association
PDs   Pharmaceutical Directorates
PhRMA Pharmaceutical Research and Manufacturers of America
PHS   Public Health Scheme
<table>
<thead>
<tr>
<th>Acronym</th>
<th>Full Form</th>
</tr>
</thead>
<tbody>
<tr>
<td>PIASA</td>
<td>Pharmaceutical Industry Association of South Africa</td>
</tr>
<tr>
<td>PMPRB</td>
<td>Patented Medicine Prices Review Board</td>
</tr>
<tr>
<td>PSSA</td>
<td>Pharmaceutical Society of South Africa</td>
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<tr>
<td>PTC</td>
<td>Pharmacy and Therapeutics Committee</td>
</tr>
<tr>
<td>QALY</td>
<td>Quality-Adjusted Life-Year</td>
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<td>SADC</td>
<td>Southern African Development Community</td>
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<tr>
<td>SAMF</td>
<td>South African Medicines Formulary</td>
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<tr>
<td>SAMJ</td>
<td>South African Medical Journal</td>
</tr>
<tr>
<td>SAPJ</td>
<td>South African Pharmaceutical Journal</td>
</tr>
<tr>
<td>SHI</td>
<td>Social Health Insurance</td>
</tr>
<tr>
<td>SEP</td>
<td>Single Exit Price</td>
</tr>
<tr>
<td>SOJA</td>
<td>System Of Objectified Judgement Analysis</td>
</tr>
<tr>
<td>UCT</td>
<td>University of Cape Town</td>
</tr>
<tr>
<td>UK</td>
<td>United Kingdom</td>
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<tr>
<td>US</td>
<td>United States</td>
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<tr>
<td>USA</td>
<td>United States of America</td>
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<td>WHO</td>
<td>World Health Organisation</td>
</tr>
</tbody>
</table>
# LIST OF APPENDICES

<table>
<thead>
<tr>
<th>Appendix I</th>
<th>Sample of a Questionnaire</th>
<th>120</th>
</tr>
</thead>
<tbody>
<tr>
<td>Appendix II</td>
<td>Sample of a Covering letter</td>
<td>126</td>
</tr>
</tbody>
</table>
SUMMARY

In an attempt to manage scarce health care resources and keep drug expenditure low, health care administrators worldwide have to make careful considerations regarding the choice of drugs to be provided to patients within their systems. One of the key strategies that is being employed to achieve this goal is the use of formularies. A major challenge in the formulary development process is to use pharmacoeconomics and outcomes research effectively to arrive at formularies that simultaneously provide patients with effective pharmacotherapy whilst maintaining financial stability. The extent to which this can be successfully achieved depends to a large extent on the availability of appropriate pharmacoeconomic data.

The primary objectives of this study were to describe the availability and quality of literature pertaining to South African based pharmacoeconomic research, and to establish the manner in and extent to which pharmacoeconomic data is used in drug formulary decision-making processes, in both the private and public health care sectors in South Africa.

A structured bibliographic search for South African pharmacoeconomic studies was conducted and a qualitative assessment of the identified studies which met the pre-determined inclusion criteria was completed, using a pre-validated quality evaluation tool.

In order to determine the use of pharmacoeconomic data in the formulary decision-making processes, by various stake holders in both the public and private of health care sectors in South Africa, a cross-sectional, descriptive study using a self-administered questionnaire was conducted.

The results suggest that there is a limited availability of pharmacoeconomic research data in South Africa. Only 16 full pharmacoeconomic studies could be identified as having been published between 01 January 1995 and 30 June 2007. The quality of 3 of these studies was considered to be ‘dubious’, one study was found to be of high standard whilst the other 12 (74.95%) were of acceptable quality and thus could be considered as suitable to be used in formulary decision-making.

The results of the national survey indicated that pharmacoeconomics is considered to be of importance and is used in formulary decision-making processes in both the public and private sectors. The primary source of pharmacoeconomic data used in formulary decisions appears to be international peer-reviewed publications. Of concern however, is
the finding that this data, mostly from studies conducted outside of South Africa, is applied directly without sensitivity analysis or modelling.

The results of the literature search and the subsequent quality appraisal suggest that pharmacoeconomic research and the use of pharmacoeconomic data in formulary decisions is at its infancy in South Africa. Thus efforts are needed to develop and grow the discipline of pharmacoeconomics in South Africa.

**Keywords:** Pharmacoeconomics, Formulary, Literature quality appraisal and South Africa.
CHAPTER 1

OVERVIEW

Concerns over the scarcity of health care resources and the cost of both medical care and medicines are being experienced in nearly all developed, as well as developing countries worldwide.\(^1\) South Africa is no exception to this,\(^2,3\) since 1994 the South African health care system has undergone a major revolution in both the public and private sectors. The former introduced the National Drug Policy (NDP) whose main goal is “to ensure an adequate and reliable supply of safe, cost-effective drugs of acceptable quality to all citizens of South Africa and the rational use of drugs by prescribers, dispensers and consumers”\(^2\). This was followed with a significant number of legislative reforms to facilitate an attainment of the NDP goals.

The private sector has adopted the managed health care model in an attempt to control the rampant increase of medical costs\(^4\), this approach has received support from the Department of Health (DOH)\(^5\). Managed health care can be defined as an organised system of health care delivery to control the cost and quality of health care by employing techniques such as mandatory drug formulary lists, case management and pre-admission screening. Providers such as pharmacists, doctors and dentists generally agree to a discounted payment and to uphold the plan’s cost and quality measures.\(^6\)

These interventions seek to ensure that the scarce health care resources are allocated in the most efficient way without compromising the quality of care given to patients. Use of drug formularies is one of the strategies that have been adopted to manage drug costs without jeopardising the quality of care to the patient.\(^7\) In South Africa drug formularies are a successful means of managing drug costs and product quality in both the private and public sectors.\(^8\)

1.1 MOTIVATION FOR THE STUDY

Decision-makers require tools that can provide them with information about cost-effectiveness of various pharmacotherapies, one such tool is pharmacoeconomics\(^9\). It can be simply defined as a branch of science that is concerned with measuring the costs and outcomes associated with the use of pharmaceuticals in health care delivery.\(^10\)

The use of pharmacoeconomics in making formulary decisions has proved successful in several countries such as Australia and Canada\(^11\). Although the NDP recognises the value and need for rational drug use decisions to be underpinned by
pharmacoeconomics, the use of pharmacoeconomics as it applies to formulary decision-making in South Africa remains an area that needs to be explored.

1.2 Hypothesis

Formulary decision-making processes in both the private and public health sectors in South Africa are not based on the use of pharmacoeconomic data as there is very little available literature that is relevant to the South African setting.

1.3 PRIMARY OBJECTIVES OF THE RESEARCH

This research project proposed to establish the manner in and extent to which pharmacoeconomic data is used in drug formulary decision-making processes.

With consideration to the development of drug formularies in both the public and private health care sectors in South Africa, this project aims to:

i. Determine and describe the processes used in the decision-making
ii. Establish the sources of pharmacoeconomic data used in the process
iii. Establish the extent of the availability and quality of data (published and unpublished) pertaining to South African based pharmacoeconomic studies
iv. Establish the background and expertise of the decision-makers
v. Arrive at recommendations that can be used to promote and aid the use of pharmacoeconomics in the process.

1.4 CHAPTER LAYOUT

The layout of the chapters is as follows:

i  Chapter 1
The intention of this chapter is to give an introduction and background to the study as well as outline the primary aims and objectives of the research.

ii  Chapter 2
A literature review is provided in this chapter which focuses on the following areas:

2.1 Escalating costs of health care worldwide
2.2 The health care scenario in South Africa
2.3 Role of health economics and pharmacoeconomics in health care
2.4 Applied Pharmacoeconomics
2.5 Formularies and the development of formularies
2.6 The use of pharmacoeconomic data in formulary decision-making processes internationally and in South Africa

2.7 Conclusion.

iii Chapter 3
This chapter outlines the research methodology that was adopted in collecting and analysing data from the medical aid schemes, managed health care organisations, private hospitals and pharmaceutical directorates.

iv Chapter 4
This chapter reports on the results and discussion of the following:
- Literature searches that were aimed at establishing the availability of pharmacoeconomic studies in South Africa
- The quality appraisal of the available pharmacoeconomic studies in order to determine their quality status.

v Chapter 5
This chapter reports on the results and discussion of the exploratory survey to establish the use of pharmacoeconomic data in formulary decision-making processes in South Africa.

vi Chapter 6
This chapter provides a conclusion of the research based on the findings, discusses the limitations of the study and provides recommendations for further study.
CHAPTER 2

THE ROLE OF PHARMACOECONOMICS IN REDUCING HEALTH CARE EXPENDITURE

2.1 Escalating costs of health care worldwide

The rapid growth of health care expenditure and scarcity of health care resources is a worldwide phenomenon. This scarcity of resources places economic constraints on the providers of services, who are often limited in their actions, and consequently the individual patient suffers. Despite significant differences in how health systems in countries worldwide are organised, financed and provided for, decision makers are all faced with similar challenges. These include sustainable financing, improving efficiency, improving health outcomes, raising quality, creating greater responsiveness, ensuring equity of access to health services, improving citizen involvement in decision making and reducing barriers between health and social care.

Good health is essential for individuals to succeed as citizens, families, workers and consumers. In virtually all the developed countries, health care costs have been rising substantially faster than their national resources. This is true with the Organisation for Economic Cooperation and Development (OECD) countries as well, who are concerned with the improvement of the health of their citizens as it can contribute to higher economic growth and improved welfare. The OECD was established in 1961 and is based in Paris, France. Its membership comprise of 30 countries with a primary aim of supporting sustainable economic growth, raising living standards, maintaining financial stability and boosting employment.

OECD countries are spending increasingly greater amounts on health care as shown in Figure 2.1, mainly as a result of the rising costs of pharmaceuticals and breakthroughs in modern medical technology. According to the OECD Health Data 2003: a comparative analysis of 30 countries, OECD countries spent an average of 8.4% of their Gross Domestic Product (GDP) on health care in 2001. This expenditure was up by 0.3% from the expenditure on health care of the preceding year. Furthermore, this report revealed that in the past decade, the health care expenditure in the OECD countries has outpaced their economies by more than one percent. GDP is the total value of a country’s annual output of goods and services.
In 2005, the United States (US) allocated $2 trillion to health care, which amounts to 16% of its GDP as shown in Figure 2.1. Despite allocating more funds on health care than any other OECD country as illustrated in Figure 2.1, there are numerous challenges the US faces such as:

i. The costs of federal and state funded health care benefits (Medicare) and private health plans are rising much faster than the GDP.

ii. Rising health care spending which is driven by factors such as medical price inflation, innovations in medical technology (e.g. new drugs, medical devices, diagnostics, therapeutic procedures etc).

iii. The increasing life span of the US population. More use of health care resources by older people has a small but persistent impact on health care costs, since older people have more health problems (chronic conditions) and thus gradually use more health care than younger people.

There is also a sharp decline in private health insurance, which is subsidised largely by the employers. The Kaiser Family Foundation, which is a non-profit, private organisation that focuses on the major health care issues facing the US estimates that there was a decrease of approximately five million jobs providing private health insurance between 2001 and 2004. This drop in the population covered by private health insurance results
in an increased load for the public sector, which places further constraints on health care resources.\textsuperscript{16,23}

The European Observatory on Health Care Systems commissioned a study in 2002 to look at the trends and challenges of health care systems in eight countries. It was found that Australia has perpetually increased its health care expenditure over the past three decades. In 2001, the government spent 8.5\% of it’s GDP on health care, which is slightly above an average of 8.4\% (of GDPs) for OECD countries in the same period.\textsuperscript{14} Furthermore, in 2004 the spending on health care was increased to 9.5\% of the country’s GDP, which is 0.5 \% in excess of an average of 9.0\% (of GDPs) for OECD countries.\textsuperscript{24}

Despite this effort there are major challenges facing the Australian health care system such as, for example:

i. Resources in health care.\textsuperscript{24}
   - There are fewer doctors per capita in comparison with other OECD countries (i.e. 2.7 practising doctors per capita in Australia as opposed to an average of 3.0 doctors per capita in the OECD countries),
   - There are fewer hospital beds in Australia per 1000 population as compared to the OECD countries (i.e. 3.6 hospital beds per 1000 population in Australia as opposed to an average of 3.9 in other OECD countries),
   - Slow growth in the availability of diagnostic technologies such as computed tomography (CT) scanners, magnetic resonance imaging (MRI) units in Australia (i.e. in Australia the number of MRI scanners in 2005 were 4.2 units per million people population when compared to an average of 9.8 units in the other OECD countries).\textsuperscript{24}

ii. Longer life spans. In 2005, an estimated life span at birth of an Australian stood at 80.9 years as opposed to two years less in the other OECD countries,\textsuperscript{24} it is a known fact that the older people consume more health care than the younger people due to their ill health.\textsuperscript{18,25}

iii. Private health insurance. The Australian government has incurred huge costs in the form of tax rebates to encourage people to take out private health insurance.\textsuperscript{14}

Globally the statistics show that the total health spending generally varies from around 2-3\% of GDP in low-income countries (<US $ 1 000 per capita) to typically 8-9\% in high-income countries (>US $ 7 000). Health expenditure expressed as a percentage of total expenditure also rises as income rises from 5-6\% up to 10\%.\textsuperscript{26} This increase in health care expenditure can largely be attributed to rising drug costs, associated with new breakthroughs in medicine, an increased volume in the use of medicines, changes in
demographics and health status of the population, as well as the irrational use of drugs.\textsuperscript{16,27}

In 2000, prescription drug costs rose by 17.3%. In the US and overall, health care costs are expected to rise by 7.3% per annum until 2011. In the United Kingdom (UK), health care costs rise on average by 3% per annum. Canada spent 10.6% more on prescription drugs in 2001 than it had the previous year.\textsuperscript{28-30}

In developing countries there is generally a low total health spending as a percentage of GDP (around 2-3\% of GDP).\textsuperscript{26} Adding to this burden of low expenditure on health the majority of developing countries are also affected by the following problems:\textsuperscript{31}

\begin{enumerate}
\item A relatively high expenditure on health services in urban areas, whilst few or no services are within reach of the majority of the population living in the rural areas
\item Resources are concentrated on hospitals, particularly teaching hospitals using high technology, rather than on primary health care programmes
\item Provision of costly training to key health personnel who are unwilling to work in rural areas creates an imbalance in the distribution of health services
\item There is a relative lack of funding for preventive medicine, including health education, compared to the funding for urban curative medicine
\item There is a heavy expenditure on a vast range of imported specialist drugs.\textsuperscript{31}
\end{enumerate}

Seven hundred and eighteen million people populate the majority of African countries, primarily in the sub-Saharan region, and their economies are amongst the poorest in the world.\textsuperscript{32} This can be highlighted by comparison of Figure 2.1 and Table 2.1 as it indicates that compared to the OECD countries (average 8.4\%), the Southern African Development Community (SADC) countries spend less of their GDP (average 6.15\%) on total health care. South Africa allocates 8.7\% of its GDP to health care which is the second highest, after Malawi, in the SADC region. Health care financing in South Africa will be discussed further in Section 2.2.

SADC was formed in 1980 with the aim of working together to ensure that people of the Southern Africa enjoy economic well-being, improved standards of living and quality of life, freedom and social justice as well as peace and security.\textsuperscript{33} Countries within the SADC are faced with the pandemics of HIV/AIDS, tuberculosis and malaria. It was reported that between 1999 and 2000 more people died of HIV/AIDS in Africa than in all the wars on the continent.\textsuperscript{34}
The key priority of the World Health Organisation (WHO) in Africa is to assist the member states in reforming their health sectors in the context of their own policies, strategies, and plans. Furthermore, the WHO urges governments to consider health issues in their agendas and translate their policies into action and reflect these priorities in their national budgets.\textsuperscript{32} South Africa has vigorously set in place a number of policies pertaining to health care delivery and legislative reforms, which will be discussed further in the next section.

### Table 2.1: SADC Health Care spending

<table>
<thead>
<tr>
<th>Country</th>
<th>Total population</th>
<th>Total Health Expenditure per capita (Intl $, 2002)</th>
<th>Total Health Care as % of GDP (2002)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Malawi</td>
<td>12 105 000</td>
<td>48</td>
<td>9.8</td>
</tr>
<tr>
<td>South Africa</td>
<td>45 026 000</td>
<td>689</td>
<td>8.7</td>
</tr>
<tr>
<td>Zimbabwe</td>
<td>12 891 000</td>
<td>152</td>
<td>8.5</td>
</tr>
<tr>
<td>Namibia</td>
<td>1 987 000</td>
<td>331</td>
<td>6.7</td>
</tr>
<tr>
<td>Lesotho</td>
<td>1 802 000</td>
<td>119</td>
<td>6.2</td>
</tr>
<tr>
<td>Botswana</td>
<td>1 785 000</td>
<td>387</td>
<td>6.0</td>
</tr>
<tr>
<td>Swaziland</td>
<td>1 077 000</td>
<td>309</td>
<td>6.0</td>
</tr>
<tr>
<td>Zambia</td>
<td>10 812 000</td>
<td>51</td>
<td>5.8</td>
</tr>
<tr>
<td>Mozambique</td>
<td>18 863 000</td>
<td>50</td>
<td>5.8</td>
</tr>
<tr>
<td>Seychelles</td>
<td>81 000</td>
<td>557</td>
<td>5.2</td>
</tr>
<tr>
<td>Angola</td>
<td>13 625 000</td>
<td>92</td>
<td>5.0</td>
</tr>
<tr>
<td>United Republic of Tanzania</td>
<td>36 977 000</td>
<td>31</td>
<td>4.9</td>
</tr>
<tr>
<td>Democratic Republic of the Congo</td>
<td>52 771 000</td>
<td>14</td>
<td>4.0</td>
</tr>
<tr>
<td>Mauritius</td>
<td>1 221 000</td>
<td>387</td>
<td>3.5</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>15 073 071</strong></td>
<td><strong>230</strong></td>
<td><strong>6.15</strong></td>
</tr>
</tbody>
</table>

Data from WHO report 2005, SADC = Southern African Development Community and Intl $ = International dollars.\textsuperscript{35}

### 2.2 The Health Care Scenario In South Africa

South Africa is a developing country with a population estimated at 47.9 million people\textsuperscript{36} and limited resources at its disposal. Health issues in South Africa like everywhere in the world are high on the agenda of national priorities. The DOH has a task of developing a unified health system capable of delivering quality health care to all citizens efficiently.\textsuperscript{37}
In 2002, Doherty, Thomas and Muirhead conducted a study on Health care Financing and Expenditure in Post-Apartheid South Africa and suggested that the health policy pre-1994, served the dominant objective of maintaining economic and political power for the white minority. The result thereof was a difference in the quality of health provided to different population groups, and resulted in a health care system that was characterised by the following:

i. Highly fragmented structure - health service delivery was delivered between a range of health authorities, namely, national, provincial, former ‘homelands’ and local government structures.

ii. Provision of curative and preventive primary care services were provided in separate facilities and administered by different health authorities. Only 11% of total public sector health care expenditure was devoted to primary health care. The main focus was on curative and higher level services.

iii. Systematic under-funding led to an inequitable bias towards historically white areas and certain geographic areas particularly the former homelands, townships and informal settlements suffered.

iv. Bias towards the wealthy minority who could afford to use the private sector. It was reported in 1992/1993 that this sector was serving only 23% of the population and not less than 61% of total health care expenditure was spent on this sector.

Post-1994 the Government deemed the correct identification of these apparent anomalies and the introduction of remedial policies as a high priority. The aim of the DOH became “to improve health status through prevention and promotion of healthy lifestyles and to consistently improve the health care delivery system by focusing on access, equity, efficiency, quality and sustainability.” However some of the apparent major challenges that still face the public sector include:

i. The HIV/AIDS pandemic, which is estimated to cost the DOH R6 billion per year, for which it is not completely compensated for by government.

ii. High expenditure on personnel, a real growth in expenditure of R3 billion per year has masked a decrease of 19000 posts.

iii. Despite increased expenditure on health per capita, spending has remained stagnant and is struggling to match the values in the mid to late 1990s. It fell by 2.5% between 1997/1998 and 1998/1999.

iv. Cost-recovery in public facilities is low and decreasing, this is due to a combination of decreased use by paying patients and poor management of billing systems.
v. Cost escalation in growth of and attraction of health personnel to private sector and overseas countries, and the implications this has for the sustainability and quality of the overall health system.\textsuperscript{40}

vi. Improvement of access to health services especially in rural areas and strengthening of primary care.\textsuperscript{37}

vii. Inefficiencies in the utilisation of resources within the public sector has made it difficult to expand its health services to provide proper care for the poor, or to absorb the growing ranks of those who are able to purchase private care.\textsuperscript{40}

The distribution of total health care expenditure in South Africa is highly concentrated on the private sector whose services are rendered mainly to residents in urban areas. The majority of health care practitioners of all categories (with the exception of the nurses) are in private practice. This sector is substantial and growing and there is an extensive network of private hospitals.\textsuperscript{41}

In 2001, a study carried out on health care financing in South Africa reported the following key findings,

i. The private sector is mainly funded by the private financing intermediaries (which include medical aid schemes, health insurance products and workplace services by private firms) and accounts for 72\% of the expenditure with population coverage of less than 20\% of the entire population.\textsuperscript{40}

ii. The second largest form of financing is on an out-of-pocket basis by non-scheme members accounting for 22.4\% of the expenditure and about 30\% population coverage.\textsuperscript{40}

The growth of private health care expenditure is increasing very rapidly. Between 1996 and 1998 it increased from R24.7 billion to R33.3 billion. This increase in expenditure was driven by escalation of costs, particularly those of private hospitals which consumed 29\% of funds spent on beneficiaries in 1998/1999.\textsuperscript{38,42} The costs of drugs also increased faster than the overall increase in benefit expenditure between 1997 and 1998.\textsuperscript{38}

The response of medical aid schemes to these sharp increases of private health care costs has been to increase member premiums. In 2001, medical scheme contributions increased by 12.4\% (this rise is over and above the inflation).\textsuperscript{39} Resultantly it was reported in the same year, that it had become increasingly unaffordable to remain a member of these schemes and population coverage of medical aid schemes was declining.\textsuperscript{41}
This shrinking population coverage increases the burden on the public sector, as an increasing proportion of the population relies on the public sector for health care particularly for hospital care. When funding does not match increases in the number of patients dependent on the public sector, the public health services are put under pressure and quality may become compromised. However, the advent of the Government Employees Medical Scheme (GEMS), which was introduced with effect from 01 January 2005, is expected to make a noticeable impact on the population coverage of medical aid schemes given its competitive pricing and 5 benefit options.

In its annual report for 2006-7 the Council for Medical Schemes reported an increase in population coverage of 2% for principal members and that of 4.3% for the beneficiaries. Furthermore, it was reported that the gross contribution income for medical aid schemes increased by 6.2% to R57.6bn and of that amount R51.3bn was paid out in benefits (i.e. to service providers). The expenditure on benefits represented an increase of 12.4% (from R45.6bn) that was paid out in the previous financial year, 2005-6. This increase in benefits expenditure is over and above the consumer price index (CPIX). Statistics SA reported in its Annual Inflation on a Monthly Basis Report that the CPIX has fluctuated from 5.3% in January 2007 to 6.4% in June 2007 and the latest figure reported in October 2007 was 7.3%. The three main drivers of the medical inflation are the private hospitals, medical specialists and medicines as shown in Figure 2.2.

Figure 2.2. Drivers of Health care inflation in South Africa. Adopted from the 2006-7 Annual Report of the Council of Medical Schemes.
The current medical inflation status is a vast improvement from what it was in 1996 where the medical inflation ranged between 18 and 25%. In the same year, 1996, about 50% of the medical aid schemes exceeded their budgets as a result of this cost explosion.\textsuperscript{45,46}

The interface between the public sector and the private sector needs to be that of promoting a competitive health care industry where both role players are equal partners in the provision of comprehensive health care.\textsuperscript{47} The DOH, in an effort to address the challenges it faces has embarked on a series of legislative reform, namely:

i. The NDP, introduced in 1996 covers the wide range of activities that contributes to the effective production, supply, storage, distribution and use of medicines\textsuperscript{2}

ii. The National Health Act No. 61 of 2003, which is intended \textit{inter alia} to remedy the inequities of the past in the distribution of health care and to create a national health system that is patient centred and for the good of all\textsuperscript{46}

iii. The Medicines and Related Substances Amendment Act No. 59 of 2002, introduced \textit{inter alia} to provide for a transparent pricing system based on the single exit price by manufacturers and the elimination of bonus and incentive schemes, thereby creating the framework within which prices can be reduced. It also introduced the regulation of the fees that can be charged by pharmacists and other legally authorised dispensers in an effort to curb the escalating costs of medicines and address the affordability issue\textsuperscript{49}

iv. The Medical Schemes Act No. 131 of 1998, sought to regulate the medical aid schemes industry and promote equitable access to health care resources.\textsuperscript{50} These included the introduction of prescribed minimum benefits by medical aid schemes to cover common chronic conditions and to do away with discriminatory policies and practices such as those that were propagated against the elderly and the sick.\textsuperscript{50}

The enactment of some of these legislations was met with a lot of resistance from the private sector and created difficulties in the relationship between these two sectors and even resulted in court actions.\textsuperscript{47} The most contested of these legislative reforms have been the National Health Act No. 61 of 2003 and the Medicines and Related Substances Amendment Act No. 101 of 2003, which both sought to regulate the services of the private sector. The former includes a requirement for health care professionals as well as private hospitals to apply for permission to practice in specific areas, i.e. they need to be issued with the “certificate of need” by the DOH under the Act. This is aimed at ensuring an equitable distribution of health care services by preventing a high concentration of services in certain areas whilst others remain underserved.\textsuperscript{49}
The Medical Schemes Act provides for the adoption of a managed health care model in the private sector with a view of providing an enabling legal framework for cost-containment. Managed health care entails risk management of the medical and financial aspects of health care. It is based on conscious decision-making or predetermined courses of action that affect one or more of the fundamental parameters of health care, namely price, quality and access to health care. The primary objective of managed health care is the containment of health care costs and the promotion of quality health care services at affordable levels.

