THE USAGE OF ANTIDIABETIC DRUGS: A MANAGED CARE APPROACH

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Soli Deo Gloria

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ABSTRACT

Title: The usage of antidiabetic drugs: a managed care approach.

Keywords: *Diabetes Mellitus, type one, type two, managed care, pharmaco-economics, drug utilisation review, oral antidiabetic agents, insulins, single exit price, cost savings, generic, innovator.*

"Diabetes mellitus" refers to a spectrum of conditions, which all present with hyperglycaemia as a common medical finding. Diabetes was once thought of as a single disease, but according to Setter *et al.* (2000:378), it includes a heterogeneous group of disorders that are secondary to various genetic predispositions and precipitating factors. Type 1 diabetes mellitus (DM) accounts for 10 to 15% of all cases of diabetes mellitus and is clinically characterised by hyperglycaemia and a propensity to diabetic keto-acidosis. Its control requires chronic insulin treatment. Although it may occur at any age, it most commonly develops in childhood or adolescence and is the predominant type of diabetes mellitus diagnosed before age 30 (Beers & Berkow, 2004). Type 2 DM is usually the type diagnosed in patients older than 30 years of age. It is also commonly associated with obesity (Berkow, 1992:1108).

The objective of this study was to review the usage and cost of antidiabetic drugs and to determine the influence of the pricing regulations on the cost of these drugs. This research can be classified as retrospective and quantitative. Data were obtained from a prescription claims database, and the study population consisted of all the antidiabetic prescriptions for the year 1 January 2004 to 31 December 2004. The one-year period was divided into three study periods, namely January to April, May to August and September to December.

Firstly diabetes mellitus was investigated in order to understand the disease and to determine the prevalence and treatment thereof. It was found that diabetes mellitus is a heterogeneous disorder acquired from both genetic and environmental factors and that education for the general population, and in particular for the patients, is the key to preventing and controlling diabetes and reducing the complications arising from it.

Secondly managed health care, pharmaco-economics and a drug utilisation review were investigated in order to understand these concepts. The influence of the South African

Government on health care was discussed, including the new pricing regulations of medicine in South Africa.

Thirdly, the utilisation patterns of antidiabetic drugs were reviewed, analysed and interpreted. It was determined that the oral antidiabetic agents are relatively less expensive than the insulins and that they are prescribed more frequently, and secondly that the biguanides presented almost half (49.4%, n = 116 138) of all the oral antidiabetic agents. It was also determined that the average cost of the oral antidiabetic drugs was between 21.0% and 28.0% lower in 2004 than in 1996 - an indication that, despite inflation, the antidiabetic drugs were less expensive in 2004 than eight years ago in 1996. It was also calculated that the total cost savings in antidiabetic medication could have been R1 448 682.26 if the lower price of antidiabetic agents had been implemented during the period January to April. And finally it was also determined that further substantial "cost savings" could have been possible if all the innovator antidiabetic products had been substituted for less expensive generic antidiabetic products.

Abstract

OPSOMMING

Titel: Die gebruik van antidiabetiese middels: 'n bestuurde gesondheidsorg benadering

Sleutelwoorde: *Diabetes mellitus, tipe een, tipe twee, bestuurde gesondheidsorg, farmako-ekonomie, geneesmiddel verbruiks oorsig, orale antidiabetiese middles, insuliene, enkel uitgangs prys, koste besparings, generies, innoveerder.*

"Diabetes mellitus" verwys na 'n spektrum van toestande wat almal hiperglukemie insluit as 'n algemene mediese teken. Daar was eers gedink dat diabetes 'n enkele siekte toestand is, maar volgens Setter, *et al.* (2000:378) is dit 'n heterogene groep siektetoestande wat sekondêr is aan verskeie genetiese predisposisies en presipiterende faktore. Tipe 1 diabetes mellitus (DM) maak 10 tot 15% van alle gevalle van diabetes mellitus op en word klinies gekarakteriseer deur hiperglukemie en 'n geneigtheid tot diabetiese keto-asidose. Dit vereis kroniese insulien behandeling. Alhoewel dit op enige ouderdom kan voorkom, ontwikkel dit meer algemeen in die kinderjare of adolessensie jare en word hierdie predominante vorm van diabetes mellitus gediagnoseer voor 'n ouderdom van 30 jaar (Beers & Berkow, 2004). Tipe 2 diabetes mellitus is gewoonlik die sort wat by pasiente ouer as 30 jaar gediagnoseer word. Dit word ook algemeen met obesiteit geassosieer (Berkow, 1992:1108).

Die doel van hierdie studie was om die gebruik en koste van antidiabetiese middels te ondersoek, en om die invloed van die eenheids prys regulasies op die koste van hierdie middels te bepaal. Hierdie navorsing kan geklassifiseer word as retrospektief en kwantitatief. Data was verkry vanaf 'n medisyne-eis databasis, en die studie populasie het bestaan uit al die antidiabetiese voorskrifte van die jaar 1 Januarie 2004 tot 31 Desember 2004. Hierdie een-jaar periode is verdeel in drie studie periodes, naamlik Januarie tot April, Mei tot Augustus en September tot Desember.

Eerstens was diabetes mellitus ondersoek sodat die siekte verstaan kan word en om die voorkoms en behandeling daarvan te bepaal. Daar is gevind dat opvoeding vir die algemene publiek, maar in besonder die pasiente, die sleutel is tot die voorkoming en beheer van diabetes asook die vermindering van die komplikasies wat daaruit kan voortspruit.

Bestuurde gesondheidsorg, farmako-ekonomie en medisyneverbruiks patrone is tweedens bestudeer, sodat hierdie konsepte verstaan kan word. Die invloed van die Suid Afrikaanse

regering op gesondheidsorg, sowel as die nuwe eenheids prysreglasies van medisyne in Suid-Afrika is ondersoek.

Derdens was die verbruikspatrone van antidiabetiese middels ondersoek, geanaliseer en geinterpreteer. Daar was eerstens bepaal dat die orale antidiabetiese middels relatief goedkoper is as insulien en dat dit meer algemeen voorgeskryf word, en tweedens is gevind dat die biguanide amper die helfte (49.4% n = 116 138) is van die orale antidiabetiese midels wat voorgeskryf word. Dit was ook bereken dat die gemiddelde koste van die antidiabetiese middels tussen 21.0% en 28.0% laer was in 2004 as in 1996 – 'n aanduiding dat , ongeag inflasie, die antidiabetiese middels goedkoper was in 2004 as agt jaar gelede in 1996. Dit was ook bereken dat die totale koste besparings vir antidiabetiese middels R1 448 682.26 kon beloop het indien die laer prys vir antidiabetiese middels geimplimenteer was gedurende die periode Januarie tot April. Laastens is daar ook bereken dat verdere koste besparings moontlik kon gewees het indien al die innoveerder antidiabetiese produkte vervang was met die goedkoper generiese antidiabetiese produk.

Opsomming

TABLE OF CONTENTS p.

LIST OF TABLES AND FIGURES p.

List of tables

LIST OF FIGURES

CHAPTER 1: Introduction and problem statement

1.1 INTRODUCTION

This dissertation will focus on the usage and cost of antidiabetic drugs, according to the database of a medicine claims database. The data of the year, 1 January 2004 to 31 December 2004, will be used to investigate the usage and cost of antidiabetic drugs in the private health care sector in South Africa.

1.2 PROBLEM STATEMENT

Diabetes is associated with a significant economic burden on health care systems around the world, and it is estimated that diabetes accounts for between 5% to 10% of a nation's health care budget (O'Dowd, 2002: 12). According to a report of the World Health Organization (WHO), diabetes mellitus is described as one of the most daunting challenges posed by chronic diseases, and that by 2025 the estimated number of people with diabetes will be approximately 300 million worldwide. (Anon : 1997 (cited by Truter, 1998: 417). In 1999 diabetes rated sixth as leading cause of disease-related deaths in the US and for every 7 dollars spent on health care, 1 dollar was spent on behalf of a person with diabetes (Stone, 1999: 146).

In Africa it is expected that the number of people living with diabetes will triple within the next 10 to 15 years. It is estimated that 3.5 to 4.0% of the white population of South Africa, 5 to 8% of the black population, 8 to10% of the coloured population and 13 to18% of Indians are diabetic (Anon : 1997 (cited by Truter, 1998: 417).

There is an increase in the number of diabetic patients and this will certainly exercise an influence on the prescribing and utilisation patterns of antidiabetic drugs. That there probably are still many undiagnosed cases, also has to be taken into account.

Other factors contributing to the high cost of the disease are expenditures for managing the disease itself, such as drugs and related supplies. Every person with diabetes faces a lifetime of treatment and monitoring of their disease, as well as treatment for any other health care problem they may develop. This places a considerable financial burden on patients, health care organisations as well as on health care systems worldwide (O'Dowd, 2002: 12, Stone, 1999: 146).

In her thesis, Truter (1998: 417), by reviewing the literature, stated that the estimated cost for diabetes in the USA in 1992 was between $92 billion and $105 billion every year. She also stated that if the same calculations were to be applied to South Africa, it could cost as much as R7 billion in 1998.

In general South Africa is facing serious problems in both the public and private health care sectors. Health care expenditure has been one of the fastest growing sectors of the South African economy (Manual, 1997). Medicines consume a considerable part of the health care expenditure in the country (Department of Health, 1996). Control of health care expenditure in the next decade will be one of the major challenges facing the South African economy. In the private sector, medicine is the single biggest cost driver. During 1998, medical schemes paid out a total of R18.745 billion of which medicine accounted for 27% (Department of Health, 1998). However, of the 28.5% of payments that were made to private hospitals, some were also for medicines used by inpatients and issued as discharge medication. Despite substantial spending on medicine, lack of access to essential medicine, irrational use of medicine, and poor quality, serious global public health problems remain (Brundtland, 1999).

In an attempt to contain rising pharmaceutical expenditure in the private health care sector, different mechanisms have been implemented such as generic substitution, a reference-based pricing system, prescribed minimum benefits and formularies.

On the 4th November 2002, changes to the Regulations of the Medical Schemes Act (Act no. 131 of 1998) were published, some of which have been implemented in 2003. On 1 January 2004 the remaining changes to the Regulations were implemented which include the introduction of Prescribed Minimum Benefits (PMBs) of the Chronic Disease List (CDL). The Chronic Disease List is a list of 27 chronic conditions, which have to be covered by all medical schemes from January 2004 (Council for Medical Schemes, 2003). Diabetes is one of the 27 chronic conditions. The Prescribed Minimum Benefits are minimum benefits which by law must be provided to all medical scheme members, including the provision of diagnosis, treatment and care costs for a range of conditions specified in the Regulations of the Medical Schemes Act (No 131 of 1998). The PMBs for the CDL differ from the general list of PMBs in that their minimum treatment is specified in the therapeutic algorithms, which have been legislated for each condition (Council for Medical Schemes, 2003).

Another factor that may influence the usage and cost of antidiabetic drugs is generic substitution. It is commonly known that most generic products are relatively cheaper than the branded product.

There are clearly potential problems with generic substitution, for example insufficient dosage, in any disease in which even small changes in the rate, pattern, or extent of drug absorption can alter the therapeutic outcome. This is particularly true in cases where changes in clinical conditions are both common and difficult to quantify, and compliance with dosing regimens is critical (Walson, 2003: 1539). It is therefore important that patients receive the correct information regarding generic substitution.

The influence of generic substitution, a reference-based pricing system, prescribed minimum benefits and formularies on the usage patterns and cost of antidiabetic drugs will be investigated in this study.

1.3 RESEARCH QUESTIONS

The following research questions can be formulated from the foregoing discussion:

a. What is diabetes mellitus?
b. What does managed care entail?
c. What does pharmaco-economics entail?
d. What does drug utilisation review entail?
e. What is the treatment cost of Diabetes Mellitus in South Africa?
f. How many different types of antidiabetic drugs are available in South Africa and how are they classified?
g. Which antidiabetic drug is most commonly used in South Africa?
h. What are the utilisation patterns of the different types of antidiabetic drugs in South Africa?
i. What does the pricing system of medicine, proposed by the Department of Health in 2004, entail?
j. How does the proposed pricing system of medicine influence the cost of antidiabetic drugs?
k. What is meant by the prescribed minimum benefits (PMBs) for chronic diseases?
l. How do the prescribed minimum benefits for the chronic disease list influence the usage of antidiabetic drugs?
m. How do the PMBs for the chronic disease list influence the cost of antidiabetic drugs?
n. How does generic substitution influence the usage and cost of antidiabetic drugs?
o. Which recommendations may be formulated regarding the usage of antidiabetic drugs?

1.4 REASERCH OBJECTIVES

This research project includes general as well as specific objectives.

1.4.1 General objective.

The general objective of this study is to review the usage and cost of antidiabetic drugs by following a managed care approach.

1.4.2 Specific objectives.

The specific objectives from the literature are to

- review diabetes mellitus as an illness and its treatment from the literature; and
- review pharmaco-economics, managed health care and drug utilisation review from the literature.

The specific objectives that are going to be addressed from the empirical study are as follows

- Determine the prevalence and medicine treatment cost of diabetes according to the database of a prescription claims database.
- Analyse the prescription patterns for different types of antidiabetic drugs according to the database.
- Investigate the influence of the new pricing structure on the cost of antidiabetic drugs according to the data of a prescription claims database.
- Determine the influence of generic substitution on the usage patterns and cost of antidiabetic drugs from a database.

1.5 RESEARCH METHOD.

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

1.5.1 Phase one: Literature review.

The literature review can be divided into two steps. The first step is a discussion of diabetes mellitus and the treatment thereof and the second is a discussion of medicine cost in South Africa, managed care, pharmaco-economics and drug utilisation review.

In the first step an overview of the diagnosis, pathogeneses and complications of the disease will be given and the different treatment algorithms will be discussed.

In the second step, managed care, pharmaco-economics and drug utilisation will be defined and discussed with special reference to the usage patterns of antidiabetic drugs. Factors that contribute to the high cost of antidiabetic medicine in the private health care sector in South Africa, as well as the mechanisms that were implemented to contain rising pharmaceutical expenditure, will be discussed briefly.

1.5.2 Phase two: Empirical investigation.

This phase consists of five phases, namely:

i. The selection of the study population
ii. The selection of the measuring instruments
iii. Data analysis
iv. The report and discussion of the results of the empirical investigation
v. Recommendations based on the results of the empirical investigation.

A retrospective drug utilisation study will be done on data provided by the database of a prescription claims database. Comparisons and analyses will be done for the year 1 January 2004 to 31 December 2004, using the Statistical Analysis System (SAS for Windows, 8.2, 2003). The one year period will be divided into three study periods, namely January to April, May to August and September to December.

1.6 DIVISION OF CHAPTERS.

Chapter 2: Aspects of diabetes mellitus.
Chapter 3: Managed care, pharmaco-economics and drug utilisation review: an overview.
Chapter 4: Empirical Investigation
Chapter 5: Results and discussion
Chapter 6: Conclusions, recommendations and limitations

1.7 SUMMARY

In this chapter an overview of the problem statement was presented. A few research questions were stated and the general and specific research objectives were formulated. The research method was described as well as the division of chapters.

In the next chapter an overview of Diabetes Mellitus as a chronic disease will be given as well as the aetiology, pathophysiology, epidemiology and management of the disease.

CHAPTER 2: Aspects of diabetes mellitus.

2.1 INTRODUCTION

In chapter 1 the planning, approach and scope of this study were discussed. This chapter focuses on diabetes mellitus as a chronic disease. Diabetes Mellitus will be defined and classified and the epidemiology, symptoms, signs, complications and pathology of the disease will be discussed shortly.

2.2 DEFINITION AND CLASSIFICATION

2.2.1 Definition of Diabetes Mellitus

The term "*diabetes*," meaning "*siphon*" or "*running through*," was used by the Greeks over 2000 years ago to describe the increased urinary volume excreted by people suffering from this disease. "*Mellitus*" meaning "*sweet*" distinguishes this urine from the large quantities of non-sweet ("insipid") urine produced by persons suffering from vasopressin deficiency (Vander *et al.*, 1998:604)

The Merck Manual (1992:1106) defines diabetes as "a syndrome characterised by hyperglycaemia resulting from impaired insulin secretion and/or effectiveness, associated with risks for diabetic ketoacidosis (DKA) or non-ketotic hyperglycaemic-hyperosmolar coma (NKHHC) and a group of late complications including retinopathy, nephropathy, atherosclerotic coronary and peripheral arterial disease, and peripheral and autonomic neuropathies" (Berkow, 1992:1106).

According to Rippey (1994:303) diabetes can also be defined as a chronic metabolic disorder in which there is a relative or absolute lack of insulin, or failure of its action. The carbohydrate metabolism is thus impaired, diagnostically featuring as a raised blood glucose level.

Beers (2004) described diabetes mellitus as a disorder in which blood sugar (glucose) levels are abnormally high because the body does not produce enough insulin.

For the purpose of this study, diabetes mellitus can be defined as a deviation of the carbohydrate metabolism, where the sugars cannot produce energy due to the lack of the pancreatic enzyme insulin.

2.2.2 Classification of Diabetes

"Diabetes mellitus" refers to a spectrum of conditions, which all present with hyperglycaemia as a common medical finding. Diabetes was once thought of as a single disease, but according to Setter *et al.* (2000:378), it includes a heterogeneous group of disorders that are secondary to various genetic predispositions and precipitating factors.

The first widely accepted classification of diabetes mellitus was published by the World Health Organisation (WHO) in 1980 and, in modified form, in 1985. The 1980 and 1985 classifications of diabetes mellitus and allied categories of glucose intolerance included clinical classes and two statistical risk classes. The 1980 Expert Committee proposed two major classes of diabetes mellitus; namely Insulin Dependant Diabetes Mellitus (IDDM) or Type 1 diabetes and Non Insulin Dependant Diabetes Mellitus (NIDDM) or Type 2 diabetes. In 1985 a new class of Malnutrition-related Diabetes Mellitus (MRDM) was introduced (Alberti & Zimmet, 1998:543).

In both the 1980 and 1985 reports other classes of diabetes were included, namely "Other Types"; "Impaired Glucose Tolerance (IGT)" as well as Gestational Diabetes Mellitus (GDM). This classification system allows for the classification of individual subjects and patients in a clinically useful manner even in cases where the specific cause or aaetiology is unknown. A new complementary classification system according to aaetiology is needed. However, according to this new classification system, all subjects with diabetes mellitus will be categorised according to clinical stages, which will be achievable in all circumstances. The stage of glycaemia may change over time depending on the extent of the underlying disease processes. The aetiological classification reflects the fact that the defect process, which may lead to diabetes, may be identifiable at any stage in the development of diabetes, even at the stage of normoglycaemia (Alberti & Zimmet, 1998:543).

Classifying the patient with diabetes into one of several categories in which hyperglycaemia is a clinical finding, is critical in developing a patient-specific treatment regimen. Table 2.1 summarises the new aetiological classification system with the updated terminology, adapted from Setter *et al.* (2000:378).

Table 2.1: Diabetes Mellitus: Aetiological Classification (adapted from Setter *et al.*, 2000:378)

1. Type 1 diabetes (β-cell destruction, usually leading to absolute insulin deficiency)
   - A. Immune mediated
   - B. Idiopathic
2. Type 2 diabetes (accompanied by insulin resistance)
3. Other specific types
   - A. Genetic defects of β-cell function
     1. Chromosome 12, HNF-1α (formerly maturity-onset diabetes of the youth)
     2. Others
   - B. Genetic defects in insulin action
     1. Type A insulin resistance
     2. Leprechaunism
     3. Others
   - C. Diseases of the exocrine pancreas
     1. Pancreatitis
     2. Neoplasia
     3. Cystic fibrosis
   - D. Endocrinopathies
     1. Acromegaly
     2. Cushing's syndrome
     3. Pheochromocytoma
     4. Others
   - E. Drug or chemical induced
     1. Nicotinic acid
     2. Glucocorticoids
     3. Thiazides
     4. Others
   - F. Infections
     1. Congenital rubella
     2. Cytomegalovirus
     3. Others
   - G. Uncommon forms of immune-mediated diabetes
     1. Stiff-man syndrome
     2. Anti-insulin receptor antibodies
     3. Others
   - H. Other genetic syndromes sometimes associated with diabetes
     1. Down's syndrome
     2. Klinefelter's syndrome
     3. Turner's syndrome
     4. Others
4. Gestational diabetes mellitus

2.2.2.1 Clinical types of diabetes

2.2.2.1.1 Insulin-Dependant Diabetes Mellitus: Type 1

Type 1 diabetes mellitus (DM) accounts for 10 to 15% of all cases of diabetes mellitus and is clinically characterised by hyperglycaemia and a propensity to diabetic keto-acidosis. Its control requires chronic insulin treatment. Although it may occur at any age, it most commonly develops in childhood or adolescence and is the predominant type of diabetes mellitus diagnosed before age 30 (Beers & Berkow, 2004).

In these patients, type 1 DM results from a genetically susceptible, immune-mediated, selective destruction of more than 90% of their insulin-secreting β-cells. Their pancreatic islets exhibit insulitis, which is characterised by an infiltration of T-lymphocytes accompanied by macrophages and B-lymphocytes and by the loss of most of the β-cells, without involvement of the glucagons-secreting α-cells. Cell-mediated immune mechanisms are believed to play the major role in the β-cell destruction. The antibodies present at diagnosis usually become undetectable after a few years. The clinical onset of type 1 DM may occur in some patients years after the insidious onset of the underlying autoimmune process (Beers & Berkow, 2004).

It has been postulated that in the most common form of IDDM (type 1A), environmental factors such as certain viral infections and possible chemical agents superimposed on genetic factors may lead to cell-mediated autoimmune destruction of β-cells (Beers & Berkow, 2004).

Masharani and Karam (2001:1161) stated that diabetes mellitus type 1 is a catabolic disorder in which circulating insulin is virtually absent, plasma glucagon is elevated, and the pancreatic β-cells fail to respond to all insulinogenic stimuli. Exogenous insulin is therefore required to reverse the catabolic state, prevent ketosis, reduce the hyperglucaemia, and reduce blood glucose.

According to Fajans (1990:348), the second type of insulin-dependant diabetes (type 1B) occurs less commonly and in approximately 10% of all cases of IDDM. Primary autoimmunity is thought to be involved in the pathogenesis of this form of diabetes. Patients with this type of IDDM are believed to have associated autoimmune diseases. They also have a higher prevalence of family history of endocrine and non-endocrine autoimmune disease.

2.2.2.1.2 *Non-insulin Dependant Diabetes Mellitus: Type 2*

This form of diabetes is clinically characterised by hyperglycaemia that is not associated with a propensity to DKA, but some patients intermittently or persistently require insulin to control or prevent symptomatic degrees of hyperglycaemia, which might lead to NKHHC. Type 2 DM is usually the type diagnosed in patients older than 30 years of age. It is also commonly associated with obesity (Berkow, 1992:1108).

According to the Merck Manual of Diagnosis and Therapy 16th edition (1982) type 2 DM is a heterogeneous group of disorders in which hyperglycaemia results from both an impaired insulin secretory response to glucose and decreased insulin effectiveness called insulin resistance.

Persistent hyperglycaemia has a "toxic" effect on β-cells, which may augment the primary abnormality in insulin secretion and explain why many type 2 DM patients show some improvement in the insulin secretory response to ingested glucose after a period of vigorous insulin control of the hyperglycaemia or aggressive diet therapy (Berkow, 1992:1108).

Patients with type 2 DM may have a body weight that ranges from normal to excessive. The intake of excessive calories leading to weight gain and obesity and resulting in insulin resistance are important factors in the pathogenesis of non-insulin dependant diabetes mellitus in the majority of patients. A genetic defect in the insulin secretory response to nutrients may be brought out for the first time when increasing insulin resistance calls forth a compensatory response that cannot be met (Fajans, 1990:348).

NIDDM patients exhibit decreased insulin effectiveness in restraining hepatic glucose output and in stimulating glucose uptake by skeletal muscle, which are important in normal plasma glucose regulation. Obesity and inadequate insulin secretion can cause similar manifestations of insulin resistance, and the existence of a primary genetically determined insulin resistance in most NIDDM patients is controversial (Berkow, 1992:1109). The insulin resistance does not appear to result from genetic alterations in insulin receptor numbers or function, but a role for genetically determined post receptor defects is possible. In obese NIDDM patients, improvement in the insulin secretory response to glucose is frequently observed after a period of weight reduction associated with decreased hyperglycaemia or after rigorous insulin treatment (Berkow, 1992:1109).

Table 2.2 summarises the general characteristics of the major clinical types of diabetes mellitus as adapted from Beers and Berkow (2004).

Table 2.2: Distinguishing features of the two major types of diabetes (adapted from Beers & Berkow, 2004:1).

	Type 1 Diabetes mellitus (IDDM)	Type 2 Diabetes mellitus (NIDDM)
Age of onset	Most commonly <30 years	Most commonly >30 years
Associated obesity	No	Very common
Propensity to keto-acidosis requiring insulin for its control	Yes	No
Endogenous insulin secretion	Extremely low to undetectable plasma insulin and C-peptide levels	Significant but variable levels of insulin secretion that are low relative to plasma glucose levels and accompanied by insulin resistance
Twin occurrence	<50%	>90%
Associated with specific Human lymphocyte antigens (HLA)-D antigens	Yes	No
Islet cell antibodies at diagnosis	Yes	No
Islet pathology	Insulitis, selective loss of most β-cells	Smaller, normal-appearing islets; amyloid deposition is common
Associated risks for retinopathy, nephropathy, athrosclerotic coronary and peripheral vascular disease in most Western populations	Yes	Yes
Hyperglycaemia responds to sulfonylureas	No	Yes, initially in many patients

2.2.2.1.3 Other types of Diabetes Mellitus

- Pancreatic disease

Pancreatic disease includes transient diabetes of the newborn, surgical removal of more than nine tenths of the pancreas, pancreatitis, pancreatic calculi with fibrosis, cystic fibrosis, cancer of the pancreas, hemochromatosis, and toxic damage to the pancreas (Marble & Ferguson, 1985:335).

- Hormonal overactivity

In a wide variety of disturbances of endocrine organs, hyperglycaemia may occur and require treatment. If the condition of the endocrine gland is one of hyperactivity and if appropriate treatment is possible against that, the diabetes may be cured (Marble & Ferguson, 1985:335).

- Drug and chemically induced conditions

Marble and Fergusson (1985:335) stated that an extremely wide variety of drugs and chemical agents may elevate the blood glucose or exacerbate an already established hyperglycaemia. In most instances the chemical agents used as medicines have only a slight effect, but the more potent types include the thiazides, diazoxide, and streptozotocin as well as some hormonally active agents (Marble & Ferguson, 1985:335).

- Insulin receptor abnormalities

Insulin receptor abnormalities include a defect in the receptor, congenital lipodistrophy, acanthosis nigricans associated with virilisation, and antibodies to insulin receptor-associated immune disorders (Marble & Ferguson, 1985:335).

- Genetic syndromes

Rare cases of diabetes mellitus, with the clinical characteristics of NIDDM, result from the heterozygous inheritance of a defective gene, leading to secretion of insulin that does not bind normally to the insulin receptor. These patients have greatly elevated plasma immunoreactive insulin (IRI) levels associated with normal plasma glucose responses to exogenous insulin (Berkow, 1992:1109).

2.2.2.2 Impaired glucose tolerance

The diagnosis for impaired glucose tolerance (IGT) is suggested for patients in whom the fasting plasma glucose level is lower than that required for the diagnosis of diabetes, but in whom, during an oral glucose tolerance test, the 2-hour value lies between ≥ 140 and > 200 mg/dl, i.e. between normal and diabetic values (Marble & Ferguson, 1985:335).

In some persons impaired glucose tolerance may represent a stage in the natural history of IDDM, and more frequently of NIDDM as recognised by prospective testing. In such patients, conversion of IGT to NIDDM, has taken years or decades. It has been found to occur in 10% to 50% of patients with IGT followed for a period of ten years. Thus, in a substantial proportion of various population groups, impaired glucose tolerance either does not progress or it reverts to normal glucose tolerance (Fajans, 1990:350).

Impaired glucose tolerance is not a clinical entity in its own right, but rather a risk category for future diabetes and/or cardiovascular diseases. IGT is often associated with the metabolic Insulin Resistance Syndrome (Alberti & Zimmet, 1998:545).

IDDM is characterised by decreased glucose tolerance due to decreased secretion of insulin in response to the glucose challenge. This is manifested by elevated blood glucose levels and glycosuria and may be accompanied by changes in fat metabolism. Tolerance to glucose declines not only in type 1 diabetes, but also in conditions where the liver is damaged; in some infections; in type 2 diabetes, which is often associated with obesity and raised levels of plasma free fatty acids; under the influence of some drugs; and sometimes in atherosclerosis (Mayes, 2000:217).

A few individuals produce antibodies directed against the insulin receptors. These antibodies prevent insulin from binding to the receptor, causing the person to develop insulin resistance syndrome. Hyperinsulinism and a syndrome characterised by severe hypoglycaemia can be caused by tumors of ß-cell origin.(Granner, 2000:622).

2.2.2.3 Gestational Diabetes

According to Albert and Zimmet (1998:546) gestational diabetes is a carbohydrate intolerance resulting in hyperglycaemia of variable severity with onset or first recognition during pregnancy. The definition applies irrespective of whether or not insulin is used for treatment or the condition persists after pregnancy. However, it does not exclude the possibility that the glucose intolerance may antedate pregnancy. This, however, has previously been unrecognised. Women who became pregnant and who are known to have diabetes mellitus, which antidate's pregnancy, are regarded as cases with "diabetes mellitus and pregnancy", and not as patients with gestational diabetes. These patients should be treated accordingly before, during, and after pregnancy.

Older women, women with a previous history of glucose intolerance, women of certain high-risk ethnic groups, and any pregnant women who have elevated fasting, or casual, blood glucose levels are at high risk for gestational diabetes. According to Alberti and Zimmet (1998:547) pregnant women belonging to high-risk populations should therefore be screened for diabetes during the first trimester of pregnancy in order to detect previously undiagnosed DM (Albert & Zimmet, 1998:547).

2.2.2.4 Risk classes

There are individuals with normal glucose tolerance who have had an abnormality of glucose tolerance in the past, or who have a close genetic relationship with a diabetic and have a high risk of developing diabetes in future. These individuals can be classified in one of two statistical risk classes namely: "previous abnormality of glucose tolerance", and, "potential abnormality of glucose tolerance" (Fajans, 1990:350).

- Previous abnormality of glucose tolerance (PreAGT)

This classification is restricted to individuals who previously had diabetic hyperglycaemia or impaired glucose tolerance but who presently have normal glucose tolerance, for example patients who had gestational diabetes but have returned to normal glucose tolerance after parturition, or patients who were obese and whose diabetes or impaired glucose tolerance returned to normal after losing weight (Fajans, 1990:351).

- Potential abnormality of glucose tolerance (PotAGT)

Patients in this class of PotAGT have never exhibited normal glucose tolerance but have substantially increased risk for the development of diabetes. PotAGT identifies the interval of time from conception until the first demonstration of impaired glucose tolerance in an individual predisposed to diabetes on genetic grounds. A particularly strong risk for developing NIDDM is being a monozygotic twin of a NIDDM patient or an offspring of two diabetic parents. PotAGT is included in the classification to identify individuals and groups of individuals for prospective research studies (Fajans, 1990:351).

2.3 PATHOPHYSIOLOGY

In patients without diabetes, insulin acts in concert with glucagon, somatostatin, growth hormone, corticosteroids, epinephrine, and parasympathetic innervation to maintain blood glucose between 40 and 169mg/dL at all times (Setter *et al.*, 2000:380).

Three cell types, α-cells, β-cells, and δ-cells, have been identified in the islets of Langerhans of the pancreas. The α-cells produce glucagon, the β-cells produce, store, and release insulin, and the δ-cells produce somatostatin, which inhibits both insulin and glucagon secretion and suppresses growth hormone. Glucagon is a hormone that acts to increase blood glucose levels. The suppression of glucagon by somatostatin decreases blood glucose levels, and its effect persists for roughly 60 to 120 minutes. The presence of insulin favours the uptake and use of glucose by insulin-sensitive sites. In skeletal muscle, glucose uptake and subsequent energy production increase. In the liver, glucose uptake and the formation of glycogen increase in the presence of insulin (Setter *et al.*, 2000:382).

Insulin is released from the pancreatic β-cells at a low basal rate and at a much higher stimulated rate in response to a variety of stimuli, especially glucose. Other stimulants such as other sugars, certain amino acids, and vagal activity are also recognised. Figure 2.1 describes one model of control of insulin release from pancreatic β-cells by glucose and sulfonylurea drugs (Nolte & Karam, 2001:713).

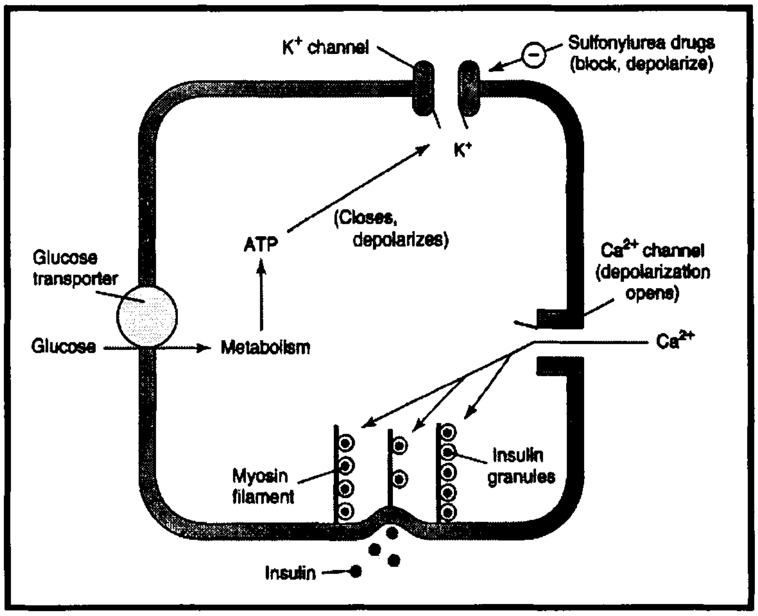


Figure 2.1 Model of control of insulin release (Nolte & Karam, 2001:713).

In the resting cell with normal (low) adenosine triphosphate (ATP) levels, potassium diffuses down its concentration gradient through ATP-gated potassium channels (ATP closes the channels), maintaining the intracellular potential at a fully polarised, negative level. Insulin release is minimal. If glucose concentration rises, ATP production increases, potassium channels close, and depolarisation of the cells results. As in muscle and nerve, voltage-gated calcium channels open in response to depolarisation, allowing more calcium to enter the cell. Increased intracellular calcium results in increased insulin secretion. Sulfonylurea hyperglycaemic drugs block the ATP-dependant potassium channel, thereby depolarising the membrane and causing increased insulin release by the same mechanism (Nolte & Karam, 2001:713).

2.3.1 General aetiology of Diabetes Mellitus

The aetiology of diabetes is incompletely understood, and numerous factors are associated with the development of the disease. Some of the factors linked with the development of diabetes are obesity, increasing age, heredity, emotional stress, autoimmune β-cell damage, endocrine disease, viral stress, vasculitis in tissues highly perfused with capillaries, insulin receptor or post-insulin receptor defects, and drugs (e.g., corticosteroids, thyroid agents, phenytoin, diazoxide, thiazides, and other diuretics etc.). Patients with type 1 diabetes have a defect in pancreatic β-cell function related to faulty genetics or other external factors. These extrinsic factors affecting β-cell function include damage caused by viruses such as mumps or Coxsackie B4, by destructive cytotoxins and antibodies released by sensitised lymphocytes, or by autodigestion in the course of an inflammatory disorder involving the exocrine pancreas (Setter *et al.*, 2000:380).

2.3.2 Aetiology of type 1 Diabetes Mellitus

Type 1 diabetes mellitus results from a T-cell-mediated autoimmune process that destroys the insulin-producing ß-cells of the pancreas. The cells, along with other types of cells, are contained in small islands of endocrine cells called the pancreatic islets (Kaufman, 2003:161).

Type I diabetes begins with a long asymptomatic stage characterised by insulitis. Insulitis can be described as an inflammatory infiltration of the islets that selectively destroys the ß-cells while leaving other cell types in the islet largely intact. The autoimmune process can be detected years before the onset of disease by the presence of cell-reactive T-cells and auto-antibodies in the blood, allowing the identification of prediabetic individuals and possible therapeutic intervention (Kaufman, 2003:161).

2.3.3 Aetiology of type 2 Diabetes Mellitus

Many patients with type 2 diabetes have excess insulin secretion and are obese. In addition to hyperinsulinemia and obesity, many patients with type 2 diabetes have hypertension, dyslipidemia, and impaired fibrinolysis, a collection of conditions called syndrome X. Patients with syndrome X, are more likely to experience cardiovascular diseases and develop long-term complications of diabetes. Hyperinsulinism and insulin resistance may be correlated with a decrease in insulin binding or post-insulin receptor signalling defects (Setter *et al.*, 2000:380).

Patients with type 2 diabetes and insulin resistance demonstrate the following two major metabolic defects: a decreased sensitivity of target tissues (primarily the liver and skeletal muscle) to the actions of insulin and a relative deficiency of endogenous insulin secretion. Because the peripheral tissues (liver and muscle) are less able to respond to insulin, patients secrete higher levels of insulin in an attempt to compensate for the diminished activity of insulin, and plasma glucose levels rise. Impaired insulin secretion and increased glucagons contribute to continued hepatic glucose output, resulting in elevated fasting glucose levels (Setter *et al.*, 2000:380).

2.4 EPIDEMIOLOGY

According to the World Health Organisation (WHO, 2004), there were an estimated 176 million people in the world in the year 2000 living with diabetes. Estimates then projected that the number would almost double to 370 million in the year 2030.

According to a study by the South African Department of Health (2003) the burden of this disease in South Africa, measured in number per 100 000 population, was relatively high compared to all other regions of the world (excluding other African regions). America had the highest incidence of people that suffer from Diabetes Mellitus; e.g. 421 per 100 000, followed by South Africa with 390 people per 100 000. Other countries with significant incidence were South East Asia, the Eastern Mediterranean, and European countries.

According to the Medical Research Council of South Africa (MRC) the top ten specific causes of death in South Africa in 2000 were: HIV/Aids, ischaemic heart disease, homicide and violence, stroke, tuberculosis, lower respiratory tract infections, road traffic accidents, diarrhoeal diseases, hypertensive heart disease and DM. Diabetes accounted for 2.4% of the total 556 586 deaths in South Africa in 2000 and for 3.2% of deaths amongst women in the same year (MRC South Africa, 2001).

Key Health Statistics from the Department of Health (2003), which summarises the number of people living with diabetes in each of the nine provinces (per 100 000) in South Africa, indicated that the Gauteng province had the highest incidence of Diabetes Mellitus, followed by the Eastern Cape and Kwa Zulu Natal. Limpopo province had the lowest incidence (refer to table 2.3).

Table 2.3 Diabetes Mellitus incidence (per 100000) amongst the population in the different provinces (adapted from SA Department of Health Monitoring and Evaluation Unit 2003).

Province	**Total number of people (per 100 000)**
Limpopo	397
Free State	781
North West	820
Western Cape	1238
Northern Cape	1254
Mpumalanga	1278
Kwa Zulu Natal	1706
Eastern Cape	2011
Gauteng	2605
Total	**12090**

The incidence of diabetes amongst women was also much higher compared to that of their male counterparts in a study of self-reported chronic conditions conducted by the Monitoring and Evaluation unit of the Department of Health (Key Health Statistics of 2003). Incidence amongst females in the Western Cape and Northern Cape was 57% (n=1238) and 58% (n=1254) respectively. In Mpumalanga the incidence amongst females calculated to 65%; and in the Free State, Kwa Zulu Natal and North West provinces, 77% were female. In the Limpopo province all self-reported cases of diabetes was from female patients, but in Gauteng, only 37%

of diabetic patients that reported diabetes were female (South Africa Department of Health Monitoring and Evaluation Unit, 2003).

According to the South African Department of Health (1998) 17.9% of the male respondents that reported diabetes as a chronic condition were in the age group 45 years and older. When the ethnicity of the patients is considered, 8.5% and 6.0% of the respondents that reported diabetes amongst men are respectively asians and whites.

The highest incidence amongst women who reported diabetes as a chronic condition was also in the age group 45 years and older (i.e. 23.7%). From these patients, 11.5% and 5.8% were from asian and coloured ethnic groups respectively (Department of Health, 1998).

2.5. CLINICAL PRESENTATION AND DIAGNOSIS

2.5.1 Type 1 Diabetes Mellitus

According to Masharani and Karam (2001:1165), type 1 diabetes presents with a characteristic symptom complex. An absolute deficiency of insulin results in accumulation of circulating glucose and fatty acids, with consequent hyperosmolality and hyperketonemia.

Type 1 diabetes mellitus is usually easy to diagnose because patients present with all off the classic symptoms of diabetes and high amounts of glucose in the urine and blood. The classic symptoms include polydipsia, polyuria, polyphagia, weakness, weight loss, dry skin and ketoacidosis (Setter *et al.*, 2000:384).

Type 1 diabetes mellitus can also be associated with increased urination due to osmotic diuresis secondary to sustained hyperglycaemia. This results in a loss of glucose as well as free water and electrolytes in the urine. Thirst is a consequence of the hyperosmolar state, as is blurred vision, which often develops as the lenses and retinas are exposed to hyperosmolar fluids. Weight loss despite normal or increased appetite is a common feature of type 1 when it develops subacutely. The weight loss is initially due to depletion of water, glycogen, and triglycerides; thereafter, reduced muscle mass occurs as amino acids are diverted to form glucose and ketone bodies. Other symptoms that can occur are, hypotension and paresthesias (Masharani & Karam, 2001:1165).

2.5.2 Type 2 Diabetes Mellitus

Patients with type 2 diabetes may or may not present with characteristic features. The presence of obesity or a strongly positive family history of mild diabetes suggests a high risk for the development of type 2 diabetes (Masharani & Karam, 2001:1165).

While many patients with type 2 diabetes present with increased urination and thirst, many others have an insidious onset of hyperglycaemia and are asymptomatic initially. This is particularly true in obese patients, whose diabetes may be detected only after glycosuria or hyperglycaemia is noted during routine laboratory studies. Occasionally, type 2 diabetes may present with evidence of neuropathic or cardiovascular complications because of occult disease present for some time prior to diagnosis. Chronic skin infections are common. Generalised pruritis and symptoms of vaginitis are frequently the initial complaints of women. Obese diabetics may have any variety of fat distribution; however, diabetes seems to be more often associated in both men and women with localisation of fat deposits on the upper segment of the body and relatively less fat on the appendages, which may be quite muscular. Mild hypertension is often present in obese diabetics (Masharani & Karam, 2001:1166).

According to the Merck Manual of Diagnosis and Therapy, an oral glucose tolerance test (OGTT) may be helpful in diagnosing type 2 diabetes mellitus in patients whose fasting glucose is between 115 and 140mg/dL in those with a clinical condition that might be related to undiagnosed diabetes mellitus. Various conditions other than diabetes mellitus, such as effect of drugs and normal ageing, can however cause abnormalities in the OGTT (Beers & Berkow, 2004).

The OGTT is not routinely used for testing for diabetes. In this test, a person fasts, has a blood sample taken to determine the fasting blood sugar level, and then drinks a special solution containing a large, standard amount of glucose. More blood samples are then obtained over the next 2 to 3 hours and are tested to determine whether the level of sugar in the blood rises abnormally high (Beers, 2004).

2.5.3 Asymptomatic Diabetes Mellitus

In asymptomatic patients, diabetes mellitus is established when the diagnostic criterion for fasting hyperglycaemia recommended by the National Diabetes Data Group (NDDG) is met: a fasting overnight glucose level of more than 140mg/dL (≥7.77 mmol/L) on two occasions in an adult or child. Recently, the American Diabetes Association recommended that fasting plasma glucose levels of more than 126mg/dL (>6.99mmol/L) be considered diagnostic for diabetes mellitus (Beers & Berkow, 2004).

The NDDG also recommends criteria for the diagnosis of impaired glucose tolerance patients who do not meet the OGTT diagnostic criteria for DM. Patients with impaired glucose tolerance may be at increased risk of developing fasting or symptomatic hyperglycaemia, but in many patients the condition does not progress or it resolves (Beers & Berkow, 2004).

The diagnostic criteria for the diagnosis of diabetes mellitus according to the NDDG are shown in table 2.4.

Table 2.4 Criteria for the diagnosis of diabetes mellitus (Beers & Berkow, 2004:1)

Symptoms of diabetes plus casual plasma glucose level ≥200mg/dL (≥11.1mmol/L). Casual is defined as any time of day with or without regard to time since last meal. The classic symptoms of diabetes include polyuria, polydipsia, and unexplained weight loss. *OR*
Fasting plasma glucose level ≥126mg/dL (≥7.0mmol/L). Fasting is defined as no caloric intake for at least 8 hours. *OR*
Two-hour plasma glucose level ≥200mg/dL (≥ 11.1mmol/L) during an oral glucose tolerance test using a glucose load containing the equivalent of 75g of anhydrous glucose dissolved in water.

Type 1 diabetes mellitus usually is easy to diagnose because patients present with all of the classic symptoms of diabetes and high amounts of glucose in the urine and blood. Type 2 diabetes is more of a challenge to diagnose because patients often do not present with the classic symptoms. The Expert Committee on the Diagnosis and Classification of Diabetes Mellitus developed screening criteria for the diagnosis of diabetes mellitus in 1997 (Setter *et al.*, 2000:384). Table 2.5 summarises these criteria.

Table 2.5 Screening criteria for Diabetes (Setter *et al.*, 2000:384).

Testing should be considered in all patients age 45 years and older. • Repeat at three-year intervals. Consider testing at younger age or test more often in patients who: • Are obese (≥120% desirable body weight) • Have a first-degree relative with diabetes • Are members of a high-risk ethnic group • Have delivered a baby weighing more than 4.1kg or have been diagnosed with gestational diabetes mellitus • Are hypertensive • Have a high-density lipoprotein cholesterol level ≤ 35mg/dL or a triglyceride level ≥ 250mg/dL • On previous testing had IGT or IFG

2.6 COMPLICATIONS

People with diabetes may experience many serious long-term complications. Some of these complications begin within months of the onset of diabetes, although most tend to develop only after a few years. Most of the complications are progressive. The more tightly a person with diabetes is to control the levels of sugar in the blood, the less likely it is that these complications will develop or become worse (Beers, 2004:3).

Late clinical manifestations of diabetes mellitus include a number of pathologic changes that involve small and large blood vessels, cranial and peripheral nerves, the skin, and the lens of the eye. These lesions lead to hypertension, renal failure, blindness, autonomic and peripheral neuropathy, and amputations of the lower extremities, myocardial infarction, and cerebrovascular accidents. These late manifestations correlate with the duration of the diabetic state subsequent to the onset of puberty. In type 1 diabetes, up to 40% of patients develop end-stage renal disease, compared with the less than 20% of patients with type 2 diabetes. As regards proliferative retinopathy, it ultimately develops in both types of diabetes but has a slightly higher prevalence in type 1 patients. In patients with type 1 diabetes, complications from end-stage renal disease are a major cause of death, whereas patients with type 2 diabetes are more likely to have myocardial infarction and stroke as the main cause of death (Masharani & Karam, 2001:1189).

2.6.1 Hypoglycaemia

Hypoglycaemia is probably the most disliked and feared complication from diabetes's point of view. Children hate the symptoms of a hypoglycaemic episode and the loss of personal control it may cause. Hypoglycaemia is a particular concern in children younger than 4 years because it may lead to possible intellectual impairment later in life (Lamb, 2004:15).

2.6.2 Nephropathy

Diabetic nephropathy is usually asymptomatic until end-stage renal disease develops, but it can cause the nephrotic syndrome prior to the development of uraemia. The cumulative incidence of nephropathy differs between the two major types of diabetes. Diabetic nephropathy develops in about one third of type 1 diabetes mellitus patients and in a smaller percentage of type 2 diabetes mellitus patients (Beers & Berkow, 2004).

Progressive diabetic nephropathy consists of proteinuria of varying severity occasionally leading to nephrotic syndrome with hypoalbuminemia, oedema, and an increase in circulating βlipoproteins as well as progressive azotemia. In contrast to all other renal disorders, the proteinuria associated with diabetic nephropathy does not diminish with progressive renal failure. As renal failure progresses, there is an elevation in the renal threshold at which glycosuria appears (Masharani & Karam, 2001:1190).

Hypertension develops with progressive renal involvement, and coronary and cerebral atherosclerosis seems to be accelerated. Approximately two-thirds of adult patients with diabetes have hypertension. Once diabetic nephropathy has progressed to the stage of hypertension, proteinuria, or early renal failure, glycaemic control is not beneficial in influencing its course. In this circumstance, antihypertensive medications, including angiotension converting enzyme (ACE) inhibitors, and restriction of dietary protein to 0.8g/kg body weight per day are recommended. Improved glycaemic control and more effective therapeutic measures to correct hypertension can reduce the development of end-stage renal disease among diabetics (Masharani & Karam, 2001:1190).

2.6.3 Neuropathy

Diabetic neuropathy commonly occurs as a distal, symmetric, predominantly sensory polyneuropathy that causes sensory deficits. Diabetic polyneuropathy may cause numbness, tingling, and paresthesias in the extremities and, less often, debilitating, severe pain and hyperesthesias. Acute, painful mononeuropathies affecting the 3rd, 4th, or 6th cranial nerve as well as other nerves, occur more frequently in older diabetics. Autonomic neuropathy occurs primarily in diabetics with polyneuropathy and can cause postural hypotension, disordered sweating, impotence and retrograde ejaculation in men, impaired bladder function, delayed gastric emptying, oesophageal dysfunction, constipation or diarrhoea and nocturnal diarrhoea (Beers & Berkow, 2004).

2.6.4 Gangrene

The incidence of gangrene of the feet in diabetics is 20 times the incidence matched in non-diabetics. The factors responsible for the development of gangrene are ischemia, peripheral neuropathy, and secondary infection. Occlusive vascular disease involves both microangiopathy and atherosclerosis of large and medium-sized arteries. The prevention of foot diseases should be emphasised, since treatment is difficult once ulceration and gangrene have developed. Patients should be instructed to inspect their feet daily for reddened areas, blisters, abrasions, or lacerations (Masharani & Karam, 2001:1190).

Foot ulcers and joint problems are important causes of morbidity in diabetes mellitus. The major predisposing cause is diabetic polyneuropathy – the sensory denervation impairs the perception of trauma from such common causes as ill-fitting shoes or pebbles (Beers & Berkow, 2004).

2.6.5 Infections

The risk of infections from fungi and bacteria is increased because of decreased cellular immunity caused by acute hyperglycaemia and circulatory deficits caused by chronic hyperglycaemia. Peripheral skin infections and oral and vaginal thrush are most common, and mycotic infection may be the initial process, leading to wet interdigital lesions, cracks, fissures, and ulcerations that favour secondary bacterial invasion. Patients with infected ulcers frequently feel no pain because of neuropathy (Beers & Berkow, 2004). Table 2.6 summarises the most important complications of uncontrolled diabetes mellitus.

Table 2.6. Long-term complications of diabetes (adapted from Beers, 2004:1).

Tissue or organ affected	What happens	Complications
Blood vessels	Atherosclerotic plaque builds up and blocks large and medium-sized arteries in the heart, brain, legs, and penis. The walls of the small blood vessels are damaged so that the vessels do not transfer oxygen normally and may leak.	Poor circulation causes wounds to heal poorly and can lead to heart disease, stroke, gangrene of the feet and hands, erectile dysfunction, and infection.
Eyes	The small blood vessels of the retina become damaged.	Decreased vision and, ultimately, blindness.
Kidney	Blood vessels in the kidney thicken; protein leaks into the urine; the blood is not filtered normally.	Poor kidney function, kidney failure.
Nerves	Nerves are damaged because glucose is not metabolised normally and because the blood supply is inadequate.	Sudden or gradual weakness of a leg, reduced sensations, tingling, and pain in the hands and feet, chronic damage to nerves.
Autonomic nervous system	The nerves that control blood pressure and digestive processes become damaged.	Swings in blood pressure, swallowing difficulties and altered digestive function, with diarrhoea.
Skin	Poor blood flow to the skin and loss of feeling result in repeated injury.	Sores, deep infections, poor healing.
Blood	White blood cell function is impaired.	Increased susceptibility to infection, especially of the urinary tract and skin.
Connective tissue	Glucose is not metabolised normally, causing tissues to thicken or contract.	Carpel tunnel syndrome, Dupuytren's contracture.

2.7 MANAGEMENT OF DIABETES MELLITUS

2.7.1 Goals of treatment

The goals of therapy for type 2 Diabetes Mellitus include (Bhattacharya, 2001a:10)

- correction of symptoms such as polyuria, nocturia, blurred vision, tiredness, pruritis vulvae in women and balanoposthitis in men;
- prevention of macrovascular and microvascular complications; and
- maintenance of a healthy, cheerful life, free of the fear of DM.

Type 2 Diabetes Mellitus is a complex metabolic disorder, and good diabetic control should include maintaining a normal body mass index, blood pressure and lipid levels. The best way of assessing glycaemic control is by estimating the glycosylated haemoglobin (HbA_{1c}) level. Lowering the HbA_{1c} to less than 2% above the upper limit (or less than 7%, as in the Diabetes Control and Complication Trial [DCCT] standard) should be the goal for which to aim. For some patients, this is difficult and often impractical, such as in the presence of significant co-morbid illness, old age, and in people with a defective state of mind. In routine clinical practice, an HbA_{1c} less than 8% should be acceptable. In certain situations, such as in pregnancy, control should be very strict. It is important to clarify that intensive glycaemic control does not mean multiple insulin injections, the use of insulin pumps or the checking of blood sugar levels 10 times a day, it simply implies that the blood glucose level should be kept as near normal as possible and hypoglycaemia avoided, no matter how simple or complex the treatment regimen is (Bhattacharya, 2001a:10).

A suggested algorithm for the treatment of type 2 diabetes is outlined in figure 2.2.

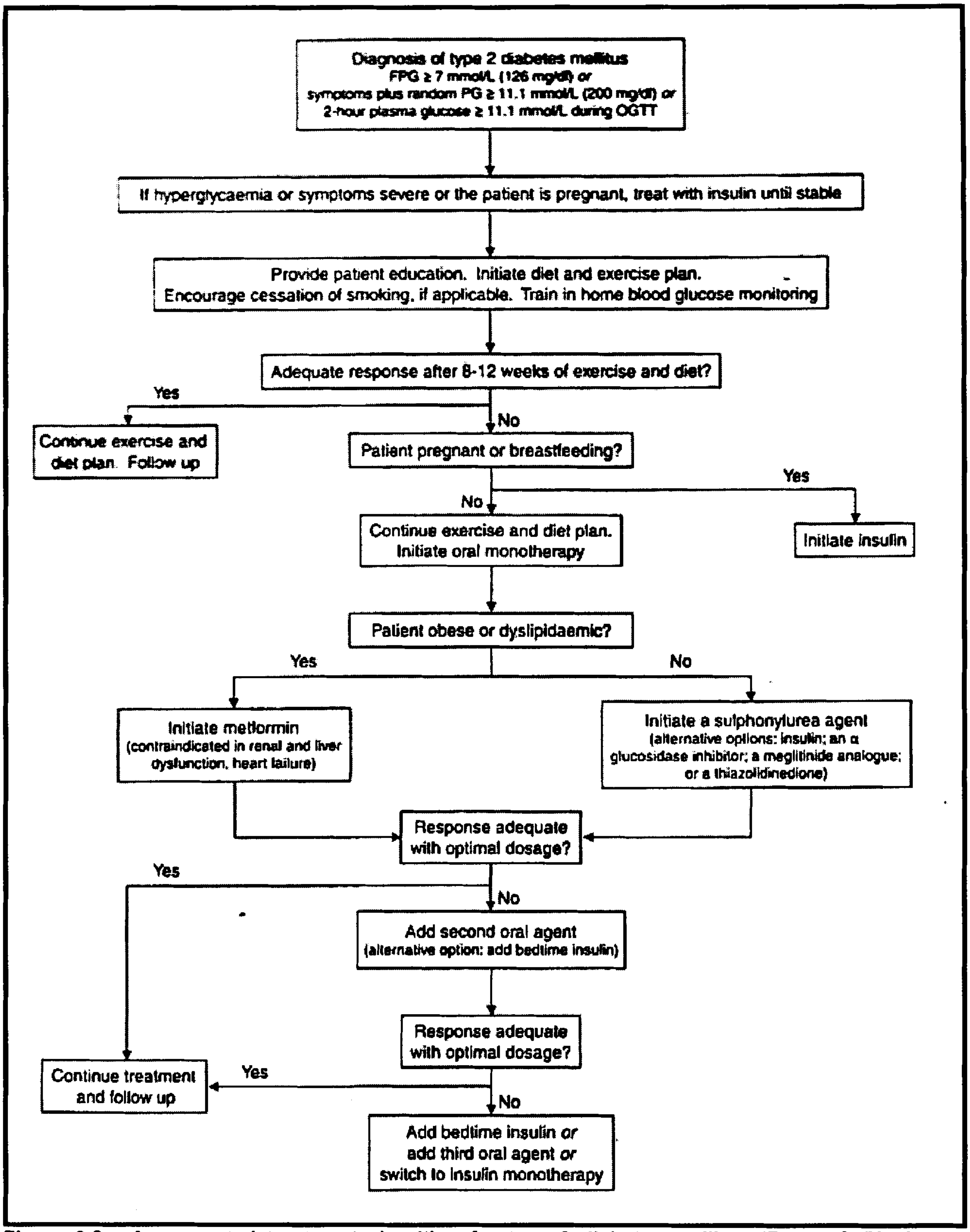


Figure 2.2: A suggested treatment algorithm for type 2 diabetes mellitus (Foster & Plosker, 2000:292).

Recommended treatment goals from the American Diabetes Association are an FPG of 4,4 to 4,7 mmol/L and a glycosylated haemoglobin level <7%. As well as the outlined treatment strategy, insulin may need to be given temporarily to control hyperglycaemia, for instance during acute illness or surgery. FPG = fasting plasma glucose; PG = plasma glucose.

2.7.2 Diabetes self-management

Self-management of diabetes is an important component of a patient's treatment plan. The management plan should be individualised for each patient by considering age, school/work schedule, physical activity, eating patterns, cultural factors, personality, and presence of complications of diabetes or other medical conditions. Goals of the treatment plan should be discussed with patients and their families and health care providers. Patient education is the key to achieving successful self-management of diabetes (Bowes, 2003:7).

2.7.3 Therapy

From a management approach, patients with diabetes fall into three broad groups (Cantrill, 2000:638):

a) The obese and mainly middle-aged or elderly patient in whom carbohydrate and total calorie restriction are sufficient to cause weight loss and produce normoglycaemia. The diabetes cannot be regarded as cured; it may reappear in times of stress or if dietary control is lost. In this group, dietary adherence, appropriate exercise and education may avoid the need for pharmacological intervention.
b) If after two months of dietary restriction the patient with NIDDM remains symptomatic or persistently has a fasting blood glucose level over 10 mmol/L, oral hypoglycaemic agents will be required.
c) All patients with IDDM require a diet containing controlled amounts of carbohydrate and insulin therapy.

In addition, patients require advice on physical activity and lifestyle modification, such as smoking cessation, etc. (Cantrill, 2000:638).

2.7.3.1 Dietary therapy

Dietary control is the mainstay of treatment for NIDDM, and plays an integral part in the management of IDDM. Dietary recommendations have undergone a considerable change in recent years, in both diabetic and non-diabetic populations (Cantrill, 2000:638).

2.7.3.2 Carbohydrates

The blood glucose level is closely affected by carbohydrate intake. Daily intake should be kept fairly constant, and the amount given should be appropriate to the level of physical activity. Most active young people will require 180g of carbohydrate per day, whereas 100g may be sufficient for an elderly person. People with diabetes should limit their sugar intake, but total exclusion from the diet is unnecessary and impractical (Cantrill, 2000:638).

2.7.3.3 Fat

One major reason for increasing the proportion of calories is to reduce fat intake. Since there is an increased risk of death from coronary artery disease in diabetics, it is wise to restrict saturated fats and to substitute unsaturated fats. Obesity is a major problem in diabetes, and fats contain more than twice the energy content per unit weight than either carbohydrates or proteins. About 30% of the total daily calories should be provided in fat. Severe restriction may be indicated for individuals with hypercholesterolaemia (Cantrill, 2000:639).

2.7.3.4 Fibre

Dietary fibre has two useful properties. Firstly, it is physically bulky and increases satiety. Secondly, fibre delays the digestion and absorption of complex carbohydrates, thereby minimising hyperglycaemia. For the average person with NIDDM, 15g of soluble fibre is likely to produce a 10% improvement in fasting blood glucose, glycated haemoglobin and low-density lipoprotein (LDL) cholesterol (Cantrill, 2000:639).

2.7.4 Medicine used for the management of Diabetes Mellitus

The therapeutic options available for the managing of diabetes mellitus have expanded greatly in the past few years. Currently, six categories of Food and Drug Administration (FDA)-approved medications for treating diabetes are available: insulin, sulfonylureas, biguanides, α-glucosidase inhibitors, thiazolidinediones, and meglitinides. All six categories of medicines can treat patients with type 2 DM effectively, but insulin is the only diabetic medication indicated for those with type 1 DM. Because of the recent expansion in the number of antidiabetic drugs available, choosing the optimal medication or combinations for the management of hyperglycaemia in patients with diabetes is not easily reduced to a single treatment algorithm. Treating the patient with diabetes remains an art and entails constant re-evaluation and assessment of the patient's response to proven therapies. Although some situations clearly warrant the use of one product over another, the choice of medications usually is not clear-cut, and cost considerations, amount of glycaemic lowering needed, compliance issues, and the patient's age, weight, and lipid profile, all influence the decision-making process (Setter *et al.*, 2000:394).

2.7.4.1 Insulins and analogues

Insulin has been used since 1922 as monotherapy in patients with type 1 disease and since the late 1950s in combination or monotherapy in patients with type 2 disease. All patients on insulin therapy should be strongly encouraged to self-monitor blood glucose levels. Insulin regimens should be tailored to each patient's individual needs, desired metabolic control, and age. Tighter glycaemic control is best achieved with three or four insulin injections per day or with an infusion pump, although not all patient populations are best served by regimens offering strict glycaemic control (Setter *et al.,* 2000:394).

The time action profile, effects of mixing, species, strength, and cost of insulin all must be considered in choosing insulin. Factors to consider when choosing insulin are the following: kinetic formulation and time activity profile, species source (human, pork, beef), strength [100 units/ml (U-100), 500 units/ml (U-500)], methods of achieving long action, purity, mixability, cost an manufacturer dependability and availability (Setter *et al.,* 2000:394).

In South Africa all varieties of insulin are biosynthetic [produced by using recombinant deoxyribonucleic acid (DNA) technology], and consists of the human molecular structure. Only a single strength, 100 units/mL, is available. Insulins differ in their duration of action, preservative content, and buffering and retarding additives (Gibbon, 2003:71).

2.7.4.1.1 Ultra fast-acting insulins

The latest human insulin analogues have an almost immediate onset of absorption and biological activity, and a reduced period of action. They are clear solutions, usually administered subcutaneously, for example Humalog®, and Novorapid® (Gibbon, 2003:71).

2.7.4.1.2 Fast-acting insulins

These soluble insulins are clear solutions and may be administered intravenously, intramuscularly or subcutaneously. They are administered subcutaneously for the everyday control of diabetes, usually in combination with longer-acting insulin. In diabetic ketoacidosis and during surgery they may be given intravenously. Examples of fast-acting insulins are Actrarapid® HM and Humulin® R (Gibbon, 2003:71).

2.7.4.1.3 Intermediate- to long-acting insulins

These are suspensions and are bound to protamine or zinc as retarding agents to prolong their duration of action. They can only be administered subcutaneously. They are usually administered once, or more commonly twice daily and may be combined with short acting insulins. Older diabetics, previously controlled by diet and oral agents alone, who require additional insulin, may be given a once-daily injection of intermediate or long-acting insulin. Examples of intermediate- to long-acting insulins are Humulin® N and Monotard® HM (Gibbon, 2003:71).

2.7.4.1.4 *Biphasic insulins*

Ready-mixed preparations containing short-acting and intermediate-acting insulin may be useful in many patients and are administered subcutaneously once, or usually twice, daily. An example of a biphasic insulin is Humulin® 30/70 (Gibbon *ed*., 2003:71).

2.7.4.1.5 *Ultra long-acting insulins*

These are conjugated with zinc molecules to delay absorption and prolong the duration of action. They are suitable for once-daily subcutaneous injection, but provide an erratic rate of absorption. An example of an ultra long-acting insulin is Ultratard® HM (Gibbon *ed*., 2003:71).

Table 2.7 summarises the insulin preparations available for the treatment of Diabetes Mellitus.

Table 2.7 Insulin preparations available in South Africa and the approximate expected time-actions (Gibbon *ed.* 2003:71).

Trade name	Manufacturer	Time action Onset	 Peak	 Duration
Ultra fast-acting insulins				
Humalog®	Eli Lily	15 minutes	1 hour	3-4 hours
Novorapid®	Novo Nordisk	10 minutes	45 minutes	3-5 hours
Fast-acting insulins				
Actrapid® HM	Novo Nordisk	30 minutes	2.5-5 hours	8 hours
Humulin® R	Eli Lily	20-30 minutes	1-3 hours	5-7 hours
Intermediate- to long-acting insulins				
Humulin® N	Eli Lily	1 hour	2-8 hours	18-20 hours
Humulin® L	Eli Lily	2 hours	6-8 hours	22-24 hours
Monotard® HM	Novo Nordisk	2.5 hours	7-15 hours	22 hours
Protaphane® HM	Novo Nordisk	1.5 hours	4-12 hours	24 hours
Biphasic insulins				
Actraphane® 30/70 HM	Novo Nordisk	30 minutes	2-12 hours	20-24 hours
Humulin® 30/70	Eli Lily	30 minutes	1-8 hours	14-15 hours
Humalog® Mix25	Eli Lily	15 minutes	0.5-2 hours	14-16 hours
Ultra long-acting insulins				
Ultratard® HM	Novo Nordisk	4 hours	8-24 hours	28 hours

2.7.4.2. Treatment regimes: Insulin

There are different types of insulin regimes available that can be followed in the management of diabetes mellitus.

- Twice-daily injections of a mixture of a short-acting and intermediate-acting insulin is the most commonly used regimen and is suitable for many young and middle aged patients with a long life expectancy. Two-thirds of the daily dose of insulin is given approximately 30 minutes before breakfast and one-third before supper (Gibbon, 2003:72).

- Where the above regimen leads to late evening and midnight hyperinsulinemia with resultant hypoglycaemia between midnight and three o'clock, the intermediate-acting insulin dosage before supper may be reduced to counteract this phenomenon. Early morning hyperglycaemia may occur, indicating early morning deficiency. Dividing the evening dose may thus better control patients, injecting the short-acting insulin at bedtime (about ten thirty), together with a snack (Gibbon, 2003:72).

- A once-daily injection of an intermediate-acting insulin may be sufficient in elderly type 2 diabetics, inadequately controlled on oral agents alone. A dose before bed may be combined with oral hypoglycaemic agents, if use of the latter alone is inadequate to provide adequate glycaemic control (Gibbon, 2003:72).

- The following, flexible regimen, the 'basal-bolus regimen', provides good control in well-motivated patients with a proper understanding of the disease. An intermediate-acting insulin is injected before bedtime to provide basal insulin requirements, supplemented by three preprandial short-acting insulin injections; alternatively, an ultra long-acting insulin is injected before bedtime providing 24-hour basal insulin requirements, supplemented by three preprandial short-acting insulin injections. If the ultra-fast, shorter-acting insulins e.g., insulin lispro, are used for the bolus component, the basal insulin may need to consist of two doses of intermediate-acting insulin, one before breakfast and the other before bedtime (Gibbon, 2003:72).

2.7.4.3 Interactions

The most important interactions of insulin with other substances or agents will be discussed.

- Insulin and non-selective beta-blockers (e.g. propranalol, nadolol, etc.).

Prolonged hypoglycaemia with masking of hypoglycaemic symptoms (i.e., tachycardia). Beta-blockers blunt sympathetic mediated responses to hypoglycaemia. Diabetic patients have deficient glucagons secretory responses to hypoglycaemia; therefore, enhanced epinephrine secretion is critical in the correction of hypoglycaemia in these patients. Both non-selective and selective beta-blockers, such as atenolol, etc., will blunt the tachycardic response to hypoglycaemia, but agents with selectivity or intrinsic sympathomimetic activity may not prolong the recovery time to normal blood glucose in mild or moderate hypoglycaemia (Tatro, 2002:726).

- Insulin and alcohol.

The serum glucose-lowering action of insulin may be potentiated by the simultaneous use of alcohol. Enhanced release of insulin following a glucose load and inhibition of gluconeogenesis will be a result of the simultaneous use of insulin and alcohol (Tatro, 2002:726).

2.7.4.4 Oral blood glucose lowering drugs

Oral therapy is very efficacious in treating patients with type 2 diabetes, but all patients should first be tried on course of diet and exercise for three months before oral therapy is used. Certain situations dictate the use of intravenous therapy over oral agents in patients with type 2 diabetes, but the importance of diet and exercise cannot be overstated. Some patients with type 2 diabetes can totally manage their disease by losing weight and following a strict exercise proramme. Even if oral medication is needed, patients who exercise regularly and are on a proper diet can manage their condition on less medicine than those not on a suitable diet or exercise proramme (Setter *et al.,* 2000:400).

Four categories of oral antidiabetic agents are currently available: insulin secretagogues (sulfonylureas), e.g. glibenclamide; biguanides, e.g. metformin; thiazolidinediones, e.g. pioglitazone and rosiglitazone; and alpha-glucosidase inhibitors, e.g. acarbose. The sulfonylureas and biguanides have been available the longest and are the traditional initial treatment choice for type 2 diabetes. A novel class of rapidly acting insulin secretagogues, the meglitinides, is an alternative to the short acting sulfonylurea tolbutamide. The thiazolidinediones are very effective agents that reduce insulin resistance. Alpha-glucosidase inhibitors have a relatively weak effect and annoying adverse effects, and they are used primarily as adjunctive therapy in individuals who cannot achieve their glycaemic goals by taking other medication (Nolte & Karam, 2001:723).

2.7.4.4.1 Sulfonylureas

The mechanism of action of the sulfonylureas when they are acutely administered is due to their insulinotrophic effect on pancreatic B cells. Sulfonylureas specifically bind to a receptor that closes an adenosine triphosphate (ATP)-sensitive potassium channel of the pancreatic ß-cell, thereby depolarising the cell membrane. This results in an influx of extracellular calcium through voltage-gated calcium channels, which causes insulin granules to move toward the cell surface, facilitating exocytosis. The sulfonylureas seem most appropriate for use in non-obese mild type 2 diabetic patients. In this group, acute administration of sulfonylureas improves the early phase of insulin release that is refractory to acute glucose stimulation. Sulfonylureas are generally contra-indicated in patients with hepatic or renal impairment (Masharani & Karam, 2001:1171).

Some of the most common side effects seen with sulfonylureas include headache, dizziness, weakness and paraesthesia; also gastrointestinal disturbances with nausea, epigastric fullness and heartburn. Allergic skin reactions are usually transient and subside with continued administration. Initially, an oral dose of 2,5mg in the morning, increased gradually with increments of no more than 2,5mg at weekly intervals, is required. The maximum dose should not be more than 15mg/day. Divided doses appear to improve the control of hyperglycaemia in patients requiring 10mg daily or more (Gibbon, 2003:75).

The sulfonylureas in common use include glibenclamide, gliclazide, glimepiride and glipizide (Gibbon, 2003:74).

- *Interactions*

The interactions of sulfonylureas with certain substances will be discussed.

❖ Sulfonylureas and alcohol

Three effects of alcohol have been identified with sulfonylureas. Alcohol may prolong but not augment glipizide-induced reductions in blood glucose. Chronic use of alcohol may decrease the half-life of tolbutamide. Alcohol ingestion by patients taking chlorpropamide may result in a disulfiram-like reaction. This reaction is characterised by facial flushing that may spread to the neck and occasionally a burning sensation, headache, nausea, and tachycardia. Typically the flush starts 10 to 20 minutes after alcohol ingestion, peaks 30 to 40 minutes, and persists for 1 to 2 hours (Tatro, 2002:1165).

❖ Sulfonylureas and anticoagulants (Warfarin®)

A greater than expected hypoglycaemic response occurs and can extend to clinical hypoglycaemia. Metabolic degradation of sulfonylurea is slowed by the oral anticoagulant leading to accumulation of the sulfonylurea (Tatro, 2002:1159).

- Sulfonylureas and beta blocking agents

The sulfonylurea-induced insulin-release from the pancreas can be inhibited by beta-blockers so that the hypoglycaemic effects are opposed to some extent. Diabetics taking oral sulfonylureas rarely seem to have serious hypoglycaemic episodes caused by beta-blockers, and any reductions in the hypoglycaemic effects of the sulfonylureas normally appear to be of little clinical importance. The selective beta-blockers are probably safer than the non-selective beta-blockers (Stockley, 2000:512).

❖ Sulfonylureas and chloramphenicol

Hypoglycaemia may occur if sulfonylureas and chloramphenicol are used simultaneously. Reduction in sulfonylurea hepatic clearance by chloramphenicol can lead to accumulation of the sulfonylurea (Tatro, 2002:1161).

❖ Sulfonylureas and clofibrate

The effects of the sulfonylurea hypoglycaemic agents can be enhanced by clofibrate in some patients, possibly advantageously in those with poorly controlled diabetes. A reduction in the dosage of the hypoglycaemic agent may be necessary (Stockley, 2000:515).

❖ Sulfonylureas and diazoxide

The addition of diazoxide to the regimen of a non-insulin-dependent diabetic stabilised on sulfonylurea therapy could destabilise the patient, resulting in hyperglycaemia. Two mechanisms have been postulated; decreased insulin release secondary to diazoxide's effect on cell membrane calcium flux or stimulation of alpha-adrenergic receptor sites in the beta cell, and diazoxide stimulation of the release of catecholamines, which results in increased glucose and free fatty acids (Tatro, 2002:1164).

❖ Sulfonylureas and MAO-inhibitors

The hypoglycaemic effects of insulin and the oral hypoglycaemic agents can be increased by the concurrent use of monoamine oxidase inhibitors (MOAI's). This may improve the control of blood sugar levels in most diabetics, but in a few it may cause undesirable hypoglycaemia. This can be controlled by reducing the dosage of the hypoglycaemic agent (Stockley, 2000:524).

❖ Sulfonylureas and sulphonamides

The co-administration of sulphonamides and sulfonylureas may increase the half-life of the sulfonylurea and therefore hypoglycaemia can occur. Sulphonamides may impair hepatic metabolism of sulfonylureas or alter plasma protein binding (Tatro, 2002:1183).

❖ Sulfonylureas and thiazide diuretics

Thiazide diuretics increase fasting blood glucose levels and may decrease sulfonylurea hypoglycaemia. This effect may occur after several days to many months of thiazide therapy. Hyponatremia may also occur. Thiazide diuretics may decrease insulin tissue sensitivity, decrease insulin secretion or increase potassium loss, causing hyperglycaemia (Tatro, 2002:1184).

❖ Sulfonylureas and urinary alkalinisers

Alkalinisation of the urine by an agent such as sodium bicarbonate may increase the elimination of chlorpropamide. This may be useful in the treatment of chlorpropamide intoxication; however, patients taking sodium bicarbonate for other reasons may have decreased therapeutic response to chlorpropamide. The renal clearance of chlorpropamide increases as urinary pH increases. It appears that urinary pH affects the ratio of renal and metabolic clearance (Tatro, 2002:1187).

2.7.4.4.2 Biguanides

The biguanides are agents of first choice in the management of obese type 2 diabetics, but the small risk of lactic acidosis demands that they be used with caution (Gibbon, 2003:73).

Metformin is a biguanide that lowers blood glucose by reducing hepatic glucose production and glycogen metabolism in the liver and enhancing insulin-mediated glucose uptake by skeletal muscle (Setter *et al.,* 2000:401).

Other proposed mechanisms include a slowing down of gastrointestinal absorption of glucose and increased glucose uptake by skeletal muscle. Because of its very high concentration in intestinal cells after oral administration, metformin increases glucose to lactate turnover, which may account for a reduction in hyperglycaemia. Metformin has a half-life of 1.5 to 3 hours, is not bound to plasma proteins, and is not metabolised in humans, being excreted unchanged by the kidneys (Masharani & Karam, 2001:1173).

Some of the most common side effects seen with metformin include gastrointestinal disturbances such as anorexia, diarrhoea, and a metallic taste in the mouth, but patients usually respond well to temporary lowering of the dosage. Lactic acidosis usually occurs only if there are predisposing factors. Symptoms of lactic acidosis include nausea, vomiting, hyperventilation, malaise and abdominal pain. An initial oral dose of 500mg twice daily or 850mg once daily, increased gradually if required, is necessary. The daily maximum is 3g, but to minimise the risk of lactic acidosis, the dose should probably not exceed 500mg three times daily or 850mg twice daily, which is sufficient in most patients (Gibbon, *ed.* 2003:74).

- *Interactions*

The most important interactions of biguanides with certain substances will be discussed.

❖ Biguanides and alcohol

There can be an increased risk of lactic acidosis if biguanides and alcohol are used simultaneously (Gibbon, 2003:74).

❖ Biguanides and cimetidine

Serum concentrations of metformin may be elevated, increasing the pharmacologic effects. Cimetidine reduces the renal clearance of metformin by inhibiting renal tubular secretion (Tatro, 2002:856).

❖ Biguanides and sulfonylureas.

There is an increased risk of serious and prolonged hypoglycaemia if biguanides and sulfonylureas are taken in combination. Care should be taken to avoid hypoglycaemia (Gibbon, 2003:74).

2.7.4.4.3 Alpha-glucosidase inhibitors

Only monosaccharides, such as glucose and fructose, can be transported out of the intestinal lumen and into the bloodstream. Complex starches, oligosaccharides, and disaccharides must therefore be broken down into individual monosaccharide molecules before being absorbed in the duodenum and upper jejunum. This digestion is facilitated by enteric enzymes, including pancreatic α-amylase and α-glucosidase, that are attached to the brush border of the intestinal cells (Nolte & Karam, 2001:729).

Alpha-glucosidase inhibitors are a family of drugs that competitively inhibit the alpha-glucosidase enzymes in the gut, which digest dietary starch and sucrose (Masharani & Karam, 2001:1174).

Acarbose, an α-glucosidase and α-amylase inhibitor, works by reducing the rate of complex carbohydrate digestion and subsequent absorption of glucose, thereby lowering postprandial glucose excursions in patients with diabetes. Acarbose is particularly effective for patients who experience postprandial hyperglycaemia. Dose-related side effects of the alpha-glucosidase inhibitors are mainly gastrointestinal in nature and include flatulence, diarrhoea, and abdominal pain. Patients who can continue to take this medicine may develop tolerance to the side effects (Setter *et al.,* 2000:401).

Careful initiation of therapy is required in order to reduce side effects. An initial dose of 25mg in the evening for the first week is given. Thereafter it can be increased to a 35mg dose twice daily for two weeks, and then a three daily dose can be given. The dosage may be increased to 50–100mg three times daily if response is inadequate (Gibbon, 2003:77).

- *Interactions*

The interactions of the alpha-glucosidase inhibitors with certain substances will be discussed below.

❖ Acarbose and hypoglycaemic agents and insulin

Acarbose may potentiate the hypoglycaemic effects of insulin (Gibbon, 2003:76).

❖ Acarbose and gastrointestinal absorbents

Concomitant use of acarbose and gastrointestinal absorbents may decrease the effect of acarbose (Gibbon, 2003:76).

2.7.4.4.4 Thiazolidinediones

Thiazolidinediones are a recently introduced class of oral antidiabetic drugs that enhance target tissue insulin sensitivity. Two members of this class are commercially available in SA: rosiglitazone and pioglitazone. Their exact mechanism of action is not yet understood, but they appear to have an acute post-receptor insulin-mimetic activity as well as chronic effects on the transcription of genes involved with glucose and lipid metabolism mediated through the peroxisome proliferator-activated receptor-gamma nuclear transport. Their major action is to diminish insulin resistance by increasing glucose uptake and metabolism in muscle adipose tissues. Rosiglitazone and pioglitazone also restrain hepatic gluconeogenesis and exert additional effects on lipid metabolism, ovarian steroidogenesis, systemic blood pressure, and the fibrinolytic system. Some of the beneficial effects of these drugs may be due to a redistribution of body fat (Nolte & Karam, 2001:728).

According to Nolte and Karam (2001:728), thiazolidinediones therapy has been associated with a decline in visceral fat mass and enhanced development of peripheral small adipocytes. Despite the increase in subcutaneous fat mass, significant weight gain has not been noted with monotherapy, probably because of the concomitant loss of central obesity.

Thiazolidinediones are considered "euglycaemics" since when used alone they can restore glucose levels into the normal or non-diabetic range without causing hypoglycaemia. Combination therapy with sulfonylureas and insulin can lead to low blood glucose values and may require dosage adjustment (Nolte & Karam, 2001:729).

Both Rosiglitazone and Pioglitazone are often referred to as an "insulin sensitiser" because they attach to the insulin receptors on cells to become more sensitive or more responsive to insulin. As a result, more glucose is removed from the blood (Marks, 2002a).

Rosiglitazone may be taken once or twice daily, with or without meals. Daily doses range from 4 to 8mg either with or without metformin. Drug interactions have not been identified with rosiglitazone as with the other thiazolidinediones. Rosiglitazone did not change the blood levels of the commonly used drugs digoxin and warfarin. Alcohol did not interact with rosiglitazone when the alcohol consumption was limited to a single episode of moderate consumption (Marks, 2002b).

The most common side effects seen with rosiglitazone alone or in combination with metformin are upper respiratory tract infection, headache, back pain, hyperglycaemia, fatigue, sinusitis, diarrhoea and hypoglycaemia. Rosiglitazone has shown to cause mild to moderate accumulation of fluid and can lead to heart failure (Marks, 2002b).

Pioglitazone also lowers the level of glucose in the blood by reducing the production and secretion of glucose into the blood and liver. Specifically, it decreases triglycerides and increases the "good" or high density lipoprotein (HDL) cholesterol (Marks, 2002a).

Pioglitazone is prescribed once daily in doses ranging from 15 to 45mg and can be taken any time of day, with or without meals. Caution should be taken if pioglitazone and an oral contraceptive are taken simultaneously, because pioglitazone may reduce the effectiveness of the oral contraceptive. Because pioglitazone interacts with the liver enzymes that eliminate some other drugs, there is the potential for pioglitazone to increase the elimination of such drugs as erythromycin, calcium channel blockers, cisapride, corticosteroids, cyclosporine, triazolam, trimetrexate, and 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase inhibitors. Pioglitazone does, however, not change the blood levels of glipizide, digoxin, warfarin, or metformin (Marks, 2002a).

The most common side effects seen with pioglitazone alone or in combination with sulfonylureas, metformin, or insulin were upper respiratory tract infections, headache, sinusitis, muscle aches, tooth disorders, hypoglycaemia, and sore throat (Marks, 2002a).

Combination therapies are becoming much more common in the treatment of patients with type 2 diabetes. A second agent may be given to a patient who is poorly controlled on a single agent, and sometimes a third drug may be needed to achieve the desired clinical goal. In general, oral agents should not be substituted for one another, but rather a second or a third drug should be added to the regimen. Insulin may be used in combination with sulfonylureas, acarbose, metformin or one of the thiazolidinediones. Keep in mind that insulin needs may decrease when oral agents are added to the regimen (Setter *et al.,* 2000:405).

2.7.4.4.5 Meglitinides

Nateglinide and repaglinide are members of a new chemical class of antidiabetic agents, which act by stimulating insulin release from the pancreas. They are structurally different from the sulfonylureas, but have a similar mode of action (Gibbon, 2003:77).

The meglitinides are used in type 2 diabetes as monotherapy or in combination with metformin. These agents are contraindicated in type 1 diabetes, diabetic ketoacidosis, severe renal or liver impairment and they should not be used in children. Combination with sulfonylureas should be avoided (Gibbon, 2003:77).

The most common adverse effects seen with the meglitinides include: hypoglycaemia, abdominal pain, diarrhoea, nausea and vomiting, and skin hypersensitivity (Gibbon, *ed.* 2003:77).

2.7.4.5 Summary of the oral antidiabetic agents in South Africa

Table 2.8 summarises all the oral antidiabetic agents according to class, active ingredient and propriety name.

Table 2.8 Oral antidiabetic agents available in South Africa (Snyman, 2004:313-317).

Class	Active ingredient	Propriety name
Biguanide	Metformin	Glucophage® Merck-Metformin® Metforal® Rolab-Metformin®
Sulfonylureas	Glimepiride	Amaryl®
	Glibenclamide	Daonil® Diacare® Glycomin® Norton-Glibenclamide® Rolab-Glibenclamide®
	Gliclazide	Diaclucide® Diamicron® Glucomed® Glycron® Merck-Gliclazide® Rolab-Gliclazide®
	Glipizide	Minidiab®
	Chlorpropamide	Hypomide®
Alpha-glucosidase inhibitors	Acarbose	Glucobay®
Thiazolidinediones	Pioglitazone Rosiglitazone	Actos® Avandia®
Meglitinides	Repaglinide Nateglinide	Novonorm® Starlix®

2.8 SUMMARY

Diabetes Mellitus is a heterogeneous disorder requiring both genetic and environmental factors. Hyperglycaemia in type 2 diabetes results from a combination of insulin resistance and relative insulin deficiency. An insight into the aetiopathogenesis helps to determine a better approach to the disease. It is crucial to identify the hidden cases of type 2 diabetes in a community. Education for the general population, and in particular, for the patients, is the key to preventing and controlling this type of diabetes and reducing the complications arising from it (Bhattacharya, 2001b:9).

In chapter three an overview will be given on managed care, pharmaco-economics and drug utilisation review.

CHAPTER 3: Managed care, pharmaco-economics and drug utilisation review: An overview.

3.1 INTRODUCTION

In the previous chapter an overview of Diabetes Mellitus as a disease was given as well as the complications thereof. The classification, diagnosis, pathophysiology and treatment of diabetes were discussed briefly.

This chapter provides an overview of the concepts of managed care, pharmaco-economics and drug utilisation review. These terms will be defined and the usage thereof in South Africa will be discussed as referred to the implementation and control of information tools for decision making.

3.2 MANAGED CARE (MC)

3.2.1 Definition of managed care

Managed care can be defined as a system of health care delivery that influences the utilisation and cost of services and measures performance. The goal is a system that delivers value by giving people access to high quality, cost-effective health care. It can also be defined as a systemised approach that seeks to ensure the provision of proper health care at a proper time, place, and cost (Wertheimer & Navarro, 1999:371).

According to Edwards (1998:4), managed care is a term that is commonly used to describe an array of health care delivery and payment systems, including health maintenance organisations (HMOs), preferred provider organisations (PPOs), and point-of-service plans (gatekeeper PPOs). Edwards (1998:4) then defined managed care as a process used to deliver cost-effective care without limiting quality or access. This is achieved by controlled access to providers, comprehensive regulatory controls, emphasis on preventive care, risk-sharing, quality, and behaviour modification of both the participants and providers.

Managed care revolves around trying to provide quality health care within the capitated financial environment, pharmaceutical formularies, and outcome guidelines. Capitated financial environments require of one to know precisely how many patients are being seen; what their demographics and diagnoses are; what tests and procedures are performed; and what the costs, both direct and indirect, associated with the delivery of care are (Kiel, 2003:16).

According to Kiel (2003:16) the delivery of health care services in a capitated environment follows a managed care model. This managed care model comprises five "players", seemingly always jockeying for "position". The employer (player 1), negotiates with the managed care organisation (player 2) for the most affordable rates and expansive coverage. The managed care organisation negotiates with the providers (player 3), mainly hospitals, pharmacists and physicians, both primary care and specialist (player 4) to garner services for its enrolled populations. The providers administer health care services to the enrolled population, patients (player 5), within the guidelines of the managed care organisation. Every player uses information technology to effectuate the managed care model.

3.2.2 Types of managed care plans

There are two basic types of managed care plans: Health Maintenance Organisations (HMO) and Preferred Provider Organisations (PPO). There are also other plans such as the Point of Service Plans (POS), which are less popular and significant. The main difference between the HMO plan and the PPO plan is, that the HMO requires that all its patients receive their care from within the network while PPO gives the patients the option of using providers either within or outside the plan's network of providers. The third type of managed health care plan is in some ways like the HMO and in some ways like the PPO. This third type is known as the Independent Practitioner Association (IPA). A managed care plan almost without exception consists of a combination of the above mentioned plans (Anon, 2004a:4).

3.2.2.1 Health Maintenance Organisations

Health maintenance organisations offer prepaid, comprehensive health coverage for both hospital and physician services. The HMO is paid monthly premiums or capitated rates by the payers, which include employers, insurance companies, government agencies, and other groups representing covered lives. There are four basic models of HMOs: group model, individual practice association, network model and staff model. An HMO contracts with health care providers. The members of an HMO are required to use participating or approved providers for all health services and generally all services will need to meet further approval by the HMO through its utilisation programme. The members of an HMO are enrolled for a specified period of time. An HMO may turn around and sub-capitate to other groups, for example, it may carve-out certain benefit categories, such as mental health, and sub-capitate these to a mental health HMO. HMOs are of the most restrictive forms of managed care benefit plans because they restrict the procedures, providers and benefits (Pam Pohly's Net Guide, 1997).

3.2.2.2 Preferred Provider Organisation

A preferred provider organisation is created for the express purpose of trading price discounts in return for a larger volume of services, achieved through the method of channelling (Curtiss, 1996:485).

According to Wertheimer and Navarro (1999:378), a PPO is a programme in which contracts are established with providers of medical care. Providers under such contracts are referred to as preferred providers. Usually, the benefit contract provides significantly better benefits for services received from preferred providers, thus encouraging covered persons to use these providers. Covered persons generally are allowed benefits for non-participating providers' services, usually on an indemnity basis and with significant co-payments. A PPO arrangement can be insured or self-funded. Providers may be paid on a discounted fee-for-service basis.

3.2.2.3 Independent Practitioner Association

This is a loosely organised network of doctors who practice from their own offices, and treat both independent practitioner association (IPA) and non-IPA patients. Usually IPA coverage is limited to a group and there is usually a small co-payment for each visit. Under the IPA plan, some of the doctor's income depends on the success of the plan. Doctors often share in losses or profits caused by the plan and in this way they share substantial financial risk, which is considered to a highly efficient outcome under antitrust analysis (Anon, 2004a:4).

3.2.2.4 Fee-for-Service

The third segment of the managed health care industry is comprised of fee-for-service (FFS) health plans that impose some management controls on the price, use, quality, or access of medical care services. Fee-for-service health plans have become "managed" most commonly through the implementation of a mandatory utilisation review requirement. Therefore, managed FFS plans can be differentiated from HMOs and PPOs in the respect that HMOs and PPOs more commonly have the ability to achieve savings by controlling use and price factors, while managed FFS plans have more commonly sought savings by reducing the use and services (Curtiss, 1996:489).

3.2.2.5 Capitation

According to Spence and Van Riper (1998:10.8), a capitation rate can be defined as the overall revenue per member per month that a managed care organisation (MCO) needs in order to recoup its expected costs and earn a targeted net income.

In a capitation arrangement, a pharmacy is paid a monthly fee for each of its patients. This fee covers all drugs and pharmacy services received by the patient, regardless of how many the patient uses. If the patient uses few drugs, the pharmacy profits; if the patient uses many expensive drugs, the pharmacy loses. Thus, the pharmacy has a financial incentive to reduce utilisation whenever possible and to use generic or less expensive products (Thomas & Larson, 1999:54).

Three difficulties arise with capitation payment to an individual pharmacy for the drugs and services received by that pharmacy's patients. This applies to capitation as a means of paying an individual pharmacy, not a network. First, because most pharmacies have a small patient base and capitation payment is based on the average utilisation by a large number of patients, the expected probabilities are not easily achieved. Within a smaller group of patients, utilisation may be much greater or much less than the overall average. Thus, an efficient provider, who should be rewarded by capitation, may actually be penalised due to the bad luck of having sicker patients. Meanwhile, a "lucky provider" with healthier patients may profit from capitation, even though that provider may be inefficient. Second, pharmacies do not directly control prescribing, which is a big factor in medicine use, and therefore cannot easily control the cost of the entire package of services for which they assume financial responsibility. Thirdly, capitation requires patients to select one pharmacy; as a result, their freedom of choice is reduced. This restriction can be minimised if a pharmacy chain is capitated rather than an individual pharmacy. A patient can then go to any capitated pharmacy in the chain (Thomas & Larson, 1999:54).

3.2.2.6 Pharmacy Benefit Manager (PBM)

The emergence of pharmacy benefit managers constitutes a major structural change that has occurred in the distribution pharmaceuticals. A key factor that has fuelled the industry's explosive growth in recent years is the increasing demand for cost control by health care payers (Grabowski & Mullins, 1997:535).

Pharmacy benefit management companies are corporate entities that control the utilisation and concomitant cost of pharmacy products on behalf of private and public payers, most commonly managed care organisations, insurance companies, and self-insured employers. A PBM conducts activities such as formulary management, utilisation review, and other programmes to promote use of pharmaceuticals in accordance to clinical practice guidelines or formulary status. Pharmacy benefit managers provide a set of health care products or services for management of the pharmacy benefit. The services are available for reimbursement by a particular health insurance plan specific to a particular group of insured individuals, and to the financial and other terms of the coverage. These activities generate cost savings to plan sponsors by reducing prescription claims processing charges, lowering ingredient and dispensing fees, and increasing patient co-payments (Grabowski & Mullins, 1997:535; Meek & Steinkellner, 2001:82,).

3.2.3 Point of service plans

The point of service plan (POS) is a hybrid of more traditional HMO and PPO models. PPOs have the following characteristics (Chetty, 2004:20):

- Primary care physicians are reimbursed through capitation payments.
- There is a withhold contingent upon achieving costs and targets.
- The primary care physician acts as gatekeeper for referral and institutional medical service.
- The patient in this scheme can retain some coverage outside that which is authorised.

3.2.4 Managed care development in South Africa

There is evidence of local and regional horizontal mergers and development of IPAs. These IPAs are mainly single disciplines with strong geographical dominance. There is a subscription of most IPAs to a National Association, e.g., the South African Managed Care Coalition, although some have opted to remain as independent units (Chetty, 2004:69).

There is also evidence of horizontal mergers with corporate buy-in. Some entities have taken on international partners. Managed care entities are employing the tools and techniques of managed care, which are pre-authorisation, chronic medicines programme, introduction of disease management and case management, introduction of medical guidelines and protocols, etc. (Chetty, 2004:69).

Managed care in general and in South Africa is provider driven or it has provider participation in programme development (Chetty, 2004:71).

Usually a managed care plan consists of a combination of the above mentioned plans, and therefore the diabetic patient is not free to use any health care provider, but is obliged to use the provider paid for by the health care plan.

3.3 PHARMACO-ECONOMIC STUDIES

3.3.1 Introduction

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

Costs are the resources consumed to perform an activity or implement a decision, while consequences are the outcomes of that action or decision. Economic evaluations assess efficiency, that is, the relationship between outputs (consequences) and inputs (costs). Their ultimate purpose is to enable the decision maker to better allocate pooled or community resources. Cost-effectiveness analysis is commonly used as a synonym for economic evaluation, although cost-effectiveness analysis is a type of method, along with cost-utility and cost-benefit analysis. Pharmaco-economics is then the application of economic evaluation methods to medicine products and pharmacist services (Larson, 2001:4).

3.3.2 Pharmaco-economics defined

Pharmaco-economics can be defined as a comparison of costs associated with competing drug therapies (e.g., acquisition costs, physician visits, laboratory tests, adverse reactions to therapies, etc.) and the adverse or beneficial effect of each therapy to determine the preferred, or most desirable, intervention (Wertheimer & Navarro, 1999:377).

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

3.3.3 Pharmaco-economic methodologies

3.3.3.1 Cost-benefit analysis (CBA)

In cost-benefit analysis, benefits are valued in the same unit as costs, that is, in monetary units as opposed to natural units or quality adjusted life years (QALYs). CBA has been used to evaluate therapies with outcomes that are difficult to measure with the conventional tool of cost-effectiveness analysis (CEA), for example, patient satisfaction with drug therapy (Hughes *et al.*, 2004:118).

According to Carriere and Huang (2001:21), cost-benefit analysis can be conducted for single- or multiple interventions to provide foundations for decision making to achieve the desired objectives. Based on the CBA, determination on whether an intervention should be implemented and, if so, which intervention should be chosen, can be made accordingly. A complete CBA can be summarised in several steps, but these steps are rather basic in that all other analyses should follow as well, with slight modifications (Carriere & Huang, 2001:21).

According to Hughes *et al.* (2004:118), there are three different approaches for measuring benefits within CBA, namely the human capital approach (HCP), the 'revealed preference' benefit measures, and the 'stated preference'. The major difference between these is that the last two reflect the preferences of individuals for health outcomes whereas the first approach is based on the market value of work contingent on such outcomes.

The human capital approach values the benefits of avoiding a premature death or disease by measuring the lost productivity from work as a result of such a negative event. The role of HCP in pharmaco-economics is now mostly limited to serve as a rough lower bound on the estimate of willingness to pay for therapies (Hughes *et al.*, 2004:118).

Revealed preference infers the benefits of a transaction to an individual by observing the choices he or she makes in terms of risk and return when buying or selling goods or services in the market (Hughes *et al.*, 2004:118).

According to Hughes *et al.* (2004:118), stated preference or contingent valuation, constructs a hypothetical market for the health care intervention in question by asking a respondent to state the maximum amount of money he or she would be willing to pay for having the health care intervention, or the minimum amount acceptable in compensation for being denied access to it. Contingent valuation allows patients or their caretakers, to indicate the intensity of their preference through their willingness to pay to obtain the therapy.

3.3.3.1.1 Steps in the conduction of a cost-benefit analysis

The first step in conducting a CBA is to identify clearly the intervention, programme, or therapeutic regimen to be evaluated (McGhan & Kitz, 1999:65).

Carriere and Huang (2001:23), stated that the perspective from which the analysis is conducted is an important consideration. They also stated that the cost savings or benefit might have different values from different perspectives, as a cost for one perspective may be a benefit from another perspective. Multiple perspectives may be included in an analysis, such as analysis from the society's perspective. All alternatives have to be identified, with specific objectives defined for the programme. A well-defined problem usually narrows the selection of alternatives.

The second step is to identify and value all the resources consumed, or costs of providing each intervention, programme, or regimen. The net benefits or benefit-to-cost ratios are calculated, based on which choice of the intervention with optimum value of net- benefit or benefit-to-cost ratio is followed (Carriere & Huang, 2001:23; McGhan & Kitz, 1996:65).

In the third step, benefits are identified and valued (McGhan & Kitz, 1996:66).

The results from the second step are adjusted by a discount rate because the monetary values at present depreciate over time. It is important to make adjustment increases if the positive return takes a long time (Carriere & Huang, 2001:23).

Finally, a sensitivity analysis is needed. The values for some factors involved in the CBA have to be estimated (Carriere & Huang, 2001:23).

3.3.3.2 Sensitivity analysis

In many pharmco-economic studies, the researchers make certain assumptions regarding the costs or probabilities of important variables. For example, the cost of a drug regimen may be estimated based on an intermediate dosing regimen, or the probability of a certain event may be estimated to occur at the most frequently reported percent of time. By using a variety of "what if" scenarios, a sensitivity analysis tests the validity of the results of a study by altering important variables and recalculating the study results. For instance, "what if" a different dosage regimen is used, or "what if" a higher or lower probability of an outcome is assumed, would the study results change? Therefore a sensitivity analysis can determine whether the results of a study will hold up under a variety of situations, or whether they are only valid under the conditions of a specific premise. Therefore, when evaluating the results of a pharmaco-economic study that is based on certain assumptions or models, one should determine whether a sensitivity analysis has been performed (McCloskey, 2001:76).

3.3.3.3 Cost-effectiveness analysis (CEA)

Cost-effectiveness analysis is a method for comparing the health outcomes (effectiveness) and the net costs of a programme or an intervention against other alternatives with similar health outcomes. CEA measures health outcomes in real terms and not in monetary terms, such as mortality, disability, or quality of life. The net costs of a programme or intervention are the costs for providing the programme and for committing the resources for treatments after subtracting the non-health benefits from the programme measured in monetary terms (Carriere & Huang, 2001:23).

Once the adequacy of CEA as the framework for analysis has been established and a proper outcome measure has been decided upon, the benefits are combined with the costs in a cost effectiveness ratio. CEA would estimate the incremental cost per unit of effectiveness gained for a medicine, relative to the standard that would provide clinicians with guidance concerning how much it costs to achieve an additional case free of the condition. This estimate is called the incremental cost-effectiveness ratio (ICER) (Hughes *et al.*, 2004:111).

$$\text{Incremental cost effectiveness} = \frac{\text{(cost of drug A – cost of drug B)}}{\text{(benefits of drug A – benefits of drug B)}}$$

$$= \frac{\text{difference in costs (A – B)}}{\text{difference in benefits (A – B)}}$$

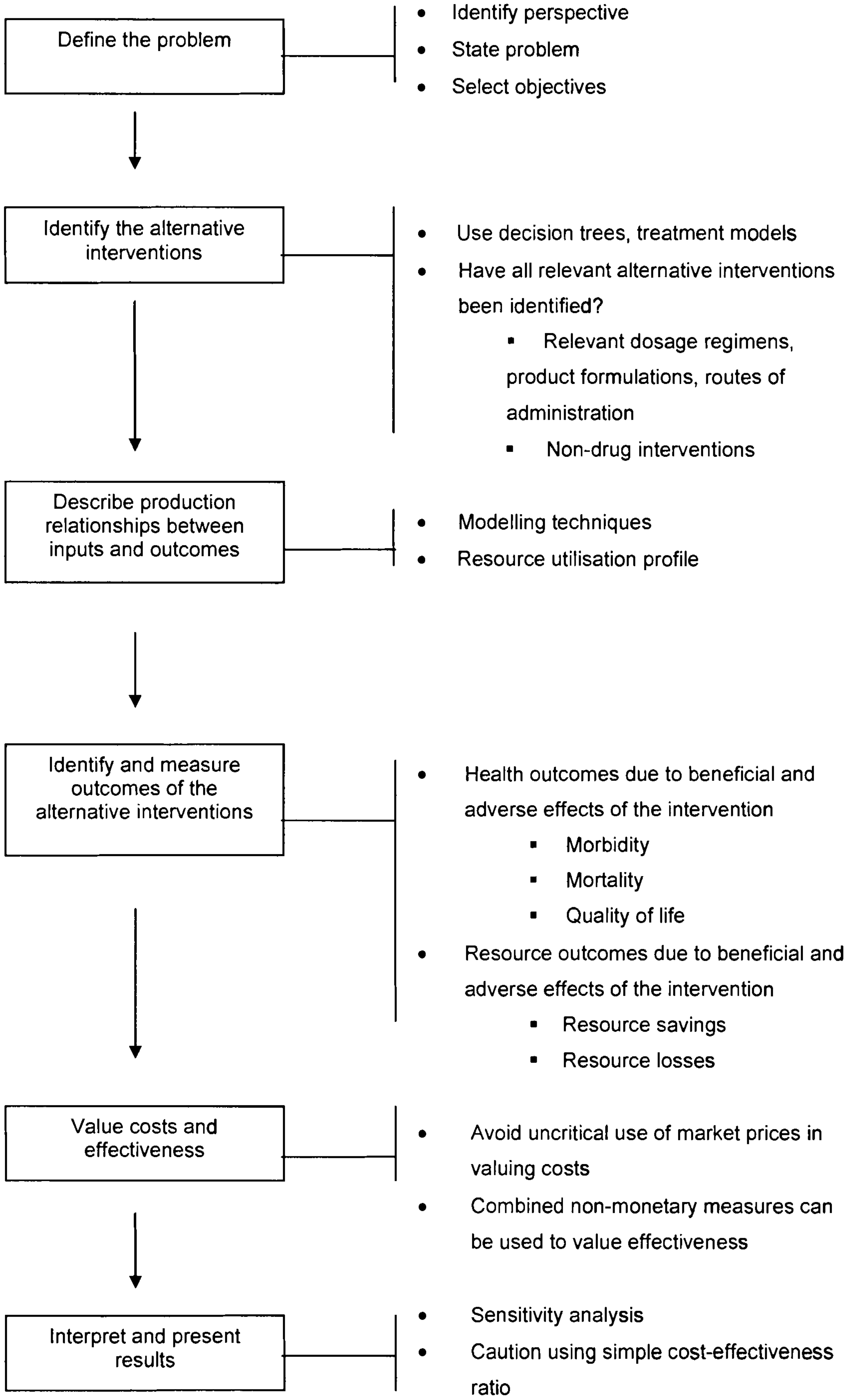
Figure 3.1: The incremental cost-effectiveness ratio

The incremental cost-effectiveness ratio reveals the cost per unit of benefit of switching from one treatment option to an alternative treatment option, i.e. the extra cost per unit of extra outcome obtained with the alternative. This differs from the average cost-effectiveness ratios, which reflect cost per unit of benefit independently of other treatments. The use of average cost-effectiveness ratios to decide between competing treatments can lead to misleading results as they fail to acknowledge their mutually exclusive character (Hughes *et al.*, 2004:111).

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

- If costs are lower and health benefits higher for one drug relative to another, the former is said to dominate and would be the preferred treatment.
- The opposite does also apply, i.e. the new drug is more expensive and less effective, and thus is considered inferior and not recommended for introduction.
- Where the new drug is both more effective and more expensive than the standard, then the ICER's judgement must be about whether the additional benefits are worth the extra costs of the new drug and, therefore, whether it is cost-effective. A threshold ICER value might then be used to define cost-effectiveness.
- The same as in the previous step, but with the roles of the new and the standard therapies reversed. Here the question arises whether the extra benefits provided by the standard therapy justify the additional costs of retaining it as preferred treatment when the option of a new, cheaper but less effective drug exists.

3.3.3.3.1 Basic steps of cost-effectiveness analysis (adapted from Chrischilles, 1996:80).



There are three steps to problem definition. A prerequisite for successful CEA is that the analyst understands the point of view or perspective from which the analysis is to be conducted. The next step is to state the basic problem being addressed. Third, specific objectives should be selected against which the alternative interventions are to be evaluated (Chrischilles, 1996:80).

The concept of cost-effectiveness is most meaningful when it is used in a relative manner. Interventions may be compared across multiple disease conditions, as is required for many formulary decisions. Other types of alternative interventions seen in drug CEA literature include the following: single drug therapy versus combination drug therapy; drug therapy alone versus drug therapy plus other diagnostic or therapeutic modality; inpatient versus outpatient drug therapy; alternative formulations of the same drug, e.g., premixed admixtures *vs.* compounded doses; and different dosage regimens of the same drug (Chrischilles, 1996:84).

Describing the production relationship ultimately results in identification and measurement of resource use required to provide each intervention. It also provides the technical framework for the quantitative assessment and comparison of net costs with net effectiveness. There are several methods for characterising these production relationships. All approaches involve development of a model that specifies how inputs are combined and how much output a given grouping of inputs will produce. Decision tree analysis has been the most commonly used modelling technique in drug therapy CEAs (Chrischilles, 1996:87).

If the problem, objectives, and alternative interventions have been carefully developed, identification of relevant health outcomes will already have been accomplished. In fact, these must be identified to complete the decision tree's linking inputs and outcomes. Health outcomes may occur as a result of both the beneficial and adverse effects of an intervention (Chrischilles, 1996:89).