Disease management is one of the core strategies for cost containment that are used in managed health care. It focuses both on the systematic evaluation of the relations between options and outcomes for patients. Essentially it entails development of compliance and management strategies and concerns itself with the measuring of outcomes and compiling reports as well as capitated risk sharing arrangements. Health care team members collaborate in ensuring the patient education, monitoring, and feedback to the patient and one another. Another strategy that is employed is Pharmaceutical Benefit Management (PBM), which involves the application of managed health care to medicines, with the goal of optimising the patient's health-related quality of life and ensuring that the positive clinical outcomes of pharmacotherapy are achieved within reasonable economic expenditure.

PMB employs techniques such as:

i. **Drug Utilisation Review (DUR)**
   This is used to ascertain the appropriateness of the prescribed medicines and their necessity, in order to prevent adverse reactions by assessing the safety and efficacy of treatment. This is achieved by instituting controls such as authorisations prior to rendering a service by providers or a retrospective review of procedures that were undertaken in treating the patient.

ii. **Medicine Formulary**
   This is a means of instituting benefit restrictions on medicines by providing a list of drugs that can be used together with step-care protocols and policies to be followed in case of substitutions and prior authorisations. Formularies are discussed further in section 2.5.

The DOH is however adamant that successful implementation of these legislative reforms will be an important step forward and a foundation for the implementation of Social Health Insurance (SHI) in the medium to long term. SHI refers to obligatory contributions into a health fund that provides health care coverage for members and their dependants. It entails social solidarity whereby low-income earners are cross-subsidised by the wealthy and the ill by the healthy.
SHI has been implemented successfully in other countries where it first focused on the formally employed individuals and was gradually extended to workers outside the formal employment sector.\textsuperscript{57} In the past decade much debate has taken place about the introduction of SHI in South Africa and a wide range of models have been proposed. The Committee of Inquiry into a National Health Insurance has made a proposal that recommends introduction of compulsory health insurance contributions for all formal sector employees and their dependants, for coverage of health care costs in public hospitals.\textsuperscript{57}

The Health Charter (2005) acknowledges the urgent need to effect transformation of the national health system in a co-operative, constructive and mutually beneficial manner that reflects the diversity and meets the various health care needs of the total population.\textsuperscript{58}

2.3 Role of health economics and pharmacoeconomics in health care

Internationally, improving the efficacy of health care systems, i.e. producing better health outcomes at the lowest possible cost, has become a major concern amongst decision-makers. This challenge has sparked an interest in the economic evaluation of health care programs and interventions, in both the developed and developing countries, with the same fundamental questions being asked.\textsuperscript{14}

i. What is the most cost-effective way of improving health?

ii. How can the health effort be redirected to provide better value for money?

iii. Insofar as this involves changing behaviour, how can the necessary changes best be secured?

iv. In the case of services what should the priorities be, how can they be equitably distributed in terms of health need, and how can they be made to secure the maximum health improvements for the money available?

All countries are faced with the same problem, namely, an increasing demand for care, to be paid for with stable or diminishing resources.\textsuperscript{59} In economic terms, the essential problem is how to maximize the health care that can be obtained from any given level of expenditure.\textsuperscript{60} Put differently, the challenge is to ascertain that health care institutions remain at the cutting edge of therapeutics but that they are also able to contain the drug budget within reasonable bounds.\textsuperscript{61}

A field of economics known as Health Economics, which may be defined as the application of economics to health, is used by decision makers to analyse the supply and
demand for health care, and provides a framework and structure for understanding health care decisions and their consequences. Health economics is based on the notion that there are not enough and will never be enough resources to achieve all the worthwhile objectives that can be identified. The demand for health care is influenced by the cost of health care services, which can be influenced by the availability and affordability of medical care. Health care systems can be described as processes that combine various inputs (pharmaceuticals, physician services, and hospital care) to produce specific outputs (medical consequences or outcomes). Health care systems, programs, policies and interventions are assessed by means of outcomes research in order to determine their true value. This is in an effort to avoid the danger of changes being made that are driven purely by cost-containment. Successful health care management as measured by the objectives of patients, physicians, and other health care providers requires that the quality of care also be maintained. Outcomes research takes into consideration the economic outcomes (e.g. costs), clinical outcomes (e.g. reduction in high blood pressure) and humanistic outcomes (e.g. improvement of quality of life).

Since pharmaceutical costs have also escalated in recent years and are an easily identifiable component of health care expenditure they too have become a major focus. Pharmaceuticals play a key role in the effectiveness, efficiency and responsiveness of health systems. In 1997, Bennet, Quick and Velasquez reported that pharmaceuticals constitute a major recurrent expense in all sectors (public and private) of health care. A report issued in the US by The National Institute for Health care Management Research and Educational Foundation (2001) cited by Van Den Bos, Watkins, Reed, and Shreve attributed the explosive pharmaceutical cost trends to several factors, including: an increase in drug utilization (39%), increases in drug prices (37%) and shifts to the use of higher priced drugs (24%). In a comparative study of drug costs per prescription and drug utilization of a thousand patients, over a period of 13 years, it was shown that drug utilization increased by 215% and the price per prescription, by 230%. In 1990, the average annual utilization in this study population was 4141 prescriptions with an average cost of $26.88 per prescription. The corresponding values in 2003 were 8900 prescriptions at an average cost of $61.78 per prescription.

An increase in the utilization of drugs can lead to an irrational and inefficient use by health care professionals that will further lead to an escalation of drug expenditure. It is problems such as these that have given birth to pharmacoeconomics, a relatively new discipline that developed in the 1970s, its conceptual principles first being published in 1978 in the American Journal of Hospital Pharmacy. It can be defined as “the science of measuring...
the costs and outcomes associated with the use of pharmaceuticals in health care delivery”. Simply stated, a pharmacoeconomic evaluation seeks to find the cheapest means by which to produce the most beneficial outcome using drugs or pharmaceuticals.

More than just determining the acquisition cost of a drug, pharmacoeconomic evaluations identify how a particular pharmaceutical agent may produce a positive outcome that lowers total health care costs. The discipline borrows from other fields such as health economics, decision analysis, and outcomes research and offers tools to decision-makers that assist in achieving the efficient allocation of resources, with regards to pharmaceuticals, in the health care system.

2.3.1 Costs in pharmacoeconomic evaluation

In pharmacoeconomic evaluations, costs and consequences of pharmacological interventions are the primary consideration. The concept of costs deals with the resources that get consumed in the production of a service or a good. The final products of an intervention are therapies that cure, prevent, or alleviate disease and consequently change the health status. The services such as prescription drugs, laboratory tests, hospital stays, physician visits, and surgical procedures are regarded as inputs and when they are converted into therapies, they become outputs.

These inputs need resources such as facilities, staff, equipment, and supplies. In this context, health services are intermediate goods; they use basic resources that get converted into therapies. In carrying out pharmacoeconomic analyses, it is important to establish what the basic inputs are, for example prior to computing the costs that are associated with the use of a drug in the hospital setup, the basic inputs of labour and equipment need to be specified. When treating an illness with drug therapy alone the inputs that need to be specified are the services that get consumed in the process.

When dealing with costs a distinction between the financial and economic concept of costs needs to be made. Financial costs deal with monetary payments and usually indicate the price of a good or service. In economics, cost is concerned with the concept of resource consumption, including those resources for which no monetary payments are made. In all good pharmacoeconomic evaluations, all relevant costs need to be included. Costs can be broadly classified into three categories, as direct, indirect and intangible costs.
A direct cost is about a transfer of money, money is exchanged for the use of a resource.\textsuperscript{64} As referred to in Table 2.2, direct costs can be categorised into direct medical cost and direct non-medical costs. Direct medical costs include spending of money on services and goods such as drugs, laboratory tests and hospitalisation including staff costs.\textsuperscript{10} Direct non-medical costs are the costs that gets incurred in dealing with an illness even though they are non medical in nature, these include costs such as hiring a person to help with home care, accommodation for family during treatment and transportation to the site of treatment.\textsuperscript{10}

Indirect costs result from production capacity changes brought about by an intervention or illness, these costs include loss of productivity or earnings as a result of a temporary or permanent disability. In this situation no money is exchanged, productivity may be measured as lost wages even if the person was paid through sick leave or another benefit program.\textsuperscript{10,64}

\begin{table}[h]
\centering
\begin{tabular}{|l|l|}
\hline
\textbf{Cost Category} & \textbf{Examples} \\
\hline
Direct medical costs & Laboratory test \\
& Drugs \\
& Hospitalization \\
Direct non-medical costs & Transport \\
Indirect cost & Days lost from work \\
& Reduced productivity \\
Intangible cost & Pain \\
& Suffering \\
\hline
\end{tabular}
\caption{Types of Costs and Consequences}
\end{table}

\begin{table}[h]
\centering
\begin{tabular}{|l|l|}
\hline
\textbf{Outcome category} & \textbf{Examples} \\
\hline
Economic outcome & Cost \\
Clinical outcome & Mortality \\
& Blood pressure in hypertension \\
& HbA1c in diabetes \\
& Number of recurrences \\
& Number of disease free patients \\
Humanistic outcome & Quality of life \\
& Patient satisfaction \\
& Patient preferences \\
\hline
\end{tabular}
\caption{Outcome of Cost and Consequences}
\end{table}

Source: Adapted from Venturini and Johnson (2002).\textsuperscript{10}
2.3.2 Methods for pharmacoeconomic evaluations

As previously stated, pharmacoeconomics is about measuring costs and outcomes associated with the use of pharmaceuticals in health care delivery and the basic purpose of pharmacoeconomic evaluations is to compare the costs and consequences of pharmacotherapeutic alternatives. Figure 2.3, provides insight into when a pharmacoeconomic evaluation or analysis is required to be undertaken. It considers both the cost and the clinical effectiveness of new proposed treatments relative to the current standard treatments in use.

When a new treatment is less effective and has a higher cost (lower left side of Figure 2.3), there will be no need to conduct a pharmacoeconomic evaluation unless there are other populations in which the new treatment might be more effective. When one considers the upper right side of Figure 2.3, where a new treatment is much more effective and of lower cost than the standard of care, the new treatment can also be adopted without the need to carry out a comprehensive pharmacoeconomic evaluation.

The four main types of pharmacoeconomic methodologies used are cost-effectiveness analysis, cost-utility analysis, cost-benefit analysis and cost-minimisation analysis. There is another type of study, cost of illness (COI), that does not compare competing alternatives but is concerned with the estimation and identification of the financial burden of the overall cost of a particular disease on a defined population.

In each type of analysis, inputs or costs of therapy are measured in monetary units. The units in which outcomes are measured depend upon the methodology of the study. Table 2.3 provides a summary of these types of pharmacoeconomic evaluations.
Another very important consideration in pharmacoeconomic evaluations is the perspective from which the analysis is performed. Patients tend to be more concerned with humanistic outcomes, health care providers with clinical outcomes, and health insurers with economic outcomes and society with a combination of all three outcomes.10

Table 2.3: Types of Pharmacoeconomic Studies

<table>
<thead>
<tr>
<th>Method</th>
<th>Cost Measure</th>
<th>Outcome Measure</th>
<th>Description</th>
<th>Advantages (A) / Disadvantages (D)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cost of Illness (COI)</td>
<td>R</td>
<td>Not applicable</td>
<td>Gives the total direct and indirect costs attributable to a given illness</td>
<td>Does not aid clinical choices (D) Useful for the estimation of the economic burden on a disease (A)</td>
</tr>
<tr>
<td>Cost-Minimization-Analysis (CMA)</td>
<td>R</td>
<td>Any (usually clinical)</td>
<td>Find the lowest cost program among those shown to be of equal benefit</td>
<td>Rarely applicable (D) Only includes limited inputs (D)</td>
</tr>
<tr>
<td>Cost-Effectiveness-Analysis (CEA)</td>
<td>R</td>
<td>Clinical (physical units)</td>
<td>Years of life Gives the cost per program-specific unit or year of life saved</td>
<td>Hard to make comparisons among studies or different diseases due to differences in the primary effectiveness measure (D) Broadly applied due to the widest range of possible clinical outcomes (A) It enables a broad range of outcomes to be combined in one summary outcome (A) Difficult to measure utilities (D)</td>
</tr>
<tr>
<td>Cost-Utility-Analysis (CUA)</td>
<td>R</td>
<td>Outcomes that include patient preferences (e.g., QALYs, HYE)</td>
<td>Gives the cost per QALY or similar measure including the notion of patient preferences</td>
<td>It allows a direct comparison of the program incremental consequences in commensurate units of measurement (A) Difficult to define a monetary value for health consequences (D)</td>
</tr>
</tbody>
</table>
| Cost-Benefit-Analysis (CBA)     | R            | R              | Full economic evaluation in which both inputs and outputs must be evaluated in monetary terms | | QALY = Quality adjusted life year, HYE = Healthy-year equivalent, R = Rands or monetary units

Source: Adapted from Venturini and Johnson (2002).10

2.3.2.1 Cost-Minimisation Analysis (CMA)

CMA is an "economic analysis where the benefits of the health care intervention are proven to be equivalent."72 In CMA the basis of comparison is solely cost as it is used to determine the most economical treatment among alternatives with equal outcomes, i.e. outcomes that have identical efficacy/efficiency and safety profiles. Because of this, CMA
has limited application in practice but it can be used to compare generic drugs with branded drugs that can be assumed to have the same therapeutic equivalence. However because generic drugs are often much cheaper than the branded alternative, with reference to Figure 2.3, a pharmacoeconomic analysis becomes unnecessary so in practice this kind of analysis is hardly ever used.¹⁰

### 2.3.2.2 Cost-effectiveness (CEA)

CEA can be defined as a series of analytical and mathematical procedures that aid in the selection of a course of action from various treatment alternatives with different efficacy/effectiveness and safety profiles.¹⁰,⁷³ As outlined in Table 2.3, CEA uses inputs measured in monetary terms and the program’s outputs are stated in terms of health improvement attained such as clinical cures expressed in physical units. Examples of these units include: disability-days avoided, quality-adjusted life-years gained, life-years saved.⁷³ With respect to drug therapy, these alternative treatments may be two or more drugs or classes of drugs. CEA can also be used to compare drug treatment with one or more types of non-drug treatment for a particular condition.

Cost-effectiveness is the most commonly used pharmacoeconomic evaluation, however the term ‘cost-effectiveness’ is often used incorrectly to refer to any therapy that is less expensive in terms of acquisition costs, or more ‘effective’ based on clinical effectiveness data only. None of these interpretations can be considered a CEA as they only consider half of the term. Chrischilles (1996) suggests that the misleading understanding is perpetuated by the drive to be cost-conscious in health care.⁷³

In computing CEA, costs and consequences of two treatment alternatives are compared in terms of the additional cost that a treatment alternative imposes over another intervention, compared with the additional effectiveness it provides in terms of outcomes. Based on this an incremental cost-effectiveness ratio (ICER) can be calculated using this formula:¹⁰

\[
\text{ICER} = \frac{(\text{Cost of treatment A}) - (\text{cost of treatment B})}{(\text{Clinical success treatment A}) - (\text{clinical success treatment B})}
\]

### 2.3.2.3 Cost-Benefit Analysis (CBA)

Figure 2.4 below outlines the steps that are followed in conducting a CBA. CBA measures both the costs and benefits of treatment in monetary terms. It is often used to evaluate therapies with outcomes that are difficult to measure with CEA.¹⁰ CBA evaluates either single or multiple interventions with different outcomes, such as diagnostic, screening or therapeutic interventions. It computes net benefits or a benefit-to-cost ratio.⁷⁴ In carrying
out the evaluation, both costs and benefits need to be stated in the same monetary terms and future costs are discounted to their current value.\textsuperscript{10}

\begin{figure}[h]
\centering
\begin{tikzpicture}
  \node[align=left] (a) {State clearly as to what interventions(s), program(s), or therapeutic regimen is to be evaluated};
  \node[align=left, below of=a] (b) {Clearly identify and value all costs incurred in providing each intervention(s), program(s), or regimen};
  \node[align=left, below of=b] (c) {Identify benefits and assign value to them};
  \node[align=left, below of=c] (d) {Determine the sum of both the costs and that of all the benefits in order to determine the net benefits. Total benefits = Total benefits – Total costs};
  \node[align=left, below of=d] (e) {Compute the cost-benefit ratio, Benefit-to-Cost Ratio = Total Benefits};
  \node[align=left, below of=e] (f) {Carry out sensitivity analysis};
  \draw[->] (a) -- (b);
  \draw[->] (b) -- (c);
  \draw[->] (c) -- (d);
  \draw[->] (d) -- (e);
  \draw[->] (e) -- (f);
\end{tikzpicture}
\caption{Steps in conducting a Cost-benefit Analysis. Source McGhan and Kitz (1996).\textsuperscript{74}}
\end{figure}

The application of CBA in health care and pharmacoconomics has proved to be limited due to the difficulties in assigning a monetary value to health outcomes and patient’s life.

\textbf{2.3.2.4 Cost-Utility Analysis (CUA)}

CUA can be defined as an economic analysis that measures benefits in quality-adjusted life-years (QALYs). QALYS incorporate in a single summary score the net health improvement gains for both the quality and the quantity of life attained by a group of individuals.\textsuperscript{75} Costs are measured in monetary terms and outcomes in clinical terms whilst taking into consideration the patient’s preferences.\textsuperscript{10} It derives its application in the evaluation of benefits that can be attained from very different health care interventions; and assists in ensuring that resources are allocated as efficiently as possible to serve health outcome goals.

CUA can be applied in the following circumstances:\textsuperscript{75}
i. When there is a need for a common unit for outcomes when comparing the interventions with a wide range of potential outcomes

ii. When both the mortality and the morbidity are affected by the intervention and a combined unit of outcome is preferred

iii. When the quality of life is a vital outcome.

CUA systematically compares ways of using the resources most efficiently to meet the demands that in any given society there are finite resources for potentially infinite demands. If conducted properly, CUA can be a very useful tool to evaluate more comprehensively the overall impact of pharmacotherapy. It assists decision-makers by highlighting the relative value of pharmaceuticals when compared with other interventions as to which intervention is the most efficient use of finite health care resources.

2.4 Applied Pharmacoeconomics

Sanchez (1999) defined Applied Pharmacoeconomics as putting pharmacoeconomic principles, methods, and theories into practice to quantify the value of pharmaceutical services and products in real-world environments. Applied Pharmacoeconomics finds its use in three common strategies:

i. Evaluation and application of pharmacoeconomic studies published in the literature

ii. Use of modelling and other data sources available in the organisation

iii. Use of data that is available within the organisation by conducting pharmacoeconomic evaluation.

The most commonly used of these three is the evaluation and use of pharmacoeconomic literature. Decision-makers, who intend to make use of pharmacoeconomic literature need to have a thorough understanding of the limitations and benefits of this data source. They need to know how to critically evaluate pharmacoeconomic studies and lastly be able to apply the published findings in the decision-making process in their local environments. Using pharmacoeconomic literature can save both time and resources. When confronted with an economic problem, a decision-maker can simply do a literature search of articles and if they identify available studies that are relevant to their situations, that were rigorously conducted, then they be used as a ready and inexpensive source of data.

In the last 30 years the field of pharmacoeconomics has grown steadily and given rise to a large number of published research studies. By 1993 approximately 35000 papers had been published in this subject area. In 1995, the international community of researchers
with an interest in the field of pharmacoeconomics convened to form an International Society for Pharmacoeconomics and Outcomes Research (ISPOR). The establishment of ISPOR was aimed at promoting the science of pharmacoeconomics and outcomes research and to facilitate the translation of this research into useful information for health care decision-makers to ensure that resource allocation of scarce health care resources is done in an efficient, fair and wise manner.\textsuperscript{78} As an organisation, ISPOR is a fully international, educational and scientific body that strives to foster excellence in the core disciplines of pharmacoeconomics and outcomes research and promote the use of this research information in health care decisions at all levels.\textsuperscript{78}

ISPOR has launched Value in Health journal which is an official publication of this organisation. This journal together with PharmacoEconomics, and Research in Pharmaceutical Economics have pharmacoeconomics as their primary focus. All of these publications are peer-reviewed making them useful resources for: formulary managers, health care providers and institutions, health care policy and decision-makers, executives in managed care and health maintenance organisations, executives in pharmaceutical companies and pharmacoeconomic academics.\textsuperscript{78,79}

2.4.1 Evaluating Pharmacoeconomic Studies

Pharmacoeconomic evaluations do not only focus on actual costs of the new interventions, but also their effectiveness, utility, benefit and other clinical and financial outcomes. Therefore, it has become increasingly important for the decision-makers to have a thorough understanding of their meaning, appropriateness and limitations. Pharmacoeconomic studies should be appropriate, straightforward, reliable, rational and easy to use.\textsuperscript{71} Furthermore, it has been suggested that unless pharmacoeconomic studies are subjected to statistical rigor and peer review analysis that is scientifically sound and valid such studies might not provide conclusive, comprehensive, convincing, and usable data on which to base clinical or financial decisions.\textsuperscript{80}

The reported increase in the quantity of published pharmacoeconomic studies as described in section 2.4 does not, unfortunately, parallel an increase in quality of evaluations.\textsuperscript{80} Thus Sacristan, Soto and Galende (1993) suggest that low quality studies, can be attributed to superficial knowledge of researchers when performing evaluations and to the journal editors who accept them for publication.\textsuperscript{80} It is therefore important that researchers, journal editors and decision-makers should become well acquainted with the methodologies of conducting good pharmacoeconomic evaluations. Furthermore, it is important that a correct use of terms should be used and adequately applied. Often, terms such as cost-effective or cost-benefit are misused. The term cost-effective is frequently
used to mean either that the use of a particular drug translates into cost savings or that the drug is effective, irrespective of its cost. In 1999, Sanchez undertook a review of methodological literature to examine various approaches that deal with the issue of quality of pharmacoeconomic evaluations. The examinations revealed that there were 6 quality appraisal tools which had been developed. In total, the guidelines had 21 criteria some of which were present in all 6 tools. Table 2.4 lists the criteria and states which tool had which criteria.

Table 2.4 Criteria in Guidelines for Pharmacoeconomic Evaluations

<table>
<thead>
<tr>
<th>Criterion</th>
<th>Drummond</th>
<th>Udvarhelyi</th>
<th>Sacristan</th>
<th>Task Force</th>
<th>PhRMA</th>
<th>PHS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Well-defined study question</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Study perspective</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Type of study design</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Choice and description of competing alternatives</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Evidence to justify competing alternatives</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Type of economic analysis</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>NA</td>
<td></td>
</tr>
<tr>
<td>Data sources and sample selection</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Description of cost</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Calculation of indirect cost</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Unclear</td>
</tr>
<tr>
<td>Description of outcome measures</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Measures of cost and outcomes (benefits)</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Valuation of cost and outcomes</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Discounting</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Incremental analysis of cost and outcomes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Time horizons</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Sensitivity analysis</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Evaluation suitable if made within a clinical trial</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Ethical problems identified and discussed</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td>Unclear</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Overall impression of quality and study</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td>Unclear</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Generalisability and limitations</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Reference case</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
</tr>
</tbody>
</table>

Adapted from Sanchez (1999).
Sanchez reported that the guidelines that were developed by Drummond et al in 1986 provided a good basis for evaluating the quality of pharmacoeconomic studies. These criteria comprised of 10 points that were posed as questions to help decision-makers to determine if the basic elements of a quality study have been considered. The criteria were as follows:

i. Well defined study question
ii. Study perspective
iii. Choice and description of competing alternatives
iv. Evidence to justify competing alternatives
v. Type of economic analysis
vi. Description of cost
vii. Description of outcome measures
viii. Measures of cost and outcome measures
ix. Measures of cost and outcomes (benefits)
x. Valuation of cost and outcomes
xi. Discounting
xii. Incremental analysis of cost and outcomes
xiii. Sensitivity analysis
xiv. Generalisability and limitations

Over the years these criteria were used as a basis to develop further criteria. Udvarhelyi, Colditz, Rai and Epstein (1992) also made recommendations as to what can be considered a minimum set of standards when performing and reporting CEA and CBA studies after they conducted a systematic methodological review of articles published between 1978 and 1987. Their set of criteria was not as comprehensive as that of Drummond et al (1986), as it only comprised of six questions which are listed below:

i. Study perspective
ii. Description of cost
iii. Description of outcomes measures
iv. Discounting
v. Incremental analysis of cost and outcomes
vi. Sensitivity analysis

The following year, 1993, Sacristan et al compiled a comprehensive checklist that can be used to assess and rate both the content and quality of published pharmacoeconomic studies. The tool comprises of a 12-section checklist, with each section made up of sub-sections with questions that range from a minimum of 1 to a maximum of 8. The questions included in the tool are:
i. Well defined study question
ii. Study perspective
iii. Type of study design
iv. Choice and description of competing alternatives
v. Evidence to justify competing alternatives
vi. Type of economic analysis
vii. Data sources and sample selection
viii. Description of cost
ix. Calculation of indirect cost
x. Description of outcome measures
xi. Measures of cost and outcomes (benefits)

Upon completion of evaluation of the sub-sections, each section is then appraised as correct, acceptable, doubtful or not applicable. This is done without assigning a value to any of the sub-sections.80

In 1995, the PhRMA which, is a body that represents members of the pharmaceutical industry, deemed it necessary to draw up a set of voluntary principles for its members to conduct an evaluation of pharmacoeconomic studies. The intention was to help the members ensure high quality and minimise the potential for bias in carrying out pharmacoeconomic evaluations during drug development.85 They included the following questions in their tool:

i. Well defined study question
ii. Study perspective
iii. Type of study design
iv. Choice and description of competing alternatives
v. Evidence to justify competing alternatives
vi. Type of economic analysis
vii. Data sources and sample selection
viii. Description of cost
ix. Calculation of indirect cost
x. Description of outcome measures
xi. Measures of cost and outcomes (benefits)
During the same year, the Task Force of Health care Technology, comprised of members of the private sector, government agencies and researchers from health care technology in the US published two sets of guidelines on the conducting and reporting of pharmacoeconomic research. They dealt primarily with researcher independence and the reporting of economic outcomes research. The former is aimed at minimising the potential for bias that can be introduced by financial and other conflicts of interest. The latter guidelines describe a systematic process for reporting an economic analysis and deals with how to evaluate the content and rigor of published studies. The questions in the guidelines included:

i. Well defined study question
ii. Study perspective
iii. Type of study design
iv. Choice and description of competing alternatives
v. Evidence to justify competing alternatives
vi. Type of economic analysis
vii. Data sources and sample selection
viii. Calculation of indirect cost
ix. Description of cost
x. Description of outcome measures
xi. Measures of cost and outcome measures
xii. Measures of cost and outcomes (benefits)

In 1997, the US Public Health Service in Health and Medicine convened to review theoretical foundations for conducting CEA studies. The following questions were included in the tool.

i. Well defined study question
ii. Study perspective
iii. Type of study design
iv. Choice and description of competing alternatives
v. Data sources and sample selection
vi. Description of cost
vii. Description of outcome measures
viii. Measures of cost and outcomes (benefits)
ix. Valuation of cost and outcomes
x. Discounting
xi. Incremental analysis of cost and outcomes
xii. Time horizons
xiii. Sensitivity analysis
xiv. Reference case

In the same year, 1997, the Journal of the American Medical Association published a set of methodological practices that can be used as a reference case when conducting a CEA study. This tool was adapted, as shown in Table 2.5, by Bradley, Iskedjian, Lanctot, Mittmann, Simone and St Pierre in 1995 by assigning numerical scores to each section as follows:

i. Correct = 4, item was deemed correct if it completely met the requirements.
ii. Acceptable = 3, if the item met the requirements only partially but was adequate for the purpose of the evaluation it was regarded as acceptable.
iii. Doubtful = 2, an item was deemed doubtful if for the purpose of the evaluation an incomplete partial and inadequate information was provided.
iv. Not reported = 1, if no information (response) was provided a score of 1 was assigned.
v. Incorrect = 0, where information that was provided was inappropriate; a score of 0 was allocated.

A score of 0 for an inappropriate question was deliberately chosen in addition to a score of 1 for not reported. The rationale provided was that, it is a possibility that an action was carried out appropriately but not reported, however those that were incorrect were clearly inappropriate. Items that were considered not applicable were labelled N/A. Furthermore, an evaluator’s overall impression of the study was included as a 13th item over and above the 12-items that were initially used by Sacritan et al.

It is this tool that was adopted in the current research project in conducting a quality appraisal of the studies that were included in the research that aimed at establishing the
availability of pharmacoeconomic studies in South Africa and their subsequent quality appraisal as discussed in detail in Section 3.1.

**Table 2.5 Checklist for quality appraisal**

<p>| | | | | | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>1. Definition of study aim</strong></td>
<td>Does a well defined question exist?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>2. Sample selection</strong></td>
<td>Are the types of patients chosen suitable and are they specified?</td>
<td>Are the diagnostic criteria adequately specified?</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>3. Analysis of alternatives</strong></td>
<td>Are all the relevant alternatives analyzed?</td>
<td>Is/are the comparison alternative(s) suitable?</td>
<td>Is this the most commonly used treatment, or the one that will be replaced by the new drug?</td>
<td>Is the indication the most relevant one? Are adequate doses used?</td>
<td>Are the treatments reproducible (doses, interval, duration, etc)? Is the “do nothing” option analyzed or should it be analyzed? Is a decision analysis applied?</td>
</tr>
<tr>
<td><strong>4. Analysis of perspective</strong></td>
<td>Is it clearly specified (society, patient, hospital, etc.)?</td>
<td>Is it justified for the question asked?</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>5. Measurement of benefits</strong></td>
<td>Is it adequate for the question asked and perspective?</td>
<td>Are the data on the effectiveness of alternatives adequately established?</td>
<td>Is the main assessment variable (end-point) objective and relevant?</td>
<td>Is the time fixed for the evaluation for the evaluation sufficient and is it specified? Are the results quantified by time?</td>
<td></td>
</tr>
<tr>
<td><strong>6. Measurement of costs</strong></td>
<td>Is it adequate for the question asked and the perspective?</td>
<td>Are the costs up to date and are the prices those of the market? Is an adjustment for future costs and benefits performed?</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>7. Is this type of analysis suitable?</strong></td>
<td>Financial terms: cost-benefit; “Physical units”: cost-effectiveness, Quality of life/utility: cost-utility; Equal benefits: cost-minimization; Cost Analysis or Cost of illness. Identify type:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>8. Analysis of results</strong></td>
<td>If intermediate variables are used, are they representative of the end benefit? Is a marginal analysis performed?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>9. Is the evaluation suitable if made within a clinical trial?</strong></td>
<td>Is the suitable methodology employed? Are the statistical methods used adequate? Is an analysis according to “intention to treat” made? Are the costs resulting from the trial, which differ from those in the normal practice, taken into account?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>10. Are the assumptions and the limitations of the study discussed?</strong></td>
<td>Is a sensitivity analysis performed? Do the assumptions have a bias? Is the exclusion of any important variable analyzed or justified? If intermediate end-points are assumed, are the limitations discussed?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>11. Are the possible ethical problems discussed and identified?</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>12. Conclusions</strong></td>
<td>Are they justified? Can they be generalized? Can they be extrapolated to daily clinical practice?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
2.4.2 Generalisability of Pharmacoeconomic Studies

In recent years, there has been a growing number of studies that have focused on the generalisability of pharmacoeconomic evaluations. This is amid a similar concern regarding the quality of pharmacoeconomic evaluations as discussed in section 2.4.1. In this context, generalisability can be defined as the extent to which a pharmacoeconomic evaluation is applicable and can be found to be consistent across various patient populations and various locations. Failure to acknowledge the statistical heterogeneity of the costs aspects of the clinical trial may lead to misleading conclusions about the generalisability of the study results.

There are numerous variables that have been identified as likely to impact on the generalisability of pharmacoeconomic evaluations. These include variability across the locations of factors such as organisation of the health care system, different types of patient population and the different prices of particular inputs into health care as it applies to various practice set-ups.

A clinical trial is defined by the U.S. National Institutes of Health as a research study to answer specific questions about new therapies or new ways of making use of known treatments. The primary goal of conducting a clinical trial is to establish whether new treatments are both safe and effective.

Clinical trials comprise of 4 phases, where Phase I trials are aimed at using the new therapy under question in a small group to determine how it is metabolised, its pharmacologic effect and side-effect profile. The study group may comprise of both healthy individuals and/or patients. Phase II is an extension of the earlier phase to a large group of people to establish the effectiveness of the treatment for a specific indication or indications in patients suffering from a disease under study. Phase III trials are conducted after sufficient evidence has been gathered regarding the actual effectiveness of the drug and to further establish the benefit-risk ratio relationship of a drug. Lastly, Phase IV trials involve post-marketing studies to elicit information regarding the drug’s risks, benefits and optimal use.

Clinical trials are based on strict adherence to a research protocol, which provides details on which the study plan is based and how the health of the patients is to be safeguarded as well as answer specific research questions. Furthermore, a research protocol provides
specific details regarding the participants (inclusion/exclusion criteria), medications and dosages, length of the study, the schedule of tests etc. Clinical trials, despite their artificial nature and strict protocols or high internal validity, provide an excellent opportunity to make unbiased estimates about the clinical effectiveness and possible impact on resource utilisation of a new drug. Increasingly, a number of clinical trials are now being conducted on a multinational basis.

From a clinical point of view, a global study design provides a number of advantages that include: ability to rapidly reach the required target sample size, obtaining approval of various regulatory bodies in different jurisdictions and evidence on medical effectiveness and greater statistical safety data than if patients were derived from a single region or clinic. Despite the variations across locations in a multi centre clinical trials, the biologic effect of the drug stays the same.

However, from an economic point of view, the multi centre trials present a number of challenges regarding the generalisability of the findings of a study from one location to another. Recently Manca, Lambert, Sculpher and Rice (2007) reviewed the use of CEA data obtained from multi centre clinical trials, and concluded that, inevitably, various countries allocate health care resources differently and thus have different unit costs of health care resources, different practice set ups, and a unique patient case mix.

Mason and Mason (2006) came to the same conclusion after reviewing the generalisability theme and forecasting on the challenges with respect to technical issues, applicability and transferability of pharmacoeconomic evaluations that emanate from multi centre trials. They concluded that, firstly, the transferability of economic findings within their original policy context (i.e. same country but different locations) can be determined as long as the best practice guidelines and economic modelling are observed. Secondly, Mason and Mason reported that the transferability of economic findings internationally requires careful consideration of changes in resource implications, unit prices and outcomes. They deemed this process to require transparent methods of reporting, adjustment of the baseline risk and the use of latest innovations in the statistical field in dealing with hierarchically structured data.

Sculpher, Pang and Manca (2004) formalised a checklist of all criteria that must be followed to ensure that findings of the economic studies are generalisable across the locations. Table 2.6 provides a summary of these criteria. Key recommendations of
these criteria are consistent with other studies that focused on the transferability of international pharmacoeconomic findings across the locations.\textsuperscript{99,92,93}

Table 2.6. Criteria for improving generalisability of studies from multi centre clinical trials

<table>
<thead>
<tr>
<th>Study element</th>
<th>Reporting recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study sites (centres)</td>
<td>Describe the characteristics of the centres participating in the trial. If these are from different countries, also report the relevant features of the various health care systems.</td>
</tr>
<tr>
<td>Patient enrolment</td>
<td>Report the types of patients excluded from the trials and the percentage of the normal caseload that these represent. Comparison with the relevant patient population outside the trial centres.</td>
</tr>
<tr>
<td>Treatment alternatives</td>
<td>Describe the alternatives in detail, so that study users can assess the relevance to the own setting.</td>
</tr>
<tr>
<td>Perspective (s)</td>
<td>Report costs and benefits by each relevant perspective</td>
</tr>
<tr>
<td>Resource use and costs</td>
<td>Report quantities separately from prices/unit costs</td>
</tr>
<tr>
<td>Health state preference values</td>
<td>Report the source of the values and any instrument used</td>
</tr>
<tr>
<td>Analysis of variability</td>
<td>Provide details of quantitative analysis of variability by location. Ideally, this will be based on statistical analysis (such as multilevel modelling), but should at least incorporate standard sensitivity analysis</td>
</tr>
<tr>
<td>Other analytical issues</td>
<td>Provide details on the extent of incomplete observations (i.e. missing and censored data). Detail the characteristics of patients with incomplete data Describe the methods used to address the problem</td>
</tr>
</tbody>
</table>

Adapted from Sculpher, Pang and Manca (2004)\textsuperscript{88}

2.4.3 Use and misuse of Pharmacoeconomics in the literature

The problem of resource constraints throughout the world has seen increases in the numbers of economic analyses that are published in the medical literature. All these studies are about health care resource allocation, however not all of them meet criteria for being classified as pharmacoeconomic analyses. In the economic field it is a convention that an analysis needs to take both the costs and the outcome into consideration.\textsuperscript{94}
Table 2.7 Standard definitions of methods of conducting economic analyses

<table>
<thead>
<tr>
<th>Method of analysis</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>A. Cost description</td>
<td>Costs of a single program; no comparison is made to an alternative</td>
</tr>
<tr>
<td>B. Cost outcome description</td>
<td>Costs and health consequences of a single program; no comparison is made to an alternative</td>
</tr>
<tr>
<td>C. Cost comparison</td>
<td>Compares only the costs of two or more programs</td>
</tr>
<tr>
<td>D. Cost minimisation analysis</td>
<td>Compares costs of two or more programs when there is evidence that the programs has equivalent outcomes</td>
</tr>
<tr>
<td>E. Cost effectiveness analysis</td>
<td>Compares costs and health consequences of two or more programs with the health consequences expressed in a single natural unit such as cost per case detected or cost of year of life gained</td>
</tr>
<tr>
<td>G. Cost benefit analysis</td>
<td>Compares costs and health consequences of two or more programs with the health consequences measured in monetary units</td>
</tr>
</tbody>
</table>

Adapted from Zarnke, Levine and O’Brien (1997).

Economic analyses that consider costs in isolation or do not take the comparator into account are referred to as partial economic analyses (Table 2.7, A-C). Analyses that account for both the costs and the outcomes are referred to as true economic analyses (Table 2.7, D-G).

2.4.4 National use of Pharmacoeconomic data in decision-making

Several developed countries worldwide have formulated guidelines on how economic evaluation data will play a role in an endeavour to maximise the value for money spent on health care services as it applies to pharmaceuticals. In this section, a brief overview of the global status of pharmacoeconomics when it comes to governments is presented. In countries such as Australia, Canada, USA and New Zealand pharmacoeconomic evaluations have become mandatory for drug choice and subsidy decisions by governments. Pharmaceutical manufacturers are required in some of these countries to make economic evaluation data available in order to aid decision-makers with regards to pricing, reimbursement, treatment guidelines and inclusion of treatments into formularies. The policies in the following countries in this regard will be further discussed: Australia, Canada, USA, UK and South Africa.
2.4.4.1 Australia

Australia assumed a leading role in the development of guidelines for incorporating economic evaluations into pharmaceutical regulation. Prescriptions are regulated by an agency affiliated to the Commonwealth known as the Pharmaceutical Benefit Scheme (PBS) and only products listed with the PBS are eligible for reimbursement. In the early 1990s the Department of Health, Housing and Community Services established two advisory committees, namely, the Pharmaceutical Benefit Scheme Advisory Committee (PBSAC) and the Pharmaceutical Benefit Pricing Authority (PBPA). They were tasked with the responsibility of advising the minister on whether, and how, a product should be listed with the PBS. Furthermore, they also regulate prices at which the products should be listed and make the final recommendations to the minister.

Pharmaceutical manufacturers of branded products are required to submit detailed economic analysis data in order to obtain a listing for a new product, receive an amended listing for an existing product or support for a request for a substantial price increase. Of primary importance to the PBSAC are the costs and the comparative benefits, and hence it is crucial for the manufacturer to select an appropriate comparator product. A comparator product can be considered a ‘gold standard’ intervention used in the country where the analysis is being undertaken. Its choice should be sufficiently justifiable and clinically sound. Economic analysis should focus exclusively on the disease under study. It is worth noting that the indirect costs incurred are not to be included in the submission.

Key aspects to the guidelines, which describe the submission process to the PBSAC, are the ones pertaining to the economic analysis, namely outcomes of therapy, assessment of outcomes and economic basis of the submission as follows:

i. Outcomes of therapy

The type of economic analysis to be undertaken is guided by the category in which a new product is classified; the following four categories exist:

- A drug with new indications that are a breakthrough
- A drug that has major advantages over existing drugs, either in greater effectiveness or less toxicity
- A drug with better effectiveness and better toxicity than existing drugs, and
- A drug that is of comparable equivalence to existing therapies in effectiveness and toxicity.

In applying the above possibilities an applicant needs to make a clear distinction between effectiveness (effect of treatment when studied in real life settings) and efficacy (effect of treatment when studied under ideal conditions like randomised controlled trial) studies.
It is favourable to express the measures of the final outcome, such as the quality of life and quality-adjusted life-years of the therapy, as opposed to the use of other intermediate variables like blood pressure changes after use of antihypertensive.60

ii. Assessment of outcome
Choice of clinical trials must be sufficiently justified and convincing arguments made for the inclusion of data gathered from overseas trials. A comparison of the subjects from the clinical trials to typical Australian patients with conditions relevant to use of the new product (effectiveness vs. efficacy) must be undertaken. Age and gender distribution need to be specified in the analysis. Parameters such as formulation, dosage and duration of therapy for the comparator must conform to the product information regarding optimal use of the particular indication.

iii. Economic basis of the submission
Guidelines require that for each form of economic analysis a particular type of outcome (CBA, CMA, CUA or CEA) should be used. Furthermore, the guidelines require that the demographic characteristics of the population and the time period for the treatment of a specific disease must be appropriate to that particular situation. Estimation of the therapies studied for both net direct medical and non medical costs must be done over relevant time periods. A report of the following must be included in the final submission, a discount rate of 5% to the present value of net costs and outcomes and the net direct cost of treating patients in the study group.70 Finally, sensitivity analysis must be performed and depending on the situation the marginal costs may be required.

2.4.4.2 Canada
Canadian provinces are responsible for provision of health care services including pharmaceutical benefits. The Patented Medicine Prices Review Board (PMPRB) controls Price regulation at federal level, it has authority over all patented (both over the counter and prescription) products and limits prices of new drugs when they are launched and at the stage where manufacturers seek to increase the price of an existing product. 60 Manufacturers must meet the requirements of the guidelines set by the PMPRB and respond to provincial government requests for drug price quotes. Consequent to this the producers need to bid competitively to get their products listed in the provincial formulary.60

In 1996, the provincial government in Ontario, Canada, required pharmaceutical manufacturers seeking to list their products on the provincial formulary to provide a formal economic analysis documenting the product’s cost-effectiveness studies.96,97 This was prompted by an effort to address the concern of increasing drug costs and to apply more
measures apart from the traditional approach by the formulary committees of focusing primarily on clinical efficacy and safety of products for formulary listing.

The decision to incorporate economic analyses in the guidelines regulating the criteria for formulary listing was met with considerable criticism by various stakeholders such as academia, and the industry. A Drug Quality and Therapeutics Committee (DQTC) was set up to advise the minister of health on how to modify the existing guidelines to include the economic analysis data.\(^7^0\) It is made up of 12 members, eight of whom are physicians, one pharmacist, one pharmacologist and two government employees.

The guidelines offer a suggested format for submissions and also stipulate the criteria to be followed in carrying out economic analyses and include the 18-point checklist by which the submission will be evaluated. In the case where the applicant fails to incorporate economic analysis in the submission, the DQTC requires a justification.\(^9^0\) A key component of every cost-effectiveness study includes:

i. All clinical outcomes and relevant costs
ii. An incremental analysis, need to specify the difference between the new product and the comparator
iii. Inclusion of the discount rate of 5.0% over time for all costs and clinical outcomes
iv. Use of the societal perspective in the analysis needs to be adopted that includes both the direct and indirect medical costs
v. Every source of data used need to be identified
vi. Carry out sensitivity analysis
vii. Include a measure of relative economic attractiveness of different interventions.

PausJenssen, Singer and Detsky carried out a study in 2003 to describe how listing decisions are made by the DQTC. The following key considerations were noted.\(^9^6\)

\textbf{2.4.4.2.1 Clinical Factors}

The key focus is placed on the clinical merit of the product; if it is found to have questionable credentials further considerations are deemed unnecessary. The composition of the committee, eight physicians, may also have a lot of influence with this approach.\(^9^6\)
2.4.4.2.2 Type of drug
Types of drugs referred to here are innovative drugs, generic drugs and the ‘me-too’ (or therapeutically similar) drugs. Approval of the innovative products for formulary listing proved to be a tricky process. The generic drugs were the easiest to decide upon, the main criterion is to prove bio-equivalence. The price determination ranges between 25-40% less than the patented product. The ‘me-too’ products proved to be relatively hassle free depending on whether the manufacturer required a price premium or not; those which required the price premium had to justify their increased cost, and those without the price premium went through with ease.96

2.4.4.2.3 Quality Factors
The validity of the economic analysis is carefully examined and on numerous occasions DQTC has found that the economic analysis conducted had overstated the benefits. It was also noted that certain data is withheld which contradicts the claim made in the submission.96

2.4.4.2.4 Consistency Factor
DQTC adopted a conscious position of reviewing its previous decisions to ascertain that those they are making at present don’t contradict them and the impact that the current decisions will have in the future. The Role of the Unit Cost and the Impact Analysis, a higher unit cost means that incremental costs are higher, and leads to less favourable cost-effectiveness ratios.97 The impact analysis is secondary to economic analysis, what is more desirable is an attractive cost-effectiveness ratio. Guidelines are however silent as to what an attractive cost-effectiveness ratio constitutes.

2.4.4.2.5 The Role of the Economic Analysis
The economic analysis only played the larger role in the case of innovative products. In some instances the analyses carried out by the manufacturers were not used and they opted for use of the costing tables.96

2.4.4.2.6 Value Judgements
Each member in the committee brought with them their own unique set of values, which after elaborate discussions, proved to broaden the ultimate decision that the committee takes. The DQTC used the best available evidence to support their recommendations. This study found the incorporation of economic analysis useful as it brings difficult issues out into the open for discussion especially in the case of expensive innovative drugs. As a result of this, it was strongly encouraged that some form of economic analysis should continue to be used in formulary decision-making.96
2.4.4.3 USA

The US does not have a national requirement to provide pharmacoconomic data for formulary submissions. However, the Food and Drug Administration (FDA) is involved in the matter and various other health care providers have also begun to require economic analysis from manufacturers for formulary listing of their products which results in the duplication of effort by the manufacturers due to lack of a standardised format.

In 2000, the Academy of Managed Care Pharmacy (AMCP) introduced a format for formulary submissions. It sought to develop guidelines as a result of a growing need to ensure that any increased utilisation of medications, biopharmaceuticals and vaccine products was appropriate and that newer products would bring added clinical and economic value to covered populations. Several initiatives were undertaken to promote its usage and consequently it got nationwide publicity and attracted considerable attention. It has been adopted by managed health care systems, Pharmaceutical Benefit Management organisations, hospitals, integrated health care systems, state Medicaid agencies, and the Department of Defence.

In October 2002, version 2.0 of the AMCP Format was published which came as a result of an ongoing attempt to issue contemporary standards for evidentiary requirements and to address user comments and concerns. Table 2.8 provides a checklist of all the necessary information that the manufacturer needs to provide. This format is aimed at gaining the confidence of clinicians, patients, and members by providing a tool that will help health systems establish a record of commitment to rational decision-making.