As with health outcomes, resource outcomes derive both from the beneficial and the adverse effects of an intervention. Resource outcomes are the induced losses and savings associated with an intervention. Beneficial effects result in resource savings, whereas adverse effects result in resource losses. Both resource savings and losses can either be direct or indirect effects of the intervention in question. Direct health resource savings refer to savings on direct medical costs of illness that would occur if the intervention were not present. Direct health resource losses are direct medical costs associated with the adverse effects of an intervention. These can include the costs of diagnosing and treating adverse effects. Indirect resource savings and losses can also be included in a CEA, depending on the perspective of the analysis. Indirect resource outcomes occur in the form of work productivity, savings and losses (Chrischilles, 1996:90).

The valuation of economic variables entails conversion of production resource use, induced savings, and induced losses into monetary values. In CEA, the economic impact of an intervention is summarised as a net cost. Net costs are calculated by aggregating the production costs, associated with delivering the intervention, and the economic outcomes, induced resource losses and savings, of an intervention. Negative net cost values mean that savings from avoided costs of illness outweigh the costs of the intervention itself. The manner in which results are displayed must be given serious consideration. The temptation is to rely solely on the cost-effectiveness ratio as an index of the relative merit of the alternative interventions. Using this ratio as a criterion, the most cost-effective intervention would be the one with the lowest net cost per unit of effectiveness (Chrischilles, 1996:92).

3.3.3.4 Cost-minimisation analysis (CMA)

Cost-minimisation analysis is a technique designed to identify the preferred choice amongst possible alternatives with equivalent outcomes or consequences by examining the cost associated with each of those alternatives (Carriere & Huang, 2001:24).

According to Hughes *et al.* (2004), cost-minimisation analysis is based on the assumption that the outcomes of two or more health care technologies being compared are equivalent and, therefore, the basis of comparison becomes cost alone. The results of a CMA, being the simplest form of economic evaluation, require little more than common sense to interpret. If drug X costs more than drug Y, yet is clinically equivalent, then clearly drug Y should be chosen. By using this simple decision rule, the optimal choice of drug can be made. One must remember though, that only where strong evidence exists that two therapies produce equivalent health outcomes across all relevant dimensions of health, can CMA legitimately be employed.

3.3.3.5 Cost-utility analysis (CUA)

Bootman *et al.* (1991) defined cost-utility analysis as an economic tool in which the intervention consequence is measured in terms of patient preference or quality of the health care outcome. It is much the same as cost-effectiveness analysis with the added dimension of a particular point of view, most often that of the patient. The results of a CUA are quite often expressed in intervention cost per quality-adjusted-life-year (QALY) gained, or changes in quality-of-life (QOL) measurement for a given intervention cost.

According to Hughes *et al.* (2004:112), there are two different types of QOL measures:

- *Specific*: these instruments evaluate a series of health dimensions specific to a disease.

- *Generic*: these instruments can be used with any population. They generally cover quality-of-life questions and also questions on social, emotional and physical functioning, pain and self-care.

Cost-utility analysis combines the effects of an intervention in a more comprehensive way than cost-effectiveness analysis because it measures both effects on morbidity (quality of life) and mortality (quantity of life). The term 'utility' is derived from statements of preference by either patients or the general public in relation to possible health states. This type of study enables the comparison of different health care interventions, irrespective of the disease or condition. A range of methods has been developed to combine quality and quantity of life and to integrate these aspects of health across health states and individuals (Hughes *et al.*, 2004:112).

The best known of these indices is the quality-adjusted life-year (QALY). In this approach any health state of illness or disability is assigned a numerical score or 'utility' weight. QALYs are calculated by aggregating the number of days/years gained from a drug or health care intervention, weighted by a proportion that represents the relative value attached to the health state that the patient happened to fall into at the time. Results can be presented as cost per QALY gained or, the incremental cost per QALY gained. Figure 3.2 gives an example of calculating QALYs (Hughes *et al.*, 2004:114).

With treatment X	Without treatment X
Estimated survival = 10 years Estimated quality of life = 0.7 QALYs = (10 x 0.7) = 7.0	Estimated survival = 5 years Estimated quality of life = 0.5 QALYs = (5 x 0.5) = 2.5

QALY gained from treatment X = 7 – 2.5 = 4.5 QALYs

If the cost of treatment X is R 18000, then the cost per QALY is R 4000 per QALY (R 18000 divided between 4.5 additional QALYs)
(Hughes *et al.*, 2004:114).

Figure 3.2: A simple example of calculating QALYs.

3.3.3.6 Cost-of-illness evaluations (COI)

Cost-of-illness evaluations can be defined as the examination of the overall (direct and indirect) costs of a particular disease to a defined population. This economic methodology attempts to define, in a macroeconomic sense, all of the costs associated with a particular disease. Several studies have attempted to examine the cost of various disease states (Bootman *et al.*, 1991:8).

COI studies bring together three sources of costs – direct, indirect and intangible – in order to measure the economic burden to society of a disease or illness. There are two measures of how common a disease is. The incidence of a disease is the number of new cases accruing during a specified time period. By contrast, the prevalence is the number of people with a disease at a specified point in time. COI studies can either be based on the incidence or the prevalence of a disease, the latter being the more common because of the less demanding data collection requirements. Incidence-based cost-of-illness studies consider the lifetime costs resulting from a disease, on the basis of the number of cases diagnosed in a given year. Prevalence-based studies measure the economic impact in a given year by all existing cases, regardless of their year of onset. Incidence-based studies are more useful since they provide information about the progress of a disease and hence where cost savings might be made as a result of implementing changes in treatment regimens. This is particularly important for chronic diseases such as diabetes, where prevalence-based studies fail to take account of the long-term consequences of the disease (Leese, 1995:24).

3.3.3.6.1 Direct costs

Direct costs are the easiest to collect, but can be problematic where relevant costs are excluded, or where they are incorrectly estimated or given an inappropriate value. For non-insulin diabetes mellitus (NIDDM or type 2 diabetes) they include all aspects of medical care associated with the disease, such as hospital and nursing home care together with the treatment of complications, drugs and equipment, outpatient and general practitioner services, as well as out-of-pocket expenses incurred by patients and their families (Leese, 1995:24).

3.3.3.6.2 Indirect costs

Indirect costs are a measure of the costs to society of illness, disability and premature mortality. These costs may be experienced by the person with diabetes and his or her caregivers (Leese, 1995:24).

3.3.3.6.3 Intangible costs

Intangible costs are more subjective. They are rarely considered in cost-of-illness studies because of the difficulties of assigning costs to factors such as stress, pain and anxiety, which may lead to a reduction in quality of life for both patients and their families. One method of ascribing a value is to consider market earnings, and the most widely used method is the human capital approach, which values life (Leese, 1995:24).

3.3.3.7 Summary

Table 3.1 summarises the different pharmaco-economic methodologies and their distinguishing features.

Table 3.1 Categories of pharmaco-economic techniques (adapted from Bonk, 1999:10, 78).

Technique	Distinguishing features
Cost-benefit	Measures the cost of treating an illness, along with monetary equivalents for the treatment's outcomes.
Cost-effectiveness	Measures the cost of treating an illness, but using *clinical* measurements for the treatment's outcome
Cost-minimisation	Directly compares the cost of treatment options for an illness, assuming *equivalence* of their outcomes.
Cost-utility	Measures the cost of treating an illness, but using *preference* equivalents for the treatment's outcomes.
Cost-of-illness	Identifies and measures the costs of the illness itself, but *not* treatment outcomes.
Cost analysis	Allows researchers to test limitations to the generalisability of pharmaco-economic findings.

3.3.4 Evaluation of costs

Economic evaluation is a process by which the costs and consequences of an intervention, be it a pharmaceutical, medical device, or service, are assessed. The outcome of an economic evaluation is to determine the influence such an intervention has on health care resource utilisation, the patient, and on society (Ortmeier, 1996:386).

The first step in conducting an economic evaluation is to identify the perspective from which the result will be viewed. In an economic analysis, the perspectives from which the study was conducted and the audience for which it is intended become very important. There are many possible perspectives to consider when conducting an economic analysis. Examples would be patients, health professionals, health care institutions, third-party payers, and society (Ortmeier, 1996:386).

3.3.5 The pharmaco-economic evaluation process

There are several steps in designing the pharmaco-economic study that should be addressed for the specific economic methodology. The steps will now be discussed shortly (Bootman *et al.,* 1991:13).

Step 1: Prior to incorporating pharmaco-economic evaluation into any clinical trial, the investigator must first establish the perspective from which to evaluate the various costs and benefits. Depending on the perspective an investigator takes, the methodology may vary greatly.

Step 2: Describe/specify the clinical treatment alternatives. The alternatives included in a pharmaco-economic evaluation should be those actually available to the decision-maker.

Step 3: For each treatment alternative, specify the possible outcomes and their probabilities. This can be retrospective, using information from clinical studies, medical literature, and/or expert panels. It can also be a product of a current clinical trial. The pathways often can be presented clearly in the form of decision trees or similar diagrams.

Step 4: Specify and monitor the health care resources consumed in each pathway. The resources include: drugs, physician services, hospital, laboratory tests, etc. This can be done retrospectively or concurrently with a clinical trial. If this is done retrospectively, each patient pathway is described in terms of the health care resources that are likely to be consumed. If concurrent with a clinical trial, the artificial use of services must be considered. The perspective of the study affects the resources that are included.

Step 5: Assign a monetary value to each resource consumed. In drug studies, hospital services require special attention because of their relative magnitude.

Step 6: Specify and monitor non-health care resources consumed in each pathway. These resources, such as the economic impact a patient's treatment has on his/her family, often are difficult to measure.

Step 7: Specify the unit of effectiveness. The appropriate unit depends on the disease/condition and the results of treatment. Some possibilities are: patient lives saved, years of life added, or reduction in morbidity attributed to the disease.

Step 8: Specify other non-economic attributes of the alternatives, for example, pain, adverse effects, etc. These may be difficult to quantify and may lead to employing QOL determination and cost-utility analysis.

Step 9: Analyse the data employing the appropriate pharmaco-economic methodology. This appropriate analysis will be determined by how the study was set up, the perspective, and the type and quality of the data gathered.

Step 10: Conduct a sensitivity analysis. Ratios are calculated, using different values for uncertain items. Sensitivity analyses essentially define a range of confidence for the results of the study (Bootman, *et al.,* 1991:13).

3.3.6 Limitations

It is important to be aware of the limitations as well as the usefulness of pharmaco-economic analyses. The questions of cost must always be followed by the inquiry "to whom?" A study conducted from different perspectives may generate different results. Pharmaco-economic evaluations provide the tools to analyse the economic results of alternative drug therapy decisions. There is always an element of uncertainty regarding the aetiology of disease, and diagnostic and curative techniques. Additionally, a consensus may never be reached on such issues as the value of the discount rate, reducing uncertainty, estimating in the face of uncertainty, and taking into account the concept of equity. Sensitivity analyses examine such uncertain events under different assumptions, indicating the confidence one can place in their results, thereby reducing but not totally eliminating uncertainty. This is why such analyses require systematic and rigorous approaches. Those involved in drug-therapy decision-making must understand the strengths and weaknesses of approaches to this emerging field and use the tools in the appropriate manner (Osterhaus & Draugalis, 1991:139).

3.4 DRUG UTILISATION REVIEW (DUR)

3.4.1 Introduction

According to Wertheimer and Navarro (1999:361) a drug utilisation review can be defined as a qualitative and quantitative evaluation of prescription drug use, physician prescribing patterns, or patient drug utilisation to determine the appropriateness of drug therapy. It is a mechanism used by health maintenance organisations (HMOs) and preferred provider organisations (PPOs) to monitor prescription usage. Typically, a DUR committee examines the number of prescriptions per member per month and average cost per prescription. Utilisation and costs are reviewed according to individual physician, physician group, specialty, retail pharmacy, employee group, and member.

A DUR study is a one-time study to assess the appropriateness of drug therapy. The purpose is to identify whether current patterns of prescribing, dispensing and use of drug therapy are consistent with criteria and standards. These criteria and standards demonstrate that drug therapy is effective, safe, appropriate and cost-effective and support optimal patient outcomes (Blackburn *et al.*, 2001:6).

A DUR programme is a structured, continuous and systematic process used within a defined health care environment to assure drug therapy is effective, safe, appropriate, and cost-effective and the goal or desired patient outcome is achieved. The criteria and standards are predetermined, clinically relevant, continuously revised, updated and agreed-upon by all involved participants (Blackburn *et al.*, 2001:6).

3.4.2 Types of drug utilisation studies

Three broad categories of drug utilisation studies are recognised – prospective-, retrospective-, concurrent studies (Truter, 1995:338).

3.4.2.1 Prospective studies

According to the Managed Health Care Dictionary (second edition) a prospective study includes the function of a utilisation review that is directed toward establishing the medical necessity, appropriateness, and validity for reimbursement of care before an admission or provision of care. Many health plans and providers adhere to listings of what services require a prospective review (Rognehaugh, 1998:202).

Blackburn (1993:15) stated, "a prospective DUR refers to a programme where the evaluation of therapy, and intervention if necessary, occurs before a patient receives the first dose of a drug."

3.4.2.2 Retrospective studies

A retrospective drug utilisation study is defined as an approved, systematic process that captures, reviews, analyses, and interprets aggregate medication-use data within specific health care environments (Blackburn *et al.*, 2001:9).

Data are collected and analysed after the prescription, dispensing and use of drugs have occurred and are thus archival in nature. Although retrospective drug utilisation studies have little impact on immediate patient care, it serves to identify trends in prescribing practices that may lead to intervention aimed at enhancing prescribing behaviour. Retrospective studies are normally inexpensive and can be conducted rapidly. It can also detect new relationships and problems among medications and diseases (Truter, 1995:338).

3.4.2.3 Concurrent studies

Concurrent studies or reviews are conducted simultaneously with the dispensing process. If a potential problem is discovered while dispensing a prescription, the dispensing process comes to a halt until authorisation is received on what steps to follow. Concurrent reviews are more expensive and time consuming than retrospective studies, but have the potential for much greater pay-offs in preventing problems (Truter, 1995:339).

3.4.2.4 Qualitative studies

Qualitative studies assess the appropriateness of drug utilisation, usually by linking prescription data to the reasons for the drug prescribing. The crucial difference between qualitative and quantitative studies is that qualitative studies include the concept of appropriateness. Explicit predetermined criteria are created against which aspects of the quality, medical necessity, and appropriateness of drug prescribing may be compared (Lee & Bergman, 1994:380).

3.4.2.5 Quantitative studies

The objective of a quantitative study is to quantify the present state, the developmental trends, and the time course of drug usage at various levels of the health care system. Routinely compiled drug statistics or drug utilisation data that are the result of such can be used to estimate drug utilisation in populations by age, sex, social class, morbidity, and other characteristics, and to identify areas of possible over- or under-utilisation. Quantitative studies can also be used as denominator data for calculating rates of reported adverse drug reactions; to monitor the utilisation of specific therapeutic categories where particular problems can be anticipated, and to monitor the effects of informational and regulatory activities. These studies can also be used as markers for every crude estimate of disease prevalence, and to plan for drug importation, production, and distribution; and to estimate drug expenditures (Lee & Bergman, 1994:380).

3.4.3 Objectives of DUR

The principal aim of drug utilisation review is to facilitate the rational use of drugs in populations. For the individual patient, the rational use of a drug implies the prescription of a well-documented drug at an optimal dose, together with the correct information, at an affordable price. DUR in itself does not necessarily provide answers, but it contributes to rational drug use in important ways, as will be described below (WHO, 2003:9).

DUR can increase our understanding of how drugs are being used, for example, it can be used to estimate the numbers of patients exposed to specified drugs within a given time period. Researchers can estimate to what extent drugs are properly used, overused or underused. DUR can be used to compare the observed patterns of drug use for the treatment of a certain disease with current recommendations or guidelines, and it can be used in the application of quality indicators to patterns of drug utilisation (WHO, 2003:9).

DUR may generate hypotheses that set the agenda for further investigations, and thus avoid prolonged irrational use of drugs. Drug utilisation patterns and costs between different regions or at different times may be compared. Hypotheses can be generated to form the basis for investigations of the reasons for, and health implications of the differences found. The observed patterns of drug use can be compared with the current recommendations and guidelines for the treatment of a certain disease (WHO, 2003:10).

DUR can be undertaken to determine whether interventions to improve drug use have had the desired impact, for example, the effects of measures taken to ameliorate undesirable patterns of drug use should be monitored and evaluated (WHO, 2003:10).

Drug use should be controlled according to a quality control cycle that offers a systematic framework for continuous quality improvement. The steps in this quality control cycle is as follows:

Step 1: Plan. Analyse the current situation to establish a plan for improvement (e.g. analyse current prescription patterns of individual prescribers, groups of prescribers, or health facilities).

Step 2: Do. Implement the plan on a small scale (e.g. provide feedback on possible overuse, underuse or drug misuse of individual drugs or therapeutic groups).

Step 3: Check. "Check" to see if expected results are obtained (e.g. evaluate whether prescription patterns really improve).

Step 4: Act. Revise plan or implement plan on large scale (e.g. guide national implementation of plan) (WHO, 2003:11).

The quality control cycle can be applied at many levels, ranging from local or regional discussion groups consisting of physicians, clinical pharmacologists or pharmacists to national and international initiatives (WHO, 2003:10).

3.4.4 Sources of data in DUR

Currently available computer databases for studies of drug utilisation may be classified as non-diagnosis-linked and diagnosis-linked. Most of these data sources lack information on morbidity and are mostly used for generating drug statistics and descriptive studies of patterns of drug consumption. Some collect data in the form of drug sales, drug movement at various levels of the drug distribution channel, pharmaceutical or medical billing data, or samples of prescriptions (Lee & Bergman, 1994:385).

3.4.5 Steps in conducting a DUR

The first step in constructing a quality DUR programme is to design an organisational structure and determine the programme objectives. DURs have become an important part of any full-service contract provided by a pharmacy benefit management company (PBMC). Measures of quality may reflect reductions in overutilisation of a certain drug class or appropriate increases in utilisation of another drug class. Assumptions must be made that label an utilisation pattern as indicative of outlier behaviour on the part of the provider and/or patient. Once criteria are defined in terms of available information, reporting of data can be a powerful tool. Patterns of drug use can be defined by region, individual HMO or employer group, provider and patient (Edgren, 1999:121).

The next step in the DUR process is the intervention. Interventions in managed care need to be structured appropriately to meet the clinical situation, reflect the philosophy or approach of the plan or employer, and utilise the resources available (Edgren, 1999:121).

The final step is to reapply criteria to evaluate the effect of the interventions. This is easily accomplished through a brief follow-up study. The ongoing nature of DUR requires that criteria be revisited to update and modify according to current standards (Edgren, 1999:121).

3.4.6 Application of criteria in DUR

Criteria are predetermined measures of quality against which actual prescribing practices are measured. Criteria are based on judgements about behaviour in the choice, prescribing, dispensing and actual use of a drug. These judgments can be developed by examination of empirical data to identify "norms" that represent actual drug utilisation data or from independent *a priori* scientific judgements about the appropriate use of a drug within its indicated use and pharmacologic actions. The application of criteria is affected by determining standards that compare performance against a criterion and specifying deviations (Truter, 2001:9).

DUR criteria must be useful, effective and relevant to measurable outcomes. Criteria and standard development should therefore be based on generally accepted literature or well documented pharmacologic rationale and should be specific to the target population. A distinction can be made between implicit criteria, that are criteria based on an individual's expert judgement, clinical experience and knowledge of the literature; and explicit criteria, that is criteria based on compendia, texts, and literature. While explicit criteria are particularly useful when applied to large populations, it is useful to validate these findings by the application of implicit criteria to sub-samples of these populations. The use of explicit criteria does not permit evaluation of the patient's total clinical status or special circumstances and it does not take into account the wisdom that comes from clinical experience and judgement. Therefore a mixed strategy that combines both explicit and implicit criteria may be an optimal approach (Truter, 2001:10).

Examples of data elements for which criteria can be constructed include those associated with:

- The prescribing process, e.g., dosage and duration of therapy.
- Quality, e.g., appropriate diagnosis and drug-drug interactions.
- Outcomes, e.g., hospitalisations and laboratory values.

Application of several of these criteria may require linkage with other databases. Criteria construction should also include measurements of the underuse and overuse of drugs, because drug prescribing does not necessarily equal drug intake. These criteria must serve as warning signals for compliance (Truter, 2001:10).

3.4.7 Interventions to improve drug therapy

In an overview of DUR studies and rational drug therapy, Truter (2001:33) reported that interventions aimed at correcting behaviour are vital to enhance optimal drug use. Many strategies have been attempted in efforts to modify behaviour. Two broad types of intervention strategies can be identified:

- Education

Truter (2001:14) reported that education is the major strategy. Educational interventions may range from face-to-face discussions between specifically trained physicians or pharmacists and prescribers, to letters to individual prescribers suggesting a review of a single patient's drug history. Education can also be preventive, in other words, the prescriber must be educated from the outset to prescribe drugs optimally, rationally and cost-effectively. Preventive education needs to occur at medical training level.

- Cost-incentive or penalty systems

Interventions may be positive, for example the prescriber may receive an incentive for good or acceptable prescribing. Interventions can however also be restrictive (e.g., the sites where a patient may obtain prescriptions may be limited) or punitive (e.g., limiting prescribing privileges) (Truter, 2001:14).

Intervention strategies can also be classified according to the stage at which they occur. Four different stages can be identified, namely:

o Intervention before a prescription is written

In an overview of DUR studies and rational drug therapy, Truter (2001:14) explains that in this approach educators set up appointments to meet individual physicians face-to-face in their consulting rooms to present them with current information on rational therapeutics. These educators use up-to-date reviews of relevant clinical literature, information about cost-effectiveness, as well as visually effective material to communicate their message to doctors. The aim of these educators is not to promote a specific product, but rather to communicate to doctors how they can improve the precision and cost-effectiveness of their therapy.

o Intervention at the moment the prescription is written

This type of intervention is only possible if the doctor captures patient data and writes prescriptions, using a computer terminal. These interventions could be accomplished with the necessary software that would be able to evaluate other medications prescribed for a given patient. The software could then alert the prescriber of possible drug-drug or drug-disease interactions. This approach could also be used to warn prescribers if they prescribe a particular medication excessively or in the absence of a documented indication (Truter, 2001:15).

o Intervention at the point of dispensing

This is historically the oldest form of drug utilisation review, as practised by the conscientious pharmacist reviewing a patient's other medication before dispensing a new prescription (Truter, 2001:15).

o Retrospective intervention

In this approach, batches of prescription claims are passed through a series of computer screening criteria to detect possible drug-drug or drug-disease interactions. This is similar to a retrospective drug utilisation review, but in this case, printouts of claims that failed the screening tests are sent to a DUR committee who reviews these claims, and then informs the physicians involved of their questionable prescribing by means of a mailed notification (Truter, 2001:15).

3.4.8 Units of measurement

3.4.8.1 Cost

In cost studies, drug use is expressed in terms of costs. While cost figures are especially suitable for an overall cost analysis of drug expenditure, they are also applicable for prescription studies of only one substance. However, using data based on drug cost can introduce measurement errors because differential pricing occurs according to distribution channels employed, quantity purchased, import duties and currency exchange rate differences between countries, as well as regulatory policies that affect pricing. Studies based on cost data do not allow for cross-national comparisons, for comparisons between different programmes within one country, or longitudinal studies. Consequently, cost data introduce considerable limitations in the interpretation of drug utilisation studies (Truter, 2001:32).

3.4.8.2 Defined Daily Dose (DDD)

According to the Prescribing Support Unit (2004) the defined daily dose methodology was developed in response to the need to convert and standardise readily available data from sales statistics or pharmacy inventory data into medically meaningful units, to make crude estimates of the number of persons exposed to a particular drug or class of drugs. The DDD is the assumed average maintenance dose for the main indication of a particular drug according to the patient's age.

The advantages of this methodology include: its usefulness for working with readily available gross drug statistics at various levels of the health chain; as a standardised unit of measurement, it allows comparisons between drugs in the same therapeutic class and between different health care settings or geographic areas, and evaluations of trends over time; and it is relatively easy and inexpensive to use. This methodology has, however, some significant limitations (Lee & Bergman, 1994:386).

The DDD is not a recommended dose, but rather a technical unit of comparison. Additional problems arise when dosages vary widely, e.g., antibiotics, when one drug is used for more than one major indication, e.g., aspirin, or when drugs are used in combination with other drugs for the same disease. The DDD does not take into account variations in compliance (Lee & Bergman, 1994:387).

3.4.8.2.1 Calculation of the DDD

Consumption in a given geographical area is usually expressed in DDD per 1 000 inhabitants per day. This parameter provides a rough idea of the proportion of the population receiving a standard drug treatment every day. It does not indicate how many patients are actually being treated, however, except in the case where drugs are used continuously, such as insulin or contraceptives (Truter, 2001:35).

If data are available on the number of units of a drug sold, the number of DDD consumed is calculated according to the following formula (Truter, 2001:36):

Amount of drug sold in one year (mg)   DDD (mg) x 365 days x number of inhabitants x 1 000 inhabitants   = DDD/1000 inhabitants/day

Figure 3.3: Calculation of the DDD

3.4.8.3 DDD/100 consumers per day

Consumption in hospitals is calculated in the same way as consumption in the general population, but is usually expressed as the number of DDD per 100 bed-days. In making the calculation, the days of admission and discharge are usually counted together as one bed-day. The following formula is applied for the calculation of the consumption in a hospital (Truter, 2001:36):

Number of units delivered in a fixed period (mg) x 100 beds   [DDD(mg)] x [number of days] x [number of beds] x [hospital occupancy index]   = DDD/100 bed-days

Figure 3.4: Calculation of the DDD/100 consumers per day

3.4.8.4 Prescribed Daily Dose (PDD)

The prescribed daily dose is another unit, developed as a means to validate the DDD's. The PDD is the average daily dose prescribed, as obtained from a representative sample of prescriptions. Problems may arise in calculating the PDD due to a lack of clear and exact indication of dosage in the prescription, as is often the case with the prescribing of insulin. For certain groups of drugs, such as the oral antidiabetics, the mean PDD may be lower than the corresponding DDD (Lee & Bergman, 1994:387).

3.4.8.5 Number of drugs per prescription

In an overview of DUR studies and rational drug therapy, Truter (2001:33) reported that in early DUR studies, gross drug sales data were the most commonly used indicator. This information is widely available and can be obtained from manufacturers or wholesalers. According to Truter (2001:33), consideration of consumption in terms of "packages sold" gives a more precise idea of drug consumption than does economic value. This unit too has its limitations.

Common physical units, and numbers of packages or tablets, are also used for quantifying drug consumption. These units can however only be applied when the use of one drug or well-defined product is evaluated. Problems arise when the consumption of whole drug groups is considered (Truter, 2001:33).

If consumption is given in terms of grams of active ingredients, drugs with a low potency will have a larger fraction of the total than drugs with a high potency, because the strengths of tablets vary, with the result that low strength preparations contribute more than high strength preparations. Counting the numbers of tablets also has disadvantages. Short-acting preparations will also often contribute more than long-acting preparations (Truter, 2001:33).

3.4.9 Drug utilisation review versus drug use evaluation

Drug use evaluation (DUE) is defined as a method of enhancing the appropriate, safe, and effective use of drugs by developing indicators, collecting and evaluating patient data, identifying potential problems, and implementing corrective action to improve drug use (WHO, 2003:23). Similar to DUR, the time frame of DUE can be concurrent, prospective, or retrospective. Criteria can be based on process indicators, such as appropriate diagnosis, drug-food, drug-laboratory, or drug-disease interactions. In their best context, criteria can be based on outcomes indicators, such as improving exercise tolerance, reaching goal blood glucose levels or blood pressure levels. These elements may involve a broader database than is classically available to a PBM company (Edgren, 1999:124).

According to Edgren (1999:124), over-utilisation is a common and popular DUE criterion for use in managed care. Obvious clinical and financial implications for over-utilisation create a win-win situation for the plan. These include excessive dosage or duration, repetitive or duplicative drug use, unnecessary medication, fraud, and abuse.

Under-utilisation is another drug use pattern easily definable through a managed care database. Correcting under-utilisation may not be a financial win for the pharmacy side, but there may be a substantial offset in other resource utilisation, including inadequate dosing, patient non-compliance, and incomplete therapy regimens (Edgren, 1999:124).

3.5 COMPARISON FOR THE SUGGESTED TREATMENT ALGORITHMS FOR DIABETES MELLITUS BETWEEN THE DIFFERENT SERVICE PROVIDERS

3.5.1 Management of Diabetes Mellitus according to the Essential Drugs Programme

In the Essential Drugs Programme the management of diabetes mellitus is divided into four steps. In step one, a dietary and lifestyle modification is recommended for all patients. The

EDL also prescribes that all adult diabetics should take 150mg aspirin daily (Pudfin *ed.*, 2003:48).

If the fasting blood glucose is above 8mmol/L after three months of compliance with treatment plan in step one, then the patient must start on a biguanide (metformin) or sulfonylurea (glibenclamide or gliclazide) (Pudfin *ed.*, 2003:48).

Metformin should be given in a dose of 500mg daily. If the blood or urine glucose is uncontrolled, the dose increments should be as follows: increase to 500mg twice daily after two weeks, increase to 850mg twice daily after another two weeks if needed, or a maximum dose of 850mg three times daily. Glibenclamide should be given in a dose of 2,5mg daily with breakfast. It is important to eat after taking a sulfonylurea. If the blood or urine glucose is uncontrolled, the dose increments should be as follows: increase by 2,5mg daily at two-weekly intervals, with a maximum dose of 15mg daily. If 7,5mg or more is needed, divide the total dose into two, with the larger dose in the morning. If an alternative is required, e.g. in the elderly, the gliclazide 40mg with breakfast can be taken. If the blood or urine glucose is uncontrolled, dose increments should be as follows: increase by 40mg daily at two weekly intervals with a maximum dose of 160mg twice daily. If 80mg or more is needed daily then divide the total daily dose into two. Continue with the lifestyle modification. The target that must be reached is a random blood glucose below 10mmol/L or fasting glucose between 6 and 8mmol/L, or urine glucose of between 0 and 0,5%. This is step two (Pudfin *ed.*, 2003:50).

After three months of compliance with treatment plan in step two and maximum dose of single agent, and fasting blood glucose above 8mmol/L, start on biguanide and metformin. The target that must be reached is a random blood glucose below 10mmol/L or fasting glucose between 6 and 8mmol/L or urine glucose between 0 and 0,5. This is step three (Pudfin *ed.*, 2003:50).

Step four includes the initiation of insulin. Insulin is indicated when oral combination therapy fails, that is after three months on a biguanide and sulfonylurea and when fasting blood glucose is still above 8mmol/L. Sulfonylurea should be discontinued when insulin is initiated. Failure to step four should be referred. Table 3.2 summarises type of insulin as well as the dose thereof (Pudfin *ed.*, 2003:51).

Table 3.2 Insulin and its doses according to the EDL (adapted from Pudfin *ed.*, 2003:51).

Insulin type	Starting dose	Increment	Maximum daily dose
Intermediate to long-acting as supplementation	10 units in the evening before bedtime	If 10 units not effective, increase to 20 units	20 units
Biphasic as substitution	twice daily total daily dose: 15 units divided as follows: • 2/3 of total daily dose, i.e. 10 units, 30 minutes before breakfast • 1/3 of total daily dose, i.e. 5 units, 30 minutes before supper • stop oral sulfonylurea only after adequate control has been achieved	4 units weekly increase 0,6 units on a daily basis first increment is added to dose before breakfast second increment is added to dose before supper	30 units refer if more than 30 units are needed

3.5.2 Management of Diabetes Mellitus according to private health care provider

Figure 3.5 illustrates the treatment algorithm for the management of Diabetes Mellitus type 2 as suggested by the Council for Medical Schemes (Council for Medical Schemes, 2003).

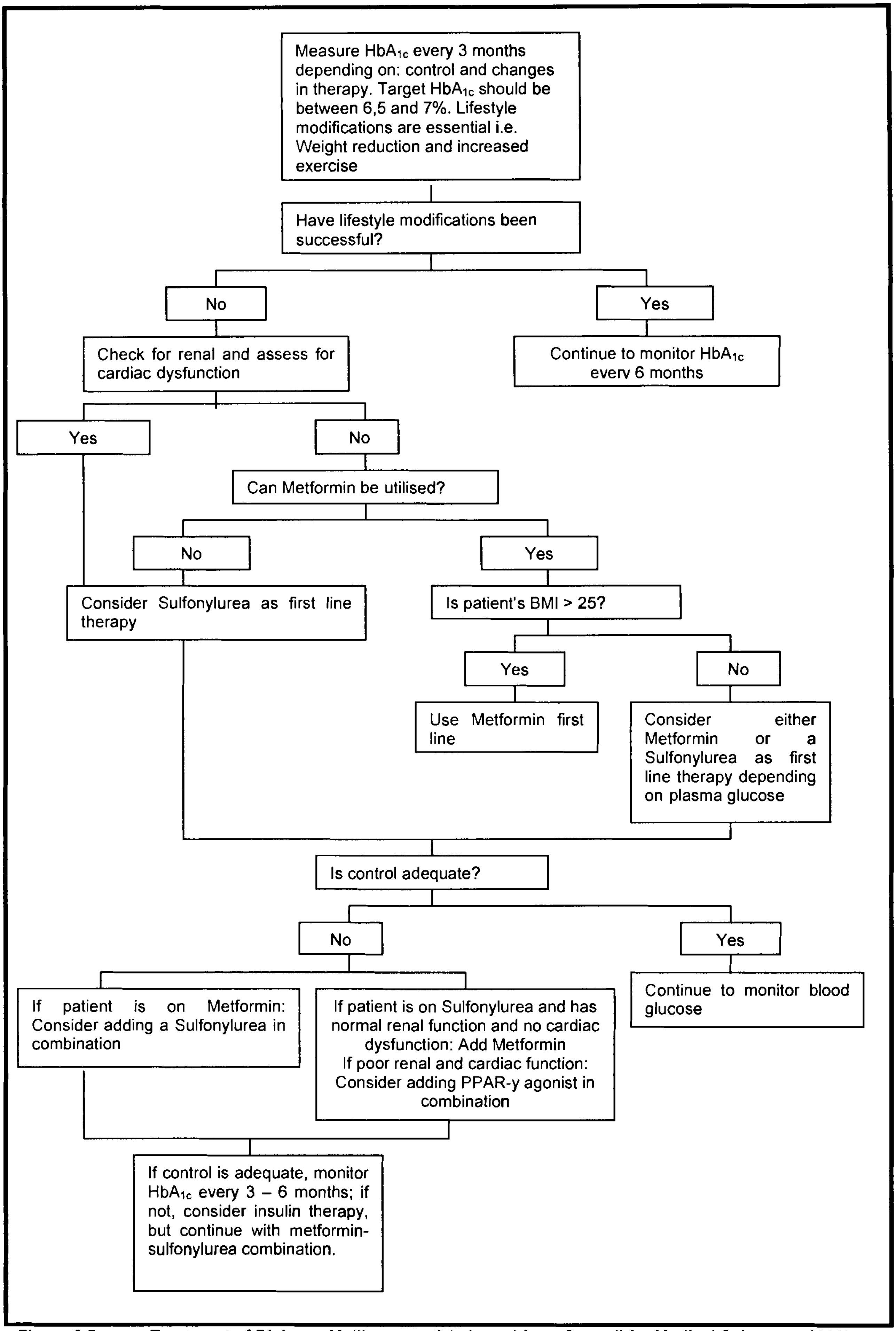


Figure 3.5 **Treatment of Diabetes Mellitus type 2 (adapted from Council for Medical Schemes, 2003).**

3.6 PRICE COMPARISONS BETWEEN THE DIFFERENT ANTIDIABETIC DRUGS

3.6.1 "Cost effectiveness" and diabetes care

Economic evaluations based on data from clinical trials and clinical practice suggests that improving glycaemic control will lead to reductions in the longer-term economic burden of diabetes by preventing expensive complications. Krumholz and colleagues (2002:603) stated that the cost-effectiveness analyses of diabetes treatment indicated that intensive glucose control improves outcome at a cost that is below other health care interventions.

The UKPDS (United Kingdom Prospective Diabetes Study) established that intensive therapy to lower glycohaemoglobin levels improves outcomes and can be highly cost-effective compared with non-intensive therapy. It is found that a sustained reduction in the glycosylated haemoglobin (HbA_{1c}) level of 1% or more in adult patients with diabetes is associated with a relative reduction in health care utilisation, particularly primary care visits, and cost savings within one to two years of the improvement in glycaemic control. These studies considered only standard medicines for diabetes, i.e. sulfonylureas, metformin, and insulin. Economic models for comparing new treatments with these established therapies must compare the costs and potential benefits of the new therapies with these standards (Veenstra *et al.*, 2002:24).

New diabetes medications all appear to reduce serum glycohaemoglobin levels effectively, however, they are more expensive than established medicines and thus will raise the cost of diabetes care in the short term. The question arises, when will the use of newer agents be cost effective in the long term? Information relevant to decision makers evaluating the appropriate use of these medicines include the following:

- Effectiveness defined as the expected reduction in the percentage of HbA_{1c} with monotherapy or in combination with other therapies.
- Persistence of clinical benefits.
- Safety, including adverse effects, drug interactions, and the need for monitoring (e.g. hepatic enzymes, renal function).
- Extra glycaemic outcomes of interest such as effects on serum lipids and consequent impact on coronary heart disease events.
- Costs, both short-term drug costs and the long-term medical costs of diabetes complications (Veenstra *et al.*, 2002:24).

Table 3.3 summarise the most important considerations in evaluating drug therapies for persons with diabetes mellitus.

Table 3.3 Important considerations in evaluating drug therapies for persons with Diabetes Mellitus (adapted from Veenstra *et al.*, 2002:25)

Efficacy		Effectiveness	Safety	Economic impact	
Surrogate markers	Clinical endpoints			Short term	Long term
% Reduction in HbA1c (monotherapy)	Macrovascular MI stroke	Compliance	Hypoglycaemia	Medicine cost	Cost savings from prevention of macrovascular complications
% Reduction in HbA1c (combination therapy)	Microvascular nephropathy retinopathy neuropathy	Adverse effects	Idiosyncratic reactions	Monitoring cost	Cost savings from prevention of micro-vascular complications
Effect on serum lipids (LDL, HDL, TG)		Impact on use of other antidiabetic drug	Drug interactions	Weight control cost (including medicines)	Cost differences due to changes in use of other antidiabetic drugs
Weight gain/loss			Monitoring		Cost issues associated with obesity and related complications

HbA_{1c} = glycosylated haemoglobin; **HDL** = high density lipoproteins; **LDL** = low density lipoproteins; **TG** = triglycerides; **MI** = myocardial infarction.

3.6.2 Clinical advantages and disadvantages of oral antidiabetic agents

3.6.2.1 Advantages of oral antidiabetic drugs

Despite the fact that most people find it easier to drink capsules than to use injections, there are a few other advantages of the oral antidiabetic drugs that make them a better option for treating diabetes mellitus. The sulfonylureas are known for their rapid fasting plasma glucose (FPG) reduction and their low cost (Luna & Feinglos, 2001:1750).

The meglitinides elevate postprandial glucose (PPG) and can therefore lead to the risk of hypoglycaemia. The meglitinides are short acting and the dose can easily be adjusted. Biguanides and thiazolidinediones have the advantage that they do not lead to a weight gain, and can therefore be given to obese or overweight patients. The alpha-glucosidase inhibitors target elevated postprandial glucose (PPG) and can therefore also lead to hypoglycaemia (Luna & Feinglos, 2001:1750).

3.6.2.2 Disadvantages of oral antidiabetic drugs

The meglitinides, biguanides, thiazolidinediones and alpha-glucosidase inhibitors all have the disadvantage that they are expensive. The sulfonylureas and thiazolidinediones can lead to weight gain, while the alpha-glucosidase inhibitors can potentiate gastro-intestinal side effects, for example flatulence, abdominal distension, etc. The thiazolidinediones have the other disadvantage that they can issue liver toxicity and they have a slow onset of action. Despite the high cost and gastro-intestinal side effects, the biguanides can also lead to lactic acidosis (Luna & Feinglos, 2001:1750).

3.6.3 Advantages and disadvantages of insulin and insulin analogues as antidiabetic agents

3.6.3.1 Advantages of insulin and insulin analogues

Insulin and insulin analogues have the advantage that they cannot cause lactic acidosis, and they cannot result in hypoglycaemia or weight gain. Because insulin is injected, gastro-intestinal side effects are excluded (GlaxoSmithKline, 2004).

3.6.3.2 Disadvantages of insulin and insulin analogues

The biggest disadvantage that insulin and insulin analogues have over oral antidiabetic drugs is the fact that they cannot be taken orally, and can therefore lead to patient non-compliance. Another disadvantage is the fact that the dosing is often dependent on meals. This is compounded by the fact that insulin is more expensive than oral antidiabetic drugs (GlaxoSmithKline, 2004).

3.6.4 Insulin and insulin analogues

As seen in chapter 2, insulin lispro is a novel, genetically engineered insulin designed to act more rapidly and with a shorter duration than human regular insulin. Numerous studies of insulin lispro in type 2 diabetes mellitus have demonstrated lower postprandial glycaemic excursions and less severe hypoglycaemic episodes (Dranitsaris *et al.*, 2000:276).

More recent reports have focused on methods to combine insulin lispro with appropriate basal insulin regimens and adjustments to meal plans. These adjustments have resulted in lower glycosylated haemoglobin (HbA_{1c}) levels without an increased risk of hypoglycaemia. Randomised clinical trials evaluating the insulin lispro (Humalog® Mix 25™) compared with human 30/70 and 20/80 insulin demonstrated that the postprandial glucose response following Humalog® Mix 25™ was closer to the normal physiological response and patients had a lower incidence of nocturnal hypoglycaemia (Dranitsaris *et al.*, 2000:276).

Dranitsaris and colleagues (2000279) did a cost-benefit analysis on the economic value of Humalog® Mix 25™ (insulin lispro). The cost proportion of the cost-benefit analysis was calculated from the monthly cost difference between Humalog® Mix 25™ and human 30/70 insulin. Since both products are usually given on a twice-daily schedule, there would be no differences in the use of syringes, supplies or other related resources. In addition, the final cost was not adjusted for reductions in number of hypoglycaemic episodes or postprandial glucose excursions because it was difficult to place a cost saving on these events.

3.6.5 Aspects of oral antidiabetic medication and economic evaluation

Current treatment algorithms for patients with type 2 diabetes mellitus are based on strategies to manage inadequate responses or treatment failures once diet and exercise have proved unsuccessful in meeting glycaemic control targets. First-line drug therapy usually consists of monotherapy with a sulfonylurea, a biguanide or an alpha-glucosidase inhibitor, while second-line therapy involves a combination of two of these oral anti-hyperglycaemic agents, with or without insulin (Hood *et al.,* 1998:317).

A number of undesired effects are associated with the most frequently prescribed antidiabetic agents. These include hypoglycaemia and body-weight gain (which are particularly associated with the sulfonylureas), gastrointestinal effects (often caused by biguanides and alpha-glucosidase inhibitors), as well as interactions with other drugs. Consequently poor compliance with medication, treatment cessation and alterations in therapy are common during the initial six months of treatment. This failure to achieve consistent metabolic control results in increased use of health care resources (Hood *et al.*, 1998:317).

Given the pressure on health care budgets worldwide, economic outcome models based on decision-analytical techniques have been developed to analyse the consequences (costs and clinical outcomes) of medical decisions (Hood *et al.*, 1998:318).

Ramsdell *et al.* (2003:821) developed a decision-analytical model to determine the direct costs of care and to evaluate six first-line oral drug treatment strategies in drug-naïve, newly diagnosed type 2 diabetes patients. The model was developed from a payer's perspective, incorporating only direct medical costs. It was assumed that all patients were treated to achieve glycosylated haemoglobin (HbA_{1c}) values of <7%. Patients who were uncontrolled (HbA_{1c} ≥7%) received add-on therapy until glycaemic control was achieved or insulin was required. In the case of primary failure (defined as little or no change in blood glucose or HbA_{1c} during the first three months of therapy) or adverse events, patients could be switched to three different first-line therapies before moving to an insulin-containing regimen. The six drugs that they used, were, glipizide GITS, metformin IR, metformin XR, glibenclamide (glyburide)/metformin, rosiglitazone, and repaglinide.

Figure 3.6 summarises a hypothetical cohort for the treatment of type 2 diabetes mellitus.

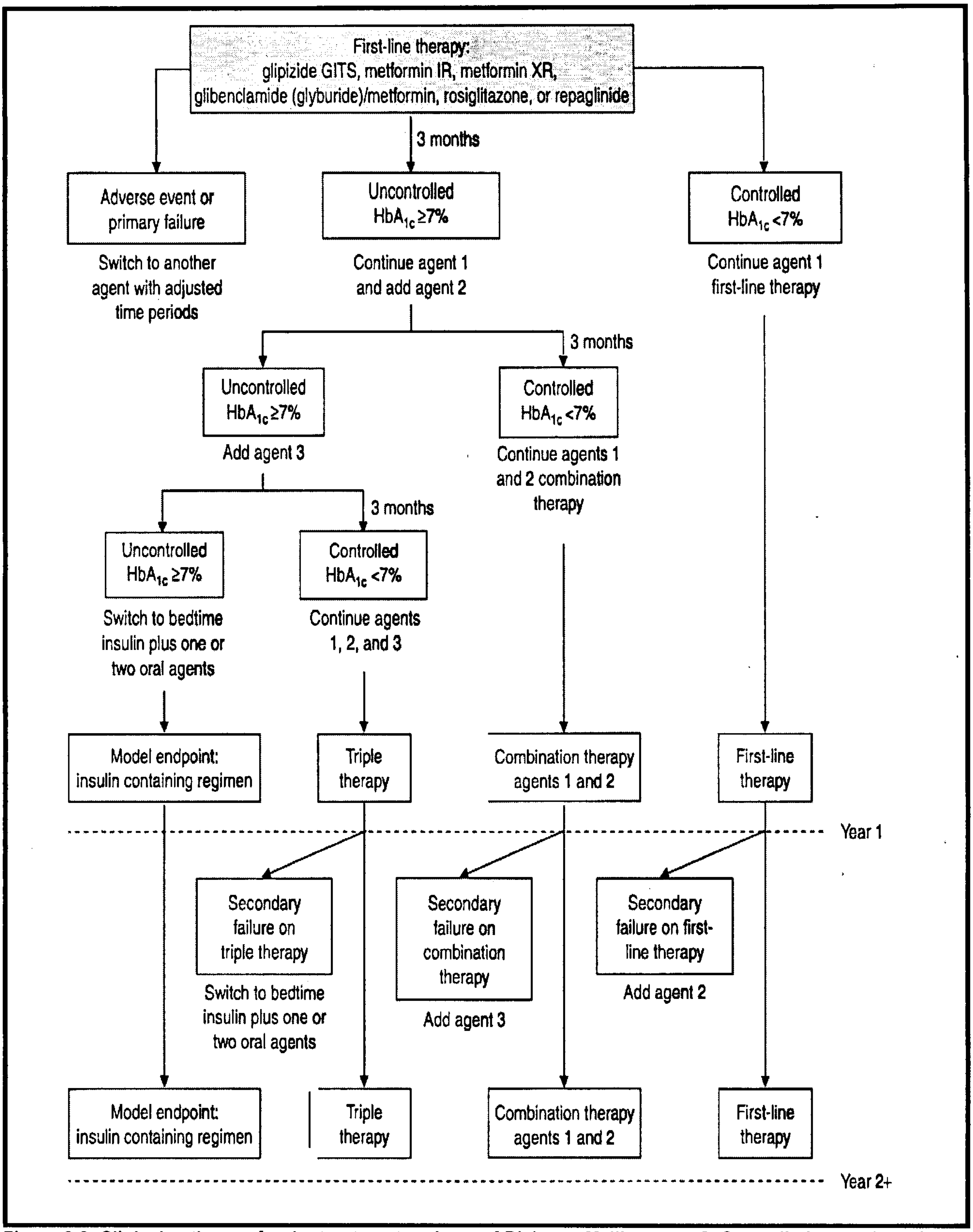


Figure 3.6: Clinical pathways for the treatment regimen of Diabetes Mellitus type 2. **Controlled** = a patient who achieves an HbA_{1c} value of <7% (goal) – patient remains on therapy; **GITS** = gastro-intestinal therapeutic system; **HbA_{1c}** = glycosylated haemoglobin; **IR** = immediate release; **primary failure** = after initiation of a first-line therapy, HbA_{1c} value does not change or changes minimally; patient is switched to another agent; **secondary failure** = HbA_{1c} value drifts to ≥7% after previously being in good control; assumed to occur after the first year of treatment; **uncontrolled** = patient experiences a reduction in HbA_{1c}, but HbA_{1c} value is ≥7% (partial response, not a goal) – another agent is added; **XR** = extended release (adapted from Ramsdell *et al.*, 2003:822).

Table 3.4 summarises the anti-hyperglycaemic drug regimens used in an economic model of first-line drug strategies for newly diagnosed type 2 diabetes.

Table 3.4 Anti-hyperglycaemic drug regimens used in an economic model of first-line drug strategies (adapted from Ramsdell *et al.*, 2003:823).

First-line therapy	+Second oral agent	+Third oral agent
Glipizide GITS	Metformin IR	Rosiglitazone
Metformin IR	Glipizide GITS	Rosiglitazone
Metformin XR	Glipizide GITS	Rosiglitazone
Glibenclamide (glyburide)/metformin	Rosiglitazone	None (progress to insulin)
Rosiglitazone	Glipizide GITS	Metformin IR
Repaglinide	Metformin IR	Rosiglitazone
Switches for adverse events[a] or primary failures[b]		
If on glipizide GITS, switch to metformin IR		
If on metformin IR/XR switch to glipizide GITS		
If on glibenclamide/metformin, switch to either glipizide GITS alone (50%) or metformin alone (50%)		
If on rosiglitazone, switch to glipizide GITS		
If on repaglinide, switch to metformin IR		

a. Adverse events = after initiation of first-line therapy, adverse event requires discontinuation of therapy; patient is switched to another agent.
b. Primary failure = after initiation of a first-line therapy, HbA_{1c} value does not change minimally; patient is switched to another agent.
GITS = gastro-intestinal therapeutic system; **IR** = immediate release; **XR** = extended release

Ramsdell *et al.* (2003:829) stated that their economic evaluation of oral anti-hyperglycaemic therapies demonstrated that careful scrutiny and selection of first-line drug strategies might provide short-term economic benefits to payers such as managed care organisations. Their findings suggested that effectiveness in achieving glycaemic goals is probably not different between various first-line strategies, as patients quickly require combination therapy to achieve the glycaemic goals. Ramsdell *et al.* (2003:829) stated that these findings are not surprising as the decision tree structures (reflecting an add-on approach to management) for each first-line strategy arm were comparable in terms of the combination and triple therapy regimens employed, as well as some of the success rates for first-line therapy.

Ramsdell *et al.* (2003:829) also stated that primary and secondary failure rates, as well as the adverse event rates, were also not substantial drivers differentiating the agents. Furthermore, they found that costs associated with adverse events and special monitoring for thiazolidinediones did not significantly contribute to the overall cost of treatment.

Table 3.5 summarises the adverse events in an economic model for newly diagnosed diabetes mellitus type 2.

Table 3.5 Adverse events in an economic model of first-line drug strategies for newly diagnosed type 2 diabetes mellitus (adapted from Ramsdell *et al.*, 2003:828).

Key adverse events associated with each anti-hyperglycaemic agent	Incidence of adverse event
Hypoglycaemia	
Mild	Varies[a]
Moderate (patient cannot tolerate therapy, and require third-party assistance)[b]:	
glipizide GITS	2.1% in first quarter
glibenclamide (glyburide)/metformin	2.1% in first quarter[c]
repaglinide	1% in first quarter
Severe (occurs with insulin only; requires third party assistance)[d]	0.7% during 7-month study period
Severe gastrointestinal discomfort[e]	
Metformin IR	6% in first quarter
Metformin XR	0.6% in first quarter
Glibenclamide/metformin	2% in first quarter
Lactic acidosis[f]	
Metformin IR	0.003% annually
Metformin XR	0.003% annually
Glibenclamide/metformin	0.003% annually
Elevated liver enzymes[g]	
Rosiglitazone	0.2%annually
Oedema[h]	
Rosiglitazone	4.8% in first quarter

a. Patient self-treats and does not require added costs from payer perspective.
b. 100% of patients with moderate hypoglycaemia require an office visit to evaluate therapy.
c. Product labelling information for glibenclamide did not include the percentage of patients discontinuing the agent due to moderate hypoglycaemia.
d.100% of patients with severe hypoglycaemia visit a physician office after the event, 35% visit an emergency department, 35% utilise an ambulance and 1% are hospitalised
e.100% of patients with severe gastrointestinal discomfort require an office visit to change therapy
f. 100% of patients with lactic acidosis visit an emergency room and are hospitalised.
g.100% of patients with elevated liver enzymes require additional ALT tests and office visit to change therapy.
h. 100%patients with oedema require office visit to change therapy and 20% receive further work-up.
ALT = alanine aminotransferase (SGPT); **GITS** = gastrointestinal therapeutic system; **IR** = immediate release; **XR** = extended release.

Ramsdell *et al.* (2003:829) concluded that for at least 95% of all models run simultaneously, the cost associated with a first-line strategy of either glipizide GITS or metformin IR was less than a first-line strategy with rosiglitazone or repaglinide. In addition, the metformin XR and glibenclamide/metformin strategies were lower in costs compared with repaglinide at least 95% of the time. Overall, the sulfonylurea strategy was less expensive compared with other agents in 86-99% of all models.

3.6.6 Insulin 70/30 Mix plus Metformin *vs.* triple oral therapy

A patient treated with three oral drugs is subjected to an additive risk of adverse events, and dose adjustments may become complex. In addition, there is the cost consideration of adding a second or third class of oral antidiabetic drug to therapeutic regimen. Where insulin therapy is instituted, the addition of metformin to insulin therapy has been shown to result in significant decreases in fasting plasma glucose (FPG) and HbA_{1c} values, as well as reduced insulin requirements (Schwartz *et al.,* 2003:2239).

Schwartz *et al.* (2003:2239) did a study to compare the efficacy, safety, and cost of two possible approaches for managing failure of combination therapy with two oral medications, namely

- adding a third class of oral antidiabetic drug, or
- switching treatment to insulin 70/30 mix twice daily plus metformin.