The format provides the means to:

i. Promote the concept of combining efficacy, safety, effectiveness and economic evaluation for the formulary decision-making process

ii. Provide a consistent and direct means for manufacturers to supply information directly to health systems to support use of their products

iii. Break down costs and emphasize that simple acquisition cost reduction is not the best approach to controlling health care expenditures.
Table 2.8 Manufacturer's formulary submission checklist

<table>
<thead>
<tr>
<th>A. Submission process</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>A.1 Have you met with health-system staff to review the submission process?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>A.2 Have you agreed to the submission date?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>A.3 Have you requested estimates to identify baseline characteristics of the</td>
<td></td>
<td></td>
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<tr>
<td>Populations represented by the health system?</td>
<td></td>
<td></td>
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<tr>
<td>A.5 Have you submitted a copy of the dossier in both paper and electronic form?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>B. Product information</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>B.1 Has a product description been provided for the product?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>B.2 Has a list of approved indications been given for the product?</td>
<td></td>
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</tr>
<tr>
<td>B.3 Has the place of this product in therapy been given for each indication?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>B.4 Have copies been provided for treatment guidelines for this product?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>B.5 Have intermediate and final outcomes of therapy for this product been tested?</td>
<td></td>
<td></td>
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<tr>
<td>B.6 Have you listed any co-prescribed drugs for this product by indication?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>B.7 Have you identified the comparator drugs for this product by indication?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>C. Supporting clinical information</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>C.1 Have you identified all relevant clinical and other studies for the product and</td>
<td></td>
<td></td>
</tr>
<tr>
<td>its comparators?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>C.2 Are copies of all summarised studies for the product and its comparators included?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>C.3 Have you provided an electronic spreadsheet summary of all studies identified</td>
<td></td>
<td></td>
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<tr>
<td>using requested format?</td>
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<td></td>
</tr>
<tr>
<td>C.4 Have you included all relevant nonexperimental studies for the product?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>C.5 Have you provided an electronic spreadsheet summary of all nonexperimental</td>
<td></td>
<td></td>
</tr>
<tr>
<td>studies using the requested format?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>D. Supporting economic information</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>D.1 Have you identified all relevant pharmacoeconomic (PE) studies for the product?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>D.2 Are copies of all summarized studies included in the submission package?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>D.3 Have you justified the relevance of these PE studies for this population?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>D.4 Have you provided an electronic spreadsheet summary of the PE studies?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>D.5 Will a disease or care management strategy be employed with the introduction of</td>
<td></td>
<td></td>
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<tr>
<td>this product?</td>
<td></td>
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<tr>
<td>D.6 Is documentation on this intervention program included in the submission?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>E. Economic model</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>E.1 Are the model structure, data, and assumptions transparent and clearly presented</td>
<td></td>
<td></td>
</tr>
<tr>
<td>for a noneconomist reader?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>E.2 Is an unlocked spreadsheet version of the model included with the submission?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>E.3 Are the results presented in a style suitable for the health system’s formulary</td>
<td></td>
<td></td>
</tr>
<tr>
<td>committee evaluation?</td>
<td></td>
<td></td>
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</tbody>
</table>

Adapted from Fry, Avey and Sullivan (2003).
**2.4.4.4 South Africa**

One of the most comprehensive policy statements to emerge from the South African DOH was the NDP in 1996. The NDP introduced a coherent set of reforms with a primary objective of ensuring that there will be more equitable access to high quality and affordable drugs throughout the country.\(^2\) One of the key strategies advocated for by the NDP is the use of Pharmacoeconomics to advance rational drug use and improved efficiency in the allocation of scarce health care resources.\(^2\)

Thomas and Muirhead reported in 2000 that provincial governments spend 6-15% of their budgets on drugs, vaccines and other medical consumables. This represents the second largest item of the total health care expenditure after personnel.\(^99\) In line with this finding, the private health sector’s expenditure on medicines was ranked third after an expenditure on private hospitals and medical specialists. This is according to the annual report (2006-7) by the Council of Medical Schemes.\(^44\)

In this context of high expenditure on medicines, the use of pharmacoeconomics as envisioned by the NDP in 1996 becomes very crucial. Nwokeji and Rascati (2005) conducted a global study aimed at establishing the level of training/education in Pharmacoeconomics outside the US. Only 3 out of 8 South African universities that offer pharmacy took part in the research. Those that participated reported that pharmacoeconomics has been incorporated into their undergraduate curriculums.\(^100\) Furthermore, one of the respondents gave a clear indication of the fact that pharmacoeconomics was a relatively new field in South Africa.\(^100\)

In line with this finding, members of the Pharmacy and Therapeutics Committees (PTCs) in South Africa were reported to have little understanding of the concepts of pharmacoeconomic analyses. This finding is based on the results of a cross-sectional survey that was conducted by Pillay, Hill and Walkom (2004). This study was conducted across the country as it included all 9 provincial PTCs in the country.\(^101\)

However, in recent times much work has been done by various stakeholders in both the public and private health care sectors to advance the use of Pharmacoeconomics in South Africa.
In 2005, the director of the Pharmaceutical Economic Policy of the DOH, Dr. A. Pillay, presented a draft of guidelines regarding the incorporation of pharmacoeconomic analyses by the drug manufacturers in submission of the application for the purposes of registration.\(^a\)

In March 2007, the Pharmaceutical Care Management Association of South Africa (PCMA) which is an organisation that strives to promote excellence in pharmacy in a managed care environment held a seminar in pharmacoeconomics.\(^b\) This seminar was organised in collaboration with DOH and the Health Economics Unit (HEU) of the University of Cape Town (UCT).

In attendance were stakeholders from various sectors of the health care industry. This seminar was aimed at discussing the strategies that are necessary to entrench the use of pharmacoeconomics in South Africa.\(^b\) Two months later, May 2007, the Pharmaceutical Industry Association of South Africa (PIASA), formerly known as the Pharmaceutical Manufactures Association also convened. PIASA represents drug manufacturers (both innovators and generic companies) in South Africa and strives to make quality medicines more accessible by promoting a favourable environment for the continued development of the pharmaceutical industry.\(^c\) The workshop was aimed at looking at how the pharmaceutical industry can advance pharmacoeconomics in South Africa. Furthermore, the industry discussed ways of preparing itself for any possible legislative reform that will make it mandatory to incorporate pharmacoeconomic evaluations in applications for the registration of drugs in line with international trends.\(^c\)

All these activities culminated in the establishment of ISPOR South Africa which held its first Annual General Meeting (AGM) on the 02\(^{nd}\) of August 2007.\(^d\) This development has increased the number of ISPOR local chapters to 23, making South Africa the first African country to belong to ISPOR.\(^e\) One of the primary objectives of ISPOR is to facilitate the exchange of scientific knowledge in the fields of pharmacoeconomics and outcomes research.\(^f\) It is to be expected that the research gap between South Africa and the international community in the field of pharmacoeconomics will be closed through this exchange of knowledge.

\(^a\) Draft Guidelines on the Submission of Economic Analysis by Dr. Anban Pillay. May 2005.
\(^b\) Seminars in Pharmacoeconomic Evaluation. Facilitated by the PCMA in collaboration with the DOH and HEU. March 2007.
2.5 Formularies and the development of formularies

In recent years, in an attempt to manage resources and contain expenses, health care systems worldwide have had to make careful considerations of which drugs to provide. One of the strategies adopted in this effort is the use of formularies. A formulary can be defined as a "list of drugs selected by formulary committees from the commercially available ones" and its primary purpose is to "discourage the use of marginally effective drugs and treatments" and to ensure the selection of medications that have been demonstrated to be safe, effective and affordable whilst maintaining or improving quality of patient care.

Formularies started in the 1950s as a simple list of drugs that were available for use in hospitals and through time their role had to be assessed as a result of financial pressures and has since evolved into a much more dynamic and independent way of choosing the appropriate drug therapy. Formularies are now routinely applied in various settings of health care such as hospitals (private and public), private health insurances, and government agencies at various levels. Most of these institutions have formulated drug therapy guidelines on how the medicines selected in their respective formularies will be prescribed and dispensed.

In this era of cost consciousness there is a tendency by the pharmacy personnel to consider the financial aspects of medicines as a main criterion in selecting the drugs for the formulary. This often evokes reactions from the medical personnel that reject this approach and tend to use clinical merits of drugs as a leading criterion. Neither an overemphasis on costs nor on clinical merits of a drug constitutes a rational and sound approach to the decision-making process. Formulary management provides a platform for pharmacists, doctors and other health care providers to work collaboratively in promoting clinically sound, and cost-effective pharmaceutical care decisions.

2.5.1 Types of Formularies

There are generally three types of formularies; open formularies, closed formularies and partially/selectively closed formularies. There are several factors that determine the type of formulary that various organisations adopt and these include the type of the managed care plan, the size of the organisation, staff availability, resources to manage the formulary and lastly the service objectives and drug benefit provisions. These are all factors that need to be taken into consideration to arrive at the type of a formulary that will best serve the needs of the organisation.
2.5.1.1 Open Formulary
Coverage is provided for all medicines regardless of whether they are present in the formulary or not, however certain Over The Counter (OTC) and cosmetic products may be excluded from coverage. Additional out of pocket expenses or co-payment can be incurred in certain instances when items that are outside the formulary are prescribed; physicians are however encouraged to prescribe within a formulary.105

2.5.1.2 Closed Formulary
The payer does not reimburse products that are not listed in the formulary, however cases are treated on merit such that where it is medically appropriate there are provisions that can be made to cover products that are not listed. This requires prescribers to follow the administrative protocol to motivate for such payment.105

2.5.1.3 Partially/Selectively Closed Formulary
This type of formulary is fundamentally an open formulary with restrictions imposed on certain groups of drugs in two ways. Firstly, certain classes of drugs do not get covered at all, such as those for cosmetic purposes. Secondly, there are drugs that require the expertise of a specialist to monitor the outcome of the treatment before coverage is provided. This is especially so for expensive drugs.105

2.5.2 The Formulary decision-making process
Decisions on formulary listing require transparency and should be justifiable to all stakeholders as they could have far-reaching consequences that may impact on a number of people such as patients, healthcare workers and employees of the manufacturers. Due to a wide variety of drugs that are available on the market, their escalating costs and the continuous introduction of new ones, a key consideration is which drugs to list in the formulary and which ones to exclude? This decision-making task is the responsibility of Pharmacy and Therapeutics Committees (PTC), whose members are appointed on the basis of their drug therapy expertise.11,105

In making a selection of drugs to be included in the formulary the PTC needs to be aware that there are several factors that can contribute to the choices that the members make. Factors influencing the selection of drugs for formularies are the following:

i. Emotional factors, a member’s dislike of a drug can be based on a case of bad side-effects that one of his/her patient(s) once experienced regardless of the assurance from research of the fact that such incidence was a rare occurrence

ii. Hidden factors, this might be influenced by the interaction (either positive or negative) that a member might have had with the pharmaceutical company
iii. Unconscious factors can result from the member’s familiarity with the drug or class of drugs as well as an influence by the opinions of colleagues and well-informed patients. It can also be simply out of a habit.

iv. Hidden factors such as financial gain or any form of incentive from a pharmaceutical company.\(^9\)

It is therefore important to exclude all the above mentioned factors as far as possible. One way of achieving that is by making use of an evidence-based drug selection system for the formulary decision-making process.\(^{10}\) There are two models that have been applied successfully in the formulary process, namely:

i. Multi Attribute Utility Theory (MAUT)

ii. System of Objectified Judgement Analysis (SOJA).

The MAUT is a structured methodology that has been developed to handle the tradeoffs among multiple alternatives by assessing the strengths and weaknesses of each alternative.\(^{10}\) It has numerous applications including the formulary process. Bettinger (2007), successfully applied MAUT in choosing the cost-effective antipsychotic agent from a choice of 5.\(^{10}\) He identified the following attributes in his selection criteria, efficacy, adverse effects, cost and adherence. The following relative weights for each identified attribute, 35%, 35%, 20% and 10%, respectively, were used.\(^{10}\) The following outcome was obtained, Aripiprazole (75.8%), Ziprasidone (71.8%), Risperidone (69.0%) and Quetiapine (65.9%). From these results it is clear that Aripiprazole is the best alternative as it achieved an overall score of 75.8%. MAUT has been used with success elsewhere as well.\(^{10,11}\)

Similarly, the SOJA model is a structured approach to the selection of drugs in the formulary process.\(^{11}\) A selection criterion for a specific group of drugs is decided upon beforehand. The degree to which each drug meets the requirements of the criterion is determined.\(^{11}\) Each individual criterion is allocated a relative weight, with efficacy, safety, and acquisition cost normally comprising around 70% of the score. SOJA has found application in a wide range of formulary decisions.\(^{11,12}\)

PTCs are tasked with ensuring that formularies are dynamic and get revised continually in order to keep them up to date. This is attained by regular meetings that review available literature, both medical and clinical, patient drug utilisation reviews, current therapeutic guidelines to determine the need to replace them with new ones, economic data, and cost-effective drugs that will give the desired goals of therapy at the most reasonable cost to the health care system.\(^{10}\)
On the basis of all these considerations decisions on product addition or deletion are then made. In 2004, Wang, Salomon and Walton presented a series of steps that are followed by the PTCs during the formulary decision-making process as outlined in Figure 2.5.\textsuperscript{115}

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{Figure2.5.png}
\caption{Flowchart of the Formulary Decision-Making Process. Adopted from Wang, Salmon and Walton (2003).\textsuperscript{115}}
\end{figure}

\textbf{2.5.2.1 Pharmacological and clinical evaluation}
At this initial stage there are two main considerations, namely; literature review and drug information from clinical trials such as efficacy, safety, tolerability, dosage, route of administration, ease of use and patient acceptance.\textsuperscript{115}

\textbf{2.5.2.2 Pharmacoeconomic evaluation}
As referred to in section 2.4 the PTCs adopt the strategies that have been described and begin to address the costs and economic benefits of the drug. Where there is not sufficient expertise to deal effectively with the pharmacoeconomic data that has been submitted and to perform modelling where necessary, independent consultants should be brought in to give expert and objective opinion. In evaluating the pharmacoeconomic data
the following factors are taken into consideration, published data and taking note of authorship, funding sources or sponsors and methodologies used. The pharmacoeconomic evaluations that are carried out by the drug companies get thoroughly scrutinised, through checking and verifying with various data sources such as databases and pharmacoeconomic literature. This is done in order to rule out any possibility of a study’s conclusions being biased in favour of the manufacturer.

2.5.2.3 Development of drug-use criteria
When the drug passes the two above-mentioned criteria the PTC then formulates clinical guidelines that will be used to ensure appropriate use of the drug in the covered population over time. These criteria include the use of strategies such as prior authorisation, limitation on quantities, evaluation prescription for appropriateness.

2.5.2.4 Approval by the PTC
Completion of these first three steps acts as the basis upon which a drug is either rejected or accepted by the PTC. The results are then disseminated to both the pharmacy and medical staff.

2.5.2.5 Administrative and ethical reviews
This mainly entails reviewing the terms of rebates contracts with manufacturers where applicable. In South Africa, this practice is forbidden by law as described in section 2.2.

2.5.2.6 Drug use monitoring
One of the key roles of the PTC is putting plans in place on how the use of the drug is going to be monitored and evaluated. This includes both continuous improvement and drug utilisation reviews.

2.5.2.7 Follow-up review by the PTC
The PTC constantly monitors the drugs that have been selected into the formulary by reviewing the results of the prospective and retrospective audits to ensure the appropriate and effective use of drugs.

2.6 Evidence Based Medicine
Another approach that is used as a guide in the health care decision-making process and resource allocation is the concept of Evidence Based Medicine (EBM). It can be defined as a careful, unambiguous, and judicious use of current best evidence in making
decisions about the care of individual patients. EBM integrates the proficiency and judgement that individual clinicians acquire through years of clinical experience and clinical practice with the best available external clinical evidence from systematic research.\textsuperscript{117}

EBM involves the use of study designs by turning clinical problems into questions and carrying out a systematic literature search, analyses, and use of current research findings to make a clinical decision on a patient-by-patient basis.\textsuperscript{117} In contrast to an approach that is focused on the care of individual patients, Evidence based health care (EBHC) incorporates improved approaches to understanding patients, families, and practitioner’s beliefs, values and attitudes by means of qualitative research methods. Furthermore, EBHC also takes into account the evidence at a population level such as the burden of disease and implication of resource utilisation as well as encompassing interventions concerned with the organisation and delivery of health care.\textsuperscript{117}

2.7 The use of pharmacoeconomic data in formulary decision-making processes internationally and in South Africa

Formulary decisions play a crucial role in the effective and efficient use of scarce health care resources to minimise the overall medical costs and improve patient access to more affordable care and improved quality of life. The formulary process can be the cornerstone of good pharmaceutical management and rational use of drugs.\textsuperscript{118} A major challenge is to use pharmacoeconomics and outcomes research effectively to arrive at formularies that simultaneously provide patients with effective drug therapy whilst maintaining financial stability within a defined budget.\textsuperscript{118,119}

It has been suggested that the use of pharmacoeconomic analyses in formulary decision-making processes is dependent on both organisational goals and the level of expertise in evaluating pharmacoeconomic information that is available.\textsuperscript{63} Several studies have been conducted worldwide in an effort to determine the extent to which pharmacoeconomic data is used in decision-making and the impact it has had on the process.

In 2000, in the United States, a survey of 3000 subscribers to the Formulary Journal, consisting of both pharmacists and physicians, was conducted. The purpose of the survey was to determine the role of pharmacoeconomics in the drug formulary decision-making process.\textsuperscript{120} The focus was on: factors considered in the choice of drugs, the use of pharmacoeconomic information, sources of pharmacoeconomic information and actions taken as a result of pharmacoeconomic information.\textsuperscript{120} Respondents were requested to
rate the factors considered in the formulary decision-making process. Ratings ranged from 1 (not important to the process) to 5 (extremely important to the process). Efficacy and safety were both cited as extremely important in the process. Cost of the drugs was found to be important whilst the use of pharmacoeconomics and health-related quality of life effects of drugs were reported to be moderately important.\textsuperscript{120}

Fifty percent (50\%) of the respondents indicated that they use pharmacoeconomic information for most or every decision, one-third used it for some decisions, and 15\% used it in few decisions.\textsuperscript{120} Formulary development was cited as the main reason that pharmacoeconomic information was used. Of the five major types of pharmacoeconomic analyses, the decision-makers were most familiar with cost-effectiveness analysis and used it the most; this was followed by cost-benefit analysis. Peer-reviewed publications were found to be the main source of pharmacoeconomic information used by decision-makers. In analysing the actions taken as a result of pharmacoeconomic information, 17\% of the respondents stated that if pharmacoeconomic studies were not available their decisions would be greatly affected, 58\% said somewhat and 25\% answered not much.\textsuperscript{120}

In a similar type of study that was undertaken by the American Society of Health-System Pharmacists in 1998, data were collected from pharmacist members of the PTCs.\textsuperscript{121} The survey focused on the formulary decision-making process and considered the extent to which pharmacoeconomic data was used, the pharmacoeconomic expertise of those involved, the perceived ease of formulary decision-making, and the usual sources of pharmacoeconomic data. Over 86\% of the respondents stated that pharmacoeconomic data was used very often or all the time in formulary decision-making. Seventy percent of the respondents had someone with pharmacoeconomic skills on staff. Sources of pharmacoeconomic data employed were in-house data (75\%), published literature (57\%), pharmaceutical industry studies (9\%), and other (2\%).\textsuperscript{121}

In line with findings of the above two studies was a survey that was carried out in the Greater New Orleans Metropolitan area in the US. The study population composed of 20 pharmacists, working or affiliated with hospitals/medical centres, that were serving on the PTC.\textsuperscript{119} The survey was designed to collect the following data; sociodemographics, area(s) of specialty, pharmacoeconomics and outcomes research training (either formal or through continuing education), which pharmacoeconomic analyses and clinical and humanistic outcomes are used in formulary decision-making, and lastly whether the subjects’ institutions had facilities and capabilities for conducting pharmacoeconomic and outcomes studies.\textsuperscript{119} The study found that 60\% or more of the pharmacists on PTCs
apply pharmacoeconomic methods. Main considerations in making formulary decisions were found to be cost of drugs, cost of administration, and cost-minimization.\textsuperscript{119}

2.7.1 Drug formularies and their development in South Africa

The NDP caters for a wide variety of activities that pertain to effective production, supply, storage, distribution and use of medicines. Furthermore, the NDP has outlined a number of objectives that are critical for its success. These objectives range from health, economics, to national development objectives. In the public health sector a comprehensive strategy that incorporates improved supply and distribution of medicines as well as extensive human resources development was adopted in the form of the Essential Drug Programme (EDP).\textsuperscript{122} Under the programme a rationalisation of the wide variety of medicines available in the public sector was a first priority. A committee was set up and tasked with the compilation of an essential drugs list (EDL) and treatment guidelines based on the World Health Organisation (WHO) model.\textsuperscript{122}

The criteria that were followed to choose the essential drugs in South Africa were amongst others: a drug that meets the health needs of the majority of the population, a drug with adequate established scientific data regarding its effectiveness, good safety and risk/benefit ratio as well as good quality. Where drugs were bioequivalent they were compared in terms of best cost-advantage, best researched and availability of a reliable local manufacturer.\textsuperscript{2} Each product on the list was assigned a level, that is, whether it can be used in primary health care, secondary or tertiary levels. The prescribing of certain drugs was restricted to specialists only, whilst others require a motivation to be made in order to be acquired and administered to the patient.\textsuperscript{122}

The NDP advocates for the establishment of PTCs at all levels of health care. In accordance with this, in an effort to ensure that the drugs that have been deemed to be essential and life saving are available and accessible to treat major health conditions of the majority of the population, provincial departments of health established their own PTCs. Provincial PTCs create their own formularies based on the national EDL by taking into consideration the prevalent health problems in their areas and level of care provided. Committees at lower levels, such as district and institutional levels are expected to restrict themselves to drugs that are on the provincial EDL.\textsuperscript{122}

The South African Medicines Formulary (SAMF), which is in its seventh edition, was first published in 1988, its objective and purpose was to promote safe, rational and cost-effective use of medicines available in South Africa.\textsuperscript{8} SAMF is widely used in public
hospitals, community and private practice by doctors, pharmacists, nurses and other health care workers as well as by hospital administrators and health policy personnel. However, the SAMF provides no economic information that would be beneficial in the selection of more cost-effective drug interventions.\(^8\)

In the private health sector in South Africa, there have also been initiatives and increased effort to contain costs. One of these has been the adoption of drug formularies by managed care organizations and medical aid schemes. Within the South African context, the use of drug utilisation studies together with pharmacoeconomic analyses could result in a more cost-effective utilisation of scarce resources and increased rational use of drugs. In doing so, at least one of the objectives of the NDP, the economic objective, could be achieved.\(^3\) Also, if based on appropriate clinical and pharmacoeconomic considerations the use of formularies can ensure quality of therapeutic decisions and control costs.\(^3\)

There is limited research on the extent to which formulary decision-makers in South Africa employ pharmacoeconomic analysis. A team of researchers at Tshwane University of Technology undertook an exploratory study to assess the knowledge, attitudes, and use of pharmacoeconomic information by South African health care funders in the private sector.\(^{123}\) Twenty-eight pharmaceutical benefit organisations were covered by means of self-administered questionnaires.

All respondents stated that pharmacoeconomic data has an impact on their formulary decision-making processes. Pharmacoeconomic data was regarded to be very important by 42.8% of the respondents and, important by 19.05% of them. Ninety one percent of the respondents favoured the use of cost-effectiveness analysis, yet only 19.05% could correctly define a cost-effectiveness analysis.\(^{123}\)

The most important data sources for formulary evaluation were considered to be clinical articles from peer-reviewed journals (100%), pharmacoeconomic data generated locally (96.45%) and pharmacoeconomic data generated internationally (86.96%). The study suggested that factors that could facilitate an increase in the use of pharmacoeconomic data include easier access to data, increased pharmacoeconomic training and the availability of guidelines. Lack of cost-effectiveness data was cited as a main barrier to using pharmacoeconomic data.\(^{123}\)
The findings of this study from the private sector perspective are in line with the conclusion that Pillay and fellow researchers came to in the research that was conducted in 2004 where the focus was on the public sector as described in Section 2.4.4.\textsuperscript{101}

2.8 Conclusion

Scarcity of health care resources is a worldwide phenomenon and South Africa is not an exception.\textsuperscript{1,3}\ The costs of medicines are one of the biggest components that consume the health care budgets in all sectors of health care.\textsuperscript{44,99} The new field of science called Pharmacoeconomics has been employed with success in many countries abroad.\textsuperscript{60} Pharmacoeconomics provides tools to decision-makers that empower them to make resource allocation decisions wisely, fairly and efficiently.\textsuperscript{13}

This literature review has highlighted the fact that pharmacoeconomics is still at an infancy stage in South Africa.\textsuperscript{100,101} This study seeks to determine the availability of pharmacoeconomic data, assess its quality and lastly establish the extent to which it is employed in formulary decision-making processes in both sectors of health care in South Africa.
CHAPTER 3

RESEARCH METHODOLOGY

This chapter presents an overview of the research design and methodology used in the assessment of the availability of and the extent to which pharmacoeconomic data is used in the development of drug formularies in South Africa. The first part of the project focused on establishing the availability of published South African pharmacoeconomic studies and determining the nature and methodological quality thereof. The second part involved a cross-sectional, descriptive and exploratory study to determine the use of pharmacoeconomic data in the formulary decision-making processes, by various stakeholders, in the health care sector in South Africa. The research design and methodology of each of these parts of the research project will be addressed separately.

The first part of the chapter (Section 3.1) will address the search strategy involved in the systematic bibliographic search for South African based pharmacoeconomic studies and the subsequent qualitative assessment of identified studies. The second part of the chapter (Section 3.2) deals with the determination of the use of pharmacoeconomic studies in formulary decision-making and provides a description and discussion of the design, methods, the instrument and procedures used for data collection and the data analysis.

3.1 DETERMINING THE AVAILABILITY OF SOUTH AFRICAN PHARMACOECONOMIC STUDIES

3.1.1 Study design

In order to understand the availability, nature and quality of published pharmacoeconomic studies in South Africa, a structured bibliographic search for pharmacoeconomic studies, meeting a pre-determined set of eligibility criteria, was undertaken, and this was followed by a quality appraisal of all qualifying studies identified. The study involved the basic steps outlined in Figure 3.1
Figure 3.1 Basic steps for the application of the inclusion or exclusion of the identified economic evaluation studies.

1. Identify eligibility criteria
2. Structured search for studies that appear to meet eligibility criteria
3. Initial screening of abstracts of possible studies identified against eligibility criteria
4. Obtain copies of and tabulate characteristics of each possible study identified
5. Apply eligibility criteria and justify any exclusions
6. Assemble a complete dataset of all eligible studies and assess and tabulate nature and characteristics of the studies
7. Conduct a methodological quality appraisal of all studies and tabulate results
8. Analyse the results to identify any emerging trends
3.1.2 Eligibility criteria

The eligibility of each identified study was assessed on the basis of the following selection criteria.

3.1.2.1 Inclusion criteria:
Economic evaluations had to meet the following criteria to be included in the sample:

i. Interrogated both the costs and the outcomes, i.e. full pharmacoeconomic evaluations such as cost-effectiveness analysis, cost-benefit analysis, etc

ii. Evaluated a drug therapy against a relevant comparator, i.e. another drug

iii. Conducted or published between 01 January 1995 and 30 June 2007

iv. Conducted in South Africa

v. Primary research such as dissertations, theses and other original research projects such as clinical trials.

3.1.2.2 Exclusion criteria:
Evaluations were excluded from the study for the following reasons:

i. Partial pharmacoeconomic evaluations such as cost–analysis where outcomes were not taken into consideration were excluded

ii. Studies that lacked the cost aspect were excluded

iii. Studies that evaluated a drug against other forms of intervention other than pharmacotherapy were excluded

iv. Editorials, commentaries, opinions or letters were excluded from any further analysis.

3.1.3 Search strategy

A comprehensive search strategy for the availability of both published and unpublished pharmacoeconomic data was conducted. It included an advanced search of four comprehensive bibliographic databases. All schools of pharmacy in South Africa were contacted by e-mail to establish the possible existence of grey literature, i.e. original research that might have been conducted but not published.

3.1.3.1 Search terms
The following search terms were used for each database, including the word South Africa in the case of international databases, in order to limit the results to those studies conducted locally. Each of the following terms was searched separately:

i. Pharmacoeconomics
ii. Formulary
iii. Cost-effectiveness analysis
iv. Cost-benefit analysis
v. Cost-utility analysis
vi. Cost-minimisation analysis
vii. Cost-drug
viii. Health economics
ix. Drug utilisation review
x. Cost-consequence

3.1.3.2 Databases searched
A choice of four databases was made of which two are South African, with a view to identifying the studies that were conducted and published locally. A further two of the chosen databases were international. This was aimed at identifying those studies that were conducted in South Africa but published in international publications, which is a common phenomenon with research collaborations. A further consideration for the inclusion of international databases is the fact that there are no pharmacoeconomic journals in South Africa, therefore, researchers are likely to publish elsewhere (internationally), especially in reputable peer-reviewed journals.

3.1.3.2.1 Nexus database system
This is a South African online database that provides information on the dissertations and theses in all fields of science. It caters for both current and completed research projects and includes abstracts for all the records. It is funded by the National Research Foundation to support and promote research in order to create knowledge, development and innovation in all fields of the natural, social sciences, humanities and technology. 124

3.1.3.2.2 Sabinet Online
Sabinet Online is a South African online database that caters for the information needs of corporate, academic and government bodies. 125 The following journals that are affiliated to Sabinet Online were searched: South African Medical Journal (SAMJ), South African Pharmaceutical Journal (SAPJ), South African Health Review and Health Systems Trust.

3.1.3.2.3 EBSCOhost
EBSCOhost is one of the world’s largest suppliers of electronic scholarly journals in the fields of humanities, social sciences and medical sciences. 126 It offers a variety of online databases that can be searched. The following databases within EBSCOhost
were selected: Academic Search Premier, Master File Premier, Medline, Health Source (Nursing, Academic, and Consumer Edition) and Clinical Pharmacology.\textsuperscript{126}

\subsection*{3.1.3.2.4 ScienceDirect}
The ScienceDirect database carries more than a quarter of the world's scientific, medical and technical information online. It features over 2000 peer-reviewed journals such as Journal of Clinical Therapeutics, Journal of Pharmacological Research and hundreds of book series and reference works.\textsuperscript{127}

\subsection*{3.1.4 Retrieval and further scrutiny of identified studies}

Titles and contents of the abstracts were scrutinised by two reviewers before retrieval of the relevant papers. Those that did not meet the inclusion criteria were excluded from further analysis. All studies that met the inclusion criteria but were unavailable online or from the university library were obtained via Inter Library Loans. These included the dissertations and theses that were held in the libraries of other institutions. The characteristics of each possible study identified were tabulated. Each study was carefully studied to determine whether or not, on close review, they still met the inclusion criteria. Those that did not comply with the inclusion criteria were also excluded.

A bibliography was generated using Reference Manager\textsuperscript{\textregistered} for all studies that met the initial inclusion criteria and were retrieved for a review. Reference Manager\textsuperscript{\textregistered} is a software tool for generating and managing literature references.\textsuperscript{128}

\subsection*{3.1.5 Quality appraisal}

The methodological quality of all studies that were included was assessed using an adopted 13 point pre-validated tool used by Bradley \textit{et al} (1995)\textsuperscript{87} as discussed in section 2.4.1. This tool is shown in Table 3.1. It involves a use of a rating scale whereby each item on the checklist was assigned a numerical value as follows: a score of 4 represented a correct answer, 3 = acceptable answer, 2 = doubtful answer, 1 = not reported and 0 = incorrect answer. Not applicable was denoted by n/a.\textsuperscript{87} The overall impression for a given study is given by an average score for all evaluated items.
Table 3.1 Checklist for quality appraisal.

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<td>Are the types of patients chosen suitable and are they specified?</td>
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<td>Are the diagnostic criteria adequately specified?</td>
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<td>3. Analysis of alternatives</td>
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<td>Are all the relevant alternatives analyzed?</td>
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<td>Is/are the comparison alternative(s) suitable?</td>
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<td>Is this the most commonly used treatment, or the one that will be replaced by the new drug?</td>
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<td>Is the indication the most relevant one? Are adequate doses used?</td>
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<td>Are the treatments reproducible (doses, interval, duration, etc)?</td>
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<td>Is the “do nothing” option analyzed or should it be analyzed?</td>
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<td>Is a decision analysis applied?</td>
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<td>4. Analysis of perspective</td>
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<td>Is it clearly specified (society, patient, hospital, etc)?</td>
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<td>Is it justified for the question asked?</td>
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<td>5. Measurement of benefits</td>
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<td>Is it adequate for the question asked and perspective?</td>
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<td>Are the data on the effectiveness of alternatives adequately established?</td>
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<td>Is the main assessment variable (end-point) objective and relevant?</td>
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<td>Is the time fixed for the evaluation for the evaluation sufficient and is it specified? Are the results quantified by time?</td>
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<td>6. Measurement of costs</td>
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<td>Is it adequate for the question asked and the perspective?</td>
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<td>Are the costs up to date and are the prices those of the market?</td>
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<td>Is an adjustment for future costs and benefits performed?</td>
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<td>7. Is this type of analysis suitable?</td>
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<td>Financial terms: cost-benefit; “Physical units”: cost-effectiveness, Quality of life/utility: cost-utility; Equal benefits: cost-minimization; Cost Analysis or Cost of illness. Identify type:</td>
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<td>8. Analysis of results</td>
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<td>If intermediate variables are used, are they representative of the end benefit?</td>
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<td>Is a marginal analysis performed?</td>
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<td>9. Is the evaluation suitable if made within a clinical trial?</td>
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<td>Is the suitable methodology employed?</td>
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<td>Are the statistical methods used adequate?</td>
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<td>Is an analysis according to “intention to treat” made?</td>
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<td>Are the costs resulting from the trial, which differ from those in the normal practice, taken into account?</td>
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<td>10. Are the assumptions and the limitations of the study discussed?</td>
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<td>Is a sensitivity analysis performed? Do the assumptions have a bias?</td>
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<td>Is the exclusion of any important variable analyzed or justified? If intermediate end-points are assumed, are the limitations discussed?</td>
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<td>11. Are the possible ethical problems discussed and identified?</td>
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<td>12. Conclusions</td>
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<td>Are they justified? Can they be generalized?</td>
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<td>Can they be extrapolated to daily clinical practice?</td>
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<td>13. Overall impression of the quality of the paper</td>
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The appraisal was conducted independently by two researchers. If the results varied the appraisal of the study was discussed until consensus was obtained. The results were analysed using descriptive statistics, mean, mode, and median.

3.1.6 Emerging trends

The results were carefully analysed for any emerging trends such as:

i. Class of drugs that constitute most of the economic evaluations

ii. General trends on the type of economic evaluations

iii. Nature of the publications in which the studies were found

iv. Check whether evaluations that were sponsored by pharmaceutical companies reported results that are biased in their favour.

3.2 DETERMINING THE USE OF PHARMACOECONOMIC DATA IN FORMULARY DEVELOPMENT

3.2.1 Research design

The research design provides the structural framework required to attain the research goals. Furthermore, it assists the researcher with the guidelines and instructions to be followed in dealing with the research problem. This helps to “increase validity and to minimise, or where possible, exclude errors within the research”. In order to determine the use of pharmacoeconomic data in formulary development, both a quantitative and qualitative approach was adopted. The literature describes a quantitative research methodology as a formal, unbiased, systematic process in which numerical data are used to obtain information about the various phenomenon. A quantitative approach provides an opportunity to describe variables, examine relationships among variables and establish the cause-effect interactions between variables. A qualitative approach attempts rather to describe the reasons and thinking behind the phenomenon that are observed.

Furthermore, this study employed an exploratory and cross-sectional descriptive design using a self-administered questionnaire to determine the extent to which pharmacoeconomic data is used in formulary decision-making processes by various stakeholders in both the private sector and the public sector in South Africa.

3.2.1.1 Exploratory study

An exploratory study was used in order to obtain basic familiarity about how formulary decision-makers use Pharmacoeconomics in South Africa. Very little was known about
their attitudes, knowledge, preferences, and activities as it relates to formulary management. Exploratory studies provide an opportunity to explore the full nature of the phenomenon in terms of how it manifests itself and other relevant factors.\textsuperscript{131}

### 3.2.1.2 Descriptive study

According to Burns and Grove (2001), descriptive studies provide an opportunity to identify problems in current practice with a view to improving practice outcomes. The purpose of descriptive research is the exploration and description of real-life situations and to solicit information about the elements as they occur.\textsuperscript{130} This study is descriptive in that observations are made, described and documented as they occur naturally without manipulating variables.

### 3.2.1.3 Cross-sectional survey

Cross-sectional studies describe the relationship between variables and other factors of interest as they occur and exist in a specified study population at a particular time. This is done without regard for what may have preceded or precipitated the observed phenomenon at the time of study.\textsuperscript{130}

A summary of the research process is provided in Figure 3.2.

```
Deciding on the sub-groups to include in the study population

Development of a survey instrument

Testing of the questionnaire

Dissemination of the questionnaire

Assessment of the response rate

Data analysis
```

Figure 3.2 Summary of steps for the research design and method
3.2.2 Study population

This study was conducted in both the private and public health sectors in South Africa.

3.2.2.1 Private Health Sector

The study population included organisations such as Medical Schemes Administrators and Managed Care Organisations which are responsible for the management of certain aspects of Medical Aid Schemes such as a formulary development. Both of these organisations are registered with the Council For Medical Schemes which is a statutory body established by the Department of Health in South Africa to provide supervision over medical schemes. There are 122 medical aid schemes in South Africa that are registered with the Council for Medical Schemes. Lastly the private sector was also represented by all registered private hospitals in South Africa.

i. **Medical schemes administrators**: A list of all 16 medical schemes administrators in South Africa together with their contact details was obtained from the website of the Council for Medical Schemes: (http://www.medicalschemes.com)

ii. **Managed Care Organisations**: A list of all 52 accredited managed care organisations in South Africa together with their contact details was also obtained from the website of the Council for Medical Schemes: (http://www.medicalschemes.com)

iii. **Private hospitals**: A list of all 198 private hospitals with their contact details was obtained from the Hospital Association of South Africa’s website (http://www.hasa.co.za).

3.2.2.2 Public Health Sector

The public sector was represented by all nine heads of the pharmaceutical directorates in the provinces in South Africa. A list of names and contact numbers for the heads of the Pharmaceutical directorates in all the nine provinces was obtained. This was done by contacting the office of the National Pharmaceutical Directorate whose contact details were obtained from the official website of the Department of Health, (http://www.doh.gov.za).

3.2.3 Development of a survey instrument

The data for this national survey was collected by means of a questionnaire (Appendix I) that was developed to achieve the research aims and objectives. A questionnaire can be described as a form designed to solicit information that can be obtained through written responses of respondents. 129
The use of questionnaires as a research instrument is advantageous because it is less costly in terms of time and money, and allows a great amount of data to be obtained over a wide range of topics from large study populations. In this, study data were gathered using a structured self-administered questionnaire. The questionnaire was designed using Microsoft Word® in such a way that allowed the participants to complete it electronically, save it and e-mail it back to the researcher. It was comprised of 19-items and was designed to collect the following data:

3.2.3.1 Composition of the formulary committees
This section focused on getting an overview of the formulary committee with respect to the educational and professional backgrounds of the members. This was covered by questions 1 – 7.

3.2.3.2 Importance of Pharmacoeconomics in formulary decisions
Guidelines that were published by Thomas and Polgar in 2000 were consulted on how to formulate questions in such a way that will elicit enough detailed information to answer the research question. A combination of open-ended and closed-ended questions was used in order to determine the importance of pharmacoeconomic data in the formulary decision-making process and the procedure that formulary committees follow in order to arrive at the formularies for their organizations. This was covered by questions 8-18.

3.2.3.3 Rating of important factors in the formulary decision-making process
Participants were requested to rank various factors that are considered in the formulary decision-making process using a Likert type format. This format allows the respondents to give an indication of how they feel about various factors by allocating a rank that has been pre-defined in terms of the weight that it carries. Respondents were requested to rank various factors on a score of 1 (most important) to 7 (least important) in order to get an understanding of what factors play a prominent role in the formulary decision-making process. This was covered by question 19.

3.2.4 Testing of the questionnaire

The questionnaire was piloted prior to use by sending it to three pharmacists in order to determine its usability and appropriateness. It was then modified according to the feedback that was received.
3.2.5 Dissemination of the questionnaire

The aim was to target individuals of the highest authority who are involved in the formulary management process within the various categories of the study population. The questionnaire was disseminated as follows:

3.2.5.1 Medical Schemes Administrators
A personalised covering letter that provided a background to the study and asked for their participation was sent to the principal officers by e-mail with an attachment of a questionnaire. The covering letter is included in Appendix II

3.2.5.2 Managed Care Organisations
Some Managed Care Organisations did not have e-mail addresses listed on the website and as a result the correspondence was done by postal mail. This involved sending the principal officers personalized covering letters that provided a background to the study and asked for their participation. A questionnaire was enclosed as well as a self-addressed stamped envelope.

3.2.5.3 Private hospitals
An e-mail was sent to the hospitals to request the contact details of the managers of their pharmaceutical services. Contact was made with the national office in the case of the hospital groups whose responses represented all the hospitals that fall under that umbrella group.

3.2.5.4 Public sector
The heads of the pharmaceutical services in all the provinces were contacted telephonically to brief them about the research and to request their participation. If willing, their e-mail addresses were obtained in order to send them a questionnaire. The questionnaires were then e-mailed to them.

3.2.6 Assessment of the response rate

An initial period of four weeks was allowed for returning the questionnaires. Where responses were not received after the specified period, a letter of reminder that included another questionnaire was sent. All responses were acknowledged with a letter of thanks. If after a further three weeks a response was still not received, a follow-up was made telephonically to establish the reason for lack of response and to make an arrangement, if
the participant was willing, for a telephonic interview in order to make it easier for the participant unless they still declined this offer or could not be contacted.

3.2.7 Data analysis

The data collected from the interviews was collated using Excel® and analyzed. The qualitative data was assessed for emerging themes, which was commented on in the discussion chapter. Due to the small sample size only descriptive statistics were used.

3.3 Dissemination of data

The findings of this research will be disseminated as follows:

i. Presentation at a relevant conference

ii. An article will be prepared for publication in an appropriate peer-reviewed journal

iii. Participants who requested feedback on the outcome of this study will also be furnished with the article.
4.1 Results of the literature review

The initial search of the databases identified 1090 records possibly fulfilling the inclusion criteria. Nine hundred and sixty seven were excluded from further analysis after a review of the titles and contents of the abstracts. Copies of all the studies were then obtained and on closer scrutiny of these a further 96 were excluded. Only 17 studies met the inclusion criteria. Figure 4.1 provides a summary of the results and the application of the selection criteria.

Fig 4.1 Summary of the results of a literature search.
4.2 Application of the selection criteria

4.2.1 Application of the exclusion criteria

The majority of the studies that were excluded were in the field of HIV/AIDS followed by antimycobacterial drugs and antihypertensive drugs. Most of the studies were obtained from EBSCOhost and Science Direct, followed by Nexus database system. No studies were found in Sabinet Online. Some of the studies were found to overlap between EBSCOhost and Science Direct. The four main reasons for exclusion were found to be:

i. Lack of the cost aspect
ii. Cost-analysis studies
iii. Book reviews, editorials, opinions and commentaries
iv. Did not evaluate a drug against a relevant comparator

Emergence of the HIV/AIDS pandemic has prompted much of research in the field of pharmacoeconomics, however, very little of this particular research can be used to inform decision-making with respect to formulary development as it was seen with the studies that were excluded. It should be noted that the studies that were included in this study could be used for the formulary process as they evaluated a drug therapy in terms of costs and outcomes against a relevant comparator (another drug therapy).

The fact that the majority of local based pharmacoeconomic studies are not suitable to be used in the formulary process is not in line with the general trends internationally where most studies show that pharmacoeconomics is a very helpful tool in the allocation of resources as it pertains to formulary development.\textsuperscript{114,120}

4.2.2 Included studies

Table 4.1 provides a summary of all studies that were included in terms of the author, drugs that were investigated, type of economic evaluations that were conducted, the journals where the studies were published and the databases where they were identified.

Although 17 studies were identified for inclusion in the study, on closer observation 2 of these were found to be the same (Wilkinson) but were published in 2 different journals. For the purposes of this study only 1 of these was included.
<table>
<thead>
<tr>
<th>Author</th>
<th>Drugs investigated</th>
<th>Type of analysis conducted</th>
<th>Journal where the study was published</th>
<th>Database</th>
</tr>
</thead>
<tbody>
<tr>
<td>Struwig</td>
<td>Metoclopramide, Trimethoprim 160 mg and Sulphamethoxazole 800 mg, Loperamide 2 mg, Terbenafine, Ketoconazole, Griseofulvin, Sertraline, Fluoxetine, Zopiclone, Nitrazepam, Temazepam, Flunitrazepam, Enoxaparin, Heparin, Ceftriaxone, Cefotaxime, Cefoxitin, Ceftazidime, Docetaxel, Paclitaxel, Vinblastine, Sumatriptan, Ondansentron</td>
<td>Cost-minimisation analysis, Cost-effectiveness analysis, Cost-benefit analysis and Cost-utility analysis.</td>
<td>Potchefstroom University (Thesis for a PhD)</td>
<td>Nexus</td>
</tr>
<tr>
<td>Rockcliffe</td>
<td>Isoniazid, Rifampicin, Ethambutol, Streptomycin, Kanamycin, Ethionamide, Thioacetazone, Ofloxacin and Ciprofloxacin</td>
<td>Cost-effectiveness analysis and Cost-minimisation analysis.</td>
<td>Rhodes University library (Dissertation for a Masters degree)</td>
<td>Nexus</td>
</tr>
<tr>
<td>Schmitt</td>
<td>Moxifloxacin 400 mg, Ceftriaxone 2000 mg, Metronidazole 500 mg &amp; Co-amoxiclav 625 mg</td>
<td>Cost-minimisation analysis.</td>
<td>University of Witwatersrand (Dissertation for a Masters degree)</td>
<td>Nexus</td>
</tr>
<tr>
<td>Wilkinson</td>
<td>Antiretroviral drugs: Lamivudine 150 mg &amp; Zidovudine 300 mg</td>
<td>Cost-effectiveness analysis.</td>
<td>South African Medical Journal and AIDS</td>
<td>EBSCOhost</td>
</tr>
<tr>
<td>Floyd</td>
<td>Antimycobacterial drugs: Isoniazid, Rifampicin, Pyrazinamide and Ethambutol</td>
<td>Cost-effectiveness analysis.</td>
<td>British Medical Journal</td>
<td>EBSCOhost</td>
</tr>
<tr>
<td>Wilton</td>
<td>Antimycobacterial drugs: Isoniazid, Rifampicin, Pyrazinamide and Ethambutol</td>
<td>Cost-effectiveness analysis.</td>
<td>The Journal Of Tuberculosis And Lung Disease</td>
<td>EBSCOhost</td>
</tr>
<tr>
<td>Wilkins</td>
<td>Antimalarial agents: Chloroquine and Sulfadoxine-pyrimethamine</td>
<td>Cost-effectiveness analysis.</td>
<td>Transactions Of The Royal Society Of Tropical Medicine And Hygiene</td>
<td>EBSCOhost and Science Direct</td>
</tr>
<tr>
<td>Sinanovic</td>
<td>Antimycobacterial drugs: Isoniazid, Rifampicin, Streptomycin, Pyrazinamide and Ethambutol</td>
<td>Cost-effectiveness analysis.</td>
<td>The Journal Of Tuberculosis And Lung Disease</td>
<td>EBSCOhost</td>
</tr>
<tr>
<td>Uzicanin</td>
<td>Immunisations: Measles vaccine</td>
<td>Cost-effectiveness analysis.</td>
<td>Vaccine</td>
<td>EBSCOhost</td>
</tr>
<tr>
<td>Gaziano</td>
<td>Antihypertensive agents</td>
<td>Cost-effectiveness analysis.</td>
<td>Circulation</td>
<td>EBSCOhost</td>
</tr>
</tbody>
</table>
### Author Drugs investigated Type of analysis conducted Journal where the study was published Database

<table>
<thead>
<tr>
<th>Author</th>
<th>Drugs investigated</th>
<th>Type of analysis conducted</th>
<th>Journal where the study was published</th>
<th>Database</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wessels.</td>
<td>Antibiotic drugs: Ceftriaxone, Cefotaxime, Cefuroxime and Amoxicillin/Clavulanic acid (co-amoxiclav)</td>
<td>Cost-effectiveness analysis</td>
<td>South African Medical Journal</td>
<td>EBSCOhost</td>
</tr>
<tr>
<td>Boule.</td>
<td>Antiretroviral drugs:</td>
<td>Cost-effectiveness analysis</td>
<td>South African Medical Journal</td>
<td>EBSCOhost</td>
</tr>
<tr>
<td>Holmes.</td>
<td>Antiretroviral drugs: Nevirapine 200 mg, Lopinavir and Ritonavir</td>
<td>Cost-effectiveness analysis</td>
<td>Clinical Infections Disease</td>
<td>EBSCOhost</td>
</tr>
<tr>
<td>Skordis.</td>
<td>Antiretroviral drugs: Zidovudine 300 mg and Nevirapine 200 mg</td>
<td>Cost-effectiveness analysis</td>
<td>Health Economics</td>
<td>EBSCOhost</td>
</tr>
</tbody>
</table>

### 4.3 Emerging trends

#### 4.3.1 Class of drugs investigated

Antiretroviral drugs were the most studied group of drugs as they represented 38% of all included studies as shown in Table 4.2.

**Table 4.2 Summary of the type of drugs investigated by class**

<table>
<thead>
<tr>
<th>Class of drugs</th>
<th>Frequency (%) (n=16)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antiretroviral drugs</td>
<td>6 (38%)</td>
</tr>
<tr>
<td>Antimycobacterial drugs</td>
<td>4 (25%)</td>
</tr>
<tr>
<td>Antihypertensive drugs</td>
<td>2 (13%)</td>
</tr>
<tr>
<td>Antimalarial drugs</td>
<td>1 (6%)</td>
</tr>
<tr>
<td>Immunosuppresants</td>
<td>1 (6%)</td>
</tr>
<tr>
<td>Vaccines</td>
<td>1 (6%)</td>
</tr>
<tr>
<td>Miscellaneous*</td>
<td>1 (6%)</td>
</tr>
<tr>
<td><strong>All types</strong></td>
<td><strong>16 (100%)</strong></td>
</tr>
</tbody>
</table>

* Miscellaneous-investigated a variety of therapeutic classes.