During their study, the following drugs were prescribed:

- Sulfonylureas: glimepiride, glipizide, sustained release glipizide, glyburide, and repaglinide.
- Thiazolidinediones: rosiglitazone and pioglitazone.
- Metformin.

The insulin used during this study included:

- Humulin® 30/70 (biosynthetic human insulin (rDNA origin) suspension – 30% regular and 70% isophane),
- Humulin® N (human insulin isophane suspension recombinant DNA origin), and
- Humulin® R (soluble biosynthetic human insulin (rDNA origin)

(Gibbon *ed.*, 2001:73; Schwartz *et al.,* 2003:2239).

Schwartz *et al.* (2003:2239) determined the cost for individual subjects upon the average daily drug administered. The average retail value cost was used. Generic drugs were used where applicable. Costs of liver function tests (recommended for certain oral agents), instruction in the use of the insulin injections and costs of needles were added to the insulin/metformin regimen costs.

Schwartz *et al.* (2003:2242) concluded that there was little overall difference in treatments when HbA_{1c} values, changes in FPG, and safety were compared. They stated that the triple oral therapy failed in 10,2% of the subjects and that there were also more dropouts due to adverse events potentially related to medication-related adverse events. Cost is an important factor in treatment decisions. Liver function tests add to the cost of therapy with oral agents, but is partially offset by needle costs involved in insulin therapy. The cost of insulin/metformin treatment regimen was substantially less than triple oral therapy with fewer treatment failures.

Schwartz *et al.* (2003:2243) concluded that a regimen of insulin 30/70 mix plus metformin showed substantial cost savings relative to a triple oral therapy approach, whereas the glycaemic improvement and safety findings of the two treatment approaches were largely similar. The failure of triple oral therapy to improve HbA_{1c} values occurred more frequently than with insulin.

3.7 THE INFLUENCE OF THE SOUTH AFRICAN GOVERNMENT ON HEALTH CARE

3.7.1 Introduction

In 1994, the newly elected democratic government faced the tremendous challenge of transforming a highly inequitable and fragmented health care system (Forman *et al.*, 2004:14).

In mid-1994, a Drug Policy Committee was appointed by the Minister of Health, with the following terms of reference: the committee was to develop a pricing plan for drugs used in South Africa in the public and private sectors. They had to develop a plan to ensure that drugs are tested and evaluated for effectiveness in the South African context of treatment using epidemiological approaches; they had to develop an Essential Drugs List to be used in the public and private sector and prepare treatment guidelines for the health personnel. The committee had to develop specific strategies to increase the use of generic drugs in South Africa (SA); they also had to prepare a plan for effective procurement and distribution of drugs in SA, particularly in the rural areas; investigate traditional medicines; and rationalise the structure for Pharmaceutical Services (Zuma, 1996a:1).

In January 1995 a Committee of Inquiry was appointed to investigate the possibility of a National Health Insurance System and how it could be financed. The Committee had to develop a plan for the provision of health care services at the primary level of care, based on the following policy objectives:

- To ensure universal and non-discriminatory access to quality primary health care for all South Africans, regardless of race, gender, income and place of residence.
- To ensure affordability and sustainability.
- Ensure efficiency and cost control.
- The plan should be consistent with the objectives of the Reconstruction and Development Programme (RDP).

This plan was approved and implemented on April 1, 1996 (Zuma, 1996b).

Public primary health care facilities, e.g. clinics, community health care centres and local authority clinics, provide services free of charge. At the hospital, services are however not free of charge, except for children and pregnant women. Medicines on the Essential Drugs List (EDL) for Primary Health Care are also free of charge in the public sector (Zuma, 1996b).
In 1997 the White Paper for the Transformation of the Health System in SA was compiled and published. This policy document elaborated the government's plan for achieving transformation and operationalising a universal right of access to equitable health care, and set the framework within which to assess the government's fulfilment of these goals in the subsequent decade. The White Paper is based on the overarching objective of developing a unified health system capable of delivering quality health care to all, guided by the strategic approach of providing comprehensive primary health care (Forman *et al.*, 2004:14).

A unified health system capable of providing quality health care to all would be achieved through the implementation of a broad range of policies and strategies including (Forman *et al.*, 2004:14)

- decentralising the management of health services with an emphasis on the creation of a district health system;
- increasing access to services by making primary health care available to all;
- ensuring the availability of safe, good quality essential drugs in health facilities; and
- rationalising health financing through budget reprioritisation.

The national, provincial and health district levels would play distinct and complementary roles, although health districts would be the major locus of implementation, and would emphasise the primary health care approach (Forman *et al.*, 2004:14).

On 4 November 2002, changes to the Regulations of the Medical Schemes Act (131/1998) were gazetted. On 1 January 2004, the introduction of Prescribed Minimum Benefits (PMBs) and the Chronic Disease List (CDL) were implemented. The list of PMBs is the basket of cases which all medical schemes are compelled to cover, and the chronic disease list shows the 27 chronic conditions which have been added to that list and which, from 2004, medical schemes are compelled to cover. Diabetes Mellitus type 2 is one of these conditions (Council for Medical Schemes, 2004:1).

3.7.2 Prescribed minimum benefits (PMBs)

PMBs are minimum benefits, which by law must be provided to all medical scheme members and include the provision of diagnosis, treatment and care costs for

- any emergency medical condition; and

- a range of conditions as specified in Annexure A of the Regulations to the Medical Schemes Act (131/1998), subject to limitations specified in Annexure A. Included in this list is the list of chronic conditions (Council for Medical Schemes, 2004:1).

An emergency medical condition is a sudden and, at the time unexpected onset of a health condition that requires immediate medical or surgical treatment, where failure to provide medical or surgical treatment would result in serious impairment to bodily functions or serious dysfunction of a bodily organ or part, or would place the person's life in serious jeopardy (Visser, 2004).

PMBs were introduced to avoid cases where individuals lose their medical scheme cover in the event of serious illness and are put at serious financial risk due to unfounded utilisation of medical services, and to encourage improved efficiency in the allocation of Public and Private health care resources. These PMBs cover a wide range of close to 300 conditions, such as meningitis, various cancers, cardiac treatment, diabetes mellitus, and many others, including medical emergencies (Visser, 2004).

The Department of Health will monitor the impact, effectiveness and appropriateness of PMB provisions. A review will be conducted at least every two years by the Department, which will involve the Council for Medical Schemes, stakeholders, provincial health departments and consumer representatives. These reviews shall provide recommendations for the revision of the Regulations on the basis of

- inconsistencies or flaws in the current regulations;
- the cost-effectiveness of health technologies or interventions;
- consistency with developments in the health policy; and
- the impact on medical scheme viability and its affordability to members (Visser, 2004).

Medical schemes are entitled to expect from its members to obtain treatment for a PMB from certain providers, the so-called "designated service providers" or DSP. Designated service provider (DSP) means a health care provider or group of providers selected by the medical scheme concerned as the preferred provider or providers to provide to its members diagnosis, treatment and care in respect of one or more PMB conditions (Visser, 2004).

A medical scheme which fails to identify a DSP in its rules will be subject to the obligation imposed by regulation 8 (1) to pay in full, without co-payment or the use of deductibles, in the diagnosis, treatment and care cost of the prescribed minimum benefits conditions. The obligation is only made subject to the provisions of regulation 8, which allow certain limitations on PMBs through the use of DSPs and other mechanisms. The medical schemes are strongly advised to identify one or more DSPs in their rules, because the Registrar of the Council of Medical Schemes will not approve rules, which do not identify a DSP, unless they provide for unlimited liability of the scheme to pay the cost of PMBs at any setting. A member that obtains a PMB from a DSP should not be faced with out-of-pocket payments. Members who voluntarily obtain a PMB from a non-DSP face co-payment, and patients who involuntarily obtain a PMB from a non-DSP do not face out-of-pocket payment. A beneficiary will be deemed to have involuntarily obtained a service from a non-DSP if, the service was not available from the DSP or would not be provided without reasonable delay; immediate medical or surgical treatment for a PMB condition was required under circumstances or at locations which reasonably precluded the beneficiary from obtaining such treatment from a designated service provider; or, there was no DSP within reasonable proximity to the beneficiary's ordinary place of business or personal residence (Visser, 2004).

The prescribed minimum benefits for the chronic disease list differ from the general list of PMBs in that their minimum treatment is specified in the therapeutic algorithms, which have been legislated for each condition (Council for Medical Schemes, 2004:2).

3.7.3 Pricing regulations of medicine in South Africa

On 16 January 2004, the Minister of Health, Dr. Manto Tshabalala-Msimang, announced draft regulations relating to a Transparent Pricing System for Medicines and Scheduled Substances made in terms of the Medicines and Related Substances Control Amendment Act of 1997, that were published in the Government Gazette (Tshabalala-Msimang, 2004a:1).

The minister stated that these regulations could be considered a major development in the Department of Health's (DOH) effort to ensure that South Africans have access to affordable, good quality medicine. In 1997, the Medicines and Related Substances Control Amendment Act, No.90 of 1997, introduced a new Section 18A to the Medicines and Related Substances Act. When this Act was passed in 1997, it was strongly opposed by pharmaceutical companies (Tshabalala-Msimang, 2004a:1).

On 30 April 2004, the Minister of Health published the finalised medicine pricing regulations in Government Gazette No. 26304. These regulations should have commenced on the 2nd of May 2004 (SA, 2004:1).

3.7.3.1 Single Exit Price

The term "single exit price" (SEP) is defined as the price set by the manufacturer or importer of a medicine or scheduled substance in terms of the regulations combined with the logistics fee and VAT, and is the price of the lowest unit of the medicine or scheduled substance within a pack multiplied by the number of units in the pack. The SEP must be clearly and legibly reflected on the package or the immediate container within which a medicine or scheduled substance is sold to a user. The manufacturer or importer must set the price if a person other than the manufacturer imports the medicine. For a one-year period, calculated from 2 May 2004, the single exit price may not be increased (Medikredit, 2004:2).

3.7.3.2 The method for setting the single exit price and dispensing fee

The draft regulations required that manufacturers set the single exit price at 50% below the official listed price contained in a publication known as the "Blue Book". The final regulations specify that the level of the exit price will be determined on a product-by-product basis, and that it will be determined in two phases. In phase one, the SEP will be the net price at which a medicine is currently being sold, and in phase two, the benchmark for the SEP will be based on an international price, calculated according to a prescribed formula. According to Health Minister, Dr. Tshabalala-Msimang, phase two will probably commence at the end of 2004 or early 2005 (Tshabalala-Msimang, 2004b:1). New products will use international pricing as the benchmark from the date of launch.

- **Single exit price for distributors and wholesalers**

In terms of the draft regulations, distributors and wholesalers can only charge a fee up to 15% of the manufacturer's exit price for a medicine that costs less than R40. Where the price is R40 or more, the maximum fee is R6. Furthermore, the regulations require of the manufacturer to set the exit price for each medicine. The Government, however, set a ceiling for the original exit price and requires that the price be increased only once a year, while it may be reduced any number of times, in the spirit of competition (Tshabalala-Msimang, 2004b:1).

- **Determination for the dispensing fee to be used by pharmacists**

With regard to medicines and scheduled substances that fall into Schedules 1 and 2 of the Act, in the absence of a prescription, the dispensing fee must, exclusive of VAT, not exceed 16% of the single exit price where the SEP is less than R100. If the medicine or scheduled substance's SEP exceeds R100, only R16 can be added to the SEP (SA, 2004:7).

With regard to medicines and scheduled substances that fall into Schedules 3,4,5,6,7 and 8 of the Act, and medicines falling into Schedules 1 and 2 in respect of which a prescription has been written, the dispensing fee, exclusive of VAT, must not exceed 26% of the SEP of a medicine or scheduled substance, where the SEP of these medicines or scheduled substance is less than R100. If the medicine or scheduled substance's SEP exceeds R100, only R26 can be added to the SEP (SA, 2004:8).

- **Determination for the dispensing fee to be used by persons that are licensed under section 22C(1)(a)**

Any other person who is licensed under section 22C(1)(a) of the Act to dispense medicine can charge a fee of no more than 16% of a single exit price of less than R100 and R16 for medicine with a price that is higher than R100, exclusive of VAT (SA, 2004:8).

Figures 3.7 and 3.8 indicate the method for the calculation of the single exit price for solid and liquid dosage forms were they are available in different pack sizes.

Two pack sizes (50 tablets and 500 tablets) of 500mg strength of a medicine.

Average 2003 price of 50 tablet pack = R50
Average 2003 price of 500 tablet pack = R300

2003 sales of 50 tablet pack = 100 000 packs
2003 sales of 500 tablet packs = 10 000 packs

Total 2003 discounts for 50 tablet pack sales in 2003 = R500 000
Total 2004 discounts for 500 tablet pack sales in 2003 = R200 000

$$\text{Unit price} = \frac{[(100\,000 \times 50) - (500\,000)] + [(10\,000 \times 300) - (200\,000)]}{[(100\,000 \times 50) + (10\,000 \times 500)]}$$

The price of the unit is R0,73/500mg tablet

The single exit price of the 50-tablet pack is R36,50
The single exit price of the 500-tablet pack is R365

Figure 3.7 Example 1: Calculation of the single exit price for solid dosage forms where it is available in different pack sizes (SA, 2004:14).

Two Pack sizes (125ml bottle and a 500ml bottle) of 5mg/ml strength of a medicine.

Average 2003 price of 125ml bottle = R50
Average 2003 price of 500ml bottle = R150

2003 sales of 125ml bottles = 10 000 bottles
2003 sales of 500ml bottles = 5 000 bottles

Total discounts for sales of 125ml bottles in 2003 = R50 000
Total discounts for sales of 500ml bottles in 2003 = R75 000

$$\text{Unit price} = \frac{[(10\,000 \times 50) - (50\,000)] + [(500 \times 150) - (75\,000)]}{[(10\,000 \times 125) + (5\,000 \times 50)]}$$

The price of the unit is R0,3

The single exit price of the 125ml bottle is R37,50
The single exit price of the 500ml bottle is R150

Figure 3.8 Example 2: Calculation of the single exit price for liquid dosage forms where it is available in different pack sizes (SA, 2004:14).

3.7.3.3 Value added tax calculations with regard to the new drug pricing regulations

There has been much uncertainty around the value added tax (VAT) calculations relating to the single exit price of drugs and the related dispensing fee. The Office of the South African Revenue Services (SARS) has informed the Department of Health that, regardless of the ambiguity, the VAT Act supersedes in this case. The ambiguity stems from the fact that the single exit price includes VAT, whilst the dispensing fee does not include VAT. It could be interpreted that the regulations imply that VAT may be calculated on VAT, but, SARS points out that this cannot be the case (BHF, 2004).

According to the Board of Health care Funders (BHF) the following method is the correct method for the determination of VAT, and is consistent with the interpretations of some tax experts with whom the BHF has consulted. The following method has been agreed upon (BHF, 2004):

- The SEP is inclusive of VAT.
- The dispensing fee, either 16%/R16 or 26%/R26, is not inclusive of VAT.
- Dispensed price = [(SEP – (VAT on SEP)) + (professional dispensing fee)] + VAT.
- The threshold of R100 refers to the threshold based on (SEP – VAT) number.
- Therefore, the VAT on the SEP plus the dispensing fee should be calculated as follows:
    - Step one: VAT should be deducted from the SEP
    - Step two: Dispensing fee should be added on the SEP less the VAT
    - Step three: VAT on both amounts combined should be added to give the final price.

Figure 3.9 describes some examples of how the VAT is determined according to the new pricing regulations.

Example 1: A drug with the SEP of R100 would be dealt with as follows:

R100 less 14% VAT = R87,72

R87,72 + 26% = R110,53

R110,53 + VAT of 14% = R126,00

Example 2: A drug with the SEP of R50 would be dealt with as follows:

R50 less 14% VAT = R43

R43 + 26% = R54,18

R54,18 + 14% VAT = R61,76.

Figure 3.9: Examples of the method for the determination of VAT with regard to the new drug pricing system.

The simple reading of the regulations say that if the SEP = R100, then the R26 dispensing fee applies, however, when the VAT is removed the SEP becomes R87,72, hence only 26% of R87,72 may be applied as the dispensing fee (BHF, 2004).

3.7.3.4 Rules relating to the services for which a pharmacist may levy a fee

On Friday, 15 October 2004, the South African Pharmacy Council published rules relating to the services for which a pharmacist may levy a fee and guidelines for levying such a fee in the Government Gazette number 26904 (South African Pharmacy Council, 2004a:3).

The services for which a pharmacist may charge a fee include, consultations, travelling and after-hour calls, collaboration with other health professionals, and certain procedures. A facility fee and dispensing fee may also be levied. All the fees are exclusive from VAT. The pharmacist's fee should be based on an hourly tariff and special units should be allocated to each procedure. Units are determined as follows: one unit = 1 minute = R6. There is also a maximum that may be allocated per procedure (South African Pharmacy Council, 2004a:6).

On Friday, 26 October 2004, the Pharmacy Council withdrew the board notice of the 15th. The Council stated that the implementation of these fees was difficult and could lead to misinterpretation. The Council decided that patients and pharmacists would benefit more if the guidelines were revised and clarified. The Council also stated that a detailed description of certain of the procedures was advisable, as they may not necessarily form part of the competencies of all pharmacists or of pharmacists in all practice settings. The Pharmacy Council has therefore decided to withdraw the Board notice, to review the content, and to develop clear directives so that the fees may be easily and fairly implemented (South African Pharmacy Council, 2004b:1).

Cost (pricing and the levy of a fee) of medicine is still a controversial matter and must still be decided on during February 2005.

The influence on the cost of the treatment of diabetics at this stage is still unclear. However, the minimum managed care plans and minimum prescribed benefits will have a large influence on the treatment of a diabetic.

3.8 SUMMARY

In this chapter an overview of managed care, pharmaco-economics and DUR was presented. The influence of the South African Government on health care was discussed including the new pricing regulations of medicine in South Africa. A comparison for suggested treatment algorithms for diabetes mellitus between different service providers was discussed, as well as the price comparison between different antidiabetic drugs.

In chapter four the empirical investigation will be described and discussed.

CHAPTER 4: Empirical Investigation

4.1 INTRODUCTION

In this chapter the research objectives, study population, data source, database and data analysis of this empirical investigation will be discussed.

4.2 RESEARCH OBJECTIVES

The research objectives are divided into general and specific objectives:

4.2.1 General objective

As explained in chapter one, the general objective of this study is to review the usage and cost of antidiabetic drugs by following a managed care approach.

4.2.2 Specific objectives

The specific objectives of the empirical study are to

- determine the prevalence and medicine treatment cost of diabetes according to the database of a prescription claims database;
- analyse the prescription patterns for different types of antidiabetic drugs according to the database;
- investigate the influence of the new pricing structure on the cost of antidiabetic drugs according to a prescription claims database;
- investigate the medication cost for the treatment of diabetes mellitus types one and two;
- determine the prevalence of the combination of insulin and oral antidiabetic agents;
- determine the defined daily dose for each oral antidiabetic agent;
- determine and analyse the prevalence and cost of the combination[a] products that are prescribed; and
- determine the prevalence, type and cost of combinations[b] between different antidiabetic agents.

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[a] Combination refers to an antidiabetic agent with more than one active ingredient, e.g. Glucovance® 250/1.25mg.
[b] Combinations refer to different antidiabetic agents prescribed together on one prescription.

4.3 STUDY POPULATION

The total population consisted of all the prescriptions on the database, while the study population consisted of all the prescriptions of patients using antidiabetic drugs for a one-year period starting on 1 January 2004 and ending on 31 December 2004. To ensure confidentiality, neither the name of the prescribing doctor nor the patient's name was revealed. A total of 2 595 254 prescriptions were used for the analysis.

The different strata were collected by following certain steps:
Step 1: All the prescriptions on the database were examined.
Step 2: Withdrawing all the prescriptions containing antidiabetic agents from the database.
Step 3: Classify the antidiabetic drugs as insulins or oral agents according to active ingredient.
Step 4: Classify the insulins according to time of action and active ingredient.
Step 5: Classify the oral antidiabetic drugs according to active ingredient.

4.4 DATA SOURCE

The data for this study were obtained from Interpharm Data Systems (Pty.) Ltd. Data were extracted from a period of 12 months, from 1 January 2004 to 31 December 2004. The study period was divided into three time periods, namely January to April, May to August and September to December. From January to April there were no limitations on the pricing structure of medicine (pre-single exit price). As seen in chapter three, section 3.7.3, new legislation that changed the pricing structure of medication came into effect in May 2004. May to August is referred to as the interim period, where the new regulations were to be phasing in. As from September 2004 the new pricing regulation was fully implemented, therefore September to December can be referred to as the post-single exit price period.

4.5 DATABASE

The database consists of all the prescriptions claimed through Interpharm Data Systems for the study period 1 January 2004 to 31 December 2004. The following fields were used in this study:

- The Nappi code of the medicine product
- The description (trade name) of the drug
- The quantity of the drug that were dispensed
- The price of the drug
- The prescription number,

- The date of dispensing
- Indicator for generic or innovator product

4.6 RESEARCH DESIGN AND METHODOLOGY

A retrospective drug utilisation study was done on data provided by the database of Interpharm Data Systems® (Pty.) Ltd. (See section 3.4.2.2 for the description of retrospective drug utilisation studies).

No experiments, e.g. clinical trials, were done, therefore, the research design can be described as a non-experimental, retrospective quantitative research.

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

- the selection of the study population (see section 4.3);
- the selection of the measuring instruments (see section 4.7.3);
- data analysis (see section 4.7);
- the report and discussion of the results of the empirical investigation (see chapter 5); and
- the recommendations based on the results of the empirical investigation (see chapter 6).

4.7 DATA ANALYSIS

The data were analysed by using different computer software programmes and by applying different classification systems. Specific measuring instruments and statistical analyses have been applied to the data.

4.7.1 Data analysis organogram

The data were analysed by employing certain steps as presented in the organogram (see Appendix A). The Statistical Analysis System® SAS 9.1® (SAS institute Inc., 2002-2003) was used to extract and analyse certain data from the database. Microsoft Word 2000® and Microsoft Excel 2000® were used to create basic tables and figures and to compute certain statistical measures.

4.7.2 Classification systems used

Different classification systems were used during this study:

4.7.2.1 The Nappi Code

A Nappi code (National Approved Product Pricing Index) is a unique nine-digit long product code implemented with electronic transactions in mind. Each code is unique for the trade name, pack size, strength, manufacturer plus exclusions, etc. (Snyman, 2004:5a).

4.7.2.2 The MIMS classification system

The MIMS (Monthly Index of Medical Specialities) classification system classifies medicine according to its pharmacological action. The MIMS classifies the antidiabetic drugs into two groups, namely insulin and oral antidiabetic drugs (Snyman, 2004:311 & 313). See Appendix B for a complete list of the MIMS classification.

4.7.2.3 Classification of agents according to the active ingredient

The SAMF (South African Medicines Formulary) classifies medicine according to its pharmacological active ingredient, and in the case of insulin, according to time of action. This classification system was used to identify the different classes of oral antidiabetic drugs and to classify the different insulins (Gibbon *ed.*, 2003:70).

Both the SAMF and MIMS were used to attain the generic and brand names of the different antidiabetic drugs.

Appendix C gives a classification of all the antidiabetic drugs with the Nappi codes according to the MIMS and SAMF.

4.7.3 Measuring instruments and statistical analysis

The different measuring instruments and statistical analysis that were used in this study are discussed below:

4.7.3.1 Measuring instruments

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

- *Prevalence*

The prevalence can be defined as the number of cases of disease, infected persons, or persons with some other attribute, present at a particular time and in relation to the size of the population from which it was drawn (Pam Pohly's Net Guide, 1997).

- *Frequency*

The frequency for a data value is the number of times the value occurs in the data set (Jaisingh, 2000:6).

Banerjee (2003:23) describes a frequency distribution as a listing of all the classes or categories of a data set and the number of observations contained within each class. This represents the relation between a set of mutually exclusive and exhaustive measurement classes and the frequency of each.

For the purpose of this study, the prevalence and frequency can be seen as the same value.

- *Prescribed Daily Dose*

The prescribed daily dose (PDD) has already been discussed in chapter 3 of this dissertation (see chapter 3, section 3.4.8.4) and will be applied to the oral antidiabetic agents in order to comment on the utilisation of these agents.

- *Economic impacts and cost- minimisation*

The influence of cost and economic concepts as related to this study is presented in:

  - Cost-minimisation (Refer paragraph 3.3.3.4);
  - Cost (refer paragraph 3.4.8.1);
  - Pricing regulations (refer paragraph 3.7);
  - Economic impacts (refer table3.3)

4.7.3.2 Statistical analysis

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

- *Arithmetic mean (average)*

Banerjee (2003:3) defines the arithmetic mean as the sum of all values making up the set of observations divided by the total number of observations in the set.

$$\textbf{Mean} = \frac{\textbf{sum of all the entries}}{\textbf{number of entries}}$$

- *Percentages*

Per cent can be defined as parts per hundred. To determine percentages, an amount has to be designated as representing the whole amount. That amount is equal to 100% (BMCC Math Tutorials,2005:1). The percentage can be calculated as follows:

$$X\% = \frac{x}{X} \times 100$$

Where: **x** = the numeric part that is to be compared, and

X = the total amount.

- *Standard deviation*

The standard deviation is a statistic that tells you how tightly a set of values is clustered around the mean in a set of data (Niles, 2005:2).

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

Mathematically:

Variance:

$$S^2_x = \frac{\sum(x_i - x)^2}{(n - 1)}$$

Standard deviation:

$$s_x = \sqrt{S^2_x}$$

- *Range*

The range can be defined as the difference between the largest and smallest values in a data set. The definition is true for a sample as well as a limited population of values (Jaisingh, 2000:45).

- *Cost prevalence index*

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

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

$$\textbf{Cost prevalence index} = \frac{\textbf{cost\%}}{\textbf{prevalence\%}}$$

The cost prevalence index is an indicator of the expensiveness of antidiabetic agents and can be analysed as follows:

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

- *d-values/ effect sizes*

According to Talheimer and Cook, (2002:3) an effect size is the difference between two means divided by the standard deviation.

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

Where:

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

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

- d = 0.2: small effect with no practical significant difference.
- d = 0.5: medium effect, which is observable and may be significant.
- d = 0.8: large effect which is significant and of practical importance.

4.8 SUMMARY

In this chapter the empirical investigation was discussed. The research objectives, study population, data source, database, research design and data analysis were described.

The results of the empirical investigation will be discussed in chapter 5.

CHAPTER 5: Results and discussion

5.1 INTRODUCTION

In this chapter the results of the empirical investigation will be reported and discussed. The results are for the period from 1 January 2004 until 31 December 2004. The results will be presented in the following categories:

- The prevalence and cost of medicine items recorded on the database.
- The prevalence and cost of endocrine system agents in the total database.
- The prevalence and cost of the antidiabetic items in the endocrine system.
- The prevalence and cost of antidiabetic agents in the total database.
- The total types of antidiabetic agents prescribed according to pharmacological classification.
- The frequency of the individually prescribed combinations of insulin and oral antidiabetic agents.
- The analysis of the prescribing patterns of each individual antidiabetic agent.
- The cost analysis of the individual antidiabetic agents.
- Determination of the average prescribed daily dose for each antidiabetic agent according to pharmacological classification.
- Determination and analysis of the cost of the combination[a] products that are prescribed.
- The frequency, type and cost of combinations[b] between different oral antidiabetic agents.

In 1998 La Grange published the results of a study on the management of type II diabetes mellitus by using a medicine claims database (the data for that study was for the period 1 October 1996 to 31 December 1996). In this dissertation comparisons will be made with her study where applicable. It is important to note that there were fewer oral antidiabetic drugs available on the South African market during 1996 if compared to 2004. As in La Grange's study, diagnostic material used by diabetic patients is not included in this study. Because the La Grange study involved only oral antidiabetic drugs only such drugs will be compared.

In 1999 Truter did a quantitative study on patients receiving antidiabetic medication. A banking medical aid provided the data, and the data for her study was for the time period 1 January

[a] Combination product refers to a product with two active ingredients, e.g. metformin/glibenclamide (Glucovance® 500/5mg).
[b] Combinations refer to more than one antidiabetic agent on the same prescription.

1996 to 31 December 1996. A total of 8 514 antidiabetic medication records of 1100 patients were selected for her study.

Furthermore the results of this study will be presented, where applicable, in the frame work of the new single exit price (SEP) as discussed in paragraph 5.8.

5.2 DEFINITIONS

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

- *Medicine item:* An agent or preparation that contains at least one active ingredient and is used to treat or prevent an illness.
- *Antidiabetic agents:* Medication that is used in the management of Diabetes Mellitus (see chapter 2 table 2.7 and 2.8), and categories in the MIMS under section 19.1.
- *Prescription:* A written instruction from a legal prescriber to a pharmacist to dispense a specific medication. A prescription may contain one or more medicine items. The abbreviation Rx will be used in tables and figures.
- *Patient:* A patient is someone receiving medication on prescription, for the purpose of this study especially antidiabetic medication and during the period 1 January 2004 to 31 December 2004.
- *Total database or total population:* All the prescriptions on the database.
- *Study population:* All the antidiabetic patient records used during this study.

5.3 STATISTICAL METHODS

Descriptive statistics were used during this study (as described in Chapter 4). Some of the tables will not add up to one hundred percent, due to rounding off.

Except if otherwise indicated the tables and figures refer to the study year 2004, or specific periods thereof, e.g. January to April, May to August, or September to December.

For the purpose of this study, prevalence and frequency will be regarded as the same. Both refer to the number of times a certain value occurs in a set of data. It is assumed that all the data obtained from the database are correct.

5.4 MEDICINE ITEMS ON THE DATABASE

5.4.1 An overview of the medicine items on the total database

On the database medicine items as well as non-medicine items (e.g. needles, plasters, etc.) were observed. For the purpose of this study only the medicine-items were analysed.

Table 5.1 summarises the prevalence and cost of all medicine items on the database for the year 1 January 2004 to 31 December 2004.

Table 5.1: The prevalence and cost of medicine items on the database (1 January-31 December 2004)

Description	Medicine items (a)	Antidiabetic drugs (b)	Percentage (%) (c)*
Number of prescriptions (N)	2 595 254	106 172	4.1
Total number of medicine items prescribed (N)	5 305 882	143 447	2.7
Average number of medicine items per prescription	2.04 ± 1.27	1.35 ± 0.52	
Minimum number of items per prescription	1	1	
Maximum numbers of items per prescription	18	5	
Total cost of items in Rand value (R) (N)	661 223 146.00	29 734 655.19	4.5
Average cost per item in Rand value (R)	124.62 ± 228.55	207.29 ± 280.92	0
Minimum cost per item in Rand value (R)	0.01	0.07	
Maximum cost per item in Rand value (R)	92 097.44	6 388.10	

From table 5.1 it can be concluded that 4.1% of the prescriptions were for antidiabetic drugs, while only 2.7% of all the medicine items were antidiabetic drugs.

5.5 FREQUENCY AND COST OF ALL THE ANTIDIABETIC AGENTS

5.5.1 Introduction

In this section objective three will be answered, namely to determine the prevalence and medicine treatment cost of diabetes. (See Chapter 1)

5.5.2 Total cost of antidiabetic agents

In this section the prevalence and cost of the antidiabetic agents will be compared to the total number of medicine items on the database as well as the cost of all the items on the database.

* Percentage (c) is determined by dividing b by a, and then multiply it with 100.

Table 5.2: Prevalence and cost of antidiabetic agents in comparison with the total database and endocrine system agents

	Prevalence	Total costs in Rand	CPI
Total medicine items on the database in one year	**5 305 882**	**661 223 146.00**	-
Total number of items for the time January-April	1 363 585	198 934 122.00	-
Total number of items for the time May-August	1 953 845	242 721 616.00	-
Total number of items for the time September-December	1 988 452	219 567 408.00	-
Total number of endocrine system agents for year 2004	**445 553**	**63 365 039.97**	
Total number of endocrine system agents for the time January-April	128 845	20 977 558.33	-
Total number of endocrine system agents for the time May-August	149 812	21 723 821.13	-
Total number of endocrine system agents for the time September-December	166 896	20 663 660.51	-
Percentage (%) of endocrine system agents on the database	8.4	9.6	1.1
Total number of antidiabetic agents for year 2004	**143 447**	**29 734 655.19**	-
Total number of antidiabetic agents for the time January-April	37 806	9 278 245.64	-
Total number of antidiabetic agents for the time May-August	47 866	10 473 206.69	-
Total number of antidiabetic agents for the time September-December	57 775	9 983 202.86	-
Percentage (%) of antidiabetic agents on total database	2.7	4.5	1.7

From table 5.2 it can be calculated that the antidiabetic agents account for almost 2.7% of all the medicine items on the database and almost 4.5% of the total cost (n = R661 223 146.00). The endocrine system agents account for almost 8.4% of the total medicine items on the database (n = 5 305 882). The total cost for the endocrine system agents was R20 977 558.33 for the time January to April, R21 723 821.13 for the time May to August and R20 663 660.51 for the time September to December. The CPI indicates that endocrine system agents, as well as antidiabetic drugs are relatively expensive.

As seen from table 5.2, antidiabetic agents constituted of 143 447 (32.2% n = 445 553) of all the endocrine system agents in the database.

5.5.3 Cost and prevalence of antidiabetic agents

Table 5.3 describes the cost and prevalence of the two (insulins and oral antidiabetic agents) pharmacological groups of antidiabetic agents according to administration route. For the purpose of this study the data were divided into three time frames, namely January to April, May to August and September to December 2004 (see chapter 3, section 3.7.3 for the implementation plans for the single exit price during 2004).

Table 5.3: Cost and prevalence of the two pharmacological groups of antidiabetic agents according to administration route (oral *vs.* insulin)

Group	Number of items (N)	Total cost in Rand (R)	% Prevalence*	Cost %**	CPI ***
January-April					
Oral	30648	3 846 942.57	81.1	41.5	0.5
Insulin	7158	5 431 303.07	18.9	58.5	3.1
Total	37806	9 278 245.64	100	100	1
May-August					
Oral	38957	4 086 107.97	81.4	39.0	0.5
Insulin	8909	6 387 098.72	18.6	61.0	3.3
Total	47866	10 473 206.69	100	100	1
September-December					
Oral	46713	3 672 255.73	81.0	36.8	0.5
Insulin	11062	6 310 947.13	19.0	63.2	3.3
Total	57775	9 983 202.86	100	100	1

* % Prevalence was determined by dividing N with the total (prevalence) per period and then multiply it by 100 (e.g. (30648/37806) x 100)

** Cost % was determined by dividing R-value with the total cost in Rand per period and then multiply it with 100 (e.g. (3846942.57/9278245.64) x 100)

*** CPI = Cost prevalence index. CPI is determined dividing the cost % and the % prevalence per period (see Chapter 4).

It can be determined from table 5.3 that the oral antidiabetic agents are relatively less expensive than the insulins and they are prescribed more frequently (a ratio of 0.81:0.18). This is a slightly higher ratio than described in the literature (refer section 2.2.2.1). A reason for the oral agents being prescribed more frequently can be because (as seen in the literature, Chapter 2 section 2.2.2.1) type one diabetes mellitus constituted only 10% to 15% of all the diabetic patients.
From the database it was calculated that the total number of insulin products for the study period January to December 2004 was 27 129, at an average cost of R668.26 ± R336.40. The number of oral antidiabetic agents for the same period was 116 318 at an average cost of R99.77 ± R99.04.

As described in chapter 4, the cost prevalence index (CPI) is an indicator of the relationship between the number of medicine items and the cost. Since the CPI of the oral agents is less than one, it is a clear indication that the therapy is relatively inexpensive. The CPI of the insulins, however, is more than 1 (3.1 and 3.3) and in comparison insulin therapy is relatively expensive.

According to the study done by Truter, the insulins accounted for almost 33% of all the antidiabetic medication prescribed during 1996. Whilst the usage of insulins reported in this study is considerably lower than reported by Truter, it is only slightly higher than the 10-15% reported in the literature (Refer to chapter 2, section 2.2.2.1).

In September 2004 the "new pricing regulations" set by the Department of Health were "fully" implemented (refer to chapter 3, section 3.7.3) and it could have made an impact on the total cost of antidiabetic agents. If the total cost of the time between May and August is compared to that of September to December there is a difference in the total costs of R490 003.83. This indicates that although there were 9909 more items prescribed between September to December (n = 57775 medicine items) in comparison with May to August (n = 47866 medicine items), the total cost for the 57775 items is less than the cost of the 47866 items, an indication of the influence of the implementation of the single exit price (SEP).

5.5.4 Average cost per medicine item, average cost per prescription and average number of medicine items per prescription

In table 5.4 the average cost per item, average cost per prescription and average number of items per prescription will be summarised.

Table 5.4: Summary of the average cost per medicine item and per prescription, and number of medicine items per prescription of the antidiabetic agents

Time	Average cost per antidiabetic item (Std. deviation) (R)	Average cost insulins (Std.deviation) (R)	Average cost oral agents (Std deviation) (R)	Average number of items	Standard Deviation	Average cost per antidiabetic prescription (R)	Standard Deviation (R)
January-April	245.42 ± 313.35	758.77 ± 383.74	125.52 ± 103.94	1.34	0.51	329.75	410.10
May-August	218.80 ± 298.99	716.93 ± 355.39	104.89 ± 106.00	1.35	0.52	295.88	379.06
September-December	172.79 ± 235.33	570.51 ± 252.55	78.61 ± 84.05	1.36	0.52	234.14	300.49
Total period (Jan-Dec 2004)	**207.29 ± 280.92**	**668.26 ± 336.40**	**99.77 ± 99.04**	**1.35**	**0.52**	**280.06**	**361.00**

According to table 5.4 the average cost per item is relatively lower for the time period September to December (R172.79 ± R235.33) in comparison with the average cost per item for the time periods January to April (R245.42 ± R313.35) and May to August (R218.80 ± R235.33). The same pattern is experienced with the average cost per antidiabetic prescription. This can also be due to the implementation of the pricing regulations that came into "full" effect in September 2004 (see section 5.3.3 and section 3.7.3). The relatively large standard deviation can be due to the fact that a variety of products were prescribed, for example oral antidiabetic agents versus insulins or generic versus innovator products. These aspects will be discussed in paragraphs 5.9.2 and 5.9.3.

La Grange (1998:140) determined the average cost per oral antidiabetic item to be R138.63 ± 92.51. Therefore it can be calculated that the average cost of antidiabetic agents is almost 1.4

times lower for the time January to December 2004 when compared to the study done by La Grange in 1998. If the different time periods is compared to La Grange's study, it can be determined that for the time January to April 2004 the average cost of antidiabetic agents was1.1 times less expensive than in 1996, for the time May to August 2004 it was 1.3 times less expensive and for the time September to December 2004 it was 1.8 times less expensive than in 1996. The average number of items per prescription was the same in 1996 study results and in 2004.

Truter (1998:136) determined the "average cost" per antidiabetic item to be R126.25 (1996 data).

Note: In this chapter the % frequency is determined by dividing the prevalence of each individual agent with the total prevalence of all the agents and then multiplying it with 100 (see section 4.7.3.2), the cost % is divided in the same manner using the total cost of each individual agent and the total cost off all the agents. See section 4.7.3.2 for formula for determining the CPI. Where the percentages do not add up to 100% it is due to rounding-off.
It is assumed that 26% is added to the single exit price for the antidiabetic drugs during the period from September to December.
VAT was not taken into account in the calculation of the gross profit.

5.6 THE PREVALENCE AND USAGE PATTERNS OF INSULINS AS ANTIDIABETIC AGENTS

5.6.1 Introduction

As described in chapter two, section 2.7.4.1 insulin is mainly used as treatment for type 1 diabetes and in combination with oral antidiabetic agents for the treatment of type 2 diabetes.

As seen in the previous section the insulins are more expensive than the oral antidiabetic agents and they are prescribed less frequently than the oral agents, because the insulins are mainly prescribed for the treatment of type one diabetes and only as final treatment regime in type two diabetics (see chapter 2 figure 2.2 page 26).

Figure 5.1 presents a summary of the prevalence of insulins for the year January to December 2004.

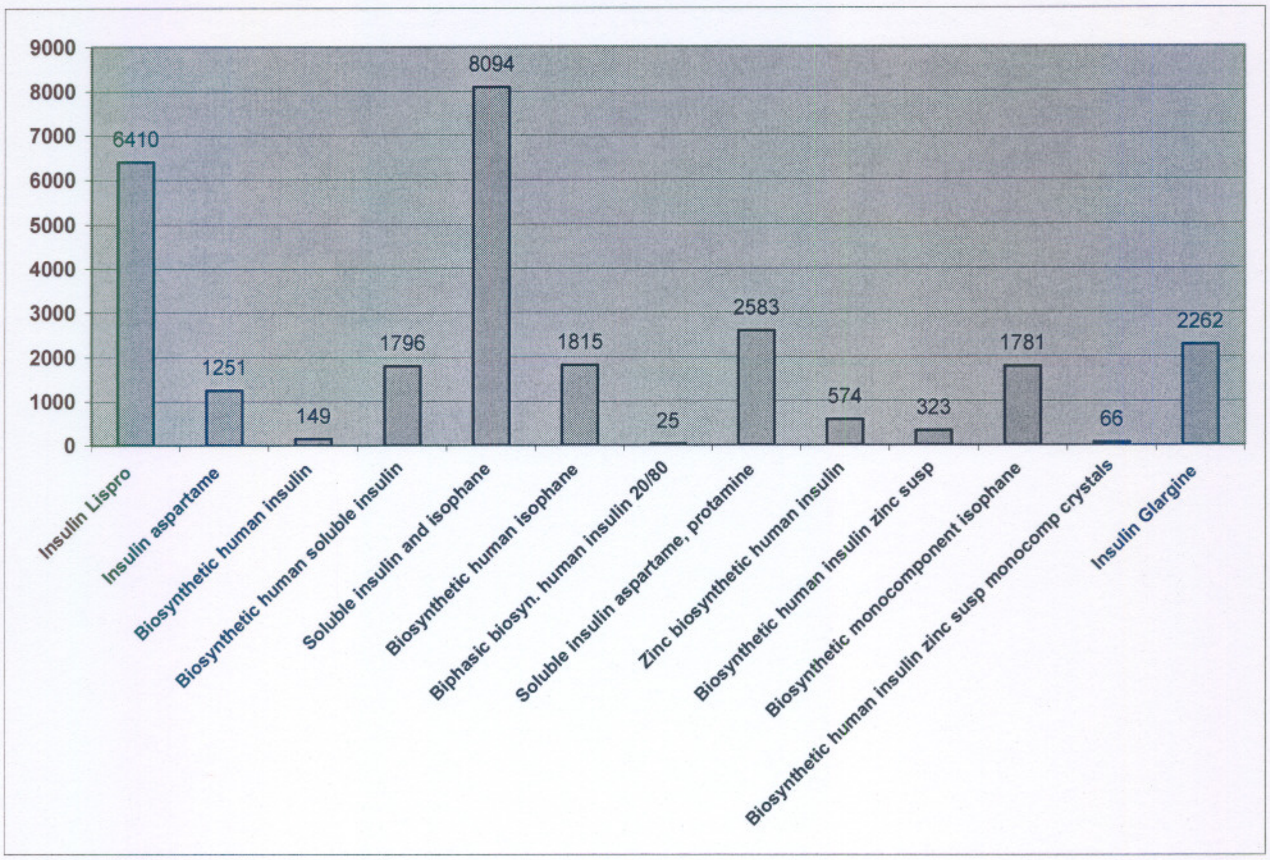

Figure 5.1: **Prevalence of insulins for the year 2004.**

The three most prescribed groups of insulin - insulin lispro; soluble insulin and isophane; and soluble insulin aspartame and protamine – amount to 63% (n = 27129) of all the insulins prescribed during the year January to December 2004.

5.6.2 Cost and prevalence of the insulins

As seen in section 5.5.3 the insulins amount to 18.9% (n = 143447) of all the antidiabetic agents in the database.

In table 5.5 the cost and prevalence of the insulins will be summarised according to the nature and active ingredients for the three study periods, namely January to April, May to August and September to December.

Table 5.5: Cost and prevalence of insulin agents according to the study periods

Active ingredient	Agent (Trade Name ®)	Prevalence	Average cost (R)	Standard deviation (R)	Total cost (R)	Frequency %	Cost %	CPI
January-April						(n = 7158)		
Insulin Lispro	Humalog Mix 25 Penset	791	767.81	561.73	607 338.67	11.1	11.2	1.0
	Humalog Mix 25 Cartridges	79	866.32	313.37	68 439.39	1.1	1.3	1.2
	Humalog Mix 25 Injection	16	861.31	637.34	13 780.94	0.2	0.3	1.5
	Humalog 10ml Ampoules	38	581.57	282.38	22 099.78	0.5	0.4	0.8
	Humalog 3ml Penset/Prefill	640	917.43	459.34	587 156.92	8.9	10.8	1.2
	Humalog 3ml Cartridge injection	92	860.54	331.76	79 169.32	1.3	1.5	1.2
Insulin aspartame	Novorapid 3ml FlexPen	289	754.65	271.44	218 094.31	4.0	4.0	1.0
	Novorapid 3ml Penfill	57	825.50	312.80	47 053.52	0.8	0.9	1.1
Biosynthetic human insulin	Humulin R 10ml vial	25	414.29	285.17	10 357.15	0.3	0.2	0.7
	Humulin R 3ml cartridges	20	794.53	515.92	15 890.67	0.3	0.3	1.0
	Humulin R Humaject Pen 5ml	5	415.33	340.86	2 076.63	0.1	0	0
Biosynthetic human soluble insulin	Actrapid HM Pensets 1.5ml	1	786.16	0	786.16	0	0	0
	Actrapid HM Pensets 3ml	333	827.56	359.45	275 577.77	4.7	5.1	1.1
	Actrapid HM Penfill 3ml	44	839.05	385.17	36 918.00	0.6	0.7	1.2
	Actrapid HM 10ml Ampoules	115	456.02	268.32	52 442.74	1.6	1.0	0.6
Soluble insulin and isophane	Actraphane HM Penset 1.5ml	1	285.83	0	285.83	0	0	0
	Actraphane HM Penset 3ml	1594	845.14	355.05	1 347 157.13	22.3	24.8	1.1
	Actraphane HM Penfill 3ml	143	809.07	434.68	115 697.65	2.0	2.1	1.1
	Actraphane HM 10ml Ampoules	287	526.19	278.62	151 017.05	4.0	2.8	0.7
Biosynthetic human isophane	Humulin 30/70 3ml cartridges	64	741.33	280.38	47 445.11	0.9	0.9	1.0
	Humulin 30/70 10ml vial	21	657.11	243.92	13 799.22	0.3	0.3	1.0
	Humulin 30/70 Humaject Injection	42	837.67	580.05	35 181.94	0.6	0.6	1.0
	Humulin N 3ml Penset	269	645.09	205.18	173 529.05	3.8	3.2	0.8
	Humulin N 3ml Cartridges	41	765.11	408.21	31 369.50	0.6	0.6	1.0
	Humulin N Humaject 3ml Injections	1	459.06	0	459.06	0	0	0
	Humulin N 10ml vial	62	378.70	122.58	23 479.28	0.9	0.4	0.4
Biphasic biosynthetic	Mixtard 20/80 Penfill	11	836.32	310.56	9 199.51	0.2	0.2	1.0

Table 5.5: (Continue) Cost and prevalence of the Insulins

Active ingredient	Agent (Trade Name ®)	Prevalence	Average cost (R)	Standard deviation (R)	Total cost (R)	Frequency %	Cost %	CPI
human insulin 20/80								
Soluble insulin aspartame and protamine	Novomix 30 Flexpen 3ml Injection	451	771.28	287.47	347 848.57	6.3	6.4	1.0
	Novomix 30 Penfill 3ml Injection	37	996.23	358.93	36 860.42	0.5	0.7	1.4
Zinc biosynthetic human insulin	Humulin L 10ml vial	173	395.18	131.90	68 365.47	2.4	1.3	0.5
Biosynthetic human insulin zinc suspension	Monotard HM 10ml Ampoules	104	445.90	200.34	46 373.50	1.5	0.9	0.6
Biosynthetic monocomponent isophane	Protaphane HM Penset 1.5ml	1	393.08	0	393.08	0	0	0
	Protaphane HM Penset 3ml	605	664.28	195.84	401 888.97	8.5	7.4	0.9
	Protaphane HM Penfill 3ml	79	694.09	268.25	54 833.48	1.1	1.0	0.9
	Protaphane HM 10ml Ampoules	95	417.15	158.78	39 629.63	1.3	0.7	0.5
Biosynthetic human insulin zinc suspension monocomponent crystals	Ultratard HM 10ml Ampoules	25	360.14	107.50	9 003.53	0.3	0.2	0.7
Insulin Glargine	Lantus 300IU/3ml	308	907.18	287.65	279 410.90	4.3	5.1	1.2
	Lantus 300IU/3ml O/T	139	830.68	256.13	115 465.07	1.9	2.1	1.1
	Lantus 1000IU/10ml	60	757.14	334.43	45 428.15	0.8	0.8	1.0
Total		**7158**	**758.77**	**383.74**	**5 431 303.07**	**100**	**100.2**	**1.0**
May-August						**(n = 8909)**		
Insulin Lispro	Humalog Mix 25 Penset	1086	872.45	438.40	947 485.12	12.2	14.8	1.2
	Humalog Mix 25 Cartridges	136	853.49	341.65	116 074.60	1.5	1.8	1.2
	Humalog Mix 25 Injection	25	901.80	587.04	22 544.88	0.3	0.4	1.3
	Humalog 10ml Ampoules	40	445.65	227.69	17 826.09	0.4	0.3	0.8
	Humalog 3ml Penset/Prefill	762	828.68	424.02	631 457.49	8.6	9.9	1.2
	Humalog 3ml Cartridge injection	110	753.88	279.24	82 926.85	1.2	1.3	1.1
	Humaject/Humalog 3ml	1	1 004.52	0	1 004.52	0	0	0
Insulin aspartame	Novorapid 3ml FlexPen	346	680.39	277.00	235 414.64	3.9	3.7	0.9
	Novorapid 3ml Penfill	57	719.02	295.04	40 984.10	0.6	0.6	1.0
Biosynthetic human insulin	Humulin R 10ml vial	24	300.24	31.83	7 205.74	0.3	0.1	0.3
	Humulin R 3ml cartridges	19	479.78	168.18	9 115.90	0.2	0.1	0.5
	Humulin R Humaject Pen 5ml	11	663.01	222.00	7 293.13	0.1	0.1	1.0

Table 5.5: (Continue) Cost and prevalence of the Insulins

Active ingredient	Agent (Trade Name ®)	Prevalence	Average cost (R)	Standard deviation (R)	Total cost (R)	Frequency %	Cost %	CPI
Biosynthetic human soluble insulin	Actrapid HM Pensets 1.5ml	1	54.21	0	54.21	0	0	0
	Actrapid HM Pensets 3ml	430	734.61	375.28	315 882.32	4.8	4.9	1.0
	Actrapid HM Penfill 3ml	63	722.45	329.88	45 514.62	0.7	0.7	1.0
	Actrapid HM 10ml Ampoules	113	386.66	162.18	43 693.00	1.3	0.7	0.5
Soluble insulin and isophane	Actraphane HM Penset 1.5ml	2	334.64	0	669.28	0	0	0
	Actraphane HM Penset 3ml	2025	762.82	349.85	1 544 714.88	22.7	24.2	1.1
	Actraphane HM Penfill 3ml	244	711.37	292.97	173 573.52	2.7	2.7	1.0
	Actraphane HM 10ml Ampoules	447	472.17	211.69	211 059.44	5.0	2.3	0.7
Biosynthetic human isophane	Humulin 30/70 3ml cartridges	104	732.23	279.13	76 151.91	1.2	1.2	1.0
	Humulin 30/70 10ml vial	16	762.05	607.05	12 192.82	0.2	0.2	1.0
	Humulin 30/70 Humaject Injection	55	790.74	479.81	43 490.70	0.6	0.7	1.2
	Humulin N 3ml Penset	329	609.72	158.89	200 598.97	3.7	3.1	0.8
	Humulin N 3ml Cartridges	43	655.21	409.74	28 173.90	0.5	0.4	0.8
	Humulin N Humaject 3ml Injections	1	524.02	0	524.02	0	0	0
	Humulin N 10ml vial	61	334.76	103.57	20 420.20	0.7	0.3	0.4
Biphasic biosynthetic human insulin 20/80	Mixtard 20/80 Penfill	9	757.19	260.20	6 814.69	0.1	0.1	1.0
Soluble insulin aspartame and protamine	Novomix 30 Flexpen 3ml Injection	715	693.89	305.50	496 131.45	8.0	7.8	1.0
	Novomix 30 Penfill 3ml Injection	30	862.15	374.34	25 864.40	0.3	0.4	1.3
Zinc biosynthetic human insulin	Humulin L 10ml vial	198	353.28	143.21	69 948.94	2.2	1.1	0.5
Biosynthetic human insulin zinc suspension	Monotard HM 10ml Ampoules	106	426	219.68	45 156.24	1.2	0.7	0.6
Biosynthetic monocomponent isophane	Protaphane HM Penset 1.5ml	0	0	0	0	0	0	0
	Protaphane HM Penset 3ml	257	672.11	218.48	172 731.80	2.9	2.7	0.9
	Protaphane HM Penfill 3ml	112	622.35	228.01	69 703.09	1.3	1.1	0.8
	Protaphane HM 10ml Ampoules	126	372.83	137.44	46 977.18	1.4	0.7	0.5

Table 5.5: (Continue) Cost and prevalence of the Insulins

Active ingredient	Agent (Trade Name ®)	Prevalence	Average cost (R)	Standard deviation (R)	Total cost (R)	Frequency %	Cost %	CPI
Biosynthetic human insulin zinc suspension monocomponent crystals	Ultratard HM 10ml Ampoules	19	339.50	119.72	6 450.47	0.2	0.1	0.5
Insulin Glargine	Lantus 300IU/3ml	432	816.16	222.08	352 582.79	4.8	5.5	1.1
	Lantus 300IU/3ml O/T	266	761.87	257.55	202 656.71	3.0	3.2	1.1
	Lantus 1000IU/10ml	88	636.75	265.69	56 034.11	1.0	0.9	0.9
Total		**8909**	**716.93**	**355.39**	**6 387 098.72**	**99.8**	**99.8**	**1.0**
September-December						**(n = 11062)**		
Insulin Lispro	Humalog Mix 25 Penset	1325	698.32	265.81	925 276.08	12.0	14.7	1.2
	Humalog Mix 25 Cartridges	161	666.80	261.66	107 354.78	1.5	1.7	1.1
	Humalog Mix 25 Injection	22	696.75	406.89	15 328.59	0.2	0.2	1.0
	Humalog 10ml Ampoules	53	393.99	202.33	20 881.51	0.5	0.3	0.6
	Humalog 3ml Penset/Prefill	916	642.59	338.54	588 609.28	8.3	9.3	1.1
	Humalog 3ml Cartridge injection	116	561.61	162.77	65 146.62	1.0	1.0	1.0
	Humaject/Humalog 3ml	1	823.35	0	823.35	0	0	0
Insulin aspartame	Novorapid 3ml FlexPen	431	559.16	236.32	240 997.74	3.9	3.8	1.0
	Novorapid 3ml Penfill	71	561.94	182.90	39 897.42	0.6	0.6	1.0
Biosynthetic human insulin	Humulin R 10ml vial	18	272.21	79.73	4 899.79	0.2	0.1	0.5
	Humulin R 3ml cartridges	16	448.89	102.94	7 182.30	0.1	0.1	1.0
	Humulin R Humaject Pen 5ml	11	508.41	133.81	5 592.54	0.1	0.1	1.0
Biosynthetic human soluble insulin	Actrapid HM Pensets 1.5ml	1	44.86	0	44.86	0	0	0
	Actrapid HM Pensets 3ml	503	555.03	260.83	279 179.50	4.5	4.4	1.0
	Actrapid HM Penfill 3ml	68	533.20	186.83	36 257.41	0.6	0.6	1.0
	Actrapid HM 10ml Ampoules	124	299.01	110.42	37 077.68	1.1	0.6	0.5
Soluble insulin and isophane	Actraphane HM Penset 1.5ml	0	0	0	0	0	0	0
	Actraphane HM Penset 3ml	2559	585.56	233.43	1 498 445.04	23.1	23.7	1.0
	Actraphane HM Penfill 3ml	262	595.62	252.71	156 053.36	2.4	2.5	1.0
	Actraphane HM 10ml Ampoules	530	422.92	194.61	224 145.88	4.8	3.6	0.8
Biosynthetic human isophane	Humulin 30/70 3ml cartridges	121	567.18	211.56	68 628.80	1.1	1.1	1.0
	Humulin 30/70 10ml vial	23	357.74	147.71	8 228.06	0.2	0.1	0.5

Table 5.5: (Continue) Cost and prevalence of the Insulins

Active ingredient	Agent (Trade Name ®)	Prevalence	Average cost (R)	Standard deviation (R)	Total cost (R)	Frequency %	Cost %	CPI
	Humulin 30/70 Humaject Injection	56	553.65	211.35	31 004.59	0.5	0.5	1.0
	Humulin N 3ml Penset	409	482.01	139.72	197 142.52	3.7	3.1	0.8
	Humulin N 3ml Cartridges	45	544.43	361.25	24 499.42	0.4	0.4	1.0
	Humulin N Humaject 3ml Injections	2	485.42	0	970.84	0	0	0
	Humulin N 10ml vial	50	339.82	145.99	16 990.81	0.5	0.3	0.6
Biphasic biosynthetic human insulin 20/80	Mixtard 20/80 Penfill	5	564.03	209.07	2820.17	0	0	0
Soluble insulin aspartame and protamine	Novomix 30 Flexpen 3ml Injection	1307	558.49	207.86	729 950.68	11.8	11.6	1.0
	Novomix 30 Penfill 3ml Injection	43	564.91	178.53	24 291.07	0.4	0.4	1.0
Zinc biosynthetic human insulin	Humulin L 10ml vial	203	285.95	109.51	58 048.20	1.8	0.9	0.5
Biosynthetic human insulin zinc suspension	Monotard HM 10ml Ampoules	113	363.54	189.33	41 080.18	1.0	0.7	0.7
Biosynthetic monocomponent isophane	Protaphane HM Penset 1.5ml	0	0	0	0	0	0	0
	Protaphane HM Penset 3ml	269	513.53	163.50	138 138.95	2.4	2.2	0.9
	Protaphane HM Penfill 3ml	125	482.12	134.06	60 265.52	1.1	1.0	0.9
	Protaphane HM 10ml Ampoules	112	334.58	120.02	37 472.91	1.0	0.6	0.6
Biosynthetic human insulin zinc suspension monocomponent crystals	Ultratard HM 10ml Ampoules	22	294.09	95.48	6 469.98	0.2	0.1	0.5
Insulin Glargine	Lantus 300IU/3ml	438	686.62	283.62	300 737.97	4.0	4.8	1.2
	Lantus 300IU/3ml O/T	435	596.36	160.40	259 418.37	3.9	4.1	1.1
	Lantus 1000IU/10ml	96	537.44	186.88	51 594.36	0.9	0.8	0.9
Total		**11062**	**570.51**	**252.55**	**6 310 947.13**	**99.8**	**100**	**1.0**

From table 5.5, tables 5.5.1 and 5.5.2 are compiled. Table 5.5.1 is an indication of insulin products with a percentage usage of >5% and a CPI of >1, which gives an indication of relatively high usage and relatively high cost.