The majority of the studies that were conducted in the field of HIV/AIDS aimed to show that the cost of providing antiretroviral treatment to HIV positive individuals is more cost-
effective than the cost of treating the conditions that are associated with this syndrome.\textsuperscript{147,149,150} Most of these studies were conducted prior to the High Court decision that forced the Department of Health to provide antiretroviral treatment to HIV positive people at the public hospitals.\textsuperscript{151} Antiretroviral drugs were followed by 4 studies on antimycobacterial drugs, then 2 antihypertensive agents and lastly one study each for antibiotics, antimalarial agents, immunosuppresants and vaccines.

4.3.2 Types of economic evaluations conducted

Table 4.3 tabulates the frequency of all included studies by type of economic analysis. The total number of actual pharmacoeconomic evaluations is 21, which is due to the fact that certain studies conducted more than one type of pharmacoeconomic evaluation. Cost-effectiveness analysis was the most used type of economic evaluation with 15 studies, followed by 3 studies for cost-minimisation studies, 2 cost-benefit analysis and lastly one cost-utility analyses.

Of all pharmacoeconomic analyses CEA & CMA are fairly straightforward to conduct when compared to CBA & CUA.\textsuperscript{10} The fact that most studies focused on CEA and CMA, could be an indication that South Africa lacks sufficient expertise in the field of pharmacoeconomics. International trends are in contrast with this finding as greater use tends to be made of complex pharmacoeconomic analyses.\textsuperscript{152}

<table>
<thead>
<tr>
<th>Type of study</th>
<th>Frequency (%) (n=21)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cost-effectiveness analysis</td>
<td>15 (71%)</td>
</tr>
<tr>
<td>Cost-minimisation analysis</td>
<td>3 (14%)</td>
</tr>
<tr>
<td>Cost-benefit analysis</td>
<td>2 (10%)</td>
</tr>
<tr>
<td>Cost-utility analysis</td>
<td>1 (5%)</td>
</tr>
<tr>
<td>All types</td>
<td>21 (100 %)</td>
</tr>
</tbody>
</table>

4.3.3 Nature of the publications

4.3.3.1 Journals

The results were carefully studied to establish any trends in journals that were used for publication of pharmacoeconomic data. The South African Medical Journal was the most used journal as it published 5 studies, followed by The Journal of Tuberculosis and Lung Disease which published 2 of the studies.
One study was found in each of the following journals British Medical Journal, Transactions of the Royal Society of Tropical Medicine and Hygiene, AIDS, Vaccine, Circulation, European Journal of Clinical Pharmacology and Health Economics.

All journals that were used were international peer-reviewed publications, with the exception of the South African Medical Journal (SAMJ) which is a local peer-reviewed journal. The South African Pharmaceutical Journal (SAPJ) which is the official publication for the association of the Pharmaceutical Society of South Africa (PSSA), was expected to be one of the leading journals to publish research in the field of pharmacy. However, no studies were found in this journal at all. This may be because it is not peer-reviewed and that most researchers prefer to publish in peer-reviewed journals.

4.3.3.2 Databases
EBSCOhost was the most useful database as 14 out of all 16 included studies were identified using it, followed by 3 publications from Nexus database of which two were dissertations for Masters Degrees and one was a thesis for a Doctorate. Science Direct identified one study that overlapped with EBSCOhost. Sabinet Online did not identify any studies despite the fact that the South African Medical Journal which published 5 of the included studies is one of the journals that it is affiliated to this database.

4.3.3.3 Unpublished studies
All 8 Schools of Pharmacy in the country were contacted in order to find out as to whether or not there is a research in the field of pharmacoeconomics that is being conducted in their respective universities. Five universities indicated that no such research is conducted at their institutions, followed whilst two universities did not reply at all. Lastly, one university provided a list of all studies that were conducted in pharmacoeconomics. The list included Struwig whose study met the inclusion criteria and was included and appraised for quality.

4.3.4 Influence of sponsorship on the quality of the evaluation
It is a well documented fact that sponsorship of economic studies by the pharmaceutical industry is likely to be biased in favour of the sponsoring company. All studies that were included were checked as to whether they were conducted under any form of financial incentive from the pharmaceutical companies. The only study that disclosed links with the pharmaceutical company and no details of financial incentive was the one by Schmitt. In as much as the finding of the study was in favour of the company, the study was
proven to be unbiased when it was subjected to the quality appraisal as it obtained an overall score of 4 which is indicative of high level of quality.

4.4 Quality Appraisal

The methodological quality of all 16 studies that complied with the inclusion criteria was assessed using a quality appraisal tool as outlined in section 3.1.4.

4.4.1 Quality appraisal of individual studies

Table 4.4 tabulates the assessment of all individual questions and provides an overall score per study. The overall impression ranged from 2 to 4 which represent doubtful and good quality respectively as per criteria presented in section 3.1.4. Only one study was found to be of high quality as it attained an overall score of 4, followed by 12 studies that attained an overall score of 3 which represents acceptable quality. Lastly, the quality of 3 studies was found to be dubious as they obtained an overall score of 2.
Table 4.4 Summary of the results of the quality appraisal

<table>
<thead>
<tr>
<th>Study aim</th>
<th>Sample</th>
<th>Alternatives</th>
<th>Perspective</th>
<th>Benefits</th>
<th>Costs</th>
<th>Suitability</th>
<th>Results</th>
<th>Clinical trial</th>
<th>Limitations</th>
<th>Ethical concerns</th>
<th>Conclusions</th>
<th>Overall impression</th>
</tr>
</thead>
<tbody>
<tr>
<td>4 4 4 4 4 4 4 4 4 4 4 4 4 4 4</td>
<td>4 4 4 4 4 4 4 4 4 4 4 4 4 4 4</td>
<td>3 3 4 4 4 4 4 4 4 4 4 4 4 1 4 4 4</td>
<td>4 4 4 4 4 4 4 4 0 4 1 4 2 4 0 4</td>
<td>3 4 4 4 4 4 4 4 4 4 4 4 4 2 4 4 4</td>
<td>1 3 4 4 4 4 4 4 4 4 4 4 4 2 4 1 4 4 4</td>
<td>4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4</td>
<td>1 1 3 4 4 4 2 4 4 2 4 4 4 4 4 4 4 4</td>
<td>1 4 4 4 n/a n/a n/a n/a 3 n/a 3 n/a n/a n/a n/a</td>
<td>2 3 2 3 0 4 4 0 0 3 4 3 4 4 0 4</td>
<td>1 0 4 0 0 0 0 0 0 0 0 0 n/a n/a 0 4</td>
<td>3 3 3 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4</td>
<td>3 3 4 3 3 3 2 2 3 2 3 3 3 3 3 3 3 3</td>
</tr>
</tbody>
</table>
4.4.2 Assessment of the level of quality adherence of economic evaluations conducted in South Africa in comparison with other countries.

Table 4.5 tabulates a comparison of the quality of pharmacoeconomic studies that were included in this study with that of those included in a quality appraisal that was conducted on studies published in the PharmacoEconomics journal for the first four years of its inception. The countries that were used for this comparison are South American countries such as Brazil, Argentina, Ecuador, Venezuela. This comparison is valid since the same quality appraisal tool that was discussed in section 3.1.4 was used in both studies.

<table>
<thead>
<tr>
<th>Quality category</th>
<th>South Africa</th>
<th>Other countries</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n  %</td>
<td>n  %</td>
</tr>
<tr>
<td>Good</td>
<td>1 6</td>
<td>9 17</td>
</tr>
<tr>
<td>Acceptable</td>
<td>13 76</td>
<td>37 69</td>
</tr>
<tr>
<td>Poor</td>
<td>3 18</td>
<td>8 15</td>
</tr>
<tr>
<td>Not reported</td>
<td>0 0</td>
<td>0 0</td>
</tr>
</tbody>
</table>

The quality of studies in other countries included in the comparative appraisal was found to be higher than those that were conducted in South Africa. There were more studies of good quality in other countries, 17% compared to 6% in South Africa. The two categories of acceptable and poor quality did not have significant differences as the former was 76% in South Africa in relation to 69% in other countries and the latter was 18% in South Africa as opposed 15% in other countries. Both groups did not have results that were scored under the “Not reported” category.

The results indicate the presence of serious methodological flaws in the manner in which the pharmacoeconomic studies were conducted as there are questions that scored 0, 1 and 2. This could be due to lack of guidelines on how to conduct good pharmacoeconomic studies as is the case in other countries such as Australia, Canada and New Zealand where there are guidelines in place on how to conduct pharmacoeconomic evaluations.
4.4.3 Quality appraisal of the individual questions for all the included studies

The mean scores for the individual questions ranged from 1 to 4 as shown in Table 4.6. Definition of study aim, sample selection, analysis of alternatives, measurement of benefits, suitability of analysis and the conclusions were mostly found to be of good quality. All these questions received a score of 4 with respect to the mean, mode and median with a standard deviation ranging from 0 to 0.77.

Analysis of the perspective, measurement of costs, analysis of the results and suitability for clinical trials received correct answers in terms of the quality appraisal criteria. They achieved a mean score of 3 whereas their mode and the median scores were 4 with a standard deviation ranging from 1.07 to 3.16. This is indicative of the high variability between the different studies in addressing these issues.

The question that dealt with the assumptions and the limitations of the studies received a score of 2 which translates into poor quality. However, the median and the mode were found to be 3 and 4 respectively with a standard deviation of 1.69. Lastly, ethical issues were not well reported on in the studies as they received a mean score of 1 with mode and median scores of 0. The standard deviation in this case was found to be 0.6.

4.4.4 Comparison of quality scores amongst various types of pharmacoeconomic evaluations

All pharmacoeconomic analyses displayed no differences in terms of the average quality scores when compared with each other as shown in Table 4.7. The mean quality score of 3 which translates into acceptable quality was obtained for all four types of pharmacoeconomic evaluations.

4.4.5 Comparison of quality scores over a period of time

The fact that the two studies that had an overall score of 2 were recent studies, i.e. 2003 and 2004 indicates that there has not been any noticeable progress in terms of improvement of quality of conducting and reporting of pharmacoeconomic studies in the past decade. This finding is in contrast with what Bradley and colleagues (1995) who found in their study where they evaluated the quality of economic studies published in pharmacy, medical and health economic journals. They came to a conclusion that over time, the quality of the economic studies follows a clear pattern of improvement. 87
Table 4.6 Summary of the quality appraisal of the individual questions for all included studies

<table>
<thead>
<tr>
<th>Question</th>
<th>Mean</th>
<th>SD</th>
<th>Mode</th>
<th>Min</th>
<th>Max</th>
<th>Median</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Definition of study aim</td>
<td>4</td>
<td>0</td>
<td>4</td>
<td>4</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>2. Sample selection</td>
<td>4</td>
<td>0</td>
<td>4</td>
<td>4</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>3. Analysis of alternatives</td>
<td>4</td>
<td>0.77</td>
<td>4</td>
<td>1</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>4. Analysis of the perspective</td>
<td>3</td>
<td>1.48</td>
<td>4</td>
<td>0</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>5. Measurement of benefits</td>
<td>4</td>
<td>0.52</td>
<td>4</td>
<td>2</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>6. Measurement of costs</td>
<td>3</td>
<td>1.07</td>
<td>4</td>
<td>1</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>7. Is this type of analysis suitable?</td>
<td>4</td>
<td>0</td>
<td>4</td>
<td>4</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>8. Analysis of the results</td>
<td>3</td>
<td>1.18</td>
<td>4</td>
<td>1</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>9. Is the evaluation suitable if made within a clinical trial?</td>
<td>3</td>
<td>3.16</td>
<td>4</td>
<td>1</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>10. Are the assumptions and the limitations of the study discussed?</td>
<td>2</td>
<td>1.69</td>
<td>4</td>
<td>0</td>
<td>4</td>
<td>3</td>
</tr>
<tr>
<td>11. Are the possible ethical problems discussed and identified?</td>
<td>1</td>
<td>0.6</td>
<td>0</td>
<td>0</td>
<td>4</td>
<td>0</td>
</tr>
<tr>
<td>12. Conclusions</td>
<td>4</td>
<td>0.39</td>
<td>4</td>
<td>3</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>13. Overall impression of the quality of the paper</td>
<td>3</td>
<td>0.48</td>
<td>3</td>
<td>0</td>
<td>4</td>
<td>3</td>
</tr>
</tbody>
</table>

SD-Standard Deviation, Min-Minimum and Max-Maximum

Table 4.7 Summary of the relationship between various economic analyses to the quality score

<table>
<thead>
<tr>
<th>Type of study</th>
<th>Frequency (n)</th>
<th>Quality score (mean)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cost-effectiveness analysis</td>
<td>15</td>
<td>3</td>
</tr>
<tr>
<td>Cost-minimisation analysis</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Cost-benefit analysis</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Cost-utility analysis</td>
<td>1</td>
<td>3</td>
</tr>
</tbody>
</table>
4.5 Conclusion

The results indicate that there is little research that is conducted in the field of pharmacoeconomics in South Africa. Furthermore, the research that is conducted lacks application with respect to formulary development as evidenced by high number of studies that were excluded. The quality of the pharmacoeconomic research in South Africa is below par with other countries, in particular those of South America.

Furthermore, with respect to quality, there were no differences that were noted amongst the various types of pharmacoeconomic evaluations. However, there were significant variations with respect to individual questions of the quality appraisal tool. Questions that dealt with limitations and assumptions were found to have poor quality as they obtained a score of 2. This is opposed to the following questions that achieved a score of 4: definition of study aim, sample selection, analysis of alternatives, measurement of benefits, suitability of analysis and the conclusions.

Lastly, the quality of pharmacoeconomic evaluations in South Africa does not appear to improve with time, as is the international trend. This finding is attributed to the fact that the two studies that achieved low scores were conducted recently. These quality concerns could possibly be attributed to a lack of national guidelines on how to conduct good pharmacoeconomic evaluations that are available in other countries.
CHAPTER 5
USE OF PHARMACOECONOMIC DATA IN FORMULARY DECISION MAKING PROCESSES

5.1 Introduction

An exploratory, cross-sectional and descriptive study design was used to obtain information on the attitudes, perceptions, knowledge and application of pharmacoeconomic data in formulary decision making processes in South Africa. The study population comprised of representatives from both the private health sector and the public health sector. The results are presented in this section and where possible graphs and tables are used to illustrate and facilitate understanding of the significance of the results.

5.2 Dissemination of questionnaires

The total number of questionnaires that were disseminated in both the private health sector and public health sector was 91. This included 42 questionnaires to Managed Care Organisations, 24 to private hospitals, 16 to Medical Schemes Administrators and 9 questionnaires to Pharmaceutical Directorates.

5.2.1 Private health sector

Although there are 125 Medical Aid Schemes in South Africa that are registered with the Council for Medical Schemes in terms of the Medical Schemes Act (131 of 1998), they are managed by 16 Medical Schemes Administrators (MSAs) and 52 Managed Care Organisations (MCOs).

These organisations (MSAs and MCOs) administer the business of medical schemes in accordance with the Medical Schemes Act (131 of 1998) as provided for in the rules of the medical schemes. Their duties include, but are not limited to, collection of premiums from the members and payment of service providers, development of treatment protocols and drug formularies.

The response rate in the private sector ranged between 20% for private hospitals and 56% for the MSAs as shown in Table 5.1.
### 5.2.1.1 Managed Care Organisations

All 52 Managed Care Organisations that are listed in the official website of the medical schemes (http://www.medicalschemes.com) were considered for inclusion in the survey. Four of the Managed Care Organisations (MCOs) were no longer in operation at the time of the survey and 8 of them did not have e-mail addresses listed on the website and could not be reached by either telephone or mail.

Three of the MCOs reported that they enlist the services of 3rd party organisations (Medical Aid Administrators) to develop their formularies. Twelve organisations declined participation listing reasons such as protection of intellectual property and lack of time. Five questionnaires were not received back and could not be tracked down/accounted for by contacting the organisations. Seven indicated that they don’t make use of formularies. In total, 18 questionnaires were received back giving an unadjusted response rate of 34.61% as shown in Table 5.1.

### 5.2.1.2 Medical aid administrators

All 16 Medical Schemes Administrators (MSA) that are listed on the official website of the medical schemes (http://www.medicalschemes.com) were approached for participation. Seven did not take part in the study due to various reasons such as not responding to e-mails and unavailability of the principal officers when following up telephonically.

A total of 9 questionnaires were received back, 4 of which were completed by a 3rd party organisation, such as a managed care organisation. Thus giving an unadjusted response rate of 56.25% as shown in Table 5.1.

### 5.2.1.3 Private hospitals

A list of all private hospitals in South Africa that are registered in terms of the provisions of the National Health Act No. 61 of 200348 was obtained from the official website of Hospitals Association of South Africa (HASA), (http://www.hasa.co.za). There are 198 individual private hospitals, most of which operate under holding groups. In total, there are 9 holding groups that are comprised of three major hospital groups that account for 144 (73%) of all the private hospitals, followed by 38 (19%) of those that are independent hospitals and lastly 16 (8%) of relatively small hospital groups.

The HASA’s website provides a list of websites for each individual private hospital, however there is a total of 26 individual hospitals whose websites are not provided. These 26 individual hospitals comprised of 21 independent hospitals, followed by 2 holding groups representing 4 hospitals and 1 hospital. In the case of the holding groups, 7 of the
national offices were approached for possible inclusion in the survey and in the case of individual hospitals, each one of 17 hospitals that were contactable was also approached for a possible inclusion in the survey. The total number of questionnaires that were disseminated was 24.

Four hospital groups representing 91 individual hospitals indicated via e-mail, without completing the questionnaire, that they do not make use of formularies. A further 2 representing 4 individual hospitals did not respond at all. In the case of individual hospitals, 15 also indicated that they do not operate formularies without completing the questionnaire. A further 2 did not respond at all. When one takes into consideration all factors that are mentioned here, 5 questionnaires were to be expected back. However, only one was returned giving an unadjusted response rate of 20%.

5.2.2 Public health sector

A list of names and contact numbers for the heads of the Pharmaceutical directorates in all the nine provinces was obtained. This was done by contacting the office of the National Pharmaceutical Directorate whose contact details were obtained from the official website of the Department of Health, (http://www.doh.gov.za).

5.2.2.1 Pharmaceutical directorates

The Pharmaceutical Directorates (PDs) in all nine provinces were approached, 5 questionnaires were received back. Four directorates did not complete the questionnaires citing a lack of time as the reason. An unadjusted response rate of 55.56% was obtained as shown in Table 5.1.

5.2.3 Survey Response Rate

Table 5.1 further provides an indication of the number of questionnaires that were to be expected if taking into consideration the factors that are listed above in terms of the eligibility of various sub groups to participate in the study. The number of questionnaires that were to be expected is 67 and the actual number of questionnaires that were received back is 33. This gives an adjusted response rate of 49.25%.
Table 5.1 Summary of the dissemination of questionnaires and organisation responses

<table>
<thead>
<tr>
<th>Study Population Details</th>
<th>MCOs</th>
<th>MSAs</th>
<th>PDs</th>
<th>PHs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Organisations approached</td>
<td>52</td>
<td>16</td>
<td>9</td>
<td>9</td>
</tr>
<tr>
<td>Organisations no longer in operation</td>
<td>4</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Organisations that could not be contacted</td>
<td>8</td>
<td>0</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>Organisations which do not use a formulary</td>
<td>7</td>
<td>0</td>
<td>0</td>
<td>4</td>
</tr>
<tr>
<td>Organisations that declined participation</td>
<td>12</td>
<td>7</td>
<td>4</td>
<td>0</td>
</tr>
<tr>
<td>Organisations that did not return the questionnaires</td>
<td>5</td>
<td>0</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>Organisations that use 3\textsuperscript{rd} party agents</td>
<td>3</td>
<td>4</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Organisations that participated</td>
<td>15</td>
<td>5</td>
<td>5</td>
<td>1</td>
</tr>
<tr>
<td>Number of questionnaires that were expected back</td>
<td>37</td>
<td>16</td>
<td>9</td>
<td>5</td>
</tr>
</tbody>
</table>

Total no of questionnaires received

18 (35%)* 9 (56%)* 5 (56%)* 1 (20%)*

*The total number of questionnaires received is expressed as a % of the number that were expected back

5.3 Formulary committees and their activities

Participants were asked whether they employ formulary committees, and if so, to provide an indication of what is the composition of such committees in terms of professional backgrounds and size is.

5.3.1 Use of formularies and formulary committees

Ninety seven percent of respondents from all sub groups reported that they make use of formularies and formulary committees to operate their medicines formularies as shown in Figure 5.1. Only 20% of the respondents, from the MCOs, reported that they don’t operate formularies such that they don’t have formulary committees in place.
Use of Formulary Committees %

<table>
<thead>
<tr>
<th>MCOs</th>
<th>MSAs</th>
<th>PDs</th>
<th>PHs</th>
<th>TOTAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>87</td>
<td>100</td>
<td>100</td>
<td>44</td>
<td>97</td>
</tr>
</tbody>
</table>

**Figure 5.1 Use of Formularies and Formulary Committees**

The results indicate that there is widespread use of formularies by all sub groups with the exception of PHs. Only one hospital group representing 30% (60) of all private hospitals reported that they make use of formularies and that they have a formulary committee that operates their formularies as explained in section 5.2.1.3. The fact that PHs are not in favour of formularies is not at all surprising as reported by Blecher and Thomas that private health care is largely financed by medical schemes. In this sense, private hospitals do make use of formularies indirectly.

The reported use of formularies is in line with the guidelines set out by the WHO’s Essential Drugs and Medicines Policy which recognises the formulary process as a cornerstone for good pharmaceutical management. Formularies provide a framework to deal with inefficient and irrational use of drugs. Well established formulary committees provide a forum for pharmacists, clinicians, administrators and other professionals to make informed decisions about the best possible ways of balancing the quality of care with financial constraints. This is done by developing treatment protocols and policies for all aspects of drug management including the development of formulary lists.

Both of these findings, use of formularies and formulary committees, are positive developments for the health care system in South Africa. They are well advocated by the World Health Organisation who further provided documented guidelines on goals and objectives, development of standard treatment guidelines, assessing medicines use to identify problems and conducting effective interventions to improve medicine use.
5.3.2 Composition of the formulary committees

In order to obtain a picture of the respective formulary committees, the participants were asked to give an indication of both the size of their respective committees and the professional backgrounds of their members.

5.3.2.1 Size of the committees

The size of the formulary committees varies considerably ranging from a minimum of 3 members in some MCOs and MSAs, to a maximum of 35 members in 1 of the PDs, as shown in Table 5.2. On average the number of members on formulary committees ranged from 6 in the case of MCOs to 22 in the case of PDs and 7 members in MSAs, followed by 7 for PHs.

Table 5.2 Summary of the number of members who constitute the formulary committees

<table>
<thead>
<tr>
<th>Members per committee</th>
<th>MCOs (n = 18)</th>
<th>MSAs (n = 9)</th>
<th>PDs (n = 5)</th>
<th>PHs (n = 1)</th>
<th>TOTAL (n = 33)</th>
</tr>
</thead>
<tbody>
<tr>
<td>3</td>
<td>3 (17%)</td>
<td>1 (11%)</td>
<td>0</td>
<td>0</td>
<td>4 (12%)</td>
</tr>
<tr>
<td>4</td>
<td>1 (6%)</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1 (3%)</td>
</tr>
<tr>
<td>5</td>
<td>3 (17%)</td>
<td>2 (22%)</td>
<td>0</td>
<td>0</td>
<td>5 (15%)</td>
</tr>
<tr>
<td>6</td>
<td>4 (22%)</td>
<td>3 (33%)</td>
<td>0</td>
<td>0</td>
<td>7 (21%)</td>
</tr>
<tr>
<td>7</td>
<td>1 (6%)</td>
<td>1 (11%)</td>
<td>1 (20%)</td>
<td>*1(100%)</td>
<td>4 (12%)</td>
</tr>
<tr>
<td>9</td>
<td>1 (6%)</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1 (3%)</td>
</tr>
<tr>
<td>10</td>
<td>2 (11%)</td>
<td>1 (11%)</td>
<td>0</td>
<td>0</td>
<td>3 (9%)</td>
</tr>
<tr>
<td>18</td>
<td>0</td>
<td>0</td>
<td>1 (20%)</td>
<td>0</td>
<td>1 (3%)</td>
</tr>
<tr>
<td>20</td>
<td>1 (11%)</td>
<td>1 (11%)</td>
<td>1 (20%)</td>
<td>0</td>
<td>3 (9%)</td>
</tr>
<tr>
<td>30</td>
<td>0</td>
<td>0</td>
<td>1 (20%)</td>
<td>0</td>
<td>1 (3%)</td>
</tr>
<tr>
<td>35</td>
<td>0</td>
<td>0</td>
<td>1 (20%)</td>
<td>0</td>
<td>1 (3%)</td>
</tr>
<tr>
<td>Mean</td>
<td>6</td>
<td>7</td>
<td>22</td>
<td>7</td>
<td>n/a**</td>
</tr>
</tbody>
</table>

*1 formulary committee of seven members develops a standard formulary for 60 individual private hospitals that belong to one holding group. **-not applicable.

If one considers that the greater the diversity of experts included on a formulary committee, the more dynamic a formulary is likely to be, a committee that is made up of three members is not likely to be effective. However, a committee as big as 35 members, as reported by one respondent from the PDs, might also prove too cumbersome to manage. It might take long before consensus is attained on the deliberations in the
process of consultation with every member, with the result that decisions might be delayed.

An average of 6 or 7 members as reported by MCOs, MSAs and PHs is desirable as opposed to an average of 22 members by the PDs. However, the size of a formulary committee will also depend on the population on whose behalf such a committee is developing the formulary. According to Harrison, the private sector served only 7 million of the general population in 2004 and has a total of 68 organisations (MCOs and MSAs) that manage 144 medical schemes.

Against this backdrop, it is to be expected that the MCOs and MSAs will have the least number of members on formulary committees as opposed to the public sector that serves about 40 million; Statistics SA estimates that the population of South Africa is 47.8 million. This finding is also consistent with the case of private hospitals as they do not serve a large number of the general population.

5.3.2.2 Composition of the committees

Ninety one percent of respondents from all the sub groups reported that doctors form part of their committees, followed by 85% including pharmacists, 52% including administrators and 45% include other professionals classified as other as shown in Figure 5.2.

![Figure 5.2 Composition of the committee members in terms of professional backgrounds](image)

**Figure 5.2 Composition of the committee members in terms of professional backgrounds**

The group referred to as “other” included various such as professional nurses (33%), specialists (12%), trustees, consultants, lawyer/ethicist at 6% and followed by professors
and dieticians at 3% as reported by respondents from all the sub groups. Table 5.3 provides a summary of the responses. With respect to the consultants none of the respondents gave details of their expertise. The presence of a lawyer/ethicist in a formulary committee is a major positive attribute as they will be able to tackle all the legal matters that might arise and play a significant role in resolving the medico-legal matters. There are two groups of professionals who were reported by only the respondent representing the private hospitals to be part of their committees, these were dieticians and professors. In the case of the former, there is a valuable contribution that they can make in assisting with drawing up the treatment guidelines and providing guidance of what diets certain patients such as diabetics will need to go on. With respect to the formularies, no details of their areas of expertise were provided. In the case of the professors it is unclear as to what their expertise is as the respondent did not provide details.

The presence of specialists is a major positive attribute as, by the nature of their training, they have a wealth of knowledge in various fields of medical care such that their contribution is likely to enhance the quality of the decisions made by the members. The presence of the trustees will ensure that the financial interests of the members of various medical aid schemes are safeguarded. In terms of the international trends, it is unusual to have professionals such as lawyers, dieticians and consultants in the formulary committees. It is however, a very good initiative that embraces diversity of skills and thereby could improve the quality of the decisions made by the committees.

Table 5.3 Description of professionals who form part of the committee referred to as “other”.

<table>
<thead>
<tr>
<th>Other Professionals</th>
<th>MCOs (n = 18)</th>
<th>MSAs (n = 9)</th>
<th>PDs (n = 14)</th>
<th>PHs (n =1)</th>
<th>TOTAL (n = 33)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Professional Nurses</td>
<td>5 (28%)</td>
<td>2 (22%)</td>
<td>4 (80%)</td>
<td>0</td>
<td>11 (33%)</td>
</tr>
<tr>
<td>Consultants</td>
<td>1 (6%)</td>
<td>1 (11%)</td>
<td>0</td>
<td>0</td>
<td>2 (6%)</td>
</tr>
<tr>
<td>Lawyer/ethicist</td>
<td>1 (6%)</td>
<td>1 (11%)</td>
<td>0</td>
<td>0</td>
<td>2 (6%)</td>
</tr>
<tr>
<td>Specialist</td>
<td>2 (13%)</td>
<td>0</td>
<td>1 (20%)</td>
<td>1 (100%)</td>
<td>4 (12%)</td>
</tr>
<tr>
<td>Professors</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1 (100%)</td>
<td>1 (3%)</td>
</tr>
<tr>
<td>Dieticians</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1 (100%)</td>
<td>1 (3%)</td>
</tr>
<tr>
<td>Trustees</td>
<td>1 (6%)</td>
<td>1 (11%)</td>
<td>0</td>
<td>0</td>
<td>2 (6%)</td>
</tr>
</tbody>
</table>
5.4 Training in Pharmacoeconomics

The majority of the respondents from various categories had formulary committee members who had received training in pharmacoeconomics. Of those that had been trained, this training was mainly in the form of continuing education. Continuing education had been received by 69% of the respondents from all the sub groups, followed by 35% with formal education and 27% of those whose training was referred to as “Other”, as shown in Figure 5.3.

![Figure 5.3: Evaluation of the training credentials of the decision-makers](image)

If we consider the nature of continuing education received, 9% of the respondents from all the sub groups, with the exception of private hospitals, reported that members of their committees had attended a programme organised by Eli Lilly (multi national pharmaceutical company) and a further 9% reported that decision-makers in their committees attended a programme organised by the Pharmaceutical Care Management Association (PCMA) in conjunction with the DOH. Lastly, 12% of the respondents from all the sub groups, excluding private hospitals, indicated that decision-makers in their committees had received a certificate in pharmacoeconomics without divulging further details of the course provider as shown in Table 5.4 below.

The training of those who had been formally trained included Masters programmes (25%), Doctorates (14%) and Master of Business Administration (MBA) degrees (8%) (Figure 5.3).
Table 5.4 Summary of training in Pharmacoeconomics by means of continuing education

<table>
<thead>
<tr>
<th>Type of Training</th>
<th>MCOs (n = 18)</th>
<th>MSAs (n = 9)</th>
<th>PDs (n = 5)</th>
<th>PHs (n = 1)</th>
<th>TOTAL (n = 33)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eli Lilly Programme</td>
<td>1 (6%)</td>
<td>2 (22%)</td>
<td>0</td>
<td>0</td>
<td>3 (9%)</td>
</tr>
<tr>
<td>PCMA with DOH</td>
<td>1 (6%)</td>
<td>1 (11%)</td>
<td>1 (20%)</td>
<td>0</td>
<td>3 (9%)</td>
</tr>
<tr>
<td>Certificate</td>
<td>3 (17%)</td>
<td>0</td>
<td>1 (20%)</td>
<td>0</td>
<td>4 (12%)</td>
</tr>
</tbody>
</table>

In a study that was conducted by Sarpong in the Greater New Orleans, USA, it was also found that the majority of the decision-makers received training in pharmacoeconomics in the form of continuing education as opposed to formal post graduate education.\(^{119}\)

Motheral, Grizzle, Armstrong, Cox and Fairman (2000) reported a similar finding in a survey carried out in Maryland, USA, which focused on the sample of subscribers to the Formulary journal.\(^{120}\)

Mullins and Wang (2002), in their review paper identified a need to develop formal post graduate capacity in the field of pharmacoeconomics, suggesting that it is currently deficient.\(^{159}\)

5.5 Formulary process

Participants were asked questions about the formulary processes in their respective organisations as it relates to: the number of formulary reviews undertaken in the past year, the use of analytical tools and software programmes in formulary development, the major considerations in the formulary decision-making process, factors that may be considered in the formulary decision-making process and the use of pharmacoeconomic data in the formulary decision-making process.

5.5.1 Formulary reviews undertaken in the past year

The number of formulary reviews undertaken by the various categories of organisations are summarised in Table 5.6 below. Regular reviewing of the formulary in response to new drugs or withdrawal of existing products from the market as a result of safety concerns is important. A formulary review is a process of ensuring that the beneficiaries have access to a wide range of medically appropriate drugs to treat various conditions and to ascertain that the formulary design remains relevant to the target group that it serves.\(^{160}\)
The majority (48%) of respondents from all the sub groups indicated that they conduct five or fewer formulary reviews per year, followed by 21% of those who indicated that they review their formularies more than 15 times in a year, 18% reported that they carry out formulary reviews between 11 and 15 times per annum and 6% reported that they conduct their formulary reviews between 6 and 10 times in a year as shown in Table 5.5.

Table 5.5 Number of formulary reviews conducted per year

<table>
<thead>
<tr>
<th>No. of formulary reviews in a year</th>
<th>MCOs (n = 18)</th>
<th>MSAs (n = 9)</th>
<th>PDs (n = 5)</th>
<th>PHs (n = 1)</th>
<th>TOTAL (n = 33)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-5</td>
<td>8 (44%)</td>
<td>3 (33%)</td>
<td>5 (100%)</td>
<td>0</td>
<td>16 (48%)</td>
</tr>
<tr>
<td>6-10</td>
<td>1 (6%)</td>
<td>0</td>
<td>0</td>
<td>1 (100%)</td>
<td>2 (6%)</td>
</tr>
<tr>
<td>11-15</td>
<td>3 (17%)</td>
<td>3 (33%)</td>
<td>0</td>
<td>0</td>
<td>6 (18%)</td>
</tr>
<tr>
<td>Other</td>
<td>3 (17%)</td>
<td>4 (44%)</td>
<td>0</td>
<td>0</td>
<td>7 (21%)</td>
</tr>
</tbody>
</table>

Respondents that conduct reviews more than 15 times a year supported their responses by indicating that they conduct reviews each time a new drug product is launched. They further suggested that formulary reviews are accompanied by clinical protocol reviews.

These results would suggest that the majority (16), of all the organisations in the sample conduct formulary reviews, five or fewer times a year, followed by 7 of all the respondents reported that they review their formularies more than 15 times a year. Although formulary reviews appear to be undertaken more in the private sector (MCOs and MSAs) than they are in the public sector (PDs) they appear to be undertaken considerably less often than is reported by other studies. In the study that was conducted by Odedina, Sullivan, Nash and Climmonos (2002) in Florida, USA, it was found that on average the formulary reviews were conducted 24 times in a year.121

The finding that new product launches influence the frequency with which formulary reviews are conducted, as reported by 7 respondents, suggests a formulary process which is dynamic and responsive to market forces. This may ultimately translate into cost savings, especially in the case of new generic drugs, as was envisaged by the Medicines and Related Substances Act of 2002 (as amended).49 This legislative reform advocates the extensive use of generic drugs and requires health care professionals who are legally authorised to dispense medicines, to inform their patients of the availability of generic equivalents, prior to dispensing.49
The Medicines Review Annual Report (2005), of Mediscor, a medical scheme administrator, suggests that this regulation is achieving its intended objectives. Mediscor reported an increase of 8.7% in the use of generic drugs, from 40.2% in 2004 to 48.9% in 2005. This increase in generic prescribing may be translated into a decrease of 8% in the average cost of drugs in the country since 2004.  

In the case of PDs all 5 respondents reported that they review their formularies only five or less time in a year. This might be attributed to the following:

i. The size of formulary committees in public sector. As was discussed in Section 5.3.2.1, 4 of the 5 public sector provinces indicated committees of 18 members or larger. It may be that with committees of this size, convening the meetings, from a logistical point of view is difficult especially when taking cognisance of the fact that the members of the committees may be dispersed through out the province which entails travelling to the major centres where formulary meetings are convened.

ii. Secondly this finding may point to issues of bureaucracy and “red tape” where changes to procedures and policies cannot be easily initiated, and it may take time to go through the hierarchical authorities in order to attain approval.

iii. Furthermore, the procurement system in the public service follows very strict practices that entail the awarding of tenders to pharmaceutical companies whose bidding was successful. Such that there are agreements in place on what specific products are to be supplied to the state and at what volumes and costs. This system locks the provinces into long-term contracts with manufacturers, which decreases their ability to be responsive to new product launches.

This lack of responsiveness is in contrast with the MSAs and MCOs, where some of the respondents reported that they review their formularies more than 15 times in a year, and went further to report that they review their formularies each time a new product is launched.

5.5.2 Use of analytical tools and software programmes in formulary development

Respondents were asked if they employed any specific methods of analysis, during the formulary decision making process, with Multi Attribute Utility Theory and System Of Objectified Judgement Analysis (SOJA) being provided as examples. None of the respondents in either sectors reported that they make use of any specific methods of analysis. This finding was found to be in contrast with the international trends where systematic tools of analysis, such as SOJA, are used in making formulary decisions.
SOJA has been described by Walkom, Robertson, Newby and Pillay (2006) as one of the frameworks that can be employed to limit the influence of "emotional criteria" on decision-making by assigning a relative weight to each criterion, in terms of importance. This is achieved by allocating weighing of around 70% to efficacy, safety, and acquisition costs.\textsuperscript{114} It is a well documented fact that each member of the formulary committee brings their own values with them to the process. These values may be related to negative or positive past experiences and may introduce bias thus influencing their formulary decisions.\textsuperscript{96} The use of software programmes such as SOJA or MAUT remains an area that requires further consideration by drug formulary committees in both the public and private sectors in South Africa.

The use of computer software programmes in the formulary decision-making process in organisations appears to be very limited. The respondent representing private hospitals indicated that they do not employ any software programmes at all. This was followed by 89\% of respondents for both the MCOs and the MSAs who indicated that they don't make use of any software programme. This is similar in the public sector, where 80\% of respondents indicated that software programmes are not used.

The respondents that did report the use of computer software programmes indicated that they were mainly in-house purpose developed programmes whilst one respondent indicated use of a programme called “Tapestry”. The only reference that could be found to Tapestry in terms of computer software suggests that it is a framework for writing web-based applications in Java, which would suggest that they were also referring to an in-house purpose built application.\textsuperscript{166}

5.5.3 Major considerations in the formulary decision-making process

Participants were requested to describe the procedure that their organisations follow in making formulary decisions and were asked to indicate what the major considerations in the process are. No respondent described the procedure in any detail although a few indicated that they employed a structured, stepwise approach.

Their responses with regards to the considerations factored into the process can be can be classified into four major categories as summarised in Table 5.6. The categories are:

i. clinical issues
ii. cost issues
iii. drug characteristics
iv. other factors.

Table 5.6 Factors that are considered important in the formulary decision-making process

<table>
<thead>
<tr>
<th></th>
<th>MCOs (n = 18)</th>
<th>MSAs (n = 9)</th>
<th>PDs (n = 5)</th>
<th>PHs (n = 1)</th>
<th>TOTAL (n = 33)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>CLINICAL ISSUES</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Efficacy</td>
<td>7</td>
<td>5</td>
<td>0</td>
<td>0</td>
<td>12 (36%)</td>
</tr>
<tr>
<td>Drug Safety</td>
<td>3</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>5 (15%)</td>
</tr>
<tr>
<td>Therapeutic equivalence</td>
<td>2</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>3 (9%)</td>
</tr>
<tr>
<td>Bioequivalence</td>
<td>2</td>
<td>4</td>
<td>0</td>
<td>0</td>
<td>6 (18%)</td>
</tr>
<tr>
<td>Side effect profile</td>
<td>1</td>
<td>3</td>
<td>0</td>
<td>0</td>
<td>4 (12%)</td>
</tr>
<tr>
<td>Clinical outcomes</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>1 (3%)</td>
</tr>
<tr>
<td><strong>COST</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Affordability</td>
<td>7</td>
<td>5</td>
<td>3</td>
<td>1</td>
<td>16 (48%)</td>
</tr>
<tr>
<td>Cost-minimisation</td>
<td>3</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>3 (9%)</td>
</tr>
<tr>
<td>Cost-effectiveness</td>
<td>7</td>
<td>5</td>
<td>0</td>
<td>0</td>
<td>12 (36%)</td>
</tr>
<tr>
<td>Cost-benefit</td>
<td>3</td>
<td>4</td>
<td>0</td>
<td>0</td>
<td>7 (21%)</td>
</tr>
<tr>
<td><strong>DRUG CHARACTERISTICS</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dosage form</td>
<td>1</td>
<td>4</td>
<td>0</td>
<td>0</td>
<td>5 (15%)</td>
</tr>
<tr>
<td>Quality</td>
<td>0</td>
<td>2</td>
<td>0</td>
<td>1</td>
<td>3 (9%)</td>
</tr>
<tr>
<td><strong>OTHER</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Evidence-based medicine</td>
<td>5</td>
<td>0</td>
<td>2</td>
<td>0</td>
<td>7 (21%)</td>
</tr>
<tr>
<td>Prescribed minimum benefit</td>
<td>5</td>
<td>3</td>
<td>0</td>
<td>0</td>
<td>8 (24%)</td>
</tr>
<tr>
<td>Availability of the drug</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>2 (6%)</td>
</tr>
<tr>
<td>Benefit design</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1 (3%)</td>
</tr>
<tr>
<td>Ethical and legal considerations</td>
<td>1</td>
<td>4</td>
<td>0</td>
<td>0</td>
<td>5 (15%)</td>
</tr>
<tr>
<td>Literature review</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1 (3%)</td>
</tr>
<tr>
<td>Benefit to the province</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>1 (3%)</td>
</tr>
<tr>
<td>Research</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>1 (3%)</td>
</tr>
<tr>
<td>Local PTC’s decisions</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>1 (3%)</td>
</tr>
<tr>
<td>Service</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>1 (3%)</td>
</tr>
<tr>
<td>Black Economic Empowerment status</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>1 (3%)</td>
</tr>
<tr>
<td>Considerations of local manufacturers</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>1 (3%)</td>
</tr>
</tbody>
</table>
5.5.3.1 Clinical issues

Of all the clinical factors, efficacy\(^a\) received the highest ranking amongst all the sub groups as it received an over all score of 36%, followed by bioequivalence\(^b\) at 18%, drug safety at 15%, side effect profile at 12%, and the therapeutic equivalence at 9%. The PHs (3%) reported that they consider clinical outcome, although is not clear as to the exact meaning of it.

These findings are consistent with studies that were conducted internationally by Motheral \textit{et al} (2000) in their survey of subscribers to the Formulary journal found out that drug efficacy and safety were rated high amongst factors considered,\(^{120}\) although in this case bioequivalence came before drug safety. This is also supported by Odedina \textit{et al} (2002), who conducted an exploratory study of pharmacist members of the PTC, of all 224 hospitals licensed in Florida, USA. In this study, drug efficacy and safety were also cited as some of the main considerations in the formulary decision-making process.\(^{121}\)

5.5.3.2 Cost

All the sub groups reported that the cost aspect plays an in important role in the formulary decision-making process. It was reported by 48% of all the respondents that the affordability of a drug is an important criterion, followed by 3 pharmacoeconomic parameters including cost-effectiveness, cost-benefit and cost-minimisation at 36%, 21% and 9% respectively. In a study that sought to determine the role of pharmacoeconomics in the formulary decision-making process, Walkom \textit{et al} (2006) described the acquisition costs as being relevant in all formulary decisions.\(^{114}\) In a review which focused on balancing the cost and value of medications, Avorn described the cost of drugs as an important factor that must be balanced against the benefits and the risks.\(^{61}\)

5.5.3.3 Drug characteristics

Fifteen percent of respondents from the sub groups, with the exception of the PDs and the PHs reported that the dosage form of a drug played an important role in formulary decisions. This finding is consistent with the results of a survey conducted by Anell and Svarvar (2000) on the attitudes of the members of a Swedish Formulary Committee in which they found that dosage form of a drug plays an important role in making formulary decisions.\(^{167}\)

\(^{a}\) the ability of an intervention to produce the desired beneficial effect in clinical trials.\(^{168}\)

\(^{b}\) having the same strength and similar bioavailability in the same dosage form as another sample of a given drug substance.\(^{168}\)
The importance of a dosage form is relevant as certain dosage forms such as parenterals require administration under medical supervision.\textsuperscript{169}

Another finding that relates to the drug characteristics was reported to be quality as reported by 9\% of the respondents. A finding that compares favourably with the observation made by Anell and Svarvar (2000) where the reputation and credibility of the manufacturer were factors that were taken into consideration, since they were considered to be important determinants of drug quality.\textsuperscript{167} This criterion is likely to be very subjective as there are no specific objective criteria that can be used as a basis to compare the quality of one drug with another. It would appear that MCOs and PDs do not consider drug characteristics as important as none of their respondents reported them as a criteria used in formulary decisions.

5.5.3.4 Other factors
Evidence based medicine was found to be the most considered criteria under the category “other factors” as reported by 21\% of respondents. This was followed by Prescribed Minimum benefit at 24\%, and followed by ethical and legal considerations at 15\% and the availability of a drug at 6\%. Lastly, at 3\%, the following factors; benefit design, literature review, benefit to the province, research, local PTC’s decisions and considerations of local manufacturers were found to be the least considered factors.

Despite the wide range of factors that were reported to be major considerations by the sub groups, there seem to be those that are common with international findings. These include the use of evidence based medicine and reliability of the manufacturer as reported by Anell and Svarvar (2000) and Fijn, Brouwers, Knaap and De Jong-Van Den Berg (1999).\textsuperscript{167,170} The rest of the other factors such as ethical and legal considerations, prescribed minimum benefit and benefit to the province were found to be unique to the South African settings as they could not be backed up by any studies that were conducted in other countries.

5.5.4 Factors that may be considered in the formulary decision-making process
Participants were asked to rate the importance of various factors that could be taken into account during the formulary-decision making process. Participants were asked to rate the factors on a scale of 1 to 7; 1 being the most important and 7 being the least important.
Figure 5.4 Participants scoring of factors that may be considered in the formulary decision-making processes.

Most participants gave drug efficacy a score of 1 indicating that it is the factor that is considered most important. Six participants scored drug effectiveness 1 or 2 and drug safety was scored as either 1 or 2 by 8 respondents.

Figure 5.5 Scoring of factors that may be considered in the formulary decision-making processes.

The extent of drug monitoring and availability of oral therapy were not considered as important by the respondents. These two factors were given a score of either 6 or 7 by the majority of the respondents as seen in Figure 5.5.
5.5.5 Use of Pharmacoeconomic data in the formulary decision-making process.

Participants were asked to give an indication of the considered importance of pharmacoeconomic data in making formulary decisions, the extent to which such data is employed, types of pharmacoeconomic evaluations that are used, sources of such data, whether they find data from overseas studies transferable to their settings and if so whether they perform sensitivity analyses in order to establish its rigour.

5.5.5.1 The considered importance of pharmacoeconomic data in the process

Participants were asked to indicate the importance of pharmacoeconomic data in their formulary decision-making processes. Sixty one percent of all the sub groups indicated that pharmacoeconomic data was somewhat important in their formulary decisions, followed by 39% of respondents across all the sub groups who reported that pharmacoeconomic data was very important in their formulary decisions. None of the individual sub groups reported that pharmacoeconomic data was not at all important to their formulary decisions as shown in Figure 5.6.

![Figure 5.6 Importance of Pharmacoeconomic data in the formulary process](image)

The fact that the majority (61%) of the respondents reported that pharmacoeconomic data is somewhat important was found to be in contrast with the international trends where the use of pharmacoeconomic data is considered to be very important.\textsuperscript{120,171}

5.5.5.2 The extent to which pharmacoeconomic data is used in the formulary decision-making process
The majority (58%) of respondents from all sub groups reported that pharmacoeconomic data is considered in some decisions, followed by 21% who reported that it is considered in few decisions, as opposed to 18% of the respondents who reported that they consider pharmacoeconomic data in every decision. Lastly, only 3% of the respondents from all the sub groups reported that pharmacoeconomic data is considered in almost no decisions as shown in Table 5.7.

Table 5.7. The extent to which PE data is used in the formulary process.

<table>
<thead>
<tr>
<th>Extent of use of Pharmacoeconomic data</th>
<th>MCOs (n = 18)</th>
<th>MSAs (n = 9)</th>
<th>PDs (n = 5)</th>
<th>PHs (n = 1)</th>
<th>TOTAL (n = 33)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Considered in every decision</td>
<td>1 (5%)</td>
<td>1 (11%)</td>
<td>3 (60%)</td>
<td>1 (100%)</td>
<td>6 (18%)</td>
</tr>
<tr>
<td>Considered in some decisions</td>
<td>12 (67%)</td>
<td>6 (67%)</td>
<td>1 (20%)</td>
<td>0</td>
<td>19 (58%)</td>
</tr>
<tr>
<td>Considered in few decisions</td>
<td>5 (28%)</td>
<td>2 (22%)</td>
<td>0</td>
<td>0</td>
<td>7 (21%)</td>
</tr>
<tr>
<td>Considered in almost no decisions</td>
<td>0</td>
<td>0</td>
<td>1 (20%)</td>
<td>0</td>
<td>1 (3%)</td>
</tr>
</tbody>
</table>

In 1996, the DOH adopted the following policy strategy, as outlined in the NDP; “to promote the acquisition, document and sharing of knowledge and experience through the establishment of advisory groups in rational drug use, pharmacoeconomics and other areas of the pharmaceutical sector”. When one takes this position of the DOH into consideration, it helps to explain the reason why, of all the sub groups, PDs were found to be the group that showed most appreciation for pharmacoeconomics. The exception is the sub group of the PHs mainly because it consists of one respondent. This policy statement is consistent with international trends with the only difference in countries such as Australia, Canada and New Zealand being that pharmacoeconomics has attained legal status with respect to drug approval/registration as explained in chapter 2.