Table 5.5.1: Summary of insulin products with prevalence >5% and CPI >1

Agent (Trade name ®)	January-April	May-August	September-December
Humalog Mix 25 Penset	√	√	√
Humalog 3ml Penset/Prefill	√	√	√
Actraphane HM Penset 3ml	√	√	-
Novomix 30 Flexpen 3ml Injection	√	-	-

√ indicates that the product has a prevalence of >5% and CPI >1

Table 5.5.2 is an indication of insulin products that have a percentage usage of >5%, but with a CPI of ≤1. If the CPI is ≤1 it indicates that these insulins are relatively less expensive than the insulins with a CPI of >1.

Table 5.5.2: Summary of insulin products with prevalence >5% and CPI ≤1

Agent (Trade name ®)	January-April	May-August	September-December
Protaphane HM Penset 3ml	√	-	-
Actraphane HM Penset 3ml	-	√	√
Novomix 30 Flexpen 3ml Injection	-	√	√

√ indicates that the product has a prevalence of >5% and CPI ≤1

- *January-April*

From table 5.5, it could be calculated that the insulins prescribed during this time period represent 26.4% of all the insulins on the database (n = 27 129). The total cost of the insulins prescribed during this time period is R5 431 303.07 (30% n = R18 129 348.92), with a CPI value of 1.1 indicating that this therapy is relativly expensive.

For this time period the item with the lowest average cost is Actraphane® HM Penset 1.5ml, with an average cost of R285.83 ± R0.00. Actraphane® HM Penset 1.5ml was also one of the products with the lowest prevalence (1). The other products with a prevalence of less than 10 were Humulin® R Humaject Pen 5ml (5), Humulin® N Humaject 3ml Injection, and Protaphane® HM Penset 1.5ml both with a prevalence of 1.

According to table 5.5 Novomix® 30 Penfill 3ml Injection was the item with the highest average cost (R996.23 ± R358.93) for this time period. The product with the highest prevalence during this time was Actraphane® HM Penset 3ml with a prevalence of 1594. This product also had the highest cost percentage and amounted to 24.8% of the total cost for this time.

Note that the items with the highest and lowest prevalence come from the same group (soluble insulin and isophane) and are in fact agents with the same active ingredients but with different strengths.

- *May-August*

According to table 5.5 the insulins prescribed during this time period presents 32.8% of the total insulins in the database (n = 27 129). The number of insulins is higher than the number of insulins prescribed during the time January to April. This can be due to the fact that there could have been an increase in the total number of patients receiving insulins.

The item with the highest prevalence for this time period is Actraphane® HM Penset 3ml with a percentage frequency of 22.7% (2025), followed by Humalog® Mix 25 Penset with a frequency of 1086 (12.2%, n = 8909).

The item with the highest average cost is Humaject®/Humalog® 3ml (R1 004.52), followed by Humalog® Mix 25 Injection with an average cost of (R901.80 ± R587.04). Note that since only one of the Humaject®/Humalog® 3ml products was prescribed the percentage frequency and cost percentage is omissible, the CPI value cannot be determined.

The item with the lowest average cost is Actrapid® HM Penset 1.5ml (R54.21). If the average cost of this product is compared with the average cost of the same product for the time January to April, it is clear that there is a difference of R731.95.
The product with the lowest average cost was Humulin® R 10ml vial, with an average cost of R300.24 ± R31.83 and a CPI value of 0.3.

Note that no Protaphane® HM Penset 1.5ml were prescribed during this time period.

- *September-December*

According to table 5.5 the insulins prescribed during this time amount to 41% of all the insulins in the database (n = 27129). The number of insulins is higher than the number of insulins prescribed during the time January to April and May to August. This can be due to the fact that there could have been an increase in the total number of patients receiving insulins. This aspect was however not investigated. The total cost of the insulins prescribed during this time period is R6 31 947.13 and amounts to 34.8% of the total cost for insulins. The CPI value can be calculated as 0.8, an indication that the therapy is relatively inexpensive.

The item with the highest prevalence for this time period is Actraphane® HM Penset 3ml Injection (2559), followed by Humalog® Mix 25 Penset (1325) and Novomix® Flexpen 3ml Injection (1307).

The items with the lowest prevalence are Humaject®/Humalog® 3ml(1), Actrapid® HM Penset 1.5ml (1), Humulin® N Humaject® 3ml Injection (2), and Mixtard® 20/80 Penfill (5).
From table 5.5 it can also be seen that the products with the highest average cost are Humaject®/Humalog® 3ml (R823.35) and Humalog® Mix 25 Penset (R698.32 ± R265.81). According to the CPI values Humalog® Mix 25 Penset (1.2) and Lantus®300IU/3ml (1.2) are relatively expensive. Since the percentage frequency and cost percentage of Humaject®/Humalog® 3ml is omissible, a CPI value cannot be determined.

According to table 5.5 Actrapid® HM Penset 1.5ml (R44.86) and Humulin® R 10ml vials (R272.21 ± R79.73) have the lowest average cost. The total average cost (R570.51 ± R252.55) of all the insulins prescribed during this time period is lower than the total average costs of the other time periods (January-April R758.77 ± R383.74, and May-August R716.93 ± R355.39).

For this time period the standard deviation for each product should have been zero or very close to zero because of the single exit price set and implemented by the Department of Health. Insulin is, however, a complex antidiabetic agent and the dosing for every patient differs according to each patient's individual needs, desired metabolic control and age (see chapter two, section 2.7.4.1 page 28).

5.6.3 Summary

Table 5.5 illustrates the relatively large variety of insulin products available according to active ingredient, package sizes and administration ways. Accordingly, many different products were prescribed during the study periods with a wide variety of "average cost per month" – ranging from R44.86 to R1 004.52.

It can be concluded that Actraphane® HM Penset 3ml (6178) has the highest prevalence, followed by Humalog® Mix 25 Penset (3202) and Novomix® 30 Flexpen 3ml Injection (2473). The average cost of these three products is R710.64 ± R327.45 for Actraphane® HM Penset 3ml, R774.55 ± R421.80 for Humalog® Mix 25 Penset and R636.45 ± R268.91 for Novomix® 30 Flexpen 3ml Injection.

Actraphane® HM Penset 3ml Injection is a biphasic insulin that contains a short and intermediate acting insulin and is usually administered only once daily (Chapter 2, section 2.7.4.1.4).

The product with the highest average cost is Humaject®/Humalog® 3ml (R1004.52 ± R0.00) in the time period May to August. This is also the product with the highest combined average (R913.94 ± R128.11) cost during the whole study period i.e. January to December. The CPI value of Humaject®/Humalog® 3ml (1.4) for the total study period is also an indication that this form of therapy is relatively expensive.

The product with the lowest average cost for a specific time period is Actrapid® HM Penset 1.5ml (R44.86 ± R0.00) during September to December. This is also the product with the lowest combined average cost (R295.08 ± R425.32) for the total study period. The CPI value (0.4) of this product is also an indication that this form of therapy is relatively inexpensive.

As seen in the discussion of the time period from September to December there is a difference in the total average cost between the different time periods. This can be due to the change in the pricing regulations that came into effect in the last quarter of 2004.

5.7 THE PREVALENCE AND USAGE PATTERNS OF ORAL ANTIDIABETIC AGENTS

5.7.1 Introduction

As seen in table 5.3, the oral antidiabetic agents have a much higher prevalence than the insulins. The oral agents account for almost 81% of the antidiabetic agents that are prescribed and the biguanides account for almost half (49.4%, 57 572) of the prescribed oral antidiabetic agents (n = 116 318), followed by the sulfonylureas (51 319 or 44.1%). The biguanides are the agents of first choice in the management of obese type 2 diabetics and that can be the reason why the biguanides have the highest prevalence (refer paragraph 3.5.1, chapter 3). The oral antidiabetic agents with the lowest frequency are the alpha-glucosidase inhibitors (777 or 0.7%).

From the study done by La Grange (1998:145), the only classes of antidiabetic agents available on the South African market were the first and second-generation sulfonylureas, biguanides and alpha-glucosidase inhibitors. In 1996 acetohexamide and tolbutamide were available, but these two agents have since been removed from the South African market. Truter (1999:137) calculated that the sulfonylureas accounted to 63.8% of all the oral antidiabetic prescriptions for the year 1996, an indication of the increase (nearly 20%) in the usage of oral antidiabetic agents in 2004.

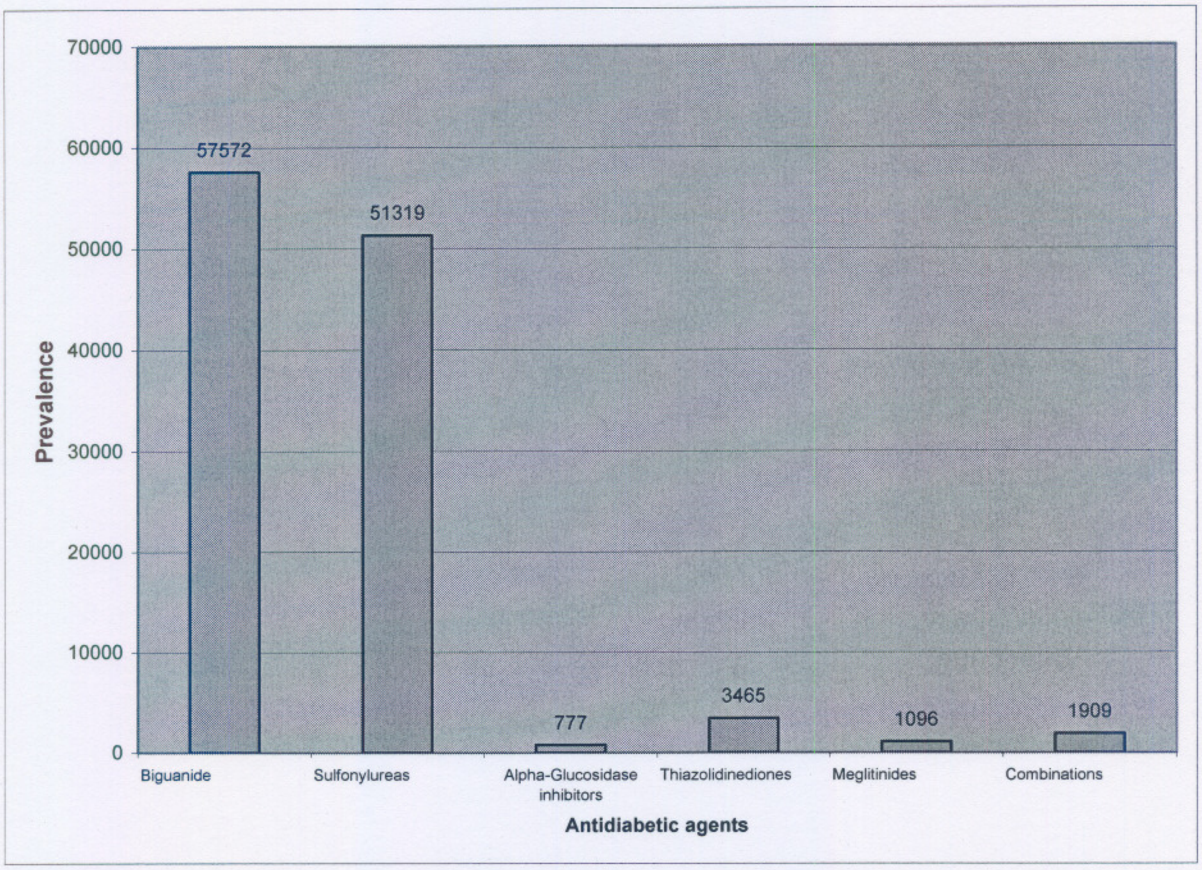

Figure 5.2: Prevalence of oral antidiabetic agents (January-December 2004)

5.7.2 Cost and prevalence of individual oral antidiabetic agents according to active ingredient

In this section the cost; prevalence and CPI of each individual oral antidiabetic agent will be discussed. Each agent will be discussed in three periods, namely January-April 2004, May-August 2004 and September-December 2004.

5.7.2.1 Biguanides

The only biguanide that is currently available on the South African market is metformin. According to the database the only innovator products of metformin are Glucophage® and Rolab-Metformin® film-coated tablets. Both of them are available in two strengths, namely Glucophage® 500mg and Glucophage® Forte 850mg; and Rolab-Metformin® FC 500mg and 850mg as will be seen in table 5.6. Rolab-Metformin® hydrochloride, Merck-Metformin®, Metforal® and Sandoz-Metformin® are the generic equivalents of the innovator products Glucophage® and Rolab-Metformin® FC. In table 5.6 the cost and prevalence of metformin will be described.

Table 5.6: The total cost and prevalence of all metformin agents (Jan-Dec 2004)

Agent	Prevalence	Average cost (R)	Standard deviation (R)	Total cost (R)	Frequency %	Cost %	CPI
January-April							
Glucophage® 500mg	4286	64.73	29.30	277 447.46	28.6	23.2	0.8
Glucophage® Forte 850mg	4243	101.69	33.37	431 473.55	28.3	36.2	1.3
Rolab-Metformin® HCL 500mg	1799	63.46	28.78	114 166.07	12	9.6	0.8
Rolab-Metformin® FC 500mg	1732	61.24	27.88	106 062.84	11.6	8.9	0.8
Rolab-Metformin® FC 850mg	1382	93.66	30.40	129 444.85	9.2	10.8	1.2
Rolab-Metformin® HCl 850mg	1074	94.14	29.63	101 108.96	7.2	8.5	1.2
Merck-Metformin® 500mg	234	58.11	27.86	13 598.99	1.6	1.1	0.7
Merck-Metformin® 850mg	231	87.52	25.80	20 216.8	1.5	1.7	1.1
Total	**14981**	**79.67**	**35.13**	**1 193 519.52**	**100**	**100**	**1**
May-August							
Glucophage® 500mg	5531	52.40	24.97	289 850.84	28.9	25.3	0.9
Glucophage® Forte 850mg	5618	74.88	31.90	420 666.87	29.4	36.7	1.2
Rolab-Metformin® HCL 500mg	2166	43.84	20.96	94 958.16	11.3	8.3	0.7
Rolab-Metformin® FC 500mg	2273	47.83	24.29	108 712.11	11.9	9.5	0.8
Rolab-Metformin® FC 850mg	1696	66.23	25.51	112 332.88	8.9	9.8	1.1
Rolab-Metformin® HCl 850mg	1208	64.10	23.51	77 428.20	6.3	6.8	1.1
Merck-Metformin® 500mg	361	55.59	25.05	20 067.49	1.9	1.8	0.9
Merck-Metformin® 850mg	238	79.46	20.35	18 910.51	1.2	1.7	1.4
Metforal® 850mg	36	57.13	16.71	2056.51	0.2	0.2	1
Metforal® 500mg	8	38.63	21.94	309.00	0	0	
Total	**19135**	**59.82**	**29.11**	**1 145 292.57**	**100**	**100**	**1**
September-December							
Glucophage® 500mg	7135	30.83	20.36	219 985.54	30.4	21.6	0.7
Glucophage® Forte 850mg	7214	57.41	18.75	414 135.90	30.8	40.4	1.3
Rolab-Metformin® HCL 500mg	639	33.72	16.62	21 548.72	2.7	2.1	0.8
Rolab-Metformin® FC 500mg	715	36.48	16.58	26 080.26	3	2.5	0.8
Rolab-Metformin® FC 850mg	434	57.22	18.93	24 835.41	1.9	2.4	1.3
Rolab-Metformin® HCl 850mg	376	54.26	20.06	20 401.65	1.6	2	1.3
Merck-Metformin® 500mg	164	45.31	23.83	7 430.17	0.7	0.7	1
Merck-Metformin® 850mg	116	65.58	24.63	7 607.67	0.5	0.7	1.4
Metforal® 850mg	128	54.83	19.22	7 017.76	0.5	0.7	1.4
Metforal® 500mg	42	35.32	18.24	1 783.40	0.2	0.1	0.5
Sandoz-Metformin® HCL 500mg	1751	33.45	15.48	58 568.15	7.5	5.7	0.8
Sandoz-Metformin® FC 500mg	2251	35.64	16.54	80 229.14	9.6	7.8	0.8

Table 5.6: (Continue) The total cost and prevalence of all metformin agents (Jan-Dec 2004)

Agent	Prevalence	Average cost (R)	Standard deviation (R)	Total cost (R)	Frequency %	Cost %	CPI
Sandoz-Metformin® HCL 850mg	1040	53.46	17.22	55 600.19	4.4	5.4	1.2
Sandoz-Metformin® FC 850mg	1445	54.92	15.54	79 420.23	6.2	7.8	1.3
Glucophage	6	56.02	0	336.12	0	0	0
Total	**23456**	**43.68**	**22.17**	**1 024 344.19**	**100**	**99.8**	**1**

From table 5.6, tables 5.6.1 and 5.6.2 were compiled. Table 5.6.1 is an indication of all the metformin products with a percentage usage of >10% and a CPI of >1, which gives an indication of relatively high usage and relatively high cost.

Table 5.6.1: Summary of the metformin products with prevalence >10% and CPI >1

Agent (Trade name ®)	January-April	May-August	September-December
Glucophage Forte 850mg	√	√	√

√ indicates that the product has a prevalence of >10% and CPI >1

Table 5.6.2 is an indication of all the metformin products that have a percentage usage of >10%, but with a CPI of ≤1.

Table 5.6.2: Summary of the metformin products with prevalence >10% and CPI ≤1

Agent (Trade name ®)	January-April	May-August	September-December
Glucophage 500mg	√	√	√
Rolab-Metformin HCl 500mg	√	√	-
Rolab-Metformin FC 500mg	√	√	-

√ indicates that the product has a prevalence of >10% and CPI ≤1

- *January-April*

The total cost of all the metformin agents for this time interval was R1 139 519.92, which amounts to 35.5% of all the metformin agents in the database. Glucophage® 500mg and Glucophage® Forte 850mg are the agents with the highest prevalence, with a % frequency of 28.9 (n = 4286) and 28.3 (n = 4243) respectively. Glucophage® 500mg, Rolab-Metformin® HCL 500mg and FC 500mg, and Merck-Metformin® 500mg all have a CPI of less than 1, meaning that the therapy is relatively inexpensive, with Merck-Metformin® 500mg the most inexpensive of all the agents (average cost = R58.11 ± 27.86).

- *May-August*

For this time interval the total cost amounts to 34.1% (n = R 1 154 292.57) of all the metformin agents in the database. For this interval it can be concluded that Metforal® 500mg and Metforal® 850mg were introduced to the South African market as generic products. Metforal® 500mg is the most inexpensive of all the agents with an average cost of R38.36 ± R21.94. A CPI value can however not be determined since only 8 Metforal® 500mg items were prescribed during this four-month period and therefore the percentage frequency and cost percentage were omissible. From table 5.6 it was observed that Glucophage® Forte 850mg has the highest prevalence.

- *September-December*

The total cost of all the metformin items for this time period was R1 024 344.19. Once again Glucophage® 500mg and Glucophage® Forte 850mg were prescribed the most of all metformin items, with a prevalence of 30.4% (n = 7135) and 30.8% (n = 7214) respectively. It can be observed that the total average cost (R 43.68 ± R22.17) of all the products for this time interval is relatively lower than those of the first two time intervals January to April (R79.67 ± R35.13) and May to August (R 58.85 ± R29.11) respectively. This can be a result of the pricing regulations that came into effect in September 2004 (see chapter 3, section 3.7.3).

In 2003 the pharmaceutical company Rolab® merged with Novartis® generic companies and changed its name to the global brand name, Sandoz (Sandoz, 2004a:1). This can be seen as the reason for the introduction of the Sandoz products at the end of table 5.6.

The CPI indicates that six out of the 14 items are relatively inexpensive, while only one product (Merck-Metformin® 500) shows to have equilibrium between cost and prevalence of the therapy.

If the prevalence and average costs of the biguanides dispensed between January and April 2004 are compared to the prevalence and average costs of the biguanides dispensed in 1996, it can be seen that in 1996 the average cost (R71.70 ± R35.49) was less than the average cost for the biguanides in January to April 2004 (R79.67 ± R35.13). The biguanides prescribed during May to August 2004 (R59.82 ± R29.11) were 1.2 times less expensive than the biguanides prescribed in 1996. For September to December 2004 (R43.68 ± R22.17) the biguanides were 1.6 times less expensive than in 1996. For the time 1 October to 31 December 1996, only 2 935 biguanides were prescribed. The average cost for the biguanides determined by Truter was R67.52 for the year 1996 (1999:139). Therefore it can be calculated that the biguanides were 35.3% to 39.1% more expensive in 1996 than the period between September and December 2004.

5.7.2.2 Sulfonylureas

As seen in chapter 2, section 2.7.4.4.1, glimeparide, glibenclamide, gliclazide, glipizide and chlorpropamide are all sulfonylureas due to their active ingredient.

In table 5.7 the cost and prevalence of the sulfonylureas will be discussed.

Table 5.7: Cost and prevalence of the sulfonylureas

Active Ingredient	Agent	Prevalence	Average cost (R)	Standard deviation (R)	Total cost (R)	Frequency %	Cost %	CPI
January-April								
Glimeparide	Amaryl® 4mg	1085	366.20	125.90	397 332.10	7.7	18.4	2.4
	Amaryl® 2mg	1513	194.97	65.07	294 996.23	10.8	13.6	1.3
	Amaryl® 1mg	1001	103.92	32.51	104 024.96	7.1	4.8	0.7
Glibenclamide	Glycomin® 5mg	2943	147.75	76.82	434 832.98	21	20.1	1
	Glyben® 5mg	402	128.39	71.79	51 613.65	2.9	2.4	0.8
	Daonil® 5mg	372	432.64	194.08	160 943.87	2.7	7.4	2.7
	Norton-Glibenclamide®	19	30.43	20.12	578.21	0.1	0	0
	Euglycon® 5mg	6	573.93	360.66	3 443.55	0	0.2	0
	Diacare® 5mg	3	55.70	4.16	167.09	0	0	0
Gliclazide	Glucomed® 80mg	3512	97.75	44.78	343 294.58	25.1	15.9	0.6
	Diamicron® 80mg	1291	116.95	59.61	150 986.78	9.2	7	0.8
	Diamicron® MR 30mg	424	135.43	61.96	57 420.55	3	2.7	0.9
	Rolab-Gliclazide®	833	92.93	39.97	77 408.38	6	3.6	0.6
	Diaglucide® 80mg	147	108.33	47.88	15 924.86	1	0.7	0.7
	Glycron® 80mg	138	93.98	41.90	12 969.01	1	0.6	0.6
	Glygard®	57	99.14	41.74	5 650.98	0.4	0.3	0.8
	Merck-Gliclazide®	39	63.19	47.12	2 464.55	0.3	0.1	0.3
	Ziclin® 80mg	4	136.79	0	547.16	0	0	0
Glipizide	Minidiab®	193	241.04	148.63	46 520.21	1.4	2.2	1.6
Chlorpropamide	Hypomide® 250mg	20	100.57	54.02	2 011.30	0.1	0.1	1
	Diabinese® 250mg	1	46.51	0	46.51	0	0	0
Total		**14003**	**154.48**	**113.96**	**2 163 177.51**	**99.8**	**100.1**	**1**
May-August								
Glimeparide	Amaryl® 4mg	1462	337.14	114.17	492 893.05	8.5	23	2.7
	Amaryl® 2mg	1719	170.76	62.96	293 529.78	10	13.7	1.4
	Amaryl® 1mg	1126	88.28	33.49	99 402.42	6.6	4.7	0.7
Glibenclamide	Glycomin® 5mg	3645	74.42	51.67	271 263.40	21.3	12.7	0.6
	Glyben® 5mg	510	50.10	59.97	25 548.92	3	1.2	0.4
	Daonil® 5mg	474	360.11	169.53	170 692.01	2.8	8	2.9
	Norton-Glibenclamide®	20	19.83	11.58	396.66	0.1	0	0
	Euglycon® 5mg	6	300.59	184.27	1 803.56	0	0.1	0

Table 5.7: (Continue) Cost and prevalence of the sulfonylureas

Active Ingredient	Agent	Prevalence	Average cost (R)	Standard deviation (R)	Total cost (R)	Frequency %	Cost %	CPI
	Diacare® 5mg	8	46.16	32.43	369.27	0	0	0
Gliclazide	Glucomed® 80mg	3822	88.38	41.55	337 772.10	22.3	15.8	0.7
	Diamicron® 80mg	1288	118.78	66.18	152 986.56	7.5	7.2	1
	Diamicron® MR 30mg	882	136.60	58.93	120 483.80	5.2	5.6	1
	Rolab-Gliclazide®	1151	64.21	31.61	73 902.91	6.7	3.5	0.5
	Diaglucide® 80mg	436	71.85	32.91	31 327.10	2.5	1.5	0.6
	Glycron® 80mg	213	89.90	48.62	19 149.36	1.2	0.9	0.8
	Glygard®	83	73.41	29.12	6 093.00	0.5	0.3	0.6
	Merck-Gliclazide®	91	63.59	29.49	5 786.42	0.5	0.3	0.6
	Ziclin® 80mg	0	0	0	0	0	0	0
Glipizide	Minidiab®	161	202.72	141.21	32 638.45	0.9	1.5	1.7
Chlorpropamide	Hypomide® 250mg	14	73.54	47.71	1 029.57	0.1	0	0
	Diabinese® 250mg	0	0	0	0	0	0	0
	Diabetix® 250mg	1	15.20	0	15.20	0	0	0
Total		**17112**	**124.89**	**106.92**	**2 137 083.54**	**99.7**	**100**	**1**
September-December								
Glimeparide	Amaryl® 4mg	1454	275.48	115.78	400 552.96	7.2	20.8	2.9
	Amaryl® 2mg	1680	148.78	56.10	249 945.89	8.3	13	1.6
	Amaryl® 1mg	1081	78.14	43.46	84 468.01	5.4	4.4	0.8
Glibenclamide	Glycomin® 5mg	4408	58.78	30.68	259 120.00	21.8	13.5	0.6
	Glyben® 5mg	685	15.02	14.51	10 287.92	3.4	0.5	0.1
	Daonil® 5mg	514	252.47	111.77	129 767.17	2.5	6.7	2.7
	Norton-Glibenclamide®	24	20.62	7.59	494.90	0.1	0	0
	Euglycon® 5mg	9	181.61	86.90	1 634.52	0	0.1	0
	Diacare® 5mg	17	13.55	10.56	230.42	0.1	0	0
Gliclazide	Glucomed® 80mg	3817	72.05	35.63	275 009.33	18.9	14.3	0.8
	Diamicron® 80mg	1136	83.74	48.12	95 130.00	5.6	4.9	0.9
	Diamicron® MR 30mg	1237	130.48	65.00	161 398.79	6.1	8.4	1.4
	Rolab-Gliclazide®	496	56.48	28.18	28 012.58	2.5	1.5	0.6
	Diaglucide® 80mg	838	62.84	26.31	52 663.96	4.1	2.7	0.7
	Glycron® 80mg	424	69.06	29.14	29 281.41	2.1	1.5	0.7
	Glygard®	229	58.61	26.30	13 421.14	1.1	0.7	0.6

Table 5.7: (Continue) Cost and prevalence of the sulfonylureas

Active Ingredient	Agent	Prevalence	Average cost (R)	Standard deviation (R)	Total cost (R)	Frequency %	Cost %	CPI
	Merck-Gliclazide®	318	53.66	28.83	17 063.04	1.6	0.9	0.6
	Ziclin® 80mg	0	0	0	0	0	0	0
	Sandoz-Gliclazide®	1660	55.72	28.37	92 501.77	8.2	4.8	0.6
Glipizide	Minidiab®	157	152.91	118.96	24 007.22	0.8	1.2	1.5
Chlorpropamide	Hypomide® 250mg	20	46.00	38.48	919.97	0.1	0	0
	Diabinese® 250mg	0	0	0	0	0	0	0
	Diabetix® 250mg	0	0	0	0	0	0	0
Total		**20204**	**95.32**	**83.49**	**1 925 911.00**	**99.9**	**99.9**	**1**

From table 5.7, tables 5.7.1 and 5.7.2 can be compiled. Table 5.7.1 is an indication of all the sulfonylurea products with a percentage usage of >10% and a CPI of >1, giving an indication of relatively high usage and relatively high cost.

Table 5.7.1: Summary of the sulfonylurea products with prevalence >10% and CPI >1

Agent (Trade name ®)	January-April	May-August	September-December
Amaryl 2mg	√	√	-

√ indicates that the product has a prevalence of >10% and CPI >1

Table 5.7.2 is an indication of all the sulfonylurea products that have a percentage usage of >10%, but with a CPI of ≤1.

Table 5.7.2: Summary of the sulfonylurea products with prevalence >10% and CPI ≤1

Agent (Trade name ®)	January-April	May-August	September-December
Glycomin 5mg	√	√	√
Glucomed 80mg	√	√	√

√ indicates that the product has a prevalence of >10% and CPI ≤1

- *January-April*

The total cost of all the sulfonylurea agents was R 2 163 177.51 for this time period, which amounts to 34,7% (n = R 6 226 172.05) of the total cost of all the sulfonylureas for the year 2004. Glucomed® 80mg has the highest prevalence with a percentage frequency of 25.1 (n = 14003). The gliclazide group has the highest prevalence and amounts to 46% of all the sulfonylurea agents. All the agents in the gliclazide group have a CPI of less than one, meaning that this form of therapy is relatively inexpensive. The two most expensive agents are Euglycon® with an average cost of R573.93 ± R360.66 per item and Daonil® with an average cost of R432.64 ± R194.08 per item. The most inexpensive agent is the generic product Norton-Glibenclamide® with an average cost of R30.43 ± R20.12 per item.

- *May-August*

For this time period the total cost amounts to 34.3% (n = R 2 137 083.54) of the total cost of all the sulfonylurea agents on the database. In this period Diabetix® 250 mg was introduced to the South African market, and was the most inexpensive agent with an average cost of R15.20 ± R0.00 per item. Since only one of these products was prescribed during this study period the standard deviation could not be determined. Glucomed® has the highest prevalence with a percentage frequency of 22.3% (n = 17112). According to CPI values, Amaryl® 4mg (CPI = 2.7) and Daonil® (CPI = 2.9) are the most expensive forms of therapy.

- *September-December*

It can be observed that the sulfonylureas prescribed during this time frame, amount to 39.4% (n = 51319) of all the sulfonylureas in the database. The gliclazides have the highest prevalence of all the groups in this time period - a total of 10 155 items or 50.2% of all the sulfonylurea items for the year 2004.

This group of sulfonylureas has a lower total cost (R 1 925 911.00) than the sulfonylureas in the other two time periods (R 2 163 177.51 for January-April, and R 2 137 083.54 for May-August) respectively. The total average cost is also lower (R95.32 ± R83.94) compared to the total average cost of the time periods January to April (R154.48 ± R113.96) and May to August (R124.89 ± R106.92).

The most inexpensive sulfonylurea for this time period was Diacare®, with an average cost of R13.55 ± R10.56. The CPI of Amaryl® 4mg (2.9) and Daonil® (2.7) is more than one, which indicates that both these items is a relatively expensive form of treatment.

According to the study done by La Grange in 1998, the sulfonylureas were divided into first- and second-generation sulfonylureas. The first generation sulfonylureas were the acetohexamide (Dimelor® 500mg), chlorpropamide (Diabinese® 250mg, Diabinese® 100mg and Hypomide® 250mg) and tolbutamide (Rastinon® 250mg). The second-generation sulfonylureas were glibenclamide, gliclazide and glipizide.

The average cost of these first and second generation sulfonylureas for the time 1 October to 31 December 1996 was R135.29 ± R54.82, almost 1.1 times more expensive than the sulfonylureas for the study period January to December 2004. If the study period January to December 2004 is compared with the study period used by La Grange (1998:149), it can be calculated that the sulfonylureas dispensed during January to April are slightly more expensive. The sulfonylureas dispensed during May to August 2004 were, however, almost 1.1 times less expensive, and the sulfonylureas dispensed during the time September to December 2004 1.4 times less expensive than the sulfonylureas dispensed during the period 1 October to 31 December 1996. The only sulfonylureas detected in the Truter study (1999:140) were gliclazide, glibenclamide, glipizide and chlorpropamide. Truter determined the average cost of the sulfonylureas to be R115,93 ± R53.25. Therefore it can be calculated that the sulfonylureas were 17.8% to 29.5% more expensive in 1996 than the period between September and December 2004.

5.7.2.3 Thiazolidinediones

The third group of oral antidiabetic agents is the thiazolidinediones. As seen in chapter 2 section 2.7.4.4.4, the thiazolidinediones are a relatively newly introduced class of oral antidiabetic agents, and not recorded as part of the La Grange or Truter studies of the 1996 data. Only two forms are available in South Africa, namely Pioglitazone® and Rosiglitazone®. Table 5.8 summarises the prevalence and cost of this group of antidiabetic agents.

Table 5.8: Cost and prevalence of all the thiazolidinediones

Active ingredient	Agent	Prevalence	Average cost (R)	Standard deviation (R)	Total cost (R)	Frequency %	Cost %	CPI
January-April								
Pioglitazone	Actos® 15mg	200	400.32	58.32	80 064.63	27	27.6	1
	Actos® 30mg	135	582.41	88.96	78 625.13	18.2	27.1	1.5
Rosiglitazone	Avandia® 4mg	287	372.41	116.69	106 881.45	38.7	36.8	0.9
	Avandia® 2mg	119	206.42	73.43	24 563.99	16.1	8.5	0.5
Total		**741**	**391.55**	**144.19**	**290 135.20**	**100**	**100**	**1**
May-August								
Pioglitazone	Actos® 15mg	382	390.06	70.63	149 001.67	27.1	26.7	1
	Actos® 30mg	352	578.66	78.37	203 686.56	25	36.6	1.5
Rosiglitazone	Avandia® 4mg	530	340.36	130.79	180 390.54	37.6	32.4	0.9
	Avandia® 2mg	144	167.30	65.41	24 091.38	10.2	4.3	0.4
Total		**1408**	**395.72**	**156.92**	**557 170.15**	**99.9**	**100**	**1**
September-December								
Pioglitazone	Actos® 15mg	366	314.36	57.60	115 057.57	24.5	23.5	1
	Actos® 30mg	380	467.58	91.25	177 678.61	25.4	36.3	1.4
Rosiglitazone	Avandia® 4mg	614	287.77	124.52	176 691.78	41	36.1	0.9
	Avandia® 2mg	136	149.23	48.06	20 295.19	9.1	4.1	0.5
Total		**1496**	**327.36**	**134.37**	**489 723.15**	**100**	**100**	**1**

From table 5.8, tables 5.8.1 and 5.8.2 can be compiled. Table 5.8.1 is an indication of all the thiazolidinedione products with a percentage usage of >10% and a CPI of >1, which gives an indication of relatively high usage and relatively high cost.

Table 5.8.1: Summary of the thiazolidinedione products with prevalence >10% and CPI >1

Agent (Trade name ®)	January-April	May-August	September-December
Actos 2mg	√	√	√

√ indicates that the product has a prevalence of >10% and CPI >1

Table 5.8.2 is an indication of all the thiazolidinedione products that have a percentage usage of >10%, but with a CPI of ≤1.

Table 5.8.2: Summary of the thiazolidinedione products with prevalence >10% and CPI ≤1

Agent (Trade name ®)	January-April	May-August	September-December
Actos 15mg	√	√	√
Avandia 4mg	√	√	√
Avandia 2mg	√	√	-

√ indicates that the product has a prevalence of >10% and CPI ≤1

- *January-April*

Rosiglitazone accounts for more than half (54.8%, n = 741) of the thiazolidinediones that were dispensed during this time period. On average cost, rosiglitazone is less expensive than pioglitazone. The CPI values of both Avandia® 4mg (0.9) and Avandia® 2mg (0.5) are an indication of this statement.

- *May-August*

During this time period, pioglitazone showed a higher prevalence (734) than rosiglitazone (674), and amounted to 52.1% (n = 1408) of the total of thiazolidinediones for this period of time. According to the CPI values, rosiglitazone is less expensive than pioglitazone.

- *September-December*

The thiazolidinediones prescribed during this period of time, amounted to 41% of all the thiazolidinediones prescribed in the total database (n = 3645). The average cost (R327.36 ± R144.19) for products prescribed during this period is lower than those of the other time periods January to April (R391.55 ± R144.19) and May to August (R395.22 ± R156.92) respectively.

If the cost % and CPI values are studied, it can be concluded that rosiglitazone is less expensive than pioglitazone, with Avandia® 2mg the most inexpensive (CPI = 0.5, average cost R149.23 ± R48.06).

5.7.2.4 Meglitinides

As seen in section 2.7.4.4.5 of chapter 2, the meglitinides form a relatively new class of oral antidiabetic agents. The meglitinides account for only 0.94% of all the oral antidiabetic agents in the total database (n = 116318). There are two classes of meglitinides namely the repaglinides and the nateglinides.

No meglitinides were recorded as part of the La Grange or Truter studies of 1996.

Table 5.9 summarises the cost and prevalence of the Meglitinides.

Table 5.9: Cost and prevalence of the meglitinides as an antidiabetic agent

Active ingredient	Agent	Prevalence	Average cost (R)	Standard deviation (R)	Total cost (R)	Frequency %	Cost %	CPI
January-April								
Repaglinide	Novonorm® 0,5mg	101	99.93	20.30	10 093.31	34.4	15.6	0.5
	Novonorm® 1,0mg	98	196.50	45.35	19 257.19	33.3	29.7	0.9
	Novonorm® 2,0mg	69	356.92	122.51	24 627.65	23.5	38	1.6
Nateglinide	Starlix® 120mg	25	426.69	60.22	10 667.17	8.5	16.4	1.9
	Starlix® 60mg	1	208.23	0	208.23	0.3	0.3	1
Total		**294**	**220.59**	**133.48**	**64 853.55**	**100**	**100**	**1**
May-August								
Repaglinide	Novonorm® 0,5mg	111	89.83	33.21	9 970.87	26	10.7	0.4
	Novonorm® 1,0mg	168	190.60	92.29	32 021.05	39.3	34.2	0.9
	Novonorm® 2,0mg	117	336.24	99.36	39 340.25	27.4	42.1	1.5
Nateglinide	Starlix® 120mg	31	393.82	100.37	12 208.33	7.3	13.1	1.8
	Starlix® 60mg	0	0	0	0	0	0	0
Total		**427**	**219.06**	**132.99**	**93 540.50**	**100**	**100.1**	**1**
September-December								
Repaglinide	Novonorm® 0,5mg	117	87.41	33.23	10 226.46	31.2	14.2	0.5
	Novonorm® 1,0mg	156	185.01	180.47	28 862.02	41.6	40.1	1
	Novonorm® 2,0mg	81	303.94	117.53	24 619.29	21.6	34.2	1.6
Nateglinide	Starlix® 120mg	20	390.10	77.19	7 802.08	5.3	10.9	2.1
	Starlix® 60mg	1	377.43	0	377.43	0.3	0.5	1.7
Total		**375**	**191.70**	**159.52**	**71 887.28**	**100**	**99.9**	**1**

From table 5.9, tables 5.9.1 and 5.9.2 can be compiled. Table 5.9.1 is an indication of all the meglitinide products with a percentage usage of >10% and a CPI of >1, which gives an indication of relatively high usage and relatively high cost.

Table 5.9.1: Summary of the meglitinide products with prevalence >10% and CPI >1

Agent (Trade name ®)	January-April	May-August	September-December
Novonorm 2.0mg	√	√	√
Starlix FCT 120mg	√	-	-

√ indicates that the product has a prevalence of >10% and CPI >1

Table 5.9.2 is an indication of all the meglitinide products that have a percentage usage of >10%, but with a CPI of ≤1.

Table 5.9.2: Summary of the meglitinide products with prevalence >10% and CPI ≤1

Agent (Trade name ®)	January-April	May-August	September-December
Novonorm 0.5mg	√	√	√
Novonorm 1.0mg	√	√	√

√ indicates that the product has a prevalence of >10% and CPI ≤1

- *January-April*

As seen in table 5.9, the meglitinides for this time period, amounted to almost 26.8% (n = 1096) of all the meglitinides in the total database for the year 2004. Novonorm® 0,5mg is the most frequently prescribed product with a prevalence of 101 (34.4%). This is also the most inexpensive item with a CPI value of 0.5.

Starlix® 60mg was prescribed only once. According to the CPI value it is clear that there is equilibrium between the cost and prevalence of the therapy.

- *May-August*

The meglitinides for this time period accounted for 39% of all the meglitinides in the database. With an average cost of R 89.83 ± R 33.21 and a CPI value of 0.4, Novonorm® 0,5mg is the most inexpensive of all the meglitinides. Once again, the repaglinides have a higher prevalence than the nateglinides, with a percentage frequency of 92.7% (n = 294).

Note that no Starlix® 60mg was prescribed or dispensed for this time period.

- *September-December*

As noted with all the other oral antidiabetic agents, once again it can be stated that the average cost of this time period (R191.70 ± R159.52) is much lower than the total average cost of the other time periods (R 220.59 ± R133.48 and R 219.06 ± R132.99).

Novonorm® 0,5mg is once again the most inexpensive drug in this group of oral antidiabetic agents, with an average cost of R87.41 ± R 33.23, and a CPI value of 0.5. The most expensive drug is Starlix® 120mg with an average cost of R 390.10 and a CPI value of 2.1.

5.7.2.5 Alpha-glucosidase inhibitors

The final group of oral antidiabetic agents that will be discussed is the alpha-glucosidase inhibitors. As seen in section 2.7.4.4.3 of chapter 2, the alpha-glucosidase inhibitors act by inhibiting the alpha-glucosidase enzymes in the gastro-intestinal tract.

Acarbose (Glucobay®) is the only agent in this group available on the South African market.

The cost and prevalence of the alpha-glucosidase inhibitors will be indicated in table 5.10.

Table 5.10: Cost and prevalence of alpha-glucosidase inhibitors

Active ingredient	Agent	Prevalence	Average cost (R)	Standard deviation (R)	Total cost (R)	Frequency %	Cost %	CPI
January-April								
Acarbose	Glucobay® 50mg	153	231.83	68.12	35 470.26	63.7	54.8	0.9
	Glucobay® 100mg	87	336.50	74.28	29 275.68	36.3	45.2	1.2
Total		**240**	**269.77**	**86.48**	**64 745.94**	**100**	**100**	**1**
May-August								
Acarbose	Glucobay® 50mg	171	207.28	63.74	35 444.85	64.3	53.9	0.8
	Glucobay® 100mg	95	318.99	100.92	30 303.87	35.7	46.1	1.3
Total		**266**	**247.18**	**95.37**	**65 748.72**	**100**	**100**	**1**
September-December								
Acarbose	Glucobay® 50mg	185	177.05	48.19	32 753.43	68.3	60.3	0.9
	Glucobay® 100mg	86	250.53	65.45	21 545.61	31.7	39.7	1.3
Total		**271**	**200.37**	**64.08**	**54 299.04**	**100**	**100**	**1**

From table 5.10, tables 5.10.1 and 5.10.2 can be compiled. Table 5.10.1 is an indication of all the alpha-glucosidase inhibitor products with a percentage usage of >10% and a CPI of >1, which gives an indication of relatively high usage and relatively high cost.

Table 5.10.1: Summary of the alpha-glucosidase inhibitor products with prevalence >10% and CPI >1

Agent (Trade name ®)	January-April	May-August	September-December
Glucobay 100mg	√	√	√

√ indicates that the product has a prevalence of >10% and CPI >1

Table 5.10.2 is an indication of all the alpha-glucosidase inhibitor products that have a percentage usage of >10%, but with a CPI of ≤1.

Table 5.10.2: Summary of the alpha-glucosidase inhibitor products with prevalence >10% and CPI ≤1

Agent (Trade name ®)	January-April	May-August	September-December
Glucobay 50mg	√	√	√

√ indicates that the product has a prevalence of >10% and CPI ≤1

- *January-April*

As calculated in table 5.10 the acarbose prescribed in this time period, presents 31% of all the acarbose prescribed in the database (n = 777). Note that the average cost for Glucobay® 50mg (R231.83 ± R68.12) and Glucobay® 100mg (R336.50 ± R74.28) is relatively higher than the average cost of Glucobay® 50mg and 100mg for the other time periods from May to August and September to December.

According to the CPI value of Glucobay® 50mg (0.9) this form of therapy is relatively inexpensive since the value is less than one.

- *May-August*

Glucobay® 50mg once more has a lower CPI (0.8) and average cost (R207.28 ± R63.74) than Glucobay® 100mg.

- *September-December*

During this time period, the most acarbose agents were prescribed with a prevalence of 271 and a percentage frequency of 34.9% (n = 777).

As with all the other oral antidiabetic agents, the average cost for this period (R200.37 ± R64.08) is relatively lower than the total average cost of the other two time periods (R269.77 ± R86.48 for Jan-Apr and R247.18 ± R95.37 for May-Aug).

Glucobay® 50mg was prescribed 185 times with a percentage frequency of 68.3% and Glucobay® 100mg was prescribed 86 times (31.7%).

If the average cost of Glucobay® 100mg prescribed during January to April is compared to the average cost of Glucobay® 100mg prescribed during September to December, a d-value of 1.2 can be calculated, which means that the difference in the average cost is of practical statistical significance, meaning that it can have an influence on possible cost savings.

If the average cost of Glucobay® 50mg prescribed during January to April is compared to the average cost of Glucobay® 50mg prescribed during September to December, a d-value of 0.8 can be calculated, which means that the difference in the average cost is of practical statistical significance.

From table 5.10 and the La Grange study (1998:149) it can be calculated that the average cost of the alpha-glucosidase inhibitors dispensed during the time January to April 2004 was almost 1.9 times more expensive than the alpha-glucosidase inhibitors (R140.73 ± R62.46) dispensed during the study period used by La Grange. It can also be calculated that the average cost for the period May to August 2004 is 1.8 times higher and the average cost for the period September to December 2004 is 1.4 times higher than the average cost calculated by La Grange on the 1996 data. Truter (1999:141) determined the average cost of the alpha-glucosidase inhibitors to be R127.22 per item. Therefore it can be calculated that the alpha-glucosidase inhibitors were 29.8% to 36.5% more expensive during the period September to December 2004 than in 1996.

5.7.2.6 Combinations

The only product that can be described as a combination product is Glucovance®. Glucovance® is a combination of metformin and glibenclamide. Currently Glucovance® is available in three strengths* on the South African market, namely a 500/2.5mg, 500/5mg and a 250/1.25mg. No combination products were recorded in the La Grange or Truter studies.

Table 5.11 summarises the cost and prevalence of the combination product Glucovance®.

* 500/2.5mg = 500mg metformin and 2.5mg glibenclamide; 500/5mg = 500mg metformin and 5mg glibenclamide; 250/1.25mg = 250mg metformin and 1.25mg glibenclamide.

Table 5.11: Cost and prevalence of the combination product Glucovance®

Active ingredient	Agent	Prevalence	Average cost (R)	Standard deviation (R)	Total cost (R)	% Frequency	Cost %	CPI
January-April								
Metformin/Glibenclamide	Glucovance® 500/2.5mg	188	187.88	70.42	35 321.88	48.3	50.1	1
	Glucovance® 500/5mg	124	237.92	111.72	29 501.77	31.9	41.8	1.3
	Glucovance® 250/1.25mg	77	73.86	27.62	5 687.20	19.8	8.1	0.4
Total		**389**	**181.26**		**70 510.85**	**100**	**100**	**1**
May-August								
Metformin/Glibenclamide	Glucovance® 500/2.5mg	268	134.16	63.95	35 953.75	44	41.2	0.9
	Glucovance® 500/5mg	228	197.40	93.24	45 006.46	37.4	51.6	1.4
	Glucovance® 250/1.25mg	113	55.86	22.84	6 312.28	18.6	7.2	0.4
Total		**609**	**143.30**	**143.30**	**87 272.49**	**100**	**100**	**1**
September-December								
Metformin/Glibenclamide	Glucovance® 500/2.5mg	434	110.14	42.53	47 798.92	47.6	45.2	0.9
	Glucovance® 500/5mg	339	150.96	59.34	51 176.75	37.2	48.4	1.3
	Glucovance 250/1.25mg	138	49.13	18.17	6 779.28	15.1	6.4	0.4
Total		**911**	**116.09**	**58.04**	**105 754.95**	**99.9**	**100**	**1**

From table 5.11, tables 5.11.1 and 5.11.2 can be compiled. Table 5.11.1 is an indication of the combination product with a percentage usage of >10% and a CPI of >1, which gives an indication of relatively high usage and relatively high cost.

Table 5.11.1: Summary of the combination product with prevalence >10% and CPI >1

Agent (Trade name ®)	January-April	May-August	September-December
Glucovance 500/5mg	√	√	√

√ indicates that the product has a prevalence of >10% and CPI >1

Table 5.11.2 is an indication of the combination product that has a percentage usage of >10%, but with a CPI of ≤1.