5.5.5.3 Type of pharmacoeconomic evaluation that are used the most

Participants were asked to indicate from a choice of four types, the type of pharmacoeconomic evaluation that they use the most. Cost-effectiveness analysis was reported by 61% of the respondents from all the sub groups as the most used type. Cost-benefit analysis was found to be the second commonly used type of pharmacoeconomic analysis as reported by 27% of all the respondents. This was followed by cost-minimisation analysis at 21%. Lastly, none of the respondents reported that they employ cost-utility analysis as shown in Figure 5.7.
The finding that CEA is the most used type of analysis is well supported by the literature.\textsuperscript{69,73} When one takes into consideration the nature of the formulary process, that it involves making decisions about the inclusion or exclusion of drugs across the therapeutic range, it becomes clear why CEA is popular. Since CEA measures the health benefits in natural units (e.g. mmHg) that can be derived from a particular intervention (e.g. using an Angiotensin Converting Enzyme inhibitor agent versus a diuretic) against costs in monetary terms.

This is opposed to other analyses where the application in practice is limited as in the case of:

i. CMA, this application only lends itself useful in situations that involve measuring the costs only where the outcomes are identical as in the case of generics drugs and innovator’s products where it is normally obvious as to which one is the cheaper option

ii. CUA evaluates the costs in monetary terms and the outcomes in terms of a unit of utility, quality adjusted life year (QALY). In practice it is difficult to draw comparisons about QALY’s that can be derived from various therapies since a QALY is not a well defined fixed unit that is transferable from one study to another

iii. CBA is also not always easy to compute since it evaluates the costs of intervention in monetary terms against the accrued benefits in monetary terms as well. In
practice, it is not always easy to quantify certain outcomes in monetary terms such as the relief of depression.

5.5.5.4. Sources of pharmacoeconomic data

Participants were also asked to indicate what the common sources of pharmacoeconomic data that they use are and to indicate whether they are local or international publications, whether they are peer-reviewed or not and lastly whether they use in-house data or not. The results suggest that decision-makers prefer the pharmacoeconomic data published in international peer-reviewed publications, followed by local (South African) peer-reviewed publications.

The majority (73%) of the respondents across the sub groups reported that they make use of international peer-reviewed journals, followed by 52% of those that reported that they make use of peer-reviewed local journals followed by 39% of respondents who indicated that they make use of in-house data. None of the respondents cited the use of unpublished research such as dissertations and theses as shown in Figure 5.8.

This finding compares well with international trends although the majority of the studies do not differentiate between nationally or internationally generated publications, only putting emphasis on the peer-review aspect.\textsuperscript{120,167} The nature of the studies that were reported to be “in-house” cannot be commented on further as details of these studies, which would be considered to be “trade-secrets” are not available and it is not even known if these studies meet the criteria for classification as pharmacoeconomic studies.
5.5.5.5 Transferability and generalisability of the pharmacoeconomic data from other settings.

When asked about the transferability and generalisability of the pharmacoeconomic data, the responses were fairly divided as 52% of all the respondents reported that they find the studies that were conducted overseas directly applicable. Whereas 45% of the respondents reported that they do not find data from other settings generalisable and transferable to their specific work environments as shown in Figure 5.9.

It is not clear whether decision-makers who reported that they use data from other settings are aware of the fact that the outcome of economic analyses are dependent on factors such as unit costs, practice setups and unique patient case mix. All of these factors are affected by how each country goes about allocating health care resources. 89 Table 2.6 in section 2.4.2 provides a checklist that was devised by Sculpher, Pang, Manca, Drummond, Golder and Urdahl (2004) to help decision-makers to establish the generalisability of economic studies from other countries.88

![Figure 5.9 Transferability and generalisability of pharmacoeconomic data](image)

5.5.5.6 Use of modelling and sensitivity analysis to appraise the quality of pharmacoeconomic data.

The majority (76%) of the respondents across all sub groups reported that they do not employ sensitivity analysis to assess the statistical rigour of pharmacoeconomic data prior to its use, as shown in Figure 5.10.
The fact that modelling and performance of sensitivity analysis is not commonly done on the pharmacoeconomic data that is used is very worrying. It is a well documented fact that all pharmacoeconomic evaluations contain some degree of uncertainty that requires testing by subjecting the evaluation to a sensitivity analysis in order to determine its robustness.\textsuperscript{76,77}

5.5.6 Supply and distribution of pharmacoeconomic data

In as much as each respondent from various sub groups described the process as it applies to their respective organisation or institution, the following emerging trends were observed:

i. Drug manufacturers appear to be the main supplier of the pharmacoeconomic data

ii. Most respondents from all the sub groups, with the exception of the PDs, reported that they conduct in-house research that includes literature reviews, claims analysis etc

iii. Pharmacoeconomic data is distributed equally to all members of the PTCs for review and comment prior to the process

iv. The majority of the respondents from all the sub groups reported that the distribution of the pharmacoeconomic data is co-ordinated by a senior member of the PTC, normally the pharmacy services manager, PTC manager or the chairperson

v. The majority of the respondents from the PDs reported that the person who submits a motivation for a drug to be included in the formulary is the one who
supplies the pharmacoeconomic data that gets distributed to the members of the PTCs with the agenda via the chairperson.

There were a few respondents whose processes were found to be different from the trends noted above, for example:

i. One respondent from the MSAs reported that their data is supplied by the actuarial analysts and that the Clinical Policies Unit conducts the literature searches and thus provide the clinical data. Furthermore, that the final models and outcomes are distributed internally (members of the PTC) for review and comment prior to the process

ii. One respondent from the PDs reported that the supply and distribution of the pharmacoeconomic data is a task of an “Individual specialized department at the tertiary complex”

iii. The respondent from the PHs reported that they gather data from the hospitals and send it through to the person who conducts the review

iv. One respondent from the MCOs just reported that “it is done on the individual basis”. This is understood to refer to the supply of pharmacoeconomic data

v. One more respondent whose organisation is an international business reported that, “data is purely pricing from our various worldwide supplier”.

It is clear from these results that the pharmacoeconomic data is distributed to each member of the committee in advance prior to the formulary decision-making process. This is a positive attribute as it affords each member an opportunity of assessing the merits (clinical and financial) of a drug(s) prior to the meeting. This way, every member is in the position to make a meaningful contribution to the process.

It is not clear as to the exact nature of the pharmacoeconomic data that the drug manufacturers provide on request of these organisations or institutions. This is more surprising in the light of the findings of a study that was conducted by Ford where it was concluded that South Africa has a lack of pharmacoeconomic data such as CEA and CBA. Furthermore, as seen with the results of the literature searches that were conducted in this study, there is very limited research that generates pharmacoeconomic data in South Africa and of those studies that met the selection criteria only one (Schmitt\textsuperscript{136}) could be linked to the drug manufacturer. Considering the fact that it is not yet a legal requirement for drug manufacturers to conduct pharmacoeconomic evaluations, it remains unclear as to the nature of the pharmacoeconomic data that the industry supplies.
The finding that the pharmacoeconomic data is generally distributed by a senior member of the PTC is a positive development. It is to be expected that by virtue of their seniority, these members will have sufficient insight and experience to ascertain the accuracy of the data prior to distribution.

5.5.7 Actions that are as a result of a pharmacoeconomic findings.

Almost every respondent from all the sub groups reported in brief that the action that is taken by their organisations or institutions as a result of a pharmacoeconomic finding is a decision to either include or exclude the drug. They further reported that they then communicate their updated formularies to all relevant people.

One respondent described the process in much detail in addition to the general response of exclusion or inclusion of the drug. This respondent, from the MSAs, described the process to be as follows:

i. After a pharmacoeconomic finding has been made recommendations, are made to the Clinical Governance Committee

ii. Then a decision to either exclude or include a drug is taken

iii. If the drug is included, then they work on the reimbursement criteria

iv. Furthermore, the respondent reported that following the inclusion of a drug they then negotiate the price with the pharmaceutical company

v. If the drug is excluded, then they work with the medical specialist to implement a registry for when/if the funding does start.

The respondents did not describe the process with sufficient detail in order to get a clear picture of their activities subsequent to the decision whether to include or exclude a drug. It was expected that a series of steps as outlined in Figure 2.5 was going to be provided with the exception of the one MSA respondent whose description was more detailed. It is not understood as to what this respondent was referring to by “negotiating the price with the drug manufacturer” as the amendment of the Medicines And Related Substances Act forbids this practice. This Act prescribed that all medicines sold by the drug manufacturer should be sold on the basis of Single Exit Price (SEP) and that no discounts or bonuses can be offered by the drug manufacturers.

5.6 Conclusion

Formularies are employed extensively in both sectors of health care. This finding complies with the WHO recommendation of using formularies in health establishments in order to promote rational use of drugs. Pharmacists and doctors were found to be key
members of the formulary committees, followed by the administrators and professional nurses. The majority of the respondents from all the sub groups reported that members of their formulary committees have received some training in pharmacoconomics. The nature of this training was mainly in the form of continuing education.

The majority of the respondents from all the sub groups reported that they conduct formulary reviews five or less time in the year. In contrast with international trends, no system of analysis is employed in the formulary decision-making process. Clinical merits (efficacy, safety, side-effect profile etc) of a drug were found to be the main criteria that are considered in the formulary decision-making process, this was then followed by the cost of the drug and other criteria such as evidence based medicine, prescribed minimum benefits etc.

The majority of the respondents from all the sub groups reported that pharmacoconomics was considered somewhat important and that the most used type of pharmacoeconomic evaluation was found to be CEA. The majority of the respondents from all the sub groups reported the international peer-reviewed journals, followed by local peer-reviewed journals as their primary source of pharmacoeconomic data.

Lastly, it is concerning that the majority of the respondents from all the sub groups reported that they find direct application of pharmacoeconomic studies that were conducted in other settings including overseas and that they do not perform sensitivity analysis or modelling. The dangers of using data from other settings without first checking its rigour are well documented in the literature and were discussed in detail in section 2.4.2.
CHAPTER 6

CONCLUSIONS, LIMITATIONS AND RECOMMENDATIONS

6.1 Introduction

This chapter revisits the study aims and objectives with a view to drawing conclusions from the results and discussing the limitations in addition to making recommendations for further investigation.

The objectives of the study were as follows:

i. Determine and describe the processes used in the formulary decision-making.
ii. Establish the sources of pharmacoeconomic data used in the formulary process.
iii. Establish the extent of the availability and quality of data (published and unpublished) pertaining to South African based pharmacoeconomic studies.
iv. Establish the background and expertise of the formulary decision-makers.
v. Arrive at recommendations that can be used to promote and aid the use of pharmacoeconomics in the formulary process

6.2 Availability of South African based pharmacoeconomic studies

The following findings were made and conclusions drawn about the availability of South African based pharmacoeconomic studies:

i. There is little research that is conducted in the field of pharmacoeconomics in South Africa. This is shown by the results of the literature searches that were conducted. Out of 1090 potentially relevant research abstracts that were identified and screened for retrieval, only 16 could be considered to meet the inclusion criteria for this study, thus implying that only 16 primary research studies in South Africa, conducted or published between 01 January 1995 and 30 June 2007, interrogated both the costs and outcomes and evaluated drug therapy against a relevant comparator, and could therefore be considered to be full pharmacoeconomic evaluations. Furthermore, five out of eight schools of pharmacy in the country reported that they do not carry out any research in the field of pharmacoeconomics.

ii. Conducted pharmacoeconomic research covers a narrow scope in terms of therapeutic drug classes.
The majority of studies that complied with the inclusion criteria focused on antiretroviral drugs.

Most of these studies aimed at providing evidence that the cost of antiretroviral drugs is much cheaper than treating the ailments that are associated with HIV/AIDS when left untreated.

Impact of the studies on the formulary decision-making process:

The limited number of local based pharmacoeconomic studies means that there are few tools that are available to facilitate the formulary decision-making process.

However, all the pharmacoeconomic evaluations that were included in this study can be applied to the formulary process with respect to the inclusion or exclusion of the drugs that they investigated.

Nature of the publications where the local based studies are published:

The majority of the studies were published locally in a peer-reviewed journal (South African Medical Journal), followed by international peer-reviewed journals.

Quality appraisal:

The results of a quality appraisal demonstrated that the quality of pharmacoeconomic evaluations conducted in South Africa is acceptable.

However, when compared with studies that were conducted in other third world countries; South African studies were found to be below par in terms of quality.

This can be attributed to the fact that pharmacoeconomics is still new in this country and there is no set of national guidelines on how to conduct good pharmacoeconomic evaluations.

This was also shown by a high degree of variability when a quality review of individual questions was undertaken which clearly shows that there is a lack of methodological rigour in conducting pharmacoeconomic evaluations.

6.3 Use of pharmacoeconomic data in formulary decision-making processes

With respect to the national survey of the use of pharmacoeconomic data in the formulary decision-making processes, the following conclusions can be made:

Use of formularies and formulary committees:

There is an extensive use of formularies in both the public and private health sectors which is in line with the WHO recommendations that are aimed at facilitating rational drug use.
• Pharmacists and doctors were found to be key members of formulary committees, followed by administrators and professional nurses
• Some respondents further indicated that lawyers, dieticians, trustees and consultants also form part of their committees. The diversity of professional skills is a positive attribute as it is likely to enhance the quality of the decisions that are taken
• The size of the committees varied considerably between the public health sector and the private health sector, with the former having an average committee made up of 22 members as opposed to an average of 6 members in the private sector. The reported sizes of the committees are adequate if one takes into consideration the sizes of the target population for each of these respective sectors

ii. Training in pharmacoeconomics
• In line with the international trends, the majority of the formulary committee members have undergone training in pharmacoeconomics
• This training was mainly in the form of continuing education. This is a positive development as it will enable the members to correctly apply the theoretical concepts of pharmacoeconomics to the formulary decision-making process
• Of those that received formal training, this was mainly in the form of Masters degrees

iii. Formulary reviews
• The majority of the respondents reported that they conduct five or less formulary reviews per annum
• However, the private sector was found to be more responsive to the market dynamics, such as new product launches, as reported by some of the private sector’s respondents that they review their formularies each time a new product is launched

vi. Use of specific methods of analysis
• None of the sub groups reported the use of any specific method of analysis such as SOJA or MAUT
• Only one respondent reported the use of a programme referred to as Tapestry, which is understood to be an in-house purpose built application
• This is in contrast with some of the international trends where SOJA and MAUT have been employed successfully in selecting drugs for the formulary
• This lack of use of objective tools to facilitate the formulary decision-making processes could indicate that South African formulary processes are open to bias by members
vii. The importance of pharmacoeconomic data and the extent of its use
   - Pharmacoeconomic data was deemed as somewhat important to the formulary process by the majority of the respondents.
   - Furthermore, it was reported by the majority of the respondents that pharmacoeconomic data is considered in some decisions. A very small percentage (3%) reported that they considered pharmacoeconomic data in almost no decision.

viii. Type and sources of pharmacoeconomic data used in the formulary process
   - Cost-effectiveness analysis is the most commonly used type of pharmacoeconomic evaluation and none of the respondents reported the use of cost-utility analysis.
   - The preferred source of pharmacoeconomic data was found to be the international peer-reviewed publications, followed by local peer-reviewed journals.
   - This preference is probably motivated by a perception of high standards and quality associated with international peer-reviewed journals.

ix. Generalisability of pharmacoeconomic data from other settings and use of sensitivity analysis
   - The majority of respondents from all the sub groups reported that they find pharmacoeconomic data from other settings such as overseas studies applicable to their settings.
   - Furthermore, they also indicated that they rarely perform sensitivity analysis to ascertain the rigour of the data that they are going to apply to their settings.
   - These findings are concerning as they indicate very limited understanding of the concepts of pharmacoeconomics and the generalisability of pharmacoeconomic data by the decision-makers. There is enough evidence that suggests that data from specific study contexts may not be easily transferrable to other settings due to variations in factors such as the unit price, different practice set ups and unique patient case mix.

x. Other factors that may be considered in the formulary decisions
   - The consideration of other factors follows only after the clinical credentials (drug efficacy, drug safety and drug effectiveness) of the drug has been established.
   - The extent of drug monitoring and the availability of oral therapy were considered to be of little importance.
With respect to the hypothesis that was outlined in section 1.2, the aspect that deals with the availability of pharmacoeconomic data was found to be true. However, based on the results of the survey, it is clear that pharmacoeconomic data is used in the formulary decision-making process in both sectors of health care in South Africa. Although pharmacoeconomic data is reported to be used in the formulary decision making process; considering the limited research that is conducted in South Africa, the value of and applicability of the data that is used needs to be questioned.

6.4 Status of Pharmacoeconomics in South Africa

Pharmacoeconomics as a branch of health economics is well developed in many industrialised countries such as Australia, New Zealand, the US, Canada and many European countries where it is applied frequently in the allocation of scarce health care resources. There is enough evidence of how highly developed and advanced pharmacoeconomics is internationally such as, for example:

i. There is a vast body of research that is generated in this field that has led to a number of peer-reviewed journals that are dedicated to publishing pharmacoeconomic research. These publications include PharmacoEconomics, Value in Health and Formulary.

ii. In countries such as Australia and New Zealand, pharmacoeconomics has attained a legal status that makes it mandatory for pharmaceutical companies that want to market new drugs to conduct and disclose the results of a full pharmacoeconomic evaluation that shows that the new drug is justifiably priced (i.e. it is cost-effective).

iii. National guidelines on how to conduct good pharmacoeconomic evaluations exist.

iv. Establishment of ISPOR which is aimed at promoting the science of pharmacoeconomics and outcomes research.

In South Africa, pharmacoeconomics is still in an infancy stage. However, the Department of Health has acknowledged its importance in the NDP and is committed to promote its advancement. Much activity has taken place in recent times to develop pharmacoeconomics in South Africa, culminating into the establishment of ISPOR SA and the drafting of guidelines on methodological considerations for conducting good pharmacoeconomic evaluations.

In 2004, Ford conducted research to gain an understanding of how pharmacoeconomics is applied to formulary decisions made by the private sector. The results of this research
could not be generalised to and extended to the public sector as the study population was comprised only of Medical Aid Administrators which represents a very small section of the private health sector.\textsuperscript{123}

In same year, Pillay \textit{et al} conducted research that focused on the public health sector and targeted the members of the PTCs in all the provinces. The aim of this research was to establish the criteria that are employed in the formulary decision-making process.\textsuperscript{101} Some of the questions were also aimed at establishing the understanding of pharmacoeconomics by the decision-makers. Both Pillay and Ford came to the same conclusion that the level of understanding of pharmacoeconomics is poor as some of the respondents could not explain the meaning of terms such as cost-effectiveness, cost-benefit etc.

There is a research gap in South Africa in the field of pharmacoeconomics in terms of:

i. Availability of local based pharmacoeconomic data
ii. Assessment of its methodological rigour and overall quality
iii. Its consequent application by decision-makers during the formulary decision-making processes in both the public health sector and the private health sector.

\textbf{6.5 Limitations of the study}

i. Although the original plan for the research had been to analyse the data statistically, in an attempt to try and describe relationships and conduct comparisons between the private and public sectors, due to the small sample size only descriptive statistical methods were possible.

ii. The fact that the questionnaire was self-administered means that if respondents had required greater clarity whilst completing the questionnaire, it would not have been available. Piloting the questionnaire with pharmacists was an attempt to try and anticipate and address any possible problems in this regard. It is however, felt that if administered interviews had been conducted probing of responses which could have provided more insightful responses may have been possible.

iii. In making follow ups telephonically, it was difficult in certain instances to get through to the relevant person as many organisations makes use of either secretaries or personal assistants to the principal officers who did not always understand the nature and importance of this research and therefore did not direct the calls on.

iv. Conclusions can not be directly drawn about the understanding of the pharmacoeconomic concepts by the respondents since no question attempted to
establish that. However, based on the answers of some of the questions inferences can be drawn on how good or poor the understanding of pharmacoeconomics is.

6.6 Recommendations

i. Education

• It is recommended that pharmacoeconomics should be incorporated (where it is not already taught) into the undergraduate curriculum for the training of pharmacists, doctors and nurses.

• Furthermore, that the post graduate capacity in the field of pharmacoeconomics should be intensified to generate more research.

ii. Development of national guidelines

• The DOH should finalise the guidelines for conducting good pharmacoeconomic evaluations and disseminate them widely to the pharmaceutical community.

iii. Professional societies

• It is recommended that the professional societies such as the PSSA and the ISPOR SA should create more awareness and educational programmes about pharmacoeconomics to the pharmacists and other professionals.

iv. Further study

• It is recommended that a study should be undertaken to establish how pharmacoeconomics can play a role in the medicines pricing regulations. This might provide a theoretical framework that could help to resolve the differences that exist between the private sector and the DOH on this matter.

• Further study into the extent and nature of pharmacoeconomic education in South Africa would be useful in an effort to identify the reasons why so little pharmacoeconomic research is being conducted.

• Conduct a study to establish the exact nature of the pharmacoeconomic data since the literature search identified very little pharmacoeconomic studies.

• Since so many organisations appear to use international research, without conducting sensitivity analysis, as the basis for their formulary-decision making process, a study determining the extent to which international research results are truly generalisable to our South African context would be of great value.

• Use pharmacoeconomics to develop a cost-justification model for a new drug that is undergoing clinical trials in South Africa in line with international trends.
REFERENCES


4. Mahlo S.J. A strategy to enhance positive working relationships among the role players within the managed health care context in Gauteng. 2000; Rand Afrikaans University (Dissertation for a Masters degree).


15. OECD. 2007. Available online: (http://www.oecd.org/pages/0,3417,en_36734052_36734103_1_1_1_1,00.html). [Accessed 12/01/2007].


Thank you for agreeing to participate in this study. The form has been designed to be completed electronically, in Word®, we ask that you complete the following questions by using the tab key to move through the questions and by selecting the correct box or by completing the space provided.

1. Does your organisation make use of a committee for making formulary decisions?

☐ Yes
☐ No

2. How many members constitute the committee?

☐

3. What is the composition of the committee in terms of the professional backgrounds?

☐ Medical practioner(s)
☐ Pharmacist(s)
☐ Administrator(s)
☐ Other (please specify)

☐

THE USE OF PHARMACOECONOMIC DATA IN THE FORMULARY DECISION-MAKING PROCESS
4. Have any members in the committee received training in pharmacoeconomics?

☐ Yes
☐ No

5. If yes, what type of training?

☐ Formal training
☐ Continuing Education

6. In the case of formal training what qualification has been obtained?

☐ Masters
☐ Doctorate
☐ MBA
☐ Other (please specify)

7. How many formulary reviews were undertaken in the last year by your organization?

☐ (0-5)
☐ (6-10)
☐ (11-15)
☐ Other (please specify)

8. Please describe the procedure that your organization follows in making formulary decisions, what are the major considerations?


9. Are any specific analysis methods such as Multi Attributry Utility Theory and System of Objectified Judgement Analysis (SOJA) employed in the formulary decision-making processes?

- Yes
- No
If yes, please specify:

10. Are any computer software programmes used in the process?

- Yes
- No
If yes, please specify:

11. How important is pharmacoeconomic data to the process?

- Very important
- Somewhat important
- Not at all important

12. To what extent is pharmacoeconomic data used in the process?

- Considered in every decision
- Considered in some decisions
- Considered in few decisions
- Considered in almost no decisions
13. What type of pharmacoeconomic evaluations are mainly used by your organisation?

☐ Cost-effective analysis
☐ Cost-minimization analysis
☐ Cost-benefit analysis
☐ Cost-consequences analysis

14. What are the sources of pharmacoeconomic information that your organisation employs?

☐ Peer-reviewed published research, international
☐ Peer-reviewed published research, local
☐ Use of unpublished research e.g. dissertations and theses
☐ In-house data

15. Who supplies the data and is it equally distributed amongst all the members of the committee prior to the process?


16. What actions are taken as a result of the pharmacoeconomic findings?


17. Do you generally consider the data from other settings and overseas studies transferable and applicable to your organisation?


18. Is pharmacoeconomic modelling and sensitivity analysis done to assess the quality of pharmacoeconomic data prior to its use?


19. Please rank the other factors that may be considered in the formulary decision-making process, on the scale 1 (most important) to 7 least (important).

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<thead>
<tr>
<th>Factor</th>
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<td>Drug efficacy</td>
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<td>Side-effect profile</td>
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<td>Extent of drug monitoring</td>
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<td>Availability of oral therapy</td>
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Please save the file and email it back to:

s205004300@nmmu.ac.za

Thank you for your co-operation.
If you have any questions or queries please do not hesitate to contact me.

Mr. Keele Godfrey (BPharm)
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6031
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Tel (+27) 41 4072061
Dear Ms …………………,

Re: Research into the use of pharmacoeconomic data in formulary decision-making processes.

I’m currently busy with a research for a Masters degree in pharmacy (MPharm) at the Nelson Mandela Metropolitan University. The focus of the research is to establish what pharmacoeconomic data is available in South Africa and the extent to which it is used by various role players in the health care sector in making formulary decisions.

As discussed telephonically yesterday, I will be very grateful if you can assist by completing the attached questionnaire and send it back to me please.

Yours Sincerely,

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