Table 5.11.2: Summary of the combination product with prevalence >10% and CPI ≤1

Agent (Trade name ®)	January-April	May-August	September-December
Glucovance 500/2.5mg	√	√	√
Glucovance 250/1.25mg	√	√	√

√ indicates that the product has a prevalence of >10% and CPI ≤1

- *January-April*

As calculated in table 5.11 the metformin/glibenclamide combination for this time period amounts to 20.4% (n = 1909) of the total metformin/glibenclamide combinations on the total database. Glucovance® 250/1.25mg is the most inexpensive item according to the average cost (R73.86 ± R27.62) and CPI value (0.4), but it has the lowest prevalence (19.8%, n = 389).

- *May-August*

During this period of time, the metformin/ glibenclamide combination products amounted to 31.9% of the total metformin/glibenclamide products in the database (n = 1909). Glucovance® 500/2.5 had the highest prevalence (268) and percentage frequency (44%, n = 609).

- *September-December*

According to table 5.11, the metformin/glibenclamide combination products for this period of time, amounted to 47.7% of all the metformin/glibenclamide products (n = 1909).

Note that from the table 5.11 it is once again clear that the items prescribed during this time period have an "average cost" (R116.09) that is much lower than the other time periods for the same item (January-April R181.26 and May-August R143.30) respectively.

5.7.3 Utilisation and cost of utilisation of oral antidiabetic agents in terms of prescribed daily dose (PDD)

The consumption and utilisation of the oral antidiabetic agents will be calculated using the following formula (PSU, 2005:3):

$$\text{Clinical measure of PDD} = \frac{\text{average number of tablets per prescription}}{\text{number of days}}$$

According to the Prescribing Support Unit (PSU) the prescribed daily dose (PDD) for a drug can be determined from prescriptions and medical or pharmacy records. The PDD is the average daily amount of the drug that is actually prescribed for a given time period. A comparison of a drug's PDD with its DDD gives an insight into the actual usage of a drug when compared to its most common and recommended use (Manitoba Centre for Health Policy, 2003:2; PSU, 2005:3).

The DDD as defined by the WHO for a particular drug is the assumed average maintenance dose per day for a drug used for its main indication in adults. The DDD is, however, only a unit of measurement and does not necessarily reflect the recommended or prescribed daily dose. Doses for individual patients and patient groups will often differ from the DDD and will necessarily have to be based on individual characteristics (e.g. age and weight) and pharmacokinetic considerations (WHO, 2005:4).

The DDD is nearly always a compromise based on a review of the available information including doses used in various countries when this information is available. The DDD is sometimes a dose that is rarely if ever prescribed, because it is an average of two or more commonly used dose sizes (WHO, 2005:5). For these and other reasons (e.g. duplication of results) only the PDD will be used as indicator of the daily intake of antidiabetic agents.

In table 5.12 the average number of tablets per prescription of each antidiabetic agent is used to calculate the average number of tablets and the average strength per day (in mg) that a patient receives. For the purpose of this study a month consists of thirty days. The average number of tablets per day was determined by dividing the average number of tablets per prescription with thirty. By multiplying the average number of tablets per day with the strength of the product, the average strength per day that a patient receives can be determined.

The prevalence for each agent is the same as the prevalence summarised in table 5.6 to table 5.11

Table 5.12: Utilisation of antidiabetic agents in terms of the PDD

		January to April			May to August			September to December		
Active ingredient	Agent (Registered trademark ®)	Jan-Apr Average number of tablets per prescription per day	Average number of tablets per day	Average strength per day (mg)	May-Aug Average number of tablets per prescription per day	Average number of tablets per day	Average strength per day (mg)	Sept-Dec Average number of tablets per prescription per day	Average number of tablets per day	Average strength per day (mg)
Acarbose	Glucobay 100mg	85.41 ± 17.20	2.85	284.70	87.96 ± 22.01	2.93	293.20	81.63 ± 18.21	2.72	272.00
	Glucobay 50mg	83.73 ± 24.97	2.79	139.55	83.65 ± 26.48	2.79	139.50	86.27 ± 35.12	2.88	144.00
Chlorpropamide	Diabinese 250mg	30.00 ± 0.00	1.00	250.00	-	-	-	-	-	-
	Diabetix 250mg	-	-	-	20.00 ± 0.00	0.67	167.50	-	-	-
	Hypomide 250mg	66.00 ± 32.67	2.20	550.00	66.43 ± 31.53	2.21	552.50	54.05 ± 38.98	1.80	450.00
Glibenclamide	Daonil 5mg	70.37 ± 32.10	2.35	11.7	66.92 ± 31.73	2.23	11.15	61.95 ± 30.71	2.07	10.35
	Diacare 5mg	60.00 ± 0.00	2	10	71.25 ± 30.79	2.38	11.90	54.71 ± 18.33	1.82	9.10
	Euglucon 5mg	82.50 ± 48.14	2.75	13.75	60.00 ± 32.86	2.00	10.00	50.00 ± 25.98	1.67	8.35
	Glyben 5mg	62.82 ± 32.49	2.09	10.47	63.70 ± 32.45	2.12	10.60	64.05 ± 32.56	2.14	10.70
	Glycomin 5mg	66.23 ± 33.67	2.21	11.04	67.67 ± 35.03	2.26	11.30	68.29 ± 34.29	2.28	11.40
	Norton-Glibenclamide 5mg	59.21 ± 23.70	1.97	9.87	64.50 ± 35.46	2.15	10.75	91.25 ± 33.66	3.04	15.20
Gliclazide	Diamicron 80mg	70.11 ± 32.91	2.34	186.96	74.73 ± 35.28	2.49	199.20	72.37 ± 35.85	2.41	192.80
	Diamicron MR 30mg	49.27 ± 22.40	1.64	49.27	51.97 ± 22.88	1.73	51.90	53.39 ± 26.37	1.78	53.40
	Diaglucide 80mg	76.01 ± 34.36	2.53	202.69	74.41 ± 32.94	2.48	198.40	76.72 ± 31.54	2.56	204.80
	Glucomed 80mg	70.89 ± 32.94	2.36	189.04	72.74 ± 32.72	2.42	193.60	72.25 ± 32.99	2.41	192.80
	Glycron 80mg	70.75 ± 28.73	2.36	188.67	76.19 ± 32.42	2.54	203.20	78.53 ± 30.84	2.62	209.60
	Glygard 80mg	72.11 ± 28.83	2.40	192.29	64.84 ± 22.02	2.16	172.80	68.38 ± 28.94	2.28	182.40
	Merck-Gliclazide 80mg	60.00 ± 23.41	2.00	160.00	64.78 ± 28.10	2.16	172.80	69.40 ± 30.40	2.31	184.80
	Rolab-Gliclazide 80mg	70.07 ± 30.95	2.34	186.85	69.69 ± 31.75	2.32	185.60	71.79 ± 31.93	2.39	191.20
	Sandoz-Gliclazide 80mg	-	-	-	-	-	-	71.62 ± 32.95	2.39	191.20
	Ziclin 80mg	90.00 ± 0.00	3.00	240.00	-	-	-	-	-	-
Glimeparide	Amaryl 1mg	31.62 ± 8.35	1.05	1.05	31.30 ± 8.06	1.04	1.04	32.42 ± 16.69	1.08	1.08
	Amaryl 2mg	31.69 ± 8.61	1.06	2.11	31.75 ± 8.01	1.06	2.12	31.96 ± 8.80	1.07	2.14
	Amaryl 4mg	31.97 ± 9.01	1.07	4.26	31.90 ± 8.51	1.06	4.24	32.15 ± 9.04	1.07	4.28
Glipizide	Minidiab 5mg	69.61 ± 39.72	2.32	11.60	73.74 ± 48.03	2.46	12.30	76.82 ± 52.10	2.56	12.80

Table 5.12: (Continue) Utilisation of antidiabetic agents in terms of the PDD

		January to April			May to August			September to December		
Active ingredient	Agent (Registered trademark ®)	Jan-Apr Average number of tablets per prescription per day	Average number of tablets per day	Average strength per day (mg)	May-Aug Average number of tablets per prescription per day	Average number of tablets per day	Average strength per day (mg)	Sept-Dec Average number of tablets per prescription per day	Average number of tablets per day	Average strength per day (mg)
Metformin	Glucophage 500mg	71.06 ± 34.35	2.37	1184.33	71.08 ± 30.42	2.37	1185.00	72.15 ± 31.53	2.41	1205.00
	Glucophage Forte 850mg	64.96 ± 20.78	2.17	1840.53	65.08 ± 20.29	2.17	1844.50	66.05 ± 22.53	2.20	1870.00
	Rolab-Metformin FC 500mg	72.84 ± 31.87	2.43	1214.00	74.35 ± 36.22	2.48	1240.00	74.59 ± 32.28	2.49	1245.00
	Rolab-Metformin FC 850mg	65.23 ± 18.49	2.17	1848.18	66.20 ± 18.27	2.21	1878.50	66.19 ± 19.97	2.21	1878.50
	Sandoz-Metformin FC 500mg	-	-	-	-	-	-	73.35 ± 33.17	2.45	1225.00
	Sandoz-Metformin FC 850mg	-	-	-	-	-	-	64.13 ± 16.92	2.14	1819.00
	Merck-Metformin 500mg	71.95 ± 35.29	2.40	1199.17	72.20 ± 32.39	2.41	1205.00	71.99 ± 32.21	2.40	1200.00
	Merck-Metformin 850mg	64.58 ± 16.32	2.15	1829.77	62.62 ± 13.74	2.09	1776.50	64.57 ± 16.06	2.15	1827.50
	Metforal 500mg	-	-	-	72.63 ± 17.75	2.42	1210.00	75.95 ± 38.89	2.53	1265.00
	Metforal 850mg	-	-	-	60.00 ± 7.17	2.00	1700.00	64.45 ± 21.98	2.15	1827.50
	Rolab-Metformin HCl 500mg	70.09 ± 32.45	2.34	1170.00	72.14 ± 33.81	2.40	1200.00	71.97 ± 31.82	2.40	1200.00
	Rolab-Metformin HCL 850mg	62.73 ± 17.25	2.09	1777.35	63.97 ± 18.36	2.13	1810.50	65.61 ± 20.42	2.19	1861.50
	Sandoz-Metformin HCl 500mg	-	-	-	-		-	71.09 ± 30.54	2.37	1185.00
	Sandoz-Metformin 850mg	-	-	-	-	-	-	64.53 ± 17.92	2.15	1827.50
Metformin/ Glibenclamide	Glucovance 250/1.25mg	42.99 ± 15.33	1.43		41.42 ± 14.63	1.38		46.67 ± 15.91	1.56	
	Glucovance 500/2.5mg	57.94 ± 20.61	1.93		57.20 ± 22.20	1.91		55.33 ± 22.23	1.84	
	Glucovance 500/5mg	76.19 ± 30.96	2.54		80.79 ± 33.35	2.69		79.10 ± 34.72	2.64	
Nateglinide	Starlix FCT 120mg	80.20 ± 12.48	2.67	320.40	72.81 ± 20.65	2.43	291.60	82.50 ± 12.60	2.75	330.00

Table 5.12: (Continue) Utilisation of antidiabetic agents in terms of the PDD

		January to April			May to August			September to December		
Active ingredient	Agent (Registered trademark ®)	Jan-Apr Average number of tablets per prescription per day	Average number of tablets per day	Average strength per day (mg)	May-Aug Average number of tablets per prescription per day	Average number of tablets per day	Average strength per day (mg)	Sept-Dec Average number of tablets per prescription per day	Average number of tablets per day	Average strength per day (mg)
	Starlix FCT 60mg	42.00 ± 0.00	1.40	84.00	-	-	-	84.00 ± 0.00	2.80	168.00
Pioglitazone	Actos 15mg	28.99 ± 5.00	0.97	14.55	29.20 ± 5.51	0.97	14.55	29.53 ± 6.70	0.98	14.70
	Actos 30mg	28.77 ± 3.44	0.96	28.80	28.91 ± 4.05	0.96	28.80	29.70 ± 7.06	0.99	29.70
Repaglinide	Novonorm 0.5mg	81.68 ± 18.55	2.72	1.36	82.34 ± 26.30	2.74	1.37	86.59 ± 28.24	2.89	1.45
	Novonorm 1.0mg	85.41 ± 20.82	2.85	2.85	87.50 ± 40.26	2.92	2.92	94.33 ± 85.40	3.14	3.14
	Novonorm 2.0mg	91.96 ± 32.73	3.07	6.14	93.08 ± 28.17	3.10	6.20	95.90 ± 35.32	3.20	6.40
Rosiglitazone	Avandia 2mg	34.91 ± 12.53	1.16	2.32	32.32 ± 14.91	1.08	2.16	32.24 ± 10.84	1.07	2.14
	Avandia 4mg	32.98 ± 10.46	1.10	4.40	33.69 ± 12.29	1.12	4.48	33.64 ± 13.68	1.12	4.48

- January to April *versus* May to August

From table 5.12 it can be seen that if the time period January to April is compared to the time period May to August the following calculations and conclusions can be made.

It appears that there was not really a change in the average number of tablets per prescription of each antidiabetic agent.

Diacare® 5mg

For Diacare® 5mg, the average number of tablets that a patient receives per day has increased, from 2 (Jan-Apr) to 2.38 (May-Aug), an increase of more that 10%. According to the MIMS (2004:314) the prescribed daily dose varies between 2.5mg and 15mg. The average number of tablets per prescription has also increased from 60.00 ± 0.00 (Jan-Apr) to 71.25 ± 30.79 (May-Aug). Although it is an increase of more than 10% the d-value, which is an indication of the practical statistical significance, is only 0.3.

Euglucon® 5mg

For Euglucon® 5mg, the average number of tablets that a patient receives per day has decreased from 2.75 for January to April, to 2.00 for May to August. The average number of tablets per prescription has also decreased from 82.50 ± 48.14 (Jan-Apr) to 60.00 ± 32.86 (May-Aug). According to the MIMS (2003:303) the maximum dose of Euglucon® 5mg is 15mg per day. It is thus clear that the average strength per day of Euglucon® 5mg is in line with the prescribed daily dose according to the MIMS (2003:303).

- January to April *versus* September to December

From table 5.12 it can be seen that if the time period January to April is compared to the time period September to December the following conclusions can be made.

It seems as if there was not really a change in the average number of tablets per prescription of each antidiabetic agent, except for these following agents:

Hypomide® 250mg

The average number of tablets per prescription for the period September to December (54.05 ± 38.98) has decreased when compared to that of January to April (66.00 ± 32.67) with more than 10%. The d-value is however 0.3 which is an indication that the decrease has no practical statistical significance. According to the MIMS (2004:315) the prescribed daily dose must be between 50mg and 500mg. From table 5.12 it can be determined that the average number of tablets per day for the time period January to April was 2.20 and for the time September to December was 1.80. If this average is multiplied by the strength (250mg per tablet) it can be determined that the average consumption of Hypomide 250mg for January to April was 550.00mg and for September to December it was 450.00mg.

Daonil® 5mg

From table 5.12 it can be seen that the average number of tablets per prescription has decreased from 70.37 ± 32.10 (January-April) to 61.98 ± 30.71 (September-December). This is a decrease of more than 10%, but once again the d-value is less than 0.8, which means that this decrease does not have any practical statistical significance. The average number of tablets per day has also decreased with more than 10 % from 2.35 (January-April) to 2.07 (September-December). The maximum prescribed daily dose is 15mg (MIMS, 2004:313) and when this is compared to the actual average strength taken per day it is 11.70mg during January to April and 10.35mg during the time September to December

Euglucon® 5mg

It can be seen from table 5.12 that for the time September to December the average number of tablets per prescription is 50.00 ± 25.98 compared to the 82.50 ± 48.14 of the time January to April, a decrease of more than 60%. The d-value of 0.7, however, shows that this decrease does not necessarily have a practical statistical significance, but that factors such as number of patients, average cost per tablet, etc. must be brought into considerations for a possible reason of this decrease in average number of tablets per prescription. The average number of tablets per day has also decrease from 2.75 (January-April) to 1.67 (September-December). According to the MIMS (2003:303) the prescribed daily dose should be between 2.5mg and 15mg. For January to April the average intake per day was 13.75mg and for September to December it was 8.35mg. Whilst a significant difference in consumption per day is experienced both the results are in the range of prescribed daily intake.

Norton-Glibenclamide® 5mg

From table 5.12 it can be seen that the average number of tablets per prescription has increased from January to April (59.21 ± 23.70) when compared with September to December (91.25 ± 33.66). From these two averages a d-value of 0.9 can be calculated which gives an indication that this increase may have an influence in the total average cost of Norton-Glibenclamide®. It is important to note that the average tablet per day has also increased from 1.97 (January-April) to 3.04 (September-December). According to the MIMS (2004:314) the maximum daily dose is three tablets, or 15mg. The possibility of 'overdosing" should be kept in mind, since the average intake per day is 15.20mg for the time September to December. However, in the absence of clinical data, e.g. blood glucose values, it is not possible to come to a conclusion on the prescribed volumes. Note should also be taken of the influence of bioavailability on the consumption and cost. This, however, is outside the scope of this study.

Glycron® 80mg

From table 5.12 it can be seen that the average number of tablets per prescription has increased from 70.25 ± 28.73 (January-April) to 78.53 ± 30.84 (September-December). The average number of tablets per day has also increased with more than 10%, from 2.36 (January-April) to 2.62 (September-December). The average strength per day that the patients received has increased with 20.93mg, but is still within the dosage range (of 40mg-320mg) according to the MIMS (2004:315).

Merck-Gliclazide® 80mg

Table 5.12 reveals that the average number of tablets per prescription has increased from 60.00 ± 23.41 for the time January to April to 69.40 ± 30.40 for the time period September to December. The average number of tablets per day has also increased from 2.00 tablets per day to 2.31 tablets per day. There was also an increase in the average strength per day. For the time period September to December the patients receiving Merck-Gliclazide® received on average 24.80mg/day more than for the time period January to December.

Starlix® FCT 60mg

From table 5.12 it can be seen that the average number of tablets per prescription, the average number of tablets per day and the average strength that a patient receives per day have doubled since January to April until September to December.

If the utilisation of oral antidiabetic agents dispensed during 2004 is compared to the utilisation of oral antidiabetic agents dispensed during the 1996 study period used by La Grange (1998:151), the following conclusions can be made.

For the period January to April 2004, the average number of tablets per prescription for the 500mg biguanides was between 70.09 to 72.84 tablets per prescription with an average of 71.49. For the period May to August 2004 the average number of tablets per prescription for the 500mg biguanides was between 71.08 to 74.35 tablets per prescription with an average of 72.48. For the period September to December 2004 the average number of tablets per prescription for the 500mg biguanides was between 71.09 to 75.95 tablets per prescription with an average of 73.01. The number of tablets per prescription for the 500mg biguanides dispensed during the 1996 study period of La Grange (1998:151) was 71.58.

For the period January to April 2004, the average number of tablets per prescription for the 850mg biguanides was between 62.73 and 65.23 tablets per prescription with an average of 64.38. For the period May to August 2004 the average number of tablets per prescription for the 850mg biguanides was between 60.00 and 66.20 tablets per prescription with an average of

63.57. For the period September to December 2004 the average number of tablets per prescription for the 850mg biguanides was between 64.13 and 66.19 tablets per prescription with an average of 65.08. The number of tablets per prescription for the 850mg biguanides dispensed during the 1996 study period of La Grange (1998:151) was 65.81.

For the period January to April 2004 the average number of tablets per prescription for the 100mg acarbose was 85.31, for the period May to August it was 87.96 and for the period September to December it was 81.63. The average number of tablets per prescription for the 100mg acarbose dispensed during the 1996 study period of La Grange (1998:151) was 81.73. The d-values for the 2004 study periods, if compared to the 1996 period, show that there is no practical statistical significance in the differences of the average number of tablets per prescription.

For the period January to April 2004 the average number of tablets per prescription for the 50mg acarbose was 83.73, for the period May to August it was 83.65 and for the period September to December it was 86.27. The average number of tablets per prescription for the 50mg acarbose dispensed during the 1996 study period of La Grange (1998:151) was 79.06. The d-values for the 2004 study periods, if compared to the 1996 period, show that there is no practical statistical significance in the differences of the average number of tablets per prescription.

For the period January to April 2004, the average number of tablets per prescription for the 250mg chlorpropamide was 48.00 tablets per prescription. For the period May to August 2004 the average number of tablets per prescription for the 250mg chlorpropamide was 43.22. For the period September to December 2004 the average number of tablets per prescription for the 250mg chlorpropamide was 54.05 tablets per prescription. The average number of tablets per prescription for the 250mg chlorpropamide dispensed during the 1996 study period of La Grange (1998:151) was 52.04.

For the period January to April 2004 the average number of tablets per prescription for glibenclamide was 66.86, for the period May to August it was 65.67 and for the period September to December it was 65.04. The average number of tablets per prescription for glibenclamide dispensed during the 1996 study period of La Grange (1998:151) was 69.09. The d-values for the 2004 study periods, if compared to the 1996 period, show that there is no practical statistical significance in the differences of the average number of tablets per prescription.

For the period January to April 2004 the average number of tablets per prescription for gliclazide was 69.91, for the period May to August it was 68.67 and for the period September to December it was 70.49. The average number of tablets per prescription for gliclazide dispensed during the 1996 study period of La Grange (1998:151) was 68.97. The d-values for the 2004 study periods, if compared to the 1996 period, show that there is no practical statistical significance in the differences of the average number of tablets per prescription.

For the period January to April 2004 the average number of tablets per prescription for glipizide was 69.61, for the period May to August it was 73.74 and for the period September to December it was 76.83. The average number of tablets per prescription for gliclazide dispensed during the 1996 study period of La Grange (1998:151) was 68.73. The d-values for the 2004 study periods, if compared to the 1996 period, show that there is no practical statistical significance in the differences of the average number of tablets per prescription.

5.7.4 Summary

In this section the cost and prevalence of the oral antidiabetic agents were discussed. From the results it is clear that the biguanides and sulfonylureas have the highest prevalence.

The total cost for all the oral antidiabetic agents for the total study period is R11 604 970 09 and it can be seen that the total cost for the period January tot April amounts to 33.1% (n = R3 846 942.57) of the total cost. The total cost of all the oral agents for the time May to August is R4 086 107.97 and for September to December it is R3 671 919.61.

The time period with the most products prescribed and dispensed was the time September to December with total items of 46713, but the lowest total cost (R3 671 919.61). The time period with the highest total average cost is the time from January to April (R125.52 ± R103.94).

It can also be seen that the price of all the oral antidiabetic products was lower during the last time period in the database. As stated earlier, this can be due to the pricing regulations that came into effect in the last quarter of 2004 (see section 3.7.3 of chapter 3).

The utilisation of antidiabetic agents was also discussed in this section. From table 5.12 it seems as if there is not an over or under consumption of the oral antidiabetic agents. Due to the complexity in the dosing schedule of the insulins, it is difficult to determine the consumption if the dosage of each individual patient is not available.
In the next section the cost and prevalence of combinations of antidiabetic agents will be discussed.

5.8 THE PREVALENCE AND USAGE PATTERNS OF COMBINATIONS OF ANTIDIABETIC AGENTS

5.8.1 Introduction

It is sometimes necessary to consider combination therapy in the treatment of diabetic patients whose diabetes is not adequately controlled by diet and single-drug therapy. According to the treatment protocol of diabetes mellitus type 2, if treatment with one oral agent (usually metformin or a sulfonylurea) has failed, a second agent can be added. If the combination of two oral antidiabetic agents is not adequate to control blood glucose concentrations a third oral agent or insulin can be added to the treatment regime (refer to Chapter 2 section2.7.1, figure 2.2). Due to the magnitude of the tables summarising the combinations of antidiabetic agents these tables will appear in Appendix E, F and G.

The antidiabetic prescriptions on the database were analysed to identify the prescriptions with only one antidiabetic agent. These agents were tabled (table 5.13 – table 5.18) together with the number of combinations for each agent (determined from table 5.5 – 5.11).

Table 5.13: Summary of total, single and combination oral antidiabetic agents for the time January to April

January-April	Agent (Trade name)	Average cost (Total prevalence)	Average cost (One alone)	Average cost (Combination)
Active ingredient		(R)	(R)	(R)
Acarbose	Glucobay 100mg	336.50 ± 74.28 (87)	347.63 ± 38.98 (36)	328.64 (51)
	Glucobay 50mg	231.83 ± 68.12 (153)	231.62 ± 83.74 (82)	232.07 (71)
Chlorpropamide	Diabinese 250mg	46.51 ± 0.00 (1)	46.51 ± 0.00 (1)	0
	Hypomide 250mg	100.57 ± 54.02 (20)	108.46 ± 65.29 (10)	92.67 (10)
Glibenclamide	Daonil 5mg	432.64 ± 194.08 (372)	356.68 ± 167.46 (170)	496.58 (202)
	Diacare 5mg	55.70 ± 4.16 (3)	0	55.70 (3)
	Euglucon 5mg	573.93 ± 360.66 (6)	358.23 ± 421.00 (3)	789.62 (3)
	Glyben 5mg	128.39 ± 71.79 (402)	108.87 ± 64.18 (167)	142.26 (235)
	Glycomin 5mg	147.75 ± 76.82 (2943)	123.78 ± 67.77 (1200)	164.46 (1743)
	Norton-Glibenclamide	30.43 ± 20.12 (19)	22.91 ± 4.20 (8)	35.91 (11)
Gliclazide	Diamicron 80mg	116.95 ± 59.61 (1291)	98.11 ± 52.85 (631)	134.97 (660)
	Diamicron MR 30mg	135.43 ± 61.96 (424)	131.92 ± 57.46 (243)	140.13 (181)
	Diaglucide 80mg	108.33± 47.88 (147)	88.69 ± 38.80 (61)	122.27 (86)
	Glucomed 80mg	97.75 ± 44.78 (3512)	84.79 ± 40.80 (1642)	109.13 (1870)
	Glycron 80mg	93.98 ± 41.90 (138)	90.67 ± 43.09 (54)	96.11 (84)
	Glygard	99.14 ± 41.74 (57)	94.28 ± 36.84 (30)	104.54 (27)
	Merck-Gliclazide 80mg	63.19 ± 47.12 (39)	40.08 ± 43.54 (11)	72.27 (28)
	Rolab-Gliclazide	92.93 ± 39.97 (833)	81.10 ± 37.77 (332)	100.76 (501)
	Ziclin 80mg	136.79 ± 0.00 (4)	136.79 ± 0.00 (4)	0
Glimeparide	Amaryl 1mg	103.92 ± 32.51 (1001)	102.05 ± 29.40 (678)	107.85 (323)
	Amaryl 2mg	194.97 ± 65.07 (1513)	194.79 ± 61.37 (817)	195.19 (696)
	Amaryl 4mg	366.20 ± 125.90 (1085)	365.96 ± 113.69 (495)	366.41 (590)
Glipizide	Minidiab 5mg	241.04 ± 148.63 (193)	214.08 ± 139.63 (99)	269.42 (94)
Metformin	Glucophage 500mg	64.73 ± 29.30 (4286)	60.64 ± 27.94 (2319)	69.56 (1967)
	Glucophage Forte 850mg	101.69 ± 33.37 (4243)	100.92 ± 31.98 (1681)	102.19 (2562)
	Rolab-Metformin HCL 500mg	63.46 ± 28.78 (1799)	57.49 ± 26.47 (1034)	71.53 (765)
	Rolab-Metformin FC 500mg	61.24 ± 27.88 (1732)	57.46 ± 26.80 (889)	65.22 (843)
	Rolab-Metformin FC 850mg	93.66 ± 30.40 (1382)	90.38 ± 29.09 (566)	95.95 (816)
	Rolab-Metformin HCl 850mg	94.14 ± 29.63 (1074)	92.60 ± 27.32 (427)	95.16 (647)
	Merck-Metformin 500mg	58.11 ± 27.86 (234)	54.66 ± 26.53 (128)	62.29 (106)
	Merck-Metformin 850mg	87.52 ± 25.80 (231)	82.67 ± 23.47 (89)	90.56 (142)

Table 5.13: (Continue) Summary of total, single and combination oral antidiabetic agents for the time January to April

January-April Active ingredient	Agent (Trade name)	Average cost (Total prevalence) (R)	Average cost (One alone) (R)	Average cost (Combination) (R)
Metformin/ Glibenclamide	Glucovance 250/1.25mg	73.86 ± 27.62 (77)	74.91 ± 27.99 (68)	65.92 (9)
	Glucovance 500/2.5mg	187.88 ± 70.42 (188)	189.08 ± 72.70 (170)	176.53 (18)
	Glucovance 500/5mg	237.92 ± 111.72 (124)	234.12 ± 111.04 (115)	286.44 (9)
Nateglinide	Starlix FCT 120mg	426.69 ± 60.22 (25)	418.81 ± 71.59 (15)	438.50 (10)
	Starlix FCT 60mg	208.23 ± 0.00 (1)	208.23 ± 0.00 (1)	0
Pioglitazone	Actos 15mg	400.32 ± 58.32 (200)	403.63 ± 80.94 (101)	396.94 (99)
	Actos 30mg	582.41 ± 88.96 (135)	592.91 ± 16.33 (55)	575.19 (80)
Repaglinide	Novonorm 0.5mg	99.93 ± 20.30 (101)	98.76 ± 21.14 (72)	102.84 (29)
	Novonorm 1.0mg	196.50 ± 45.35 (98)	199.84 ± 42.45 (49)	193.16 (49)
	Novonorm 2.0mg	356.92 ± 122.51 (69)	356.22 ± 124.02 (21)	357.23 (48)
Rosiglitazone	Avandia 2mg	206.42 ± 73.43 (119)	200.07 ± 65.02 (77)	218.05 (42)
	Avandia 4mg	372.41 ± 116.69 (287)	376.44 ± 123.95 (144)	170.75 (143)

Table 5.14: Summary of total, single and combination oral antidiabetic agents for the time May to August

May-August Active ingredient	Agent (Trade name)	Average cost (Total prevalence) (R)	Average cost (One alone) (R)	Average cost (Combination) (R)
Acarbose	Glucobay 100mg	318.99 ± 100.92 (95)	299.59 ± 77.08 (35)	330.30 (60)
	Glucobay 50mg	207.28 ± 63.74 (171)	203.62 ± 57.38 (63)	209.41 (108)
Chlorpropamide	Diabetix 250mg	15.20 ± 0.00 (1)	15.20 ± 0.00 (1)	0
	Hypomide 250mg	73.54 ± 47.71 (14)	108.12 ± 47.79 (6)	47.61 (8)
Glibenclamide	Daonil 5mg	360.11 ± 169.53 (474)	291.16 ± 136.34 (189)	405.83 (285)
	Diacare 5mg	46.16 ± 32.43 (8)	75.17 ± 60.05 (2)	36.49 (6)
	Euglucon 5mg	300.59 ± 184.27 (6)	216.34 ± 167.91 (4)	469.11 (2)
	Glyben 5mg	50.10 ± 59.97 (510)	43.09 ± 49.74 (193)	54.36 (317)
	Glycomin 5mg	74.42 ± 51.67 (3645)	64.95 ± 51.03 (1377)	80.17 (2268)
	Norton-Glibenclamide	19.83 ± 11.58 (20)	12.86 ± 6.23 (13)	32.78 (7)
Gliclazide	Diamicron 80mg	118.78 ± 66.18 (1288)	99.66 ± 59.65 (542)	132.67 (746)
	Diamicron MR 30mg	136.60 ± 58.93 (882)	131.20 ± 56.36 (478)	143.00 (404)
	Diaglucide 80mg	71.85 ± 32.91 (436)	62.59 ± 32.71 (154)	76.91 (383)
	Glucomed 80mg	88.38 ± 41.55 (3822)	79.32 ± 39.90 (1698)	95.62 (2124)
	Glycron 80mg	89.90 ± 48.62 (213)	78.29 ± 48.21 (70)	95.59 (143)
	Glygard	73.41 ± 29.12 (83)	71.62 ± 32.31 (45)	75.53 (38)
	Merck-Gliclazide 80mg	63.59 ± 29.49 (91)	54.19 ± 22.22 (31)	68.44 (60)
	Rolab-Gliclazide	64.21 ± 31.61 (1151)	56.67 ± 28.66 (436)	68.80 (715)
Glimeparide	Amaryl 1mg	88.28 ± 33.49 (1126)	85.36 ± 28.15 (743)	93.95 (383)
	Amaryl 2mg	170.76 ± 62.96 (1719)	169.95 ± 56.88 (929)	171.70 (790)
	Amaryl 4mg	337.14 ± 114.17 (1462)	341.40 ± 120.93 (596)	334.40 (866)
Glipizide	Minidiab 5mg	202.73 ± 141.21 (161)	171.31 ± 122.77 (76)	230.54 (85)
Metformin	Glucophage 500mg	52.40 ± 24.97 (5531)	49.20 ± 22.87 (2838)	55.78 (2693)
	Glucophage Forte 850mg	74.88 ± 31.90 (5618)	72.93 ± 29.94 (2139)	76.08 (3479)
	Rolab-Metformin HCL 500mg	43.84 ± 20.96 (2166)	39.99 ± 19.09 (1139)	46.09 (1027)
	Rolab-Metformin FC 500mg	47.83 ± 24.29 (2273)	43.75 ± 22.32 (1151)	52.01 (1122)
	Rolab-Metformin FC 850mg	66.23 ± 25.51 (1696)	63.84 ± 25.03 (672)	67.80 (1024)
	Rolab-Metformin HCl 850mg	64.10 ± 23.51 (1208)	61.50 ± 22.61 (519)	66.05 (689)
	Merck-Metformin 500mg	55.59 ± 25.05 (361)	54.17 ± 25.04 (202)	57.39 (159)
	Merck-Metformin 850mg	79.46 ± 20.35 (238)	80.23 ± 18.80 (86)	79.02 (152)
	Metforal 500mg	38.63 ± 21.19 (8)	37.02 ± 24.27 (6)	43.46 (2)

Table 5.14: (Continue) Summary of total, single and combination oral antidiabetic agents for the time May to August

May-August Active ingredient	Agent (Trade name)	Average cost (Total prevalence) (R)	Average cost (One alone) (R)	Average cost (Combination) (R)
	Metforal 850mg	57.13 ± 16.71 (36)	51.26 ± 26.59 (13)	60.44 (23)
Metformin/ Glibenclamide	Glucovance 250/1.25mg	55.86 ± 22.84 (113)	57.64 ± 23.35 (95)	46.45 (18)
	Glucovance 500/2.5mg	134.16 ± 63.95 (268)	133.30 ± 63.99 (224)	138.53 (44)
	Glucovance 500/5mg	197.40 ± 93.24 (228)	193.17 ± 89.15 (189)	217.89 (39)
Nateglinide	Starlix FCT 120mg	393.82 ± 100.37 (31)	403.82 ± 78.91 (17)	381.67 (14)
Pioglitazone	Actos 15mg	390.06 ± 70.63 (382)	387.02 ± 78.21 (204)	393.54 (178)
	Actos 30mg	578.66 ± 78.37 (352)	574.67 ± 62.11 (155)	581.79 (197)
Repaglinide	Novonorm 0.5mg	89.83 ± 33.21 (111)	86.71 ± 38.17 (69)	94.95 (42)
	Novonorm 1.0mg	190.60 ± 92.29 (168)	202.51 ± 149.56 (55)	184.80 (113)
	Novonorm 2.0mg	336.24 ± 99.36 (117)	312.03 ± 130.94 (27)	343.50 (90)
Rosiglitazone	Avandia 2mg	167.30 ± 65.41 (144)	168.33 ± 52.45 (79)	166.05 (65)
	Avandia 4mg	340.36 ± 130.79 (530)	346.95 ± 132.56 (215)	335.86 (315)

Table 5.15: Summary of the total, single and combination oral antidiabetic agents for the time September to December

January-April	Agent (Trade name)	Average cost (Total prevalence)	Average cost (One alone)	Average cost (Combination)
Active ingredient		(R)	(R)	(R)
Acarbose	Glucobay 100mg	250.53 ± 65.45 (86)	256.48 ± 61.66 (37)	246.04 (49)
	Glucobay 50mg	177.05 ± 48.19 (185)	170.60 ± 39.95 (75)	181.44 (110)
Chlorpropamide	Hypomide 250mg	46.00 ± 38.48 (20)	46.48 ± 38.89 (13)	45.11 (7)
Glibenclamide	Daonil 5mg	252.47 ± 111.77 (514)	218.77 ± 99.37 (218)	277.28 (296)
	Diacare 5mg	13.55 ± 10.56 (17)	9.94 ± 4.63 (5)	15.06 (12)
	Euglucon 5mg	181.61 ± 86.90 (9)	114.26 ± 10.64 (5)	265.81 (4)
	Glyben 5mg	15.02 ± 14.51 (685)	13.79 ± 12.98 (240)	15.68 (445)
	Glycomin 5mg	58.78 ± 30.68 (4408)	49.47 ± 27.10 (1638)	64.29 (2770)
	Norton-Glibenclamide	20.62 ± 30.68 (24)	13.58 ± 6.75 (7)	23.52 (17)
Gliclazide	Diamicron 80mg	83.74 ± 48.12 (1136)	66.72 ± 38.23 (401)	93.03 (735)
	Diamicron MR 30mg	130.48 ± 65.00 (1237)	123.75 ± 59.55 (618)	137.19 (619)
	Diaglucide 80mg	62.84 ± 26.31 (838)	56.30 ± 26.58 (295)	66.40 (543)
	Glucomed 80mg	72.05 ± 35.63 (3817)	63.99 ± 33.16 (1617)	77.97 (2200)
	Glycron 80mg	69.06 ± 29.14 (424)	61.58 ± 29.43 (147)	73.03 (277)
	Glygard	58.61 ± 26.30 (229)	51.24 ± 22.96 (95)	63.83 (134)
	Merck-Gliclazide 80mg	53.66 ± 23.83 (318)	44.36 ± 21.43 (132)	60.25 (186)
	Rolab-Gliclazide	56.48 ± 28.18 (496)	50.44 ± 27.73 (204)	60.69 (202)
	Sandoz-Gliclazide	55.72 ± 28.37 (1660)	49.47 ± 27.66 (633)	59.58 (1027)
Glimeparide	Amaryl 1mg	78.14 ± 43.46 (1081)	73.22 ± 28.73 (717)	87.82 (364)
	Amaryl 2mg	148.78 ± 56.10 (1680)	146.62 ± 52.57 (878)	151.13 (802)
	Amaryl 4mg	275.48 ± 115.78 (1454)	273.06 ± 115.67 (591)	277.14 (863)
Glipizide	Minidiab 5mg	152.91 ± 118.96 (157)	133.52 ± 113.66 (68)	167.73 (89)
Metformin	Glucophage 500mg	30.83 ± 20.36 (7135)	27.97 ± 18.36 (3601)	33.75 (3534)
	Glucophage Forte 850mg	30.83 ± 18.75 (7214)	55.57 ± 16.25 (2659)	58.48 (4555)
	Glucophage	56.02 ± 0.00 (6)	56.02 ± 0.00 (2)	56.02 (4)
	Rolab-Metformin HCL 500mg	33.72 ± 16.62 (639)	30.82 ± 14.26 (331)	36.84 (308)
	Rolab-Metformin FC 500mg	36.48 ± 16.58 (715)	33.15 ± 15.15 (362)	39.89 (353)
	Rolab-Metformin FC 850mg	57.22 ± 18.93 (434)	56.29 ± 20.79 (183)	57.91 (251)
	Rolab-Metformin HCl 850mg	54.26 ± 20.06 (376)	52.08 ± 19.52 (148)	55.67 (228)
	Merck-Metformin 500mg	45.31 ± 23.83 (164)	41.28 ± 27.58 (65)	47.95 (99)
	Merck-Metformin 850mg	65.58 ± 24.63 (116)	46.20 ± 21.83 (190	69.38 (97)

Table 5.15: (Continue) **Summary of total, single and combination oral antidiabetic agents for the time September to December**

January-April Active ingredient	Agent (Trade name)	Average cost (Total prevalence) (R)	Average cost (One alone) (R)	Average cost (Combination) (R)
	Metforal 500mg	35.32 ± 18.24 (42)	33.05 ± 17.13 (260	39.01 (16)
	Metforal 850mg	54.83 ± 19.22 (128)	52.69 ± 17.94 (60)	56.71 (68)
	Sandoz-Metformin HCl 500mg	33.45 ± 15.48 (1751)	30.81 ± 14.37 (854)	35.96 (897)
	Sandoz-Metformin FC500mg	35.64 ± 16.54 (2251)	32.16 ± 14.73 (1158)	39.33 (1093)
	Sandoz-Metformin FC850mg	54.96 ± 15.54 (1445)	53.47 ± 14.02 (551)	55.88 (894)
	Sandoz-Metformin HCl 850mg	53.46 ± 17.22 (1040)	52.79 ± 17.54 (398)	53.88 (642)
Metformin/ Glibenclamide	Glucovance 250/1.25mg	49.13 ± 18.17 (138)	48.95 ± 17.61 (126)	50.97 (12)
	Glucovance 500/2.5mg	110.14 ± 42.53 (434)	110.68 ± 41.58 (388)	105.58 (46)
	Glucovance 500/5mg	150.96 ± 59.34 (339)	145.75 ± 52.51 (268)	170.64 (71)
Nateglinide	Starlix FCT 120mg	390.10 ± 77.19 (20)	378.61 ± 60.01 (10)	401.60 (10)
	Starlix FCT 60mg	337.43 ± 0.00 (1)	0	0
Pioglitazone	Actos 15mg	314.36 ± 57.60 (366)	317.68 ± 50.87 (176)	311.30 (190)
	Actos 30mg	467.58 ± 91.25 (380)	468.08 ± 46.08 (160)	467.21 (220)
Repaglinide	Novonorm 0.5mg	87.41 ± 33.23 (117)	83.53 ± 35.63 (68)	92.79 (49)
	Novonorm 1.0mg	185.01 ± 180.47 (156)	201.34 ± 297.03 (52)	176.85 (104)
	Novonorm 2.0mg	303.94 ± 117.53 (81)	277.45 ± 111.86 (17)	310.98 (64)
Rosiglitazone	Avandia 2mg	149.23 ± 48.06 (136)	154.99 ± 51.71 (80)	140.99 (56)
	Avandia 4mg	287.77 ± 124.52 (614)	274.45 ± 93.31 (230)	295.75 (384)

Table 5.16: Summary of the total, single and combination of insulins (January-April)

Active ingredient	Agent	Average cost (Total prevalence)	Average cost (One alone)	Average cost (Combination)
January-April				
Insulin Lispro	Humalog Mix 25 Penset	767.81 ± 561.73 (791)	775.31 ± 569.77 (584)	746.66 (207)
	Humalog Mix 25 Cartridges	866.32 ± 313.37 (79)	862.12 ± 344.21 (43)	871.34 (36)
	Humalog Mix 25 Injection	861.31 ± 637.34 (16)	933.79 ± 684.28 (13)	547.21 (3)
	Humalog 10ml Ampoules	581.57 ± 282.38 (38)	575.18 ± 251.40 (16)	586.23 (22)
	Humalog 3ml Penset/Prefill	917.43 ± 459.34 (640)	825.08 ± 325.73 (239)	972.47 (401)
	Humalog 3ml Cartridge injection	860.54 ± 331.76 (92)	728.14 ± 139.74 (37)	949.60 (55)
Insulin aspartame	Novorapid 3ml FlexPen	754.65 ± 271.44 (289)	767.03 ± 297.79 (150)	741.29 (139)
	Novorapid 3ml Penfill	825.50 ± 312.80 (57)	786.29 ± 324.70 (24)	854.02 (33)
Biosynthetic human insulin	Humulin R 10ml vial	414.29 ± 285.17 (25)	377.98 ± 114.47 (5)	423.36 (20)
	Humulin R 3ml cartridges	794.53 ± 515.92 (20)	647.16 ± 0.01 (6)	857.70 (14)
	Humulin R Humaject Pen 5ml	415.33 ± 340.86 (5)	3.43 ± 0.00 (1)	518.30 (4)
Biosynthetic human soluble insulin	Actrapid HM Pensets 1,5ml	786.16 ± 0.00 (1)	786.00 ± 0.00 (1)	0
	Actrapid HM Pensets 3ml	827.56 ± 359.45 (333)	806.96 ± 331.79 (165)	847.80 (168)
	Actrapid HM Penfill 3ml	839.05 ± 385.17 (44)	776.89 ± 319.63 (17)	878.18 (27)
	Actrapid HM 10ml Ampoules	456.02 ± 268.32 (115)	371.89 ± 109.61 (33)	489.88 (82)
Soluble insulin and isophane	Actraphane HM Penset 1,5ml	285.83 ± 0.00 (1)	0	285.83 (1)
	Actraphane HM Penset 3ml	845.14 ± 355.05 (1594)	829.32 ± 329.72 (1310)	918.11 (284)
	Actraphane HM Penfill 3ml	809.07 ± 434.68 (143)	823.09 ± 454.73 (123)	722.90 (20)
	Actraphane HM 10ml Ampoules	526.19 ± 278.62 (287)	534.24 ± 283.97 (260)	448.70 (27)
Biosynthetic human isophane	Humulin 30/70 3ml Cartridges	741.33 ± 280.38 (64)	744.52 ± 285.25 (49)	730.89 (15)
	Humulin 30/70 10ml vial	657.11 ± 243.92 (21)	657.11 ± 243.92 (21)	0
	Humulin 30/70 Humaject Inj	837.67 ± 580.05 (42)	725.15 ± 386.22 (38)	1906.57 (4)
	Humulin N 3ml Penset	645.09 ± 205.18 (269)	606.15 ± 197.99 (64)	657.25 (205)
	Humulin N 3ml Cartridges	765.11 ± 408.21 (41)	617.82 ± 503.09 (16)	859.37 (25)
	Humulin N Humaject 3ml Inj	459.06 ± 0.00 (1)	459.06 ± 0.00 (1)	0
	Humulin N 10ml vial	378.70 ± 122.58 (62)	330.87 ± 57.04 (17)	396.77 (45)
Biphasic biosynthetic human insulin 20/80	Mixtard 20/80 Penfill	836.32 ± 310.56 (11)	820.02 ± 333.25 (4)	845.63 (7)

Table 5.16: (Continue) Summary of the total, single and combination of insulins (January-April)

Active ingredient	Agent	Average cost (Total prevalence)	Average cost (One alone)	Average cost (Combination)
January-April				
Soluble insulin aspartame, protamine	Novomix 30 Flexpen 3ml Inj.	771.28 ± 287.47 (451)	765.78 ± 278.33 (315)	784.03 (136)
	Novomix 30 Penfill 3ml Inj.	996.23 ± 358.93 (37)	840.02 ± 322.58 (20)	1180.00 (17)
Zinc biosynthetic human insulin	Humulin L 10ml vial	395.18 ± 131.90 (173)	399.02 ± 139.59 (61)	393.08 (112)
Biosynthetic human insulin zinc susp	Monotard HM 10ml Ampoules	445.90 ± 200.34 (104)	449.00 ± 163.22 (51)	442.92 (53)
Biosynthetic monocomponent isophane	Protaphane HM Penset 1,5ml	393.08 ± 0.00 (1)	393.08 ± 0.00 (1)	0
	Protaphane HM Penset 3ml	664.28 ± 195.84 (605)	641.69 ± 186.04 (213)	676.55 (392)
	Protaphane HM Penfill 3ml	694.09 ± 268.25 (79)	663.08 ± 347.04 (19)	703.92 (60)
	Protaphane HM 10ml Ampoules	417.15 ± 158.78 (95)	385.13 ± 147.67 (39)	439.46 (56)
Biosynthetic human insulin zinc suspension monocomponent crystals	Ultratard HM 10ml Ampoules	360.14 ± 107.50 (25)	330.22 ± 36.32 (16)	413.33 (9)
Insulin Glargine	Lantus 300IU/3ml	907.18 ± 287.65 (308)	819.50 ± 223.20 (119)	962.38 (189)
	Lantus 300IU/3ml O/T	830.68 ± 256.13 (139)	792.25 ± 198.27 (56)	856.50 (83)
	Lantus 1000IU/10ml	757.14 ± 334.43 (60)	722.17 ± 274.88 (32)	797.10 (28)

Table 5.17: Summary of the total, single and combinations of insulins (May-August)

Active ingredient	Agent	Average cost (Total prevalence)	Average cost (One alone)	Average cost (Combination)
May-August				
Insulin Lispro	Humalog Mix 25 Penset	872.45 ± 438.40 (1086)	847.51 ± 431.83 (752)	928.60 (334)
	Humalog Mix 25 Cartridges	853.49 ± 341.65 (136)	855.48 ± 361.96 (97)	848.54 (39)
	Humalog Mix 25 Injection	901.80 ± 587.04 (25)	901.80 ± 587.04 (25)	0
	Humalog 10ml Ampoules	445.65 ± 227.69 (40)	385.07 ± 176.84 (24)	536.52 (16)
	Humalog 3ml Penset/Prefill	828.68 ± 424.02 (762)	796.91 ± 390.56 (325)	852.32 (437)
	Humalog 3ml Cartridge injection	753.8 ± 279.24 (110)	624.47 ± 65.04 (43)	838.21 (67)
	Humaject/Humalog 3ml	1004.52 ± 0.00 (1)	0	1004.52 (1)
Insulin aspartame	Novorapid 3ml FlexPen	680.39 ± 277.00 (346)	680.92 ± 271.38 (210)	679.58 (136)
	Novorapid 3ml Penfill	719.02 ± 295.04 (57)	668.26 ± 285.80 (32)	783.99 (25)
Biosynthetic human insulin	Humulin R 10ml vial	300.24 ± 31.83 (24)	308.10 ± 65.22 (2)	299.52 (22)
	Humulin R 3ml cartridges	479.78 ± 168.18 (19)	526.30 ± 106.46 (3)	471.06 (16)
	Humulin R Humaject Pen 5ml	663.01 ± 222.00 (11)	532.52 ± 55.64 (2)	692.01 (9)
Biosynthetic human soluble insulin	Actrapid HM Pensets 1,5ml	54.21 ± 0.00 (1)	54.21 ± 0.00 (1)	0
	Actrapid HM Pensets 3ml	734.61 ± 375.28 (430)	720.52 ± 388.98 (293)	764.75 (137)
	Actrapid HM Penfill 3ml	722.45 ± 329.88 (63)	638.39 ± 292.70 (27)	785.50 (36)
	Actrapid HM 10ml Ampoules	386.66 ± 162.18 (113)	370.61 ± 132.71 (33)	393.29 (80)
Soluble insulin and isophane	Actraphane HM Penset 1,5ml	334.64 ± 0.00 (2)	0	334.64 (2)
	Actraphane HM Penset 3ml	762.82 ± 349.85 (2025)	744.43 ± 346.37 (1600)	832.05 (425)
	Actraphane HM Penfill 3ml	711.37 ± 292.97 (244)	727.24 ± 319.68 (189)	656.83 (55)
	Actraphane HM 10ml Ampoules	472.17 ± 211.69 (447)	478.59 ± 213.74 (363)	444.44 (84)
Biosynthetic human isophane	Humulin 30/70 3ml Cartridges	732.23 ± 279.13 (104)	713.86 ± 276.28 (65)	762.85 (39)
	Humulin 30/70 10ml vial	762.05 ± 607.05 (16)	773.76 ± 626.49 (15)	586.47 (1)
	Humulin 30/70 Humaject Inj	790.74 ± 479.81 (55)	753.76 ± 477.75 (36)	860.80 (19)
	Humulin N 3ml Penset	609.72 ± 158.89 (329)	636.96 ± 191.10 (100)	597.87 (229)
	Humulin N 3ml Cartridges	655.21 ± 409.74 (43)	427.94 ± 206.32 (12)	743.18 (31)
	Humulin N Humaject 3ml Inj	524.02 ± 0.00 (1)	0	524.02 (1)
	Humulin N 10ml vial	334.76 ± 103.57 (61)	321.09 ± 69.56 (19)	340.94 (42)
Biphasic biosynthetic human insulin 20/80	Mixtard 20/80 Penfill	757.19 ± 260.20 (9)	865.00 ± 249.58 (6)	541.57 (3)
Soluble insulin aspartame, protamine	Novomix 30 Flexpen 3ml Inj.	693.89 ± 305.50 (715)	667.91 ± 288.01 (464)	741.91 (251)
	Novomix 30 Penfill 3ml Inj.	862.15 ± 374.15 (30)	763.44 ± 269.96 (12)	927.95 (18)

Table 5.17: (Continue) Summary of the total, single and combinations of insulins (May-August)

Active ingredient	Agent	Average cost (Total prevalence)	Average cost (One alone)	Average cost (Combination)
May-August				
Zinc biosynthetic human insulin	Humulin L 10ml vial	353.28 ± 143.21 (198)	378.11 ± 168.73 (77)	337.48 (121)
Biosynthetic human insulin zinc susp	Monotard HM 10ml Ampoules	426.00 ± 219.68 (106)	411.06 ± 164.22 (45)	437.02 (61)
Biosynthetic monocomponent isophane	Protaphane HM Penset 1,5ml	0	0	0
	Protaphane HM Penset 3ml	672.11 ± 218.48 (257)	681.29 ± 248.37 (81)	667.88 (176)
	Protaphane HM Penfill 3ml	622.35 ± 228.01 (112)	563.31 ± 166.60 (45)	662.00 (67)
	Protaphane HM 10ml Ampoules	372.83 ± 137.44 (126)	377.91 ± 155.43 (70)	366.49 (56)
Biosynthetic human insulin zinc suspension monocomponent crystals	Ultratard HM 10ml Ampoules	339.50 ± 119.72 (19)	282.50 ± 9.95 (3)	350.19 (16)
Insulin Glargine	Lantus 300IU/3ml	816.16 ± 222.08 (432)	771.82 ± 178.08 (179)	847.53 (253)
	Lantus 300IU/3ml O/T	761.87 ± 257.55 (266)	747.23 ± 203.12 (101)	770.82 (165)
	Lantus 1000IU/10ml	636.75 ± 265.69 (88)	562.79 ± 225.44 (38)	692.96 (50)

Table 5.18: Summary of the total, single and combination of insulins (September-December)

Active ingredient	Agent	Average cost (Total prevalence)	Average cost (One alone)	Average cost (Combination)
September-December				
Insulin Lispro	Humalog Mix 25 Penset	698.32 ± 265.81 (1325)	684.49 ± 247.54 (901)	727.71 (424)
	Humalog Mix 25 Cartridges	666.80 ± 261.66 (161)	650.31 ± 251.07 (106)	698.58 (55)
	Humalog Mix 25 Injection	696.75 ± 406.89 (22)	696.75 ± 406.89 (22)	0
	Humalog 10ml Ampoules	393.99 ± 202.33 (53)	341.04 ± 93.95 (21)	428.74 (32)
	Humalog 3ml Penset/Prefill	642.59 ± 338.54 (916)	594.67 ± 260.99 (372)	675.35 (544)
	Humalog 3ml Cartridge injection	561.61 ± 162.77 (116)	534.95 ± 138.02 (53)	584.03 (63)
	Humaject/Humalog 3ml	823.35 ± 0.00 (1)	0	823.35 (1)
Insulin aspartame	Novorapid 3ml FlexPen	559.16 ± 236.32 (431)	539.60 ± 222.18 (242)	584.20 (189)
	Novorapid 3ml Penfill	561.94 ± 182.90 (71)	581.52 ± 184.96 (38)	539.38 (33)
Biosynthetic human insulin	Humulin R 10ml vial	272.21 ± 79.73 (18)	237.56 ± 0.00 (8)	299.93 (10)
	Humulin R 3ml cartridges	448.89 ± 102.94 (16)	401.62 ± 0.00 (3)	459.80 (13)
	Humulin R Humaject Pen 5ml	508.41 ± 133.81 (11)	438.11 ± 0.00 (2)	524.04 (9)
Biosynthetic human soluble insulin	Actrapid HM Pensets 1,5ml	44.86 ± 0.00 (1)	44.86 ± 0.00 (1)	0
	Actrapid HM Pensets 3ml	555.03 ± 260.83 (503)	560.69 ± 289.58 (333)	543.94 (170)
	Actrapid HM Penfill 3ml	533.20 ± 186.83 (68)	492.29 ± 194.54 (27)	560.14 (41)
	Actrapid HM 10ml Ampoules	299.01 ± 110.42 (124)	299.74 ± 110.74 (39)	298.68 (85)
Soluble insulin and isophane	Actraphane HM Penset 1,5ml	0	0	0
	Actraphane HM Penset 3ml	585.56 ± 233.43 (2559)	562.50 ± 203.36 (2005)	669.02 (554)
	Actraphane HM Penfill 3ml	595.62 ± 252.71 (262)	594.85 ± 257.36 (196)	597.93 (66)
	Actraphane HM 10ml Ampoules	422.92 ± 194.61 (530)	408.47 ± 173.74 (425)	481.41 (105)
Biosynthetic human isophane	Humulin 30/70 3ml Cartridges	567.18 ± 211.56 (121)	584.95 ± 222.31 (69)	543.60 (52)
	Humulin 30/70 10ml vial	357.74 ± 147.71 (23)	363.21 ± 148.79 (22)	237.45 (1)
	Humulin 30/70 Humaject Inj	553.65 ± 211.35 (56)	519.61 ± 193.52 (41)	692.91 (14)
	Humulin N 3ml Penset	482.01 ± 139.72 (409)	521.68 ± 184.00 (110)	467.42 (299)
	Humulin N 3ml Cartridges	544.43 ± 631.25 (45)	378.40 ± 104.92 (16)	636.04 (29)
	Humulin N Humaject 3ml Inj	485.42 ± 0.00 (2)	485.42 ± 0.00 (2)	0
	Humulin N 10ml vial	339.82 ± 145.99 (50)	285.37 ± 73.66 (14)	360.99 (36)
Biphasic biosynthetic human insulin 20/80	Mixtard 20/80 Penfill	564.03 ± 209.07 (5)	793.06 ± 0.00 (2)	411.35 (3)
Soluble insulin aspartame, protamine	Novomix 30 Flexpen 3ml Inj.	558.49 ± 207.86 (1307)	537.58 ± 182.96 (823)	594.06 (484)
	Novomix 30 Penfill 3ml Inj.	564.91 ± 178.53 (43)	509.25 ± 142.61 (30)	693.35 (13)

Table 5.18: (Continue) **Summary of the total, single and combination of insulins (September-December)**

Active ingredient	Agent	Average cost (Total prevalence)	Average cost (One alone)	Average cost (Combination)
September-December				
Zinc biosynthetic human insulin	Humulin L 10ml vial	285.95 ± 109.51 (203)	296.13 ± 141.38 (71)	280.48 (132)
Biosynthetic human insulin zinc susp	Monotard HM 10ml Ampoules	363.54 ± 189.33 (113)	364.84 ± 153.20 (45)	362.68 (68)
Biosynthetic monocomponent isophane	Protaphane HM Penset 1,5ml	0	0	0
	Protaphane HM Penset 3ml	513.53 ± 163.50 (269)	526.75 ± 160.38 (56)	510.05 (213)
	Protaphane HM Penfill 3ml	482.12 ± 134.06 (125)	463.49 ± 120.47 (34)	489.09 (91)
	Protaphane HM 10ml Ampoules	334.58 ± 120.02 (112)	348.74 ± 135.87 (69)	311.86 (43)
Biosynthetic human insulin zinc suspension monocomponent crystals	Ultratard HM 10ml Ampoules	294.09 ± 95.48 (22)	352.85 ± 111.96 (3)	284.81 (19)
Insulin Glargine	Lantus 300IU/3ml	686.62 ± 283.62 (438)	631.22 ± 178.80 (175)	723.48 (263)
	Lantus 300IU/3ml O/T	596.36 ± 160.40 (435)	601.95 ± 159.75 (163)	341.74 (272)
	Lantus 1000IU/10ml	537.44 ± 186.88 (96)	501.33 ± 155.02 (37)	560.09 (59)

From table 5.13 to table 5.15, table 5.15.1 can be compiled. It illustrates the percentage prevalence of oral antidiabetic agents in combination, in comparison to the total prevalence of the oral antidiabetic agents on the database for the different time periods. The n-values were calculated by adding-up the total prevalence of the oral agents with the same active ingredient. The number in brackets is the n-value or prevalence.

Table 5.15.1: Percentage prevalence of the combination of oral antidiabetic agents

Active ingredient	January-April	May-August	September-December
	% prevalence (n-value)	%prevalence (n-value)	% prevalence (n-value)
Acarbose	50.8 (240)	63.2 (266)	58.7 (271)
Chlorpropamide	47.6 (21)	53.3 (15)	35.0 (20)
Glibenclamide	58.7 (3745)	61.9 (4663)	62.6 (5657)
Gliclazide	53.3 (6445)	57.9 (7966)	58.3 (10 155)
Glimeparide	44.7 (3599)	47.3 (4307)	48.1 (4215)
Glipizide	48.7 (193)	52.8 (161)	56.7 (157)
Metformin	52.4 (14 981)	54.2 (19 135)	55.6 (23 456)
Metformin/Glibenclamide	9.3 (389)	16.6 (609)	14.2 (911)
Nateglinide	38.5 (26)	45.2 (31)	47.6 (21)
Pioglitazone	53.4 (335)	51.1 (734)	55.0 (746)
Repaglinide	47.0 (268)	61.9 (396)	61.3 (354)
Rosiglitazone	45.6 (406)	56.4 (674)	58.7 (750)

From tables 5.13 and 5.14 it can be calculated that a total of 14 795 (48.3%, n = 30 648) prescriptions for oral antidiabetic agents alone was issued during the period January to April 2004. For the period May to August 2004, 17 775 (45.6%, n = 38 957) antidiabetic prescriptions were issued with only one oral antidiabetic agent, and during the period September to December 2004, 21 031 (45.0%, n = 46 713) antidiabetic prescriptions were issued containing only one oral agent. It can therefore be concluded that 53 601 (46.1%, n = 116 318) prescriptions were issued during 2004 that contain only one oral antidiabetic agent, meaning that only 37.4% (n = 143 447) of all the antidiabetic prescriptions were for one oral antidiabetic agent. According to the Truter study (1999:120), 64.4% prescriptions were issued containing only one oral antidiabetic agent. This indicates that more diabetic patients are using more than one antidiabetic drug in 2004 than in 1996.

From table 5.16 to table 5.18, table 5.18.1 can be compiled, which gives an indication of the percentage prevalence of insulin agents in combination, in comparison to the total prevalence of the insulin agents on the database for the different time periods.

Table 5.18.1: Percentage prevalence of the combination of insulins

Active ingredient	January-April	May-August	September-December
	% prevalence (n-value)	%prevalence (n-value)	% prevalence (n-value)
Insulin lispro	43.7 (1656)	41.4 (2160)	43.1 (2594)
Insulin aspartame	49.7 (346)	40.0 (403)	44.2 (502)
Biosynthetic human insulin	76.0 (50)	87.0 (54)	71.1 (45)
Biosynthetic human soluble insulin	56.2 (493)	41.7 (607)	42.5 (696)
Soluble insulin and isophane	16.4 (2025)	20.8 (2718)	21.6 (3351)
Biosynthetic human isophane	58.8 (500)	59.4 (609)	61.0 (706)
Biphasic biosynthetic human insulin 20/80	63.6 (11)	33.3 (9)	60.0 (5)
Soluble insulin aspartame and protamine	31.4 (488)	36.1 (745)	36.8 (1350)
Zinc biosynthetic human insulin	64.7 (173)	61.1 (198)	65.0 (203)
Biosynthetic human insulin zinc suspension	51.0 (104)	57.5 (106)	60.2 (113)
Biosynthetic monocomponent isophane	65.1 (780)	60.4 (495)	68.6 (506)
Biosynthetic human insulin zinc suspension monocomponent crystals	36.0 (25)	84.2 (19)	86.4 (22)
Insulin glargine	59.2 (507)	59.5 (786)	61.3 (969)

From tables 5.16 to 5.18 it can be calculated that a total of 6576 (91.9% n = 7158) prescriptions for insulin alone was issued during the period January to April 2004. For the period May to August 2004, 5389 (60.5%, n = 8909) antidiabetic prescriptions were issued with only one insulin product, and during the period September to December 2004, 4179 (37.8%, n = 11 062) antidiabetic prescriptions were issued containing only one insulin product. It can therefore be concluded that 59.5% (16 144, n = 27 129) prescriptions were issued during 2004 that contain only one insulin product, meaning that only 11.3% (n = 143 447) of all the antidiabetic prescriptions were for one insulin product. According to the study done by Truter (1999:121) on data of 1996, 30.5% prescriptions were issued containing only one insulin product. This indicates that more diabetic patients are using more than one insulin product in 2004 than in 1996.

From table 5.13 to 5.18, tables 5.19 and 5.20 can be derived which summarise the average cost, standard deviation and prevalence of all the oral agents and insulins that were prescribed as single agent for the three periods January to April, May to August and September to December.

Table 5.19: Summary of average cost, standard deviation and prevalence of oral antidiabetic agents prescribed as single agents (2004)

January-April	Agent (Trade name)	January-April	May-August	September-December
Active ingredient		Average cost (One alone)	Average cost (One alone)	Average cost (One alone)
Acarbose	Glucobay 100mg	347.63 ± 38.98 (36)	299.59 ± 77.08 (35)	256.48 ± 61.66 (37)
	Glucobay 50mg	231.62 ± 83.74 (82)	203.62 ± 57.38 (63)	170.60 ± 39.95 (75)
Chlorpropamide	Hypomide 250mg	108.46 ± 65.29 (10)	108.12 ± 47.79 (6)	46.48 ± 38.89 (13)
	Diabinese 250mg	46.51 ± 0.00 (1)		
Glibenclamide	Daonil 5mg	356.68 ± 167.46 (170)	291.16 ± 136.34 (189)	218.77 ± 99.37 (218)
	Diacare 5mg	0	75.17 ± 60.05 (2)	9.94 ± 4.63 (5)
	Euglucon 5mg	358.23 ± 421.00 (3)	216.34 ± 167.91 (4)	114.26 ± 10.64 (5)
	Glyben 5mg	108.87 ± 64.18 (167)	43.09 ± 49.74 (193)	13.79 ± 12.98 (240)
	Glycomin 5mg	123.78 ± 67.77 (1200)	64.95 ± 51.03 (1377)	49.47 ± 27.10 (1638)
	Norton-Glibenclamide	22.91 ± 4.20 (8)	12.86 ± 6.23 (13)	13.58 ± 6.75 (7)
Gliclazide	Diamicron 80mg	98.11 ± 52.85 (631)	99.66 ± 59.65 (542)	66.72 ± 38.23 (401)
	Diamicron MR 30mg	131.92 ± 57.46 (243)	131.20 ± 56.36 (478)	123.75 ± 59.55 (618)
	Diaglucide 80mg	88.69 ± 38.80 (61)	62.59 ± 32.71 (154)	56.30 ± 26.58 (295)
	Glucomed 80mg	84.79 ± 40.80 (1642)	79.32 ± 39.90 (1698)	63.99 ± 33.16 (1617)
	Glycron 80mg	90.67 ± 43.09 (54)	78.29 ± 48.21 (70)	61.58 ± 29.43 (147)
	Glygard	94.28 ± 36.84 (30)	71.62 ± 32.31 (45)	51.24 ± 22.96 (95)
	Merck-Gliclazide 80mg	40.08 ± 43.54 (11)	54.19 ± 22.22 (31)	44.36 ± 21.43 (132)
	Rolab-Gliclazide	81.10 ± 37.77 (332)	56.67 ± 28.66 (436)	50.44 ± 27.73 (204)
	Sandoz-Gliclazide	-	-	49.47 ± 27.66 (633)
	Zicilin 80mg	136.79 ± 0.00 (4)		
Glimeparide	Amaryl 1mg	102.05 ± 29.40 (678)	85.36 ± 28.15 (743)	73.22 ± 28.73 (717)
	Amaryl 2mg	194.79 ± 61.37 (817)	169.95 ± 56.88 (929)	146.62 ± 52.57 (878)
	Amaryl 4mg	365.96 ± 113.69 (495)	341.40 ± 120.93 (596)	273.06 ± 115.67 (591)
Glipizide	Minidiab 5mg	214.08 ± 139.63 (99)	171.31 ± 122.77 (76)	133.52 ± 113.66 (68)
Metformin	Glucophage 500mg	60.64 ± 27.94 (2319)	49.20 ± 22.87 (2838)	27.97 ± 18.36 (3601)
	Glucophage Forte 850mg	100.92 ± 31.98 (1681)	72.93 ± 29.94 (2139)	55.57 ± 16.25 (2659)
	Glucophage	-		56.02 ± 0.00 (2)
	Rolab-Metformin HCL 500mg	57.49 ± 26.47 (1034)	39.99 ± 19.09 (1139)	30.82 ± 14.26 (331)
	Rolab-Metformin FC 500mg	57.46 ± 26.80 (889)	43.75 ± 22.32 (1151)	33.15 ± 15.15 (362)
	Rolab-Metformin FC 850mg	90.38 ± 29.09 (566)	63.84 ± 25.03 (672)	56.29 ± 20.79 (183)

Table 5.19: (Continue) Summary of average cost, standard deviation and prevalence of oral antidiabetic agents prescribed as single agents (2004)

January-April	Agent (Trade name)	January-April	May-August	September-December
Active ingredient		Average cost (One alone)	Average cost (One alone)	Average cost (One alone)
	Rolab-Metformin HCl 850mg	92.60 ± 27.32 (427)	61.50 ± 22.61 (519)	52.08 ± 19.52 (148)
	Merck-Metformin 500mg	54.66 ± 26.53 (128)	54.17 ± 25.04 (202)	41.28 ± 27.58 (65)
	Merck-Metformin 850mg	82.67 ± 23.47 (89)	80.23 ± 18.80 (86)	46.20 ± 21.83 (190
	Metforal 500mg	-	37.02 ± 24.27 (6)	33.05 ± 17.13 (260
	Metforal 850mg	-	51.26 ± 26.59 (13)	52.69 ± 17.94 (60)
	Sandoz-Metformin HCl 500mg	-	-	30.81 ± 14.37 (854)
	Sandoz-Metformin FC500mg	-	-	32.16 ± 14.73 (1158)
	Sandoz-Metformin FC850mg	-	-	53.47 ± 14.02 (551)
	Sandoz-Metformin HCl 850mg	-	-	52.79 ± 17.54 (398)
Metformin/ Glibenclamide	Glucovance 250/1.25mg	74.91 ± 27.99 (68)	57.64 ± 23.35 (95)	48.95 ± 17.61 (126)
	Glucovance 500/2.5mg	189.08 ± 72.70 (170)	133.30 ± 63.99 (224)	110.68 ± 41.58 (388)
	Glucovance 500/5mg	234.12 ± 111.04 (115)	193.17 ± 89.15 (189)	145.75 ± 52.51 (268)
Nateglinide	Starlix FCT 120mg	418.81 ± 71.59 (15)	403.82 ± 78.91 (17)	378.61 ± 60.01 (10)
	Starlix FCT 60mg	208.23 ± 0.00 (1)	-	0
Pioglitazone	Actos 15mg	403.63 ± 80.94 (101)	387.02 ± 78.21 (204)	317.68 ± 50.87 (176)
	Actos 30mg	592.91 ± 16.33 (55)	574.67 ± 62.11 (155)	468.08 ± 46.08 (160)
Repaglinide	Novonorm 0.5mg	98.76 ± 21.14 (72)	86.71 ± 38.17 (69)	83.53 ± 35.63 (68)
	Novonorm 1.0mg	199.84 ± 42.45 (49)	202.51 ± 149.56 (55)	201.34 ± 297.03 (52)
	Novonorm 2.0mg	356.22 ± 124.02 (21)	312.03 ± 130.94 (27)	277.45 ± 111.86 (17)
Rosiglitazone	Avandia 2mg	200.07 ± 65.02 (77)	168.33 ± 52.45 (79)	154.99 ± 51.71 (80)
	Avandia 4mg	376.44 ± 123.95 (144)	346.95 ± 132.56 (215)	274.45 ± 93.31 (230)

Table 5.20: Summary of average cost, standard deviation and prevalence of insulin products prescribed as single agents (2004)

Class	Agent	January-April	May-August	September-December
		Average cost (One alone)	Average cost (One alone)	Average cost (One alone)
Insulin lispro	Humalog Mix 25 Penset	775.31 ± 569.77 (584)	847.51 ± 431.83 (752)	684.49 ± 247.54 (901)
	Humalog Mix 25 Cartridges	862.12 ± 344.21 (43)	855.48 ± 361.96 (97)	650.31 ± 251.07 (106)
	Humalog Mix 25 Injection	933.79 ± 684.28 (13)	901.80 ± 587.04 (25)	696.75 ± 406.89 (22)
	Humalog 10ml Ampoules	575.18 ± 251.40 (16)	385.07 ± 176.84 (24)	341.04 ± 93.95 (21)
	Humalog 3ml Penset/Prefill	825.08 ± 325.73 (239)	796.91 ± 390.56 (325)	594.67 ± 260.99 (372)
	Humalog 3ml Cartridge injection	728.14 ± 139.74 (37)	624.47 ± 65.04 (43)	534.95 ± 138.02 (53)
	Humaject/Humalog 3ml	0	0	0
Insulin aspartame	Novorapid 3ml FlexPen	767.03 ± 297.79 (150)	680.92 ± 271.38 (210)	539.60 ± 222.18 (242)
	Novorapid 3ml Penfill	786.29 ± 324.70 (24)	668.26 ± 285.80 (32)	581.52 ± 184.96 (38)
Biosynthetic human insulin	Humulin R 10ml vial	377.98 ± 114.47 (5)	308.10 ± 65.22 (2)	237.56 ± 0.00 (8)
	Humulin R 3ml cartridges	647.16 ± 0.01 (6)	526.30 ± 106.46 (3)	401.62 ± 0.00 (3)
	Humulin R Humaject Pen 5ml	3.43 ± 0.00 (1)	532.52 ± 55.64 (2)	438.11 ± 0.00 (2)
Biosynthetic human soluble insulin	Actrapid HM Pensets 1,5ml	786.00 ± 0.00 (1)	54.21 ± 0.00 (1)	44.86 ± 0.00 (1)
	Actrapid HM Pensets 3ml	806.96 ± 331.79 (165)	720.52 ± 388.98 (293)	560.69 ± 289.58 (333)
	Actrapid HM Penfill 3ml	776.89 ± 319.63 (17)	638.39 ± 292.70 (27)	492.29 ± 194.54 (27)
	Actrapid HM 10ml Ampoules	371.89 ± 109.61 (33)	370.61 ± 132.71 (33)	299.74 ± 110.74 (39)
Soluble insulin and isophane	Actraphane HM Penset 1,5ml	0	0	0
	Actraphane HM Penset 3ml	829.32 ± 329.72 (1310)	744.43 ± 346.37 (1600)	562.50 ± 203.36 (2005)
	Actraphane HM Penfill 3ml	823.09 ± 454.73 (123)	727.24 ± 319.68 (189)	594.85 ± 257.36 (196)
	Actraphane HM 10ml Ampoules	534.24 ± 283.97 (260)	478.59 ± 213.74 (363)	408.47 ± 173.74 (425)
Biosynthetic human isophane	Humulin 30/70 3ml Cartridges	744.52 ± 285.25 (49)	713.86 ± 276.28 (65)	584.95 ± 222.31 (69)
	Humulin 30/70 10ml vial	657.11 ± 243.92 (21)	773.76 ± 626.49 (15)	363.21 ± 148.79 (22)
	Humulin 30/70 Humaject Inj	725.15 ± 386.22 (38)	753.76 ± 477.75 (36)	519.61 ± 193.52 (41)
	Humulin N 3ml Penset	606.15 ± 197.99 (64)	636.96 ± 191.10 (100)	521.68 ± 184.00 (110)
	Humulin N 3ml Cartridges	617.82 ± 503.09 (16)	427.94 ± 206.32 (12)	378.40 ± 104.92 (16)
	Humulin N Humaject 3ml Inj	459.06 ± 0.00 (1)	0	485.42 ± 0.00 (2)
	Humulin N 10ml vial	330.87 ± 57.04 (17)	321.09 ± 69.56 (19)	285.37 ± 73.66 (14)
Biphasic biosynthetic human insulin 20/80	Mixtard 20/80 Penfill	820.02 ± 333.25 (4)	865.00 ± 249.58 (6)	793.06 ± 0.00 (2)

Table 5.20: (Continue) Summary of average cost, standard deviation and prevalence of insulin products prescribed as single agents (2004)

Class	Agent	January-April	May-August	September-December
		Average cost (One alone)	Average cost (One alone)	Average cost (One alone)
Soluble insulin aspartame and protamine	Novomix 30 Flexpen 3ml Inj.	765.78 ± 278.33 (315)	667.91 ± 288.01 (464)	537.58 ± 182.96 (823)
	Novomix 30 Penfill 3ml Inj.	840.02 ± 322.58 (20)	763.44 ± 269.96 (12)	509.25 ± 142.61 (30)
Zinc biosynthetic human insulin	Humulin L 10ml vial	399.02 ± 139.59 (61)	378.11 ± 168.73 (77)	296.13 ± 141.38 (71)
Biosynthetic human insulin zinc suspension	Monotard HM 10ml Ampoules	449.00 ± 163.22 (51)	411.06 ± 164.22 (45)	364.84 ± 153.20 (45)
Biosynthetic monocomponent isophane	Protaphane HM Penset 1,5ml	393.08 ± 0.00 (1)	0	0
	Protaphane HM Penset 3ml	641.69 ± 186.04 (213)	681.29 ± 248.37 (81)	526.75 ± 160.38 (56)
	Protaphane HM Penfill 3ml	663.08 ± 347.04 (19)	563.31 ± 166.60 (45)	463.49 ± 120.47 (34)
	Protaphane HM 10ml Ampoules	385.13 ± 147.67 (39)	377.91 ± 155.43 (70)	348.74 ± 135.87 (69)
Biosynthetic human insulin zinc suspension monocomponent crystals	Ultratard HM 10ml Ampoules	330.22 ± 36.32 (16)	282.50 ± 9.95 (3)	352.85 ± 111.96 (3)
Insulin glargine	Lantus 300IU/3ml	819.50 ± 223.20 (119)	771.82 ± 178.08 (179)	631.22 ± 178.80 (175)
	Lantus 300IU/3ml O/T	792.25 ± 198.27 (56)	747.23 ± 203.12 (101)	601.95 ± 159.75 (163)
	Lantus 1000IU/10ml	722.17 ± 274.88 (32)	562.79 ± 225.44 (38)	501.33 ± 155.02 (37)

From tables 5.19 and 5.20 it can be seen that there was on average a decrease in the price of antidiabetic agents. It can be calculated by subtracting the average cost of the time period September to December from the average cost of the period January to April. From table 5.19 it can therefore be calculated that the only oral antidiabetic agents that did not have a lowering in price were Merck-Gliclazide® (R4.28) and Novonorm® 1.0mg (R1.50). The product that showed the biggest lowering in price was Euglucon® 5mg (R243.97). The class of oral antidiabetic agents that exercised the biggest influence on the cost savings was metformin (R242 738.90). Only thirteen oral antidiabetic agents had d-values of less than 0.8. These agents are Diamicron® 80mg (0.6), Diamicron® MR 30mg (0.1), Euglucon® 5mg (0.6), Glucobay® 50mg (0.7), Glucomed® 80mg (0.5), Glycron® 80mg (0.7), Merck-Gliclazide® 80mg (0.1), Merck-Metformin® 500mg (0.5), Minidiab® 5mg (0.6), Novonorm® 0.5mg (0.4), Novonorm® 1.0mg (0.01), Novonorm® 2.0mg (0.6) and Starlix® FCT 120mg (0.6). (Note: if the d-value is more than 0.8 it means that the difference in price is of statistical and practical significance).

From tables 5.19 and 5.20 the average cost saving per unit price in rand and as percentage, as well as the "cost savings" for the different time periods can be calculated. Table 5.21 summarises these "cost savings" for all the oral antidiabetic agents and table 5.22 summarises these "cost savings" for the insulins.

Table 5.21: Average cost saving per unit price and cost savings of the oral antidiabetic agents for the different time periods

Active ingredient	Trade name ®	Average cost saving per unit price* (R) (percentages) Jan-Apr vs. May-Aug	Cost savings (R) January-April vs. May-August	Average cost saving per unit price* (R) (percentages) Jan-Apr vs. Sept-Dec	Cost savings (R) January-April vs. September-December	Average cost saving per unit price* (R) (percentages) May-Aug vs. Sept-Dec	Cost savings (R) May-August vs. September-December
Acarbose	Glucobay 100mg	48.06 (13.8)	1 729.44	91.15 (26.2)	3 281.40	43.11 (14.4)	1 508.85
	Glucobay 50mg	28.00 (12.1)	18 585.60	61.02 (26.3)	5 003.64	33.02 (16.2)	2 080.26
Chlorpropamide	Hypomide 250mg	0.34 (0.3)	3.40	61.98 (57.1)	619.80	61.64 (57.0)	369.84
Glibenclamide	Daonil 5mg	65.52 (18.4)	11 138.40	137.91 (38.7)	23 444.70	72.39 (24.9)	13 681.71
	Diacare 5mg	-	-	-	-	65.23 (86.8)	130.46
	Euglucon 5mg	141.89 (36.9)	425.67	243.97 (68.1)	731.91	102.08 (47.2)	408.32
	Glyben 5mg	65.78 (60.4)	10 985.26	95.08 (87.3)	15 878.36	29.30 (68.0)	5 654.90
	Glycomin 5mg	58.83 (47.5)	70 596.00	74.31 (60.0)	89 172.00	15.48 (23.8)	21 315.96
	Norton-Glibenclamide	10.05 (43.9)	80.40	9.33 (40.7)	74.64	+0.72 (+5.6)	+9.36
Gliclazide	Diamicron 80mg	+1.55 (+1.6)	+978.05	31.39 (32.0)	19 807.09	32.94 (33.1)	17 853.48
	Diamicron MR 30mg	0.72 (0.5)	174.96	8.17 (6.2)	1 985.31	7.45 (5.7)	3 561.10
	Diaglucide 80mg	26.10 (29.4)	1 592.10	32.39 (36.5)	1 975.79	6.29 (10.0)	856.06
	Glucomed 80mg	5.47 (6.5)	8 981.74	20.80 (24.5)	34 153.60	15.33 (19.3)	26 030.34
	Glycron 80mg	12.38 (13.7)	668.52	29.09 (32.1)	1 570.86	16.71 (21.3)	1 169.70
	Glygard	22.66 (24.0)	679.80	43.04 (45.7)	1 291.20	20.38 (28.5)	917.10
	Merck-Gliclazide 80mg	+14.11 (+35.2)	+155.21	+4.28 (+10.7)	+47.08	9.83 (18.1)	304.73
	Rolab-Gliclazide	24.43 (30.1)	8 110.76	30.66 (37.8)	10 179.12	6.23 (11.0)	2 716.28
Glimeparide	Amaryl 1mg	16.69 (16.4)	11 315.82	28.83 (28.3)	19 546.74	12.14 (14.2)	9 020.02
	Amaryl 2mg	24.84 (12.8)	20 294.28	48.17 (24.7)	39 354.89	23.33 (13.7)	21 673.57
	Amaryl 4mg	24.56 (6.7)	12 157.20	92.90 (25.4)	45 985.50	68.34 (20.0)	40 730.64
Glipizide	Minidiab 5mg	42.77 (20.0)	4 234.23	80.56 (37.6)	7 975.44	37.79 (22.1)	2 872.04
Metformin	Glucophage 500mg	11.44 (18.9)	26 529.36	32.67 (53.9)	75 761.73	21.23 (43.2)	60 250.74
	Glucophage Forte 850mg	27.99 (27.7)	47 051.19	45.35 (44.9)	76 233.35	17.36 (23.8)	37 133.04
	Rolab-Metformin HCL 500mg	17.50 (30.4)	18 001.94	26.67 (46.4)	27 576.78	9.17 (22.9)	10 444.63
	Rolab-Metformin FC 500mg	13.71 (23.9)	12 188.19	24.31 (42.3)	21 611.59	10.60 (24.2)	12 200.60
	Rolab-Metformin FC 850mg	26.54 (29.4)	15 021.64	34.09 (37.7)	19 294.94	7.55 (11.8)	5 073.60
	Rolab-Metformin HCl 850mg	31.10 (33.6)	13 279.70	40.52 (43.8)	17 302.04	9.42 (15.3)	4 883.79

Table 5.21: (Continue) Average cost saving per unit price and cost savings of the oral antidiabetic agents for the different time periods

Active ingredient	Trade name ®	Average cost saving per unit price* (R) (percentages) Jan-Apr vs. May-Aug	Cost savings (R) January-April vs. May-August	Average cost saving per unit price* (R) (percentages) Jan-Apr vs. Sept-Dec	Cost savings (R) January-April vs. September-December	Average cost saving per unit price* (R) (percentages) May-Aug vs. Sept-Dec	Cost savings (R) May-August vs. September-December
	Merck-Metformin 500mg	0.49 (0.9)	62.72	13.38 (24.5)	1 712.64	12.89 (23.8)	2 603.78
	Merck-Metformin 850mg	2.44 (29.5)	217.16	36.47 (44.1)	3 245.83	34.03 (42.4)	2 926.58
	Metforal 500mg	-	-	-	-	3.97 (10.7)	23.82
	Metforal 850mg	-	-	-	-	+1.43 (+2.8)	+18.59
Metformin/ Glibenclamide	Glucovance 250/1.25mg	17.27 (36.0)	1 174.36	25.96 (34.7)	1 765.28	8.69 (17.8)	825.55
	Glucovance 500/2.5mg	55.78 (29.5)	9 482.60	78.40 (41.5)	13 328.00	22.62 (20.4)	5 066.88
	Glucovance 500/5mg	40.95 (17.5)	4 709.25	88.37 (37.7)	10 162.55	47.42 (32.5)	8 962.38
Nateglinide	Starlix FCT 120mg	14.99 (3.6)	224.85	40.20 (9.6)	603.00	25.21 (6.2)	428.57
Pioglitazone	Actos 15mg	16.61 (4.1)	1 677.61	85.95 (21.3)	8 680.95	69.34 (17.9)	14 145.36
	Actos 30mg	18.24 (3.1)	1 003.20	124.83 (21.1)	6 865.65	106.59 (18.5)	16 521.45
Repaglinide	Novonorm 0.5mg	12.05 (12.2)	867.60	15.23 (15.4)	1 069.56	3.18 (3.7)	219.42
	Novonorm 1.0mg	+2.67 (+1.3)	+130.83	+1.50 (+0.8)	+73.50	1.17 (0.6)	64.35
	Novonorm 2.0mg	44.19 (12.4)	927.99	78.77 (22.1)	1 654.17	34.58 (11.1)	933.66
Rosiglitazone	Avandia 2mg	31.74 (15.9)	2 443.98	45.08 (22.5)	3 471.16	13.34 (7.9)	1 053.86
	Avandia 4mg	29.49 (7.8)	4 246.56	101.99 (27.1)	14 686.56	72.50 (20.9)	15 587.50

* "Unit price" can be defined as the number of tablets or capsules or injection in milliliter prescribed per month

Table 5.21 reveals that the oral antidiabetic agent with the highest average cost saving per unit price for the time January to April *vs.* May to August was Euglucon® 5mg (R141.89), while the agent with the lowest average cost saving was Hypomide® 250mg (R0.34). Glyben® 5mg (60.4%) showed the biggest lowering in average cost if presented in percentage. According to table 5.21, Diamicron® 80mg (+R21.55), Merck-Gliclazide® (+R14.11) and Novonorm®1.0mg (+R2.67) showed an increase in the average total cost for the period January to April *vs.* May to August.

For the period January to April *vs.* September to December it can be seen from table 5.21 that Glyben® 5mg has the highest cost saving presented in percentage (87.3%), and Euglucon® 5mg has the highest average cost saving in rand (R243.97). Diamicron® MR 30mg shows the lowest average cost saving (R8.17 or 6.2%). The only two oral antidiabetic agents that showed an increase in price were Merck-Gliclazide® 80mg (+R4.28) and Novonorm® 1.0mg (+R1.50).

From table 5.21, table 5.21.1 can be compiled which summarises the ten oral antidiabetic agents with the highest cost saving and the ten oral antidiabetic agents with the lowest cost savings for the different periods.

Table 5.21.1: Summary of the oral agents with the ten highest and ten lowest cost savings (2004)

	Highest			Lowest		
No.	Jan-Apr *vs.* May-Aug	Jan-Apr *vs.* Sept-Dec.	May-Aug *vs.* Sept.-Dec.	Jan-Apr *vs.* May-Aug	Jan-Apr *vs.* Sept-Dec.	May-Aug *vs.* Sept.-Dec.
1	Euglucon® 5mg R141.89	Euglucon® 5mg R243.97	Actos® 30mg R106.59	Hypomide® 250mg R0.34	Diamicron® MR 30mg R8.17	Novonorm® 1.0mg R1.17
2	Glyben® 5mg R65.78	Daonil® 5mg R137.91	Euglucon® 5mg R102.08	Merck-Metformin® 500mg R0.49	Norton-Glibenclamide ® R9.33	Novonorm® 0.5mg R3.18
3	Daonil® 5mg R65.52	Actos® 30mg R124.83	Avandia® 4mg R72.50	Diamicron® MR 30mg R0.72	Merck-Metformin® 500mg R13.38	Metforal® 500mg R3.97
4	Glycomin® 5mg R58.83	Avandia® 4mg R101.99	Daonil® 5mg R72.39	Merck-Metformin® 850mg R2.44	Novonorm® 0.5mg R15.23	Rolab-Gliclazide® R6.23
5	Glucovance® 500/2.5mg R55.78	Glyben® 5mg R95.08	Actos® 15mg R69.34	Glucomed® 80mg R5.47	Glucomed® 80mg R20.80	Diaglucide® 80mg R6.29
6	Glucobay® 100mg R48.06	Amaryl® 4mg R92.90	Amaryl® 4mg R68.34	Norton-Glibenclamide ® R10.05	Rolab-Metformin® FC 500mg R24.31	Diamicron® MR 30mg R7.45
7	Minidiab® 5mg R42.77	Glucobay® 100mg R91.15	Diacare® 5mg R65.23	Glucophage® 500mg R11.44	Glucovance® 250/1.25mg R25.96	Rolab-Metformin® FC 850mg R7.55

Table 5.21.1: (Continue) Summary of the oral agents with the ten highest and ten lowest cost savings (2004)

	Highest			**Lowest**		
No.	**Jan-Apr *vs.* May-Aug**	**Jan-Apr *vs.* Sept-Dec.**	**May-Aug *vs.* Sept.-Dec.**	**Jan-Apr *vs.* May-Aug**	**Jan-Apr *vs.* Sept-Dec.**	**May-Aug *vs.* Sept.-Dec.**
8	Novonorm® 2.0mg R44.19	Glucovance® 500/5mg R88.37	Hypomide® 250mg R61.64	Novonorm® 0.5mg R12.05	Rolab-Metformin® HCl 500mg R26.67	Glucovance® 250/1.25mg R8.69
9	Glucovance® 500/5mg R40.95	Actos® 15mg R85.95	Glucovance® 500/5mg R47.42	Glycron® 80mg R12.38	Amaryl® 1mg R28.83	Rolab-Metformin® HCl 500mg R9.17
10	Avandia®2mg R31.74	Minidiab® 5mg R80.56	Glucobay® 100mg R43.11	Rolab-Metformin® FC 500mg R13.71	Glycron® 80mg R29.09	Rolab-Metformin® HCl 850mg R9.42

From table 5.21.1 it can be seen that for the period January to April versus May to August, the cost savings on oral antidiabetic agents was the lowest with a variation of between R0.34 and R141.89. For the period January to April versus September to December, the cost savings on oral antidiabetic agents was the highest with a variation of between R8.17 and R243.97.

Table 5.22: Average cost saving per unit price and cost savings of the insulins for the different time periods

Class	Agent	Average cost saving per unit price (R) and percentages (Jan-Apr vs. May-Aug)	Cost savings (R) January-April vs. May-August	Average cost savings per unit price (R) and percentages (Jan-Apr vs. Sept-Dec)	Cost savings (R) January-April vs. September-December	Average cost savings per unit price (R) and percentages (May-Aug vs. Sept-Dec)	Cost savings (R) May-August vs. September-December
Insulin lispro	Humalog Mix 25 Penset	+72.20 (+9.3)	+42 164.80	90.82 (11.7)	53 038.88	163.02 (19.3)	122 591.04
	Humalog Mix 25 Cartridges	6.64 (0.8)	285.52	211.81 (24.6)	9 107.83	205.17 (24.0)	19 901.49
	Humalog Mix 25 Injection	31.99 (3.4)	415.87	237.04 (25.4)	3 081.52	205.05 (22.7)	3 698.25
	Humalog 10ml Ampoules	190.11 (33.3)	3 041.76	234.14 (40.7)	3 746.24	44.03 (11.4)	1 056.72
	Humalog 3ml Penset/Prefill	28.17 (3.4)	6 732.63	230.41 (27.9)	55 067.99	202.24 (25.4)	65 728.00
	Humalog 3ml Cartridge injection	103.67 (14.2)	3 835.79	193.13 (26.5)	7 148.03	89.52 (14.3)	3 849.36
Insulin aspartame	Novorapid 3ml FlexPen	86.11 (11.2)	12 916.50	227.43 (29.7)	34 114.50	141.32 (20.8)	29 677.20
	Novorapid 3ml Penfill	118.03 (15.0)	2 832.72	204.77 (26.0)	4 914.48	86.74 (13.0)	2 775.68
Biosynthetic human insulin	Humulin R 10ml vial	69.88 (18.5)	349.40	140.42 (2.8)	702.10	70.54 (22.9)	141.08
	Humulin R 3ml cartridges	120.86 (18.7)	725.16	245.54 (37.9)	1 473.24	124.68 (23.7)	374.04
	Humulin R Humaject Pen 5ml	+529.09 (+154.3)	+529.09	-	-	94.41 (17.7)	188.82
Biosynthetic human soluble insulin	Actrapid HM Pensets 1,5ml	731.79 (93.1)	731.79	741.14 (94.3)	741.14	9.35 (17.2)	9.35
	Actrapid HM Pensets 3ml	86.44 (10.7)	14 262.60	246.27 (30.5)	40 634.55	159.83 (22.2)	46 830.19
	Actrapid HM Penfill 3ml	138.50 (17.8)	2 354.50	284.60 (36.8)	4 838.20	146.10 (22.9)	3 944.70
	Actrapid HM 10ml Ampoules	1.28 (3.9)	42.24	72.15 (19.4)	2 380.59	70.87 (19.1)	2 338.71

Table 5.22: (Continue) Average cost saving per unit price and cost savings of the insulins for the different time periods

Class	Agent	Average cost saving per unit price (R) and percentages (Jan-Apr vs. May-Aug)	Cost savings (R) January-April vs. May-August	Average cost savings per unit price (R) and percentages (Jan-Apr vs. Sept-Dec)	Cost savings (R) January-April vs. September-December	Average cost savings per unit price (R) and percentages (May-Aug vs. Sept-Dec)	Cost savings (R) May-August vs. September-December
Soluble insulin and isophane	Actraphane HM Penset 3ml	84.89 (10.2)	111 205.90	329.82 (39.8)	349 534.20	181.93 (24.4)	291 088.00
	Actraphane HM Penfill 3ml	95.85 (11.6)	11 789.55	228.24 (27.7)	28 073.52	132.39 (18.2)	25 021.71
	Actraphane HM 10ml Ampoules	55.65 (10.4)	14 469.00	125.77 (23.5)	32 700.20	70.12 (14.7)	25 453.56
Biosynthetic human isophane	Humulin 30/70 3ml Cartridges	30.66 (4.1)	1 502.34	159.57 (21.4)	7 818.93	128.91 (18.1)	8 379.15
	Humulin 30/70 10ml vial	+116.65 (+17.75)	+2 449.65	293.90 (44.7)	6 171.90	410.55 (53.1)	6 156.90
	Humulin 30/70 Humaject Inj	+28.61 (+3.9)	+1 087.18	205.54 (28.3)	7 810.52	234.15 (31.1)	8 429.40
	Humulin N 3ml Penset	+30.81 (+5.1)	+1 971.84	84.47 (13.9)	5 406.08	115.28 (18.1)	11 528.00
	Humulin N 3ml Cartridges	189.88 (30.7)	3 038.08	239.42 (38.8)	3 830.72	49.54 (11.6)	594.48
	Humulin N Humaject 3ml Inj			+26.36 (+5.7)	+26.36	-	-
	Humulin N 10ml vial	9.78 (3.0)	166.26	45.50 (13.8)	773.50	35.72 (11.1)	678.68
Biphasic biosynthetic human insulin 20/80	Mixtard 20/80 Penfill	+44.98 (+5.5)	+179.92	26.96 (3.3)	107.84	74.94 (8.7)	431.64
Soluble insulin aspartame and protamine	Novomix 30 Flexpen 3ml Inj.	97.87 (12.8)	30 829.05	228.20 (29.8)	71 883.00	130.33 (19.5)	60 473.12
	Novomix 30 Penfill 3ml Inj.	76.58 (9.1)	1 531.60	330.77 (39.4)	6 615.40	254.19 (33.3)	3 050.28
Zinc biosynthetic human insulin	Humulin L 10ml vial	20.91 (5.2)	1 275.51	102.89 (25.8)	6 276.29	81.98 (21.7)	6 312.46

Table 5.22: (Continue) Average cost saving per unit price and cost savings of the insulins for the different time periods

Class	Agent	Average cost saving per unit price (R) and percentages (Jan-Apr vs. May-Aug)	Cost savings (R) January-April vs. May-August	Average cost savings per unit price (R) and percentages (Jan-Apr vs. Sept-Dec)	Cost savings (R) January-April vs. September-December	Average cost savings per unit price (R) and percentages (May-Aug vs. Sept-Dec)	Cost savings (R) May-August vs. September-December
Biosynthetic human insulin zinc suspension	Monotard HM 10ml Ampoules	37.94 (8.4)	1 934.94	84.16 (18.7)	4 292.16	46.22 (11.2)	2 079.90
Biosynthetic monocomponent isophane	Protaphane HM Penset 3ml	+39.60 (+10.1)	+8 434.80	114.94 (29.2)	24 482.22	154.54 (22.7)	12 517.74
	Protaphane HM Penfill 3ml	99.77 (15.0)	1 895.63	199.59 (30.1)	3 792.21	99.82 (17.7)	4 491.90
	Protaphane HM 10ml Ampoules	7.22 (1.9)	281.58	36.39 (9.4)	1 419.21	29.17 (7.7)	2 041.90
Biosynthetic human insulin zinc suspension monocomponent crystals	Ultratard HM 10ml Ampoules	47.22 (14.3)	763.52	+22.63 (+6.9)	+362.08	+70.35 (+24.9)	+211.05
Insulin glargine	Lantus 300IU/3ml	47.68 (5.8)	5 673.92	188.28 (23.0)	22 405.32	140.60 (18.2)	25 167.40
	Lantus 300IU/3ml O/T	45.02 (5.7)	2 521.12	190.30 (24.0)	10 656.80	145.28 (19.4)	14 673.28
	Lantus 1000IU/10ml	159.38 (22.1)	5 100.16	220.84 (30.6)	7 066.88	61.46 (10.9)	2 335.48
Total			**185 687.25**		**794 106.55**		**814 068.56**

From table 5.22 it can be seen that the insulin with the highest average cost saving per unit price for the time January to April *vs.* May to August was Actrapid® HM Penset 1.5ml (R731.79), while the agent with the lowest average cost saving was Actrapid® HM 10ml Ampoules (R1.28). Actrapid® HM Penset 1.5ml (93.1%) also showed the biggest lowering in average cost if presented in percentage. According to table 5.21, Humalog® Mix 25 Penset (+R72.20), Humulin® R Humaject Pen 5ml (+R529.09), Humulin® 30/70 Humaject Injection (+R28.61), Humulin® 30/70 10ml vial (+R116.65), Humulin® N 3ml Penset (+R30.81), Mixtard® 20/80 Penfill (+R44.98) and Protaphane® HM Penset 3ml (+R39.60) showed an increase in the average total cost for the time January to April *vs.* May to August.

For the time January to April *vs.* September to December it can be seen from table 5.22 that Actrapid® HM Penset 1.5ml (94.3%) has the highest cost saving presented in percentage as well as the highest average cost saving in rand (R741.14). Mixtard® 20/80 Penfill shows the lowest average cost saving (R26.96 or 3.3%). The only two insulins that showed an increase in price were Humulin® N Humaject 3ml Injection (+R26.36) and Ultratard® HM 10ml Ampoules (+R22.63).

From table 5.22, table 5.22.1 can be compiled which summarises the ten insulin products with the highest cost saving and the ten insulin products with the lowest cost savings for the different periods

Table 5.22.1: Summary of the insulin products with the ten highest and ten lowest cost savings (2004)

	Highest			**Lowest**		
No.	**Jan-Apr *vs.* May-Aug**	**Jan-Apr *vs.* Sept-Dec.**	**May-Aug *vs.* Sept.-Dec.**	**Jan-Apr *vs.* May-Aug**	**Jan-Apr *vs.* Sept-Dec.**	**May-Aug *vs.* Sept.-Dec.**
1	Actrapid® HM Penset 1.5ml R731.79	Actrapid® HM Penset 1.5ml R741.14	Humulin® 30/70 vial R410.55	Actrapid® HM 10ml Ampoules R1.28	Mixtard® 20/80 Penfill R26.96	Actrapid® HM Pensets 1.5ml R9.35
2	Humalog® 10ml Ampoules R190.11	Novomix® 30 Penfill 3ml injection R330.77	Novomix® 30 Penfill 3ml injection R254.19	Humalog® Mix 25 Cartridges R6.64	Protaphane® HM 10ml Ampoules R36.39	Protaphane® HM 10ml Ampoules R29.17
3	Humulin® N 3ml Cartridges R189.88	Actraphane® HM Penset 3ml R329.82	Humulin® 30/70 Humaject injection R234.15	Protaphane® HM 10ml Ampoules R7.22	Humulin® N 10ml vial R45.50	Humulin® N 10ml vial R35.72
4	Lantus® 1000IU/10ml R159.38	Humulin® 30/70 10ml vial R293.90	Humalog® Mix 25 Cartridges R205.17	Humulin® N 10ml vial R9.78	Actrapid® HM 10ml Ampoules R72.15	Humalog® 10ml Ampoules R44.03
5	Actrapid® HM Penfill 3ml R138.50	Actrapid® HM Penfill 3ml R284.60	Humalog® Mix 25 injection R205.05	Humulin® L 10ml vial R20.91	Monotard® HM 10ml Ampoules R84.16	Monotard® HM 10ml Ampoules R46.22

Table 5.22.1: (Continue) Summary of the insulin products with the ten highest and ten lowest cost savings (2004)

No.	Highest			Lowest		
	Jan-Apr *vs.* May-Aug	Jan-Apr *vs.* Sept-Dec.	May-Aug *vs.* Sept.-Dec.	Jan-Apr *vs.* May-Aug	Jan-Apr *vs.* Sept-Dec.	May-Aug *vs.* Sept.-Dec.
6	Humulin® R 3ml Cartridges R120.86	Actrapid® HM Pensets 3ml R246.27	Humalog® 3ml Penset/Prefill R202.24	Humalog® 3ml Penset/Prefill R28.17	Humulin® N 3ml Penset R84.47	Humulin® N 3ml Cartridges R49.54
7	Novorapid® 3ml Penfill R118.03	Humulin® R 3ml Cartridge R245.54	Actraphane® HM Penset 3ml R181.93	Humulin® 30/70 3ml Cartridges R30.66	Humalog® Mix 25 Penset R90.82	Lantus® 1000IU/ 10ml R61.46
8	Humalog® 3ml Cartridge injection R103.67	Humulin® N 3ml Cartridge R239.42	Humalog® Mix 25 Penset R163.02	Humalog® Mix 25 injection R31.99	Humulin® L 10ml vial R102.89	Humulin® R 10ml vial R70.54
9	Protaphane® HM Penfill 3ml R99.77	Humalog® Mix 25 injection R237.04	Actrapid® HM Pensets 3ml R159.83	Monotard® HM 10ml Ampoules R37.94	Protaphane® HM Penset 3ml R114.94	Actrapid®HM 10ml Ampoules R70.87
10	Novomix® 30 Flexpen 3ml injection R97.87	Humalog® 10ml Ampoules R234.14	Protaphane® HM Penset 3ml R154.54	Lantus® 300IU/3ml O/T R45.02	Actraphane® 10ml Ampoules R125.77	Mixtard® 20/80 Penfill R74.94

From table 5.22.1 it can be seen that for the period January to April versus May to August, the cost savings on insulin products were the lowest with a variation of between R1.28 and R731.79. For the period January to April versus September to December, the cost savings on insulin products were the highest with a variation of between R26.96 and R741.14.

From table 5.19 the total cost savings can be calculated if an agent that was prescribed during the time period January to April was dispensed at the cost of the same agent during the time September to December. Table 5.23 summarises these cost savings.

Table 5.23: Summary of the total cost savings for each class of oral antidiabetic agent

Class	Active ingredient	Total cost savings (R) (Jan-Apr vs. May-Aug)	Total cost savings (R) (Jan-Apr vs. Sept-Dec)	Total cost savings (R) (May-Aug vs. Sept-Dec)
Alpha-glucosidase inhibitors	Acarbose	20 315.04	8 285.04	3 589.11
Biguanides	Metformin	132 351.90	242 738.90	135 521.99
Sulfonylureas	Glimeparide	43 767.30	104 887.13	71 424.23
	Glibenclamide	93 225.73	129 301.61	41 181.99
	Gliclazide	19 074.62	70 915.85	53 408.79
	Glipizide	4 234.23	7 975.44	2 872.04
	Chlorpropamide	3.40	619.80	369.84
Thiazolidinediones	Pioglitazone	2 680.81	15 546.60	30 666.81
	Rosiglitazone	6 690.54	18 157.72	16 641.36
Meglitinides	Repaglinide	1 664.76	2 677.23	1 217.43
	Nateglinide	224.85	603.00	428.57
Combination	Metformin/Glibenclamide	15 366.21	25 255.83	14 854.81
TOTAL		**339 599.39**	**626 964.15**	**372 176.97**

When the cost savings of a product are studied, there are two things that must be looked at, namely the price per unit and the volume that is prescribed. For the purpose of this study the volume was kept constant, because the influence of the changes in the pricing regulations was investigated.

From table 5.23 it can be concluded that if the average cost of the oral antidiabetic agents for the time January to April were the same as the average cost of the oral antidiabetic agents for the time September to December, the claims house could have saved R626 964.15.

From table 5.23 and table 5.3 it can be calculated that for the period January to April *vs.* May to August there could have been a cost saving of 8.8% or R339 599.39. For the period January to April *vs.* September to December there could have been a cost saving of 16.3% or R626 964.15. For the time May to August *vs.* September to December there could have been a cost saving of 9.1% or R372 176.97 on the total cost of May to August.

From table 5.20 it can be calculated that the only insulin products that did not have a lowering in price were Humulin® N Humaject 3ml injection (R26.36) and Ultratard® HM 10ml ampoules (R22.63). Only twelve insulin products have d-values of more than 0.8. These agents are Humalog® 10ml ampoules (0.9), Humalog® 3ml Cartridge injection (1.3), Novorapid® 3ml Flexpen (0.8), Humulin® R 10ml vial (1.2), Actrapid® HM Penfill 3ml (0.9), Actrapid® HM Penset 3ml (0.8), Humulin®30/70 10ml vial (1.2), Novomix® 30 Flexpen 3ml injection (0.8), Novomix® 30 Penfill 3ml injection (1.0), Lantus® 300IU/3ml (0.8), Lantus® 300IU/3ml O/T (1.0) and Lantus® 1000IU/10ml (0.8). The product that showed the biggest lowering in price was Actrapid® HM Pensets 1.5ml (R741.14). The class of insulins that exercised the biggest influence on the cost savings were soluble insulin and isophane (R410 307.92). Table 5.24 summarises these cost savings.

Table 5.24: Summary of the total cost savings for each class of insulin

Active ingredient	Total cost savings (R) (Jan-Apr vs. May-Aug)	Total cost savings (R) (Jan-Apr vs. Sept-Dec)	Total cost savings (R) (May-Aug vs. Sept-Dec)
Insulin lispro	+27 853.31	131 190.49	217 094.86
Insulin aspartame	15 749.22	39 028.98	32 452.88
Biosynthetic human insulin	545.47	2 175.34	703.94
Biosynthetic human soluble insulin	17 391.13	48 594.84	53 122.95
Soluble insulin and isophane	137 464.45	410 307.92	341 563.27
Biosynthetic human isophane	+801.99	31 785.29	35 766.61
Biphasic biosynthetic human insulin 20/80	+179.92	107.84	431.64
Soluble insulin aspartame and protamine	32 360.65	78 498.40	63 523.40
Zinc biosynthetic human insulin	1 275.51	6 276.29	6 312.46
Biosynthetic human insulin zinc suspension	1 934.94	4 292.16	2 079.90
Biosynthetic monocomponent isophane	+6 257.59	29 693.64	19 051.54
Biosynthetic human insulin zinc suspension monocomponent crystals	763.52	+362.08	+211.05
Insulin glargine	13 295.20	40 129.00	42 176.16
TOTAL	**185 687.28**	**821 718.11**	**814 068.56**

+ indicates that there was an increase in the price of a product.

From table 5.24 it can be concluded that if the average cost of the insulins for the time January to April were the same as the average cost of the insulins for the time September to December, the cost savings on antidiabetic agents could have been a further R821 718.11.

From table 5.24 and table 5.3 it can be calculated that for the time January to April *vs.* May to August there could have been a cost saving of 3.4% or R185 687.28. For the time January to April *vs.* September to December there could have been a cost saving of 15.1% or R821 718.11. For the time May to August *vs.* September to December there could have been a cost saving of 12.7% or R814 068.56 on the total cost of May to August.

From tables 5.23 and 5.24 it can be concluded that the total cost savings in antidiabetic medication could have been R1 448 682.26 (15.6%, n = R9 278 245.64) if the lower price of antidiabetic medication had been implemented during the study period January to April 2004.

5.8.2 Summary of the total cost savings

From tables 5.2, 5.23, and 5.24 the cost savings on the total cost of all the items on the database for the different time periods can be calculated. For the time January to April *vs.* May to August the cost saving was 0.3% or R525 286.67, for January to April *vs.* September to December the cost saving was 0.7% or R1 448 682.26, and for the time period May to August *vs.* September to December the cost saving was 0.5% or R1 186 245.53.

The cost saving of the total endocrine system agents on the database can also be calculated from table 5.23, 5.24 and section 5.2.2. For the time January to April *vs.* May to August the cost saving on the endocrine system agents could have been 2.5%, for the time May to August *vs.* September to December, the total savings on the endocrine system agents could have been 5.5%. During the time period January to April *vs.* September to December, 6.9% could have been saved on endocrine system agents.

From tables 5.23, 5.24 and 5.3 the total cost savings for the antidiabetic agents can be calculated. For the time January to April *vs.* May to August, the cost savings are 5.7%, for the time period May to August *vs.* September to December the cost savings are 11.3% and for the time January to April *vs.* September to December the cost savings are 15.6%.

5.9 COMPARISON BETWEEN GENERIC AND INNOVATOR DRUGS AS RELATED TO COST AND PREVALENCE

In this section generic drugs and innovator drugs will be compared. Sandoz (2004b:1) describes generic drugs as pharmaceutical preparations that contain the same active ingredients in the same concentration as the better-known originator or innovator drugs.

According to the United States Food and Drug Administration's Centre for Drug Evaluation and Research (CDER) (2005:1) generic drugs are identical or bioequivalent to a brand name drug in dosage form, safety, strength, route of administration, quality, performance characteristics and intended use. Although generic drugs are chemically identical to their branded counterparts, they are sold at substantial discounts in comparison with the branded price.

Generic drugs are usually less expensive because generic manufacturers do not have the investment costs of the developer of a new drug. New drugs are developed under patent protection. The patent protects the investment by giving the company the sole right to sell the drug while it is in effect. The patent expires twenty years from the start of drug development to drug marketing. When patents or other periods of exclusivity expire, manufacturers can apply to the FDA to sell generic versions. Because those manufacturers do not have the same development costs, they can sell their product at substantial discounts. Once generic drugs are approved there is greater competition that keeps the price down (United States Food and Drug Administration's CDER, 2005:1; United States Food and Drug Administration's CDER, 2004:2).

5.9.1 The cost analysis of the innovator drugs and their generic substitute

Table 5.25 lists the cost and prevalence of the innovator and generic drugs in order to draw a comparison between these two groups of drugs.

Table 5.25: The cost analysis of innovator versus generic drugs of the total database

Type of drug	Number of items	Average cost (R)	Standard deviation (R)	Total cost (R)	% Frequency	Cost %
Innovator drugs	3 529 046	155.75	269.93	549 658 776.00	66.5	83.1
Generic drugs	1 776 836	62.79	74.26	111 564 370.00	33.5	16.9
Total	5 305 882	124.62	228.55	661 223 146.00	100	100

From table 5.25 it can be seen that innovator products prescribed for the whole study period (January-December 2004) amount to 66.5% of the total products (5 305 882) that were prescribed. The total cost of the innovator products amounts to 83.1% of the total cost of all the products on the database (R661 223 146.00).

The average cost of the generic products (R62.79 ± R74.26) is much lower than that of the innovator products (R155.75 ± R269.93).

In table 5.26 the cost of the innovator and generic antidiabetic agents will be summarised.

Table 5.26: The cost analysis of innovator versus generic drugs of the antidiabetic agents

Type of drug	Number of items	Average cost (R)	Standard deviation (R)	Total cost (R)	% Frequency	Cost %	CPI
Innovator	97976	257.34	315.75	25 212 750.67	68.3	84.8	1.2
Generic	45471	99.45	130.81	4 521 904.52	31.7	15.2	0.5
Total	143447	207.29	280.92	29 734 655.19	100	100	-

Table 5.26 shows that the antidiabetic innovator products have a higher prevalence (97976) than the generic products (45471). The average cost of the antidiabetic generic products (R99.45 ± R130.81) is however relatively lower than the average cost of the innovator products (R257.34 ± R315.75). The CPI values show that the antidiabetic innovator products are relatively more expensive than the generic products.

5.9.2 Oral antidiabetic agents

In this section all the oral antidiabetic agents with the same active ingredient and strength will be compared in relation to the innovator drug versus the generic drug in order to differentiate the costs between them.

Table 5.27 summarises the utilisation patterns of the innovator products versus the generic alternatives during the three different time periods, based on the therapeutic classes of the oral antidiabetic agents.

Table 5.27: Cost and prevalence of the generic and original antidiabetic agents according to the active ingredient

Time	Group	Type Innovator (I) or Generic(G)	Number of items	Average cost in Rand (R)	Standard deviation in Rand (R)	Total cost in Rand (R)	% Frequency	Cost %
January-April	Biguanide	I	11643	81.12	35.74	944 428.70	38	24.5
		G	3338	74.62	32.39	249 090.82	10.9	6.5
	Sulfonylureas	I	5880	206.17	142.42	1 212 271.21	19.2	31.5
		G	8123	117.06	66.13	950 906.30	26.5	24.7
	Alpha-glucosidase inhibitors	I	240	269.77	86.48	64 745.94	0.8	1.7
	Thiazolidinediones	I	454	403.64	158.07	183 253.75	1.5	4.8
		G	287	372.41	116.69	106 881.45	0.9	2.8
	Meglitinides	I	294	220.59	133.48	64 853.55	0.9	1.7
	Combination	I	389	181.26	99.16	70 510.85	1.3	1.8
	Total		30648	125.52	103.94	3 846 942.57	100	100
May-August	Biguanide	I	15118	61.62	29.92	931 562.70	38.8	22.8
		G	4017	53.21	24.73	213 729.87	10.3	5.2
	Sulfonylureas	I	7112	191.6	129.53	1 362 626.07	18.2	33.3
		G	10000	77.45	47.07	774 457.47	25.7	19
	Alpha-glucosidase inhibitors	I	266	247.18	95.37	65 748.72	0.7	1.6
	Thiazolidinediones	I	878	429.13	161.92	376 779.61	2.2	9.2
		G	530	340.36	130.79	180 390.54	1.4	4.4
	Meglitinides	I	427	219.06	132.99	93 540.50	1.1	2.3
	Combination	I	609	143.30	87.71	87 272.49	1.6	2.1
	Total		38957	104.89	106.00	4 086 107.97	100	99.9
September-December	Biguanide	I	19200	44.01	22.58	845 022.60	41.1	23
		G	4256	42.21	20.17	179 657.71	9.1	4.9
	Sulfonylureas	I	7259	157.77	106.40	1 145 270.04	15.5	31.2
		G	12945	60.30	33.45	780 640.96	27.7	21.3
	Alpha-glucosidase inhibitors	I	271	200.37	64.08	54 299.04	0.6	1.5
	Thiazolidinediones	I	882	354.91	134.16	313 031.37	1.9	8.5
		G	614	287.77	124.52	176 691.78	1.3	4.8
	Meglitinides	I	375	191.70	159.52	71 887.28	0.8	1.9
	Combination	I	911	116.09	58.04	105 754.95	2	2.9
	Total		46713	78.61	84.05	3 672 255.73	100	100

- *January-April*

From table 5.27 it is evident that the majority of items prescribed were for the innovator product (61.7% n = 30 648). There are, however, only three groups of agents that have a generic substitute, namely the biguanides, sulfonylureas and thiazolidinediones.

The only class of agents where the generic product had a higher prevalence was for the sulfonylureas. In this group of drugs 58% (n = 14 003) of the items that were prescribed were for the generic product and only 42% (n = 14 003) were for the innovator product.

- *May-August*

The innovator products for this time period amount to 62.7% (n = 38 957) of all the products prescribed and dispensed. There are still only three groups of drugs with generic substitutes, namely the biguanides, sulfonylureas and the thiazolidinediones.

The generic substitute of the sulfonylureas, amounts to 58.4% of all the sulfonylureas (n = 17 112) prescribed during this time period.

- *September-December*

For this time period the generic products prescribed and dispensed amount to 37.3% of all the products (n = 38 957). This can be explained by the fact that only the biguanides, sulfonylureas and thiazolidinediones have a generic substitute. The generic substitute of the sulfonylureas amounts to 68.7% of all the generic products (n = 14 547) prescribed.

5.9.2.1 Summary

Figure 5.3 illustrates the prevalence of the generic and or innovator products of the antidiabetic agents for the whole study period, i.e. January to December 2004.

CHAPTER 6: Conclusions, recommendations and limitations

6.1 INTRODUCTION

In this chapter the conclusions and limitations will be discussed. Certain recommendations to this study will also be made.

6.2 CONCLUSIONS

The following conclusions can be discussed based on the specific objectives of the research.

The ***first specific research objective*** was to review diabetes mellitus as an illness, and the treatment thereof. This was done through an extensive literature review (refer to Chapter 2). Diabetes mellitus was defined and classified. The epidemiology, symptoms and signs, complications and pathology of the disease were discussed.

It was concluded that diabetes mellitus is a heterogeneous disorder requiring both genetic and environmental factors. Hyperglycaemia in type 2 diabetes results from a combination of insulin resistance and relative insulin deficiency. An insight into the aetiopathogenesis helps to determine a better approach to the disease. It is crucial to identify the hidden cases of type 2 diabetes in a community. Education for the general population, and in particular, for the patients, is the key to preventing and controlling this type of diabetes and reducing the complications arising from it (Bhattacharya, 2001b:9).

The ***second research objective*** was to review pharmaco-economics, managed health care and drug utilisation review. This was done through an extensive literature review. Chapter three provided an overview of the concepts of managed care, pharmaco-economics and drug utilisation review. These terms were defined and the usage thereof in South Africa was discussed as referred to the implementation and control of information tools for decision making.

The ***first specific research objective*** that was to be answered ***from the empirical study***, was to determine the prevalence and medicine treatment cost of diabetes according to the database of a prescription claims database. This was done in chapter five. From the database it was calculated that 143 447 antidiabetic agents were prescribed during the time 1 January 2004 to 31 December 2004, at a total cost of R29 734 655.19. It was determined that the oral antidiabetic agents are relatively less expensive than the insulins and that they are prescribed more frequently. A reason for the oral agents being prescribed more frequently can be because type one diabetes mellitus amounts to only 10% to 15% of all the diabetic patients (as seen in the literature, Chapter 2 section 2.2.2.1). The cost prevalence index (CPI) is an indicator of the relationship between the number of medicine items and the cost. Since the CPI of the oral agents is less than one, it is a clear indication that the therapy is relatively inexpensive. The CPI of the insulins is, however more than 1 (3.1 and 3.3) and it is thus clear that the therapy is relatively expensive.

From the results (refer to paragraph 5.6, table 5.5), it can be seen that there is a wide variety of insulin products available on the South African market, e.g. vials, ampoules, cartridges, penfills, etc. The “pre-filled” or “pre-packed” products (e.g. pensets or penfills) have a higher average cost than the “ordinary” insulin products (e.g. ampoules, cartridges, vials, etc). It seems as if the “pre-filled” or “pre-packed” products have the highest prevalence (almost 75%, n = 27 129). This can be due to the fact that these products are easier to use in an active lifestyle, and therefore can assure better patient compliance. Since the clinical profiles of the patients were not available, the effectiveness of these products could not be determined.

From the results (refer paragraph 5.7, table 5.6 to 5.11) it must be noted that there are often two oral antidiabetic agents with the same active ingredient but with different strengths, for example Rolab-Metformin® HCl 500mg and Rolab-Metformin® HCl 850mg. The average tablet consumption per person per day is in most cases the same, or almost the same (refer to paragraph 5.7.3, table 5.12). However, since the blood glucose levels of the patients are not available, an explanation for this cannot be offered.

The ***second specific research objective*** that was to be answered ***from the empirical study*** was to analyse the prescription patterns for the different types of antidiabetic drugs. From the database it was calculated that the oral antidiabetic agents have a higher prevalence than the insulins, and the oral agents account for almost 81% of the antidiabetic agents that are prescribed. As seen in figure 5.2 the biguanides account for almost half (69.4%) of the prescribed oral antidiabetic agents (n = 116 138), followed by the sulfonylureas (51319). The biguanides are the agents of first choice in the management of obese type 2 diabetics and that can be the reason why the biguanides have the highest prevalence. The oral antidiabetic agent with the lowest frequency is the alpha-glucosidase inhibitors (777). As seen in section 5.5.3 the insulins amount to only 18.9% (n = 143447) of all the antidiabetic agents in the database.

The ***third specific research objective*** that was to be answered ***from the empirical study*** was to investigate the influence of the new pricing structure on the cost of antidiabetic drugs. This was calculated in section 5.8.1 and 5.8.2 of chapter five.

From tables 5.23 and 5.24 it was calculated that the total cost savings in antidiabetic medication could have been R1 448 682.26 if the lower price of antidiabetic medication were implemented during the time period January to April.

If the average cost of oral antidiabetic drugs issued in 2004 is compared to the average cost of oral antidiabetic drugs issued in 1996, it can be concluded that the average cost in 2004 (R99.77 ± R99.04) was lower than the average cost in 1996 (R138.63 ± 92.51, La Grange, and R126.25, Truter). Therefore it can be stated that the average cost of oral antidiabetic drugs was approximately 21.0% to 28.0% less expensive in 2004 than in 1996.

If an expected yearly inflation rate of 6% is added to the average cost of the oral antidiabetic drugs of 1996, it can be calculated that the average cost of the oral antidiabetic drugs could have been between R201.22 and R220.96 in the year 2004, this indicates that the average cost of the oral antidiabetic drugs is 50.4% to 54.8% lower than the expected average cost in 2004.

A further aspect of the influence of the pricing system is on the possible income of the provider. Taking the above example, the gross profit per product could have been reduced from R46.00 in 1996 to R16.00 in 2004. This may influence the readily availability of antidiabetic drugs due to the risk of carrying products that are only available on prescription from a legal prescriber.

The ***fourth specific research objective*** that was to be answered ***from the empirical study*** was to determine the influence of generic substitution on the usage patterns and cost of antidiabetic drugs. This was calculated in sections 5.9.2 and 5.9.3 of chapter five.

From the results (table 5.26) it was calculated that the average cost of the generic antidiabetic agents is 61.4% lower than the average cost of the innovator antidiabetic agents.

The oral innovator antidiabetic agents have a higher prevalence than the oral generic antidiabetic agents, except for the sulfonylureas where the generic agents have a higher prevalence (60.5%, n = 51319) than the innovator products.

The possible cost savings due to generic substitution could have been between R811 375.40 and R1 429 043.85 for the time January to April. For the period May to August the possible cost savings due to generic substitution could have been between R724 996.89 and R1 364 820.23

and for the period September to December it could have been between R430 334.54 and R993 826.54.

For the insulins the possible cost savings due to generic substitution could have been R29 518.37 for the period January to April. For the period May to August it could have been R325 504.21 and for the period September to December the possible cost savings due to generic substitution could have been between R61 912.71 and R125 519.21.

This can be an indication that there is a possible under utilisation of generic antidiabetic products.

6.3 LIMITATIONS

Based on the results and discussion in chapter five, certain limitations were identified, which could restrict or limit the scope of this study. The following limitations were detected:

- No clinical data were available on the database, therefore the relevance of some of the utilisation patterns could not be determined.
- No demographic information, such as age, gender and race was available on the database.
- No patient information was available on the database and therefore the number of newly diagnosed patients could not be determined.
- Compliance could not be determined.
- The researcher was not responsible for compiling the database.

6.4 RECOMMENDATIONS

The following recommendations could be formulated after analysis of the data and research study:

- The prescriptions dispensed by different health care providers must be separated to determine and evaluate the prescribing and dispensing patterns of the different dispensers, e.g. combination and type of product prescribed and dispensed.
- The influence of the single exit price on the provider and on the availability of the product must be investigated.
- The availability and cost aspects of the variety of pre-filled insulin preparations should be investigated, e.g. convenience *vs.* cost.

- The development of a sustainable pharmaco-economic model to address the cost-effectiveness of antidiabetic treatment as well as quality of health aspects must be investigated.
- An investigation to determine the possible undiagnosed diabetics in a population as this can have a considerable influence on the health care providers.
- The indication of clinical data, e.g. blood glucose levels, of the study population should also be taken into consideration in future studies, and not only cost aspects.

6.5 SUMMARY

In this chapter the conclusions, limitations and recommendations were discussed.

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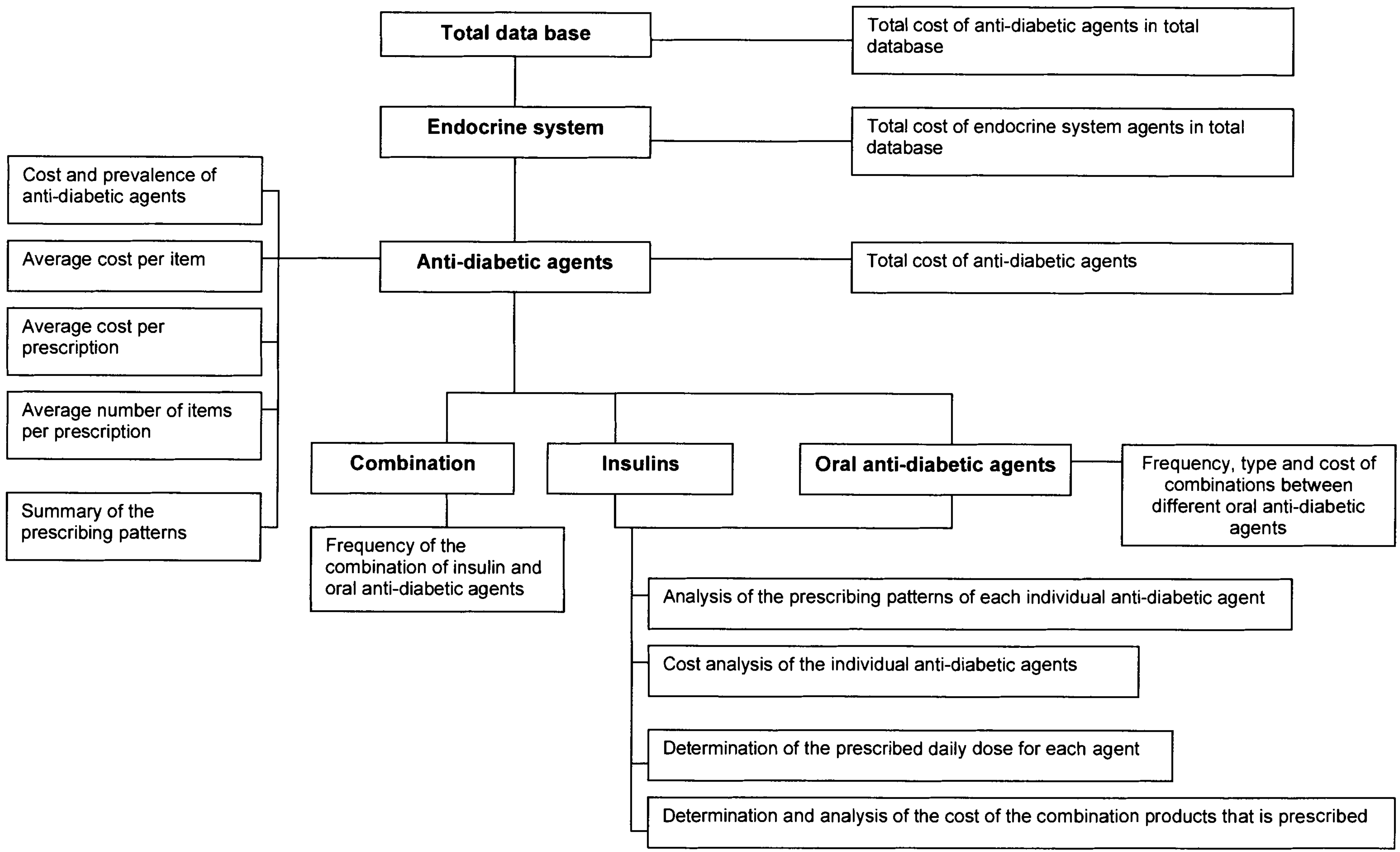
Appendix A



Total data base
Total cost of anti-diabetic agents in total database
Endocrine system
Total cost of endocrine system agents in total database
Cost and prevalence of anti-diabetic agents
Average cost per item
Anti-diabetic agents
Total cost of anti-diabetic agents
Average cost per prescription
Average number of items per prescription
Summary of the prescribing patterns
Combination
Insulins
Oral anti-diabetic agents
Frequency, type and cost of combinations between different oral anti-diabetic agents
Frequency of the combination of insulin and oral anti-diabetic agents
Analysis of the prescribing patterns of each individual anti-diabetic agent
Cost analysis of the individual anti-diabetic agents
Determination of the prescribed daily dose for each agent
Determination and analysis of the cost of the combination products that is prescribed

Appendix B

Table B1: The MIMS classification (MIMS, 2004:9a-11a).

1. CENTRAL NERVOUS SYSTEM

1.1. Central nervous system stimulants

1.1.1 Central analeptics

1.1.2 Respiratory stimulants

1.1.3 Others

1.2. Sedative Hypnotics

1.2.1 Benzodiazepines

1.2.2 Barbiturate

1.2.3 Others

1.3. Anxiolytics

1.3.1 Benzodiazepines

1.3.2 Others

1.4. Anti-depressants

1.4.1 Tricyclic

1.4.2 Non-Tricyclic

1.4.3 Mono-Amine Oxidase inhibitors

1.4.3.1 Non-selective mono-amine oxidase inhibitors

1.4.3.2 Selective mono-amine oxidase inhibitors

1.4.4 Selective serotonin re-uptake inhibitors

1.4.5 Serotonin and nor-adrenaline re-uptake inhibitors

1.4.6 Lithium

1.4.7 Others

1.5. Anti-psychotics

1.5.1 Phenothiazines

1.5.2 Butyrophenones

1.5.3 Others

1.6. Anti-epileptics

1.7. Anti-Parkinson agents

1.7.1 Dopaminergics

1.7.2 Anticholinergics

1.7.3 Others

1.8. Anti-vertigo and anti-emetic agents

1.9. Anti-migraine agents

1.10. Alzheimer's disease
2. ANAESTHETICS **2.1 General anaesthetics** 2.1.1 Inhalation anaesthetics 2.1.2 Parenteral anaesthetics **2.2 Local anaesthetics** 2.2.1 Surface anaesthetics **2.3 Muscle relaxants**
3. ANALGESICS **3.1 Narcotic analgesics** **3.2 Analgesics and antipyretics** **3.3 Combinations** **3.4 Others**
4. MUSCULO-SKELETAL AGENTS **4.1 Non-steroidal anti-inflammatory agents** 4.1.1 COX inhibitors 4.1.2 Selective COX2 inhibitors 4.1.3 Specific cyclo-oxigenase-2 inhibitor (COXIB) **4.2 Anti-gout** **4.3 Topical agents** **4.4 Gold** **4.5 Centrally acting muscle relaxants** **4.6 Others** **4.7 Osteoporosis (and other metabolic bone disorders)** 4.7.1 Bisphosphonates 4.7.2 Selective oestrogen receptor modulators 4.7.3 Calcitonin 4.7.4 Minerals and vitamin
5. AUTONOMIC **5.1 Sympathomimetics** **5.2 Sympatholytics** **5.3 Cholinergics** **5.4 Anti-cholinergics** **5.5 Others**
6. AUTACOIDS **6.1 Anti-histamines** **6.2 Serotonin antagonists** **6.3 Others**

Appendix B

7. CARDIO-VASCULAR AGENTS **7.1 Positive inotropic agents** 7.1.1 Cardiac glycosides 7.1.2 Others **7.2 Anti-arrhythmics** **7.3 Anti-hypertensives** 7.3.1 Central acting sympathetic nervous system inhibitors 7.3.2 Alpha-receptor blockers 7.3.3 Beta-receptor blockers 7.3.4 Alpha- and beta-receptor blockers 7.3.5 Sympathetic nervous blockers 7.3.6 Direct-acting vasodilators 7.3.7 Calcium channel blockers 7.3.8 ACE inhibitors 7.3.9 Angiotensin receptor antagonists 7.3.10 Others **7.4 Anti-anginal agents** 7.4.1 Calcium channel blockers 7.4.2 Beta-receptor blockers 7.4.3 Organic nitrates **7.5 Other vasodilators** 7.5.1 After-load reducers 7.5.2 Peripheral vasodilators **7.6 Vasoconstrictors** **7.7 Hipolipidaemic agents** 7.7.1 Fibrates 7.7.2 HMG-CoA reductase inhibitors (Statins) 7.7.3 Others **7.8 Plasma expanders**
8. BLOOD AND HAEMOPOEITIC **8.1 Haemostatics** **8.2 Anticoagulants** **8.3 Fibrinolytics** **8.4 Platelet aggregation inhibitors** **8.5 Sclerosing agents** **8.6 Haematinics** **8.7 Others**
9. ALCOHOLISM

Appendix B

10. RESPIRATORY SYSTEM **10.1 Coughs and colds** 10.1.1 Antitussives and expectorants 10.1.2 Decongestant, analgesic combinations 10.1.3 Decongestants **10.2 Bronchodilators** 10.2.1 Sympathomimetics 10.2.2 Methylxanthines and combinations 10.2.3 Anticholinergics 10.2.4 Combinations **10.3 Mucolytics** **10.4 Anti-asthmatics** 10.4.1 Glucocorticoids 10.4.2 Leukotriene receptor antagonists 10.4.3 Chromones 10.4.4 Other anti-asthmatics **10.5 Surfactants** **10.6 Others**
11. EAR, NOSE AND THROAT **11.1 Topical nasal preparations** 11.1.1 Antimicrobial and combinations 11.1.2 Glucocorticosteroids 11.1.3 Chromones 11.1.4 Decongestants 11.1.5 Antihistamines 11.1.6 Mucolytics 11.1.7 Others **11.2 Ear drops and ointments** **11.3 Mouth and throat preparations**
12. GASTRO-INTESTINAL TRACT **12.1 Digestants** **12.2 Appetite suppressants** **12.3 Anti-spasmodics** **12.4 Acid reducers** 12.4.1 Antacids 12.4.2 Antacids and combinations 12.4.3 Histamine-2 receptor antagonists 12.4.4 Proton pump inhibitors

Appendix B

12.4.5 Cytoprotective agents 12.4.6 Other acid reducers **12.5 Motility enhancers** **12.6 Laxatives** **12.7 Antidiarrhoels** **12.8 Liver, gall bladder and bile** **12.9 Suppositories and anal ointments** **12.10 Others**
13. ANTHELMINTICS
14. DERMATOLOGICALS **14.1 Anti-bacterial antiseptic agents** **14.2 Anti-parasitics** **14.3 Fungicides** **14.4 Cortico-steroids** 14.4.1 Cortico-steroids with anti-infective agents **14.5 Psoriasis** **14.6 Acne** **14.7 Melanin inhibitors** **14.8 And stimulants** **14.9 Others**
15. OPHTHALMICS **15.1 Anti-infectives** **15.2 Corticoids** **15.3 Combinations (anti infectives with corticoids)** **15.4 Decongestants** **15.5 Mydriatics** **15.6 Glaucoma** **15.7 Others**
16. URINARY SYSTEM **16.1 Diuretics** **16.2 Anti-diuretics** **16.3 Urinary alkalinisers** **16.4 Urinary antiseptics** **16.5 Others**
17. GENITAL SYSTEM **17.1 Contraceptives** 17.1.1 Hormonal (including oral) 17.1.2 Locally acting

Appendix B

17.1.3 Contraceptive devices

17.2 Vaginal preparations

17.3 Oxytocics

17.4 Uterine antispasmodics

17.5 Sexual dysfunction

17.5.1 Others

17.5.2 Erectile dysfunction

18. ANTI-MICROBIALS

18.1 Beta-lactams

18.1.1 Penicillins

18.1.2 Cephalosporins

18.1.3 Others

18.2 Erythromycin and other macrolides

18.3 Aminoglycosides

18.4 Tetracyclines

18.5 Chloramphenicols

18.6 Sulphonamides and combinations

18.7 Quinolones

18.8 Mycobacteria

18.8.1 Tuberculostatics

18.8.2 Anti-leprotics

18.9 Other anti-bacterial agents

18.10 Anti-fungal agents

18.11 Anti-protozoal agents

18.12 Anti-viral agents

19. ENDOCRINE SYSTEM

19.1 Anti-diabetic agents

19.1.1 Insulins

19.1.2 Oral agents

19.2 Anti-hypoglycaemic agents

19.3 Thyroid

19.4 Parathyroid and calcitonin

19.5 Corticosteroids

19.6 Sex hormones

19.6.1 Androgens and anabolic steroids

19.6.2 Oestrogens

19.6.3 Progestogens

19.6.4 Combinations

Appendix B

19.6.5 Others **19.7 Tropic hormones** **19.8 Hormone inhibitors**
20. VITAMINS, TONICS, MINERALS AND ELECTROLYTES **20.1 Vitamins** 20.1.1 Vitamin combinations **20.2 Vitamins with minerals** **20.3 Tonics** **20.4 Minerals and electrolytes**
21. AMINO-ACIDS
22. SPECIAL FOODS
23. CYTOSTATICS
24. Immunological **24.1 Immunosuppressants** **24.2 Immunostimulants**
25. CHELATING AGENTS, ION EXCHANGE PREPARATIONS
26. BIOLOGICALS
27. ENZYMES
28. POISON ANTIDOTES
29. OTHERS
30. MEDICAL GASES

Appendix B

Appendix C

The Nappi codes for all the anti-diabetic drugs as it appears in the MIMS (2004:311-317).

Oral anti-diabetic agents

Dosage form	Nappi-code	Quantity
Biguanides		
Metformin:		
Glucophage (Merck):		
(S3) Tabs	729159-019	500mg (100)
	729159-027	500mg (500)
	729167-003	850mg (60)
	729167-011	850mg (300)
Merck Metformin:		
(S3) Tabs	897957-024	500mg (56)
	897957-032	500mg (84)
	897957-016	500mg (500)
	897961-022	850mg (56)
	897961-014	850mg (300)
Metforal (Al Pharm Ltd):		
(S3) Tabs	702385-001	500mg (100)
	702385-011	500mg (400)
	702363-001	850mg (60)
	702363-001	850mg (240)
Rolab-Metformin HCl 500; 850 (Sandoz):		
(S3) Tabs	719285-003	500mg (100)
	719285-011	500mg (500)
	719293-006	850mg (30)
	719293-014	850mg (300)
Rolab-Metformin HCl 500 FC; 850FC:		
(S3) Tabs	815225-008	500mg (100)
	815225-016	500mg (500)
	815233-019	850mg (60)
	815233-027	850mg (300)
Sulfonylureas		
Glimepiride:		
Amaryl (Aventis):		
(S3) Tabs	831557-001	1mg (30)
	831565-004	2mg (30)
	831537-007	4mg (30)
Glibenclamide:		
Daonil (Aventis):		

(S3) Tabs	717452-018	5mg (30)
	717452-026	5mg (100)
	717452-034	5mg (500)
Diacare (Be-Tabs):		
(S3) Tabs	894502-007	5mg (1000)
Glycomin (Aspen Pharmacare: Pharma):		
(S3) Tabs	729361-004	5mg (30)
	729361-012	5mg (100)
	729361-020	5mg (500)
Norton-Glibenclamide (Aspen Pharmacare: Pharma):		
(S3) Tabs	827053-002	5mg (500)
Rolab-Glibenclamide 5 (Sandoz):		
(S3) Tabs	781258-006	5mg (30)
	781258-002	5mg (500)
Gliclazide:		
Diaglucide (Biogaran) Tema:		
(S3) Tabs	868906-018	80mg (60)
Diamicron (Servier)		
(S3) Tabs	719643-009	80mg (60)
	719463-017	80mg (500)
(S3) MR Tabs	702923-001	30mg (60)
Glucomed (Al Pharm Ltd)		
(S3) Tabs	834599-007	80mg (60)
	834599-015	80mg (500)
Glycron (Aspen Pharmacare: Pharma):		
(S3) Tabs	729361-004	5mg (30)
	729361-012	5mg (100)
	729361-020	5mg (500)
Merck-Gliclazide (Merck Gen):		
(S3) Tabs	700639-003	80mg (60)
	700639-006	80mg (500)
Rolab-Gliclazide 80 (Sandoz)		
(S3) Tabs	834866-005	80mg (60)
	834866-013	80mg (500)
Glipizide:		
Minidiab (Pharmacia):		
(S3) Tabs	743666-003	5mg (100)
Chlorpropamide:		
Hypomide (Aspen Pharmacare:Pharma):		
(S3) Tabs	714062-006	250mg (100)

Appendix C

	714062-014	250mg (500)
Alpha-glucosidase inhibitors		
Acarbose: Glucobay (Bayer): (S4) Tabs	 808156-004 808164-007	 50mg (90) 100mg (90)
Thiazolidinediones		
Pioglitazone: Actos (Eli Lilly): (S3) Tabs	 878243-003 878251-006	 15mg (28) 30mg (28)
Rosiglitazone: Avandia (GSK): (S3) Tabs	 899496-008 899499-003	 2mg (28) 4mg (28)
Meglitinides		
Repaglinide: Novonorm (Novo Nordisk): (S3) Tabs	 861324-005 861332-008 861340-019	 0.5mg (90) 1mg (90) 2mg (90)
Nateglinide: Starlix (Novartis): (S3) Tabs	 893897-001 893900-001	 60mg (84) 120mg (84)

Insulin and Insulin analogues

Dosage form	Nappi-code	Quantity
Ultra fast-acting insulins		
Insulin lispro:		
Humalog (Eli Lilly):		
(S3) Inj	819468-002	10ml vial
	862355-001	5x3ml cartridges
	833142-003	5x3ml humaject pens
	853445-001	5x3ml disposable pen
(S3) Mix 25 Susp	853437-009	10ml vial
	861782-003	5x3ml cartridges
	853445-001	5x3ml disposable pens
Insulin aspartame:		
Novorapid (NovoNordisk):		
(S3) Sol for injection	897767-001	5x3ml multi dose FlexPen
	897775-004	5x3ml multi dose Penfill cartridges
Fast-acting insulins		
Biosynthetic human insulin:		
Humulin R (Eli Lilly):		
(S3) Sol for injection	733431-003	10ml vial
	863564-003	5x3ml cartridge
	833126-008	5x3ml Humaject Pen
Biosynthetic human soluble insulin:		
Actrapid HM (NovoNordisk):		
(S3) Inj	733415-008	1x10ml vial
	824283-007	5x3ml Penfill
	816221-006	5x3ml Penset
Biphasic insulin and insulin analogues		
Soluble insulin and isophane:		
Actraphane HM (NovoNordisk):		
(S3) Inj	733512-003	1x10ml vial
	793876-001	5x3ml Penfill
	816213-003	5x3ml Penset
Biosynthetic human isophane:		
Humulin N (Eli Lilly):		
(S3) Susp. for injection	733458-009	10ml vial
	863556-019	5x3ml cartridges
	825786-002	5x3ml humaject pen
	853453-004	5x3ml disposable pens
Humulin 30/70 (Eli Lilly):		
(S3) Sol. for injection	783811-004	1x10ml vial
	863572-006	5x3ml cartridges
	825794-005	5x3ml humaject pens

Biphasic biosynthetic human insulin, 20% soluble & 80% isophane:		
Mixtard 20/80 (NovoNordisk):		
(S3) Inj.	794619-002	5x3ml Penfill
Insulin glargine:		
Lantus (Aventis):		
(S3) Sol. for inj.	700310-001	1x10ml vial
	700308-001	5x3ml cart.for use with non-disp.pen
	701783-001	5x dispos.pen +3ml cart.
Soluble insulin aspartame & protamine crystalline insulin, 30/70 ratio:		
Novomix 30 (NovoNordisk):		
(S3) Inj.	702086-003	5x3ml multidose FlexPen
	702089-003	5x3ml multidose Penfill cartridges
Intermediate to long-acting insulins		
Zinc biosynthetic human insulin:		
Humulin L (Eli Lilly):		
(S3) Susp. for inj.	733520-006	10ml
Biosynthetic human insulin zinc suspension; 30% amorphous, 70% crystalline:		
Monotard HM (NovoNordisk):		
(S3) Inj.	733423-019	1x10ml vial
Biosynthetic monocomponent isophane insulin:		
Protaphane HM (NovoNordisk):		
(S3) Inj.	733482-007	1x10ml vial
	793884-004	5x3ml Penfill cartridges
	700183-001	5x3ml FlexPen disposable syringes
Ultra long-acting insulins		
Biosynthetic human insulin zinc susp. of monocomponent insulin crystals:		
Ultratard HM (NovoNordisk):		
(S3) Inj.	733563-007	1x10ml vial

Appendix D

Oral anti-diabetic agents			
Class	**Active ingredient**	**Propriety name**	**DDD**
Biguanide	Metformin	Glucophage®	2g
		Merck-Metformin®	2g
		Metforal®	2g
		Rolab-Metformin®	2g
Sulfonylureas	Glimepiride	Amaryl®	2mg
	Glibenclamide	Daonil®	10mg
		Diacare®	10mg
		Glycomin®	10mg
		Norton-Glibenclamide®	10mg
		Rolab-Glibenclamide®	10mg
	Gliclazide	Diaclucide®	0.16g
		Diamicron®	0.16g
		Glucomed®	0.16g
		Glycron®	0.16g
		Merck-Gliclazide®	0.16g
		Rolab-Gliclazide®	0.16g
	Glipizide	Minidiab®	10mg
	Chlorpropamide	Hypomide®	0.375g
Alpha-glucosidase inhibitors	Acarbose	Glucobay®	0.3g
Thiazolidinediones	Pioglitazone	Actos®	30mg
	Rosiglitazone	Avandia®	6mg
Meglitinides	Repaglinide	Novonorm®	6mg
	Nateglinide	Starlix®	0.36g

Insulin and insulin analogues			
Class	**Active ingredient**	**Propriety name**	**DDD**
Ultra fast-acting insulins	Insulin lispro	Humalog®	40 U
	Insulin aspartame	Novorapid®	40U
Fast-acting	Biosynthetic human insulin	Humulin® R	40U
	Biosynthetic human soluble insulin	Actrapid® HM	40U
Biphasic insulin and analogues	Soluble insulin and isophane	Actraphane®	40U
	30% biosynthetic regular human insulin; 70% biosynthetic isophane human insulin	Humulin® 30/70	40U
	Biphasic biosynthetic human insulin suspension comprising 20% soluble and 80% isophane insulin	Mixtard® 20/80	40U
	Insulin glargine	Lantus®	40U
	Soluble insulin aspartame and protamine crystalline insulin in a 30/70 ratio	Novomix® 30	40U
Intermediate to long-acting	Zinc biosynthetic human insulin	Humulin® L	40U
	Biosynthetic human insulin zinc suspension comprising 30% in amorphous state and 70% crystalline	Monotard® HM	40U
	Biosynthetic monocomponent isophane insulin	Protaphane® HM	40U
Ultra long-acting insulin	Biosynthetic human insulin zinc suspension of monocomponent insulin crystals	Ultratard® HM	40U

Appendix D

Appendix E

Table E1: Utilisation of combination of two antidiabetic agents for the time January to April

Agents in combination		No of Rx	Average cost	Std deviation	Total cost
Actos® 15mg	Actraphane® HM Penset 3ml	5	1116.28	31.31	5581.38
	Amaryl® 1mg	5	493.82	3.87	2469.11
	Amaryl® 2mg	7	601.66	17.34	4211.6
	Amaryl® 4mg	8	950.5	345.65	7603.99
	Daonil®	1	588.68	0	588.68
	Diamicron® 80mg	3	551.16	72.51	1653.49
	Glucomed®	3	465.93	0	1397.79
	Glucophage® 500mg	5	475.3	16.58	2376.48
	Glucophage Forte® 850mg	5	494.27	11.81	2471.36
	Glucovance® 500/5mg	2	585.04	0	1170.08
	Glycomin®	3	651.43	37.72	1954.3
	Humalog® Mix 25 Penset	4	401.51	0	1606.04
	Lantus® 1000IU 10ml	1	975.58	0	975.58
	Lantus® 300IU 3ml	1	1256.37	0	1256.37
	Rolab-Metformin® HCl 500mg	3	473.47	7.38	1420.42
	Rolab-Metformin® FC 500mg	3	485.37	58.1	1456.1
	Rolab-Metformin® HCL 850mg	4	472.32	23.35	1889.29
Actos® 30mg	Actraphane® HM Penfill 3ml	1	1238.37	0	1238.37
	Actraphane® HM Penset 3ml	3	1332.04	1.44	3996.13
	Actraphane® HM 10ml Ampoules	2	654.11	0	1308.22
	Amaryl® 2mg	5	781.6	3.96	3908.01
	Amaryl® 4mg	8	1066.69	184.1	8533.54
	Avandia® 4mg	1	1219.25	0	1219.25
	Diamicron® 80mg	3	744.15	52.84	2232.45
	Glucomed®	6	765.76	1.77	4594.56
	Glucophage® 500mg	7	642.06	26.24	4494.44
	Glucophage Forte® 850mg	12	575.49	248.35	6905.85
	Glycomin®	1	744.32	0	744.32
	Glycron®	1	687.85	0	687.85

Table E1: (Continue) Utilisation of combination of two antidiabetic agents for the time January to April

Agents in combination		No of Rx	Average cost	Std deviation	Total cost
	Humalog® 3ml Penset/Prefill	1	2801.56	0	2801.56
	Humalog® Mix 25 Cartridges	1	1847.91	0	1847.91
	Protaphane® HM Penset 3ml	1	1282.43	0	1282.43
	Rolab-Metformin® HCl 500mg	1	651.46	0	651.46
	Rolab-Metformin® FC 850mg	1	690.77	0	690.77
Actraphane® HM Penfill 3ml	Actrapid® HM Penfill 3ml	2	1325.49	8.19	2650.98
	Actrapid® HM Pensets 3ml	1	1340.78	0	1340.78
	Diamicron® 80mg	1	306.06	0	306.06
	Glucophage® 500mg	2	743.85	18.31	1487.69
	Glucophage Forte® 850mg	3	713.96	61.09	2141.89
	Protaphane® HM Penfill 3ml	1	1307.15	0	1307.15
	Rolab-Metformin® HCl 500mg	2	719.96	0.01	1439.91
	Rolab-Metformin® FC 500mg	3	1377.88	3.35	4133.63
	Rolab-Metformin® FC 850mg	1	748.71	0	748.71
	Rolab-Metformin® HCL 850mg	1	709.82	0	709.82
Actraphane® HM Penset 3ml	Actrapid® HM 10ml Ampoules	3	1797.07	40.44	5391.22
	Actrapid® HM Pensets 3ml	3	1423.62	40.43	4270.86
	Amaryl® 2mg	2	1019.3	170.36	2038.6
	Avandia® 2mg	4	1270.52	441.28	5082.09
	Avandia® 4mg	12	1407.08	312.49	16884.93
	Glucobay® 100mg	2	1092.68	951.5	2185.36
	Glucomed®	9	775.01	198.52	6975.12
	Glucophage® 500mg	46	929.06	395.93	42736.7
	Glucophage Forte® 850mg	86	1118.59	524.47	96198.8
	Glucovance® 500/2.5mg	2	897.75	0	1795.5
	Glycomin®	3	1471.01	574.55	4413.04
	Glycron®	1	1051.38	0	1051.38
	Merck-Metformin® 500	2	766.2	0	1532.4
	Merck-Metformin® 850	4	818.9	24.37	3275.61
	Novorapid® 3ml Flexpen	2	1437.57	49.59	2875.13
	Protaphane® HM Penset 3ml	3	2157.36	70.45	6472.09
	Rolab-Gliclazide®	2	727.63	130.29	1455.26
	Rolab-Metformin® HCl 500mg	13	1227.62	442.56	15959.11
	Rolab-Metformin® FC 500mg	19	1006.85	676.34	19130.07

Table E1: (Continue) Utilisation of combination of two antidiabetic agents for the time January to April

Agents in combination		No of Rx	Average cost	Std deviation	Total cost
	Rolab-Metformin® FC 850mg	15	971.03	408.02	14565.43
	Rolab-Metformin® HCL 850mg	14	995.69	488.31	13939.68
	Ultratard® HM 10ml Ampoules	2	849.09	0	1698.18
Actraphane® HM 10ml Ampoules	Actraphane® HM 10ml Ampoules	1	1417.74	0	1417.74
	Amaryl® 2mg	1	552.28	0	552.28
	Glucomed®	2	708.07	0	1416.14
	Glucophage® 500mg	3	647.09	205.21	1941.28
	Glucophage® Forte 850mg	4	409.87	58.2	1639.46
	Glycomin®	1	989.7	0	989.7
	Merck-Metformin® 850	1	789.06	0	789.06
	Novonorm® 0.5mg	1	463.55	0	463.55
	Novonorm® 1.0mg	1	560.62	0	560.62
	Protaphane® HM 10ml Ampoules	1	843.85	0	843.85
	Rolab-Metformin® FC 500mg	1	295.23	0	295.23
	Rolab-Metformin® FC 850mg	2	803.39	5.83	1606.77
	Rolab-Metformin® HCL 850mg	2	403.79	63.47	807.58
Actrapid® HM 10ml Ampoules	Actrapid® HM Penfill 3ml	1	1018.83	0	1018.83
	Glucophage Forte® 850mg	1	448.64	0	448.64
	Humulin® L 10ml Vial	4	2105.95	0	8423.8
	Humulin® N 10ml Vial	1	678.58	0	678.58
	Lantus® 1000IU 10ml	1	671.89	0	671.89
	Lantus® 300IU 3ml	2	1231.66	0	2463.32
	Monotard® HM 10ml Ampoules	30	910.93	374.86	27327.88
	Protaphane® HM 10ml Ampoules	32	1031.4	406.48	33004.89
Actrapid® HM Penfill 3ml	Humalog® 3ml Penset/Prefill	1	1339.16	0	1339.16
	Humulin® L 10ml Vial	2	1012.61	0	2025.22
	Monotard® HM 10ml Ampoules	2	1197.82	560.47	2395.64
	Protaphane® HM Penfill 3ml	13	1641.55	641.01	21340.17
	Ultratard® HM 10ml Ampoules	1	1009.98	0	1009.98
Actrapid® HM Pensets 3ml	Glucophage® 500mg	2	760.23	0	1520.46
	Glucophage Forte® 850mg	4	762.02	143.35	3048.07
	Humulin® L 10ml Vial	4	1062.74	16.81	4250.95
	Humulin® N 10ml Vial	8	1387.47	12.38	11099.74

Table E1: (Continue) Utilisation of combination of two antidiabetic agents for the time January to April

Agents in combination		No of Rx	Average cost	Std deviation	Total cost
	Lantus® 1000IU 10ml	2	1298.2	24.76	2596.39
	Lantus® 300IU 3ml	7	2074.67	842.33	14522.7
	Lantus® 300IU/3ml O/T	4	1369.54	449.82	5478.16
	Monotard® HM 10ml Ampoules	9	1082.61	447.98	9743.45
	Novorapid® 3ml Flexpen	1	1472.58	0	1472.58
	Protaphane® HM Penset 3ml	101	1548.92	579.55	156440.49
	Protaphane® HM 10ml Ampoules	1	843.76	0	843.76
	Rolab-Metformin® HCL 850mg	2	859.47	34.98	1718.93
Amaryl® 1mg	Amaryl® 2mg	33	286.64	55.65	9458.97
	Amaryl® 4mg	8	420.94	122.75	3367.52
	Avandia® 2mg	2	452.99	18.9	905.97
	Diamicron® 80mg	4	224.57	32.52	898.27
	Glucobay® 50mg	2	353.05	0	706.1
	Glucomed®	2	217.49	2.3	434.97
	Glucophage® 500mg	79	185.77	59.21	14675.86
	Glucophage Forte® 850mg	64	215.88	51.56	13816.62
	Glycomin®	3	247.41	0	742.23
	Humalog® Mix 25 Penset	3	1020.96	102.56	3062.87
	Merck-Metformin® 850	2	174.26	0	348.52
	Rolab-Metformin® HCl 500mg	18	167.89	25.14	3022.01
	Rolab-Metformin® FC 500mg	14	183.13	85.43	2563.87
	Rolab-Metformin® FC 850mg	17	199.94	44.46	3398.9
	Rolab-Metformin® HCL 850mg	18	209.65	31.15	3773.71
Amaryl® 2mg	Amaryl® 4mg	25	497.48	144.94	12436.9
	Avandia® 2mg	9	417.54	116	3757.9
	Avandia® 4mg	3	366.86	0	1100.58
	Diamicron® MR 30mg	1	460.38	0	460.38
	Glucophage® 500mg	158	250.15	67.94	39524.44
	Glucophage Forte® 850mg	177	302.29	108.74	53505.68
	Glucovance® 500/2.5mg	4	395.84	0	1583.36
	Glucovance® 500/5mg	1	246.64	0	246.64
	Glycomin®	5	423.24	72.17	2166.18
	Humalog® Mix 25 Penset	3	994.85	0	2984.55
	Humulin® N 3ml Penset	1	853.05	0	853.05

Table E1: (Continue) **Utilisation of combination of two antidiabetic agents for the time January to April**

Agents in combination		No of Rx	Average cost	Std deviation	Total cost
	Merck-Metformin® 500	7	184.95	61.62	1294.68
	Merck-Metformin® 850	1	285.18	0	285.18
	Novonorm® 0.5mg	4	301.64	0	1206.56
	Novonorm 1.0mg	1	406.5	0	406.5
	Novorapid 3ml Flexpen	1	784.64	0	784.64
	Rolab-Metformin HCl 500mg	38	281.14	83.78	10683.35
	Rolab-Metformin FC 500mg	48	263.98	78.42	12671.13
	Rolab-Metformin FC 850mg	35	287.32	65.31	10056.37
	Rolab-Metformin HCL 850mg	27	300.07	52.28	8101.85
Amaryl 4mg	Avandia 2mg	1	533.82	0	533.82
	Avandia 4mg	7	680.18	12.74	4761.29
	Daonil	1	563.64	0	563.64
	Glucomed	13	475.19	41.44	6177.49
	Glucophage 500mg	96	442.05	104.4	42437.11
	Glucophage Forte 850mg	200	474.44	160.31	94888.32
	Glucovance 250/1.25mg	4	395.42	40.7	1581.69
	Glucovance 500/2.5mg	2	559.79	0	1119.58
	Glycomin	3	504.71	17.79	1514.13
	Humulin 30/70 Humaject Injection	1	1745.8	0	1745.8
	Humulin N 3ml Penset	2	1017	0.01	2033.99
	Lantus 300IU/3ml O/T	1	963.65	0	963.65
	Merck-Metformin 500	9	419.39	24.41	3774.49
	Merck-Metformin 850	3	442.93	10.73	1328.8
	Rolab-Gliclazide	1	444.91	0	444.91
	Rolab-Metformin HCl 500mg	28	421.01	153.64	11788.26
	Rolab-Metformin FC 500mg	29	438.15	58.16	12706.4
	Rolab-Metformin FC 850mg	33	480.65	257.66	15861.34
	Rolab-Metformin HCL 850mg	26	433.6	90.8	11273.58
Avandia 2mg	Diamicron 80mg	1	344.02	0	344.02
	Glucomed	6	333.03	128.14	1998.17
	Glucophage 500mg	4	229.72	2.1	918.88
	Humulin 30/70 Humaject Injection	1	1039.06	0	1039.06
	Merck-Metformin 850	3	385.22	68.71	1155.66
	Rolab-Metformin FC 850mg	1	267.09	0	267.09

Table E1: (Continue) Utilisation of combination of two antidiabetic agents for the time January to April

Agents in combination		No of Rx	Average cost	Std deviation	Total cost
	Rolab-Metformin HCL 850mg	1	301.15	0	301.15
Avandia 4mg	Daonil	1	521.95	0	521.95
	Diamicron 80mg	2	418.05	41.2	836.1
	Diamicron MR 30mg	3	558.1	222.14	1674.3
	Glucomed	10	441.63	38.36	4416.27
	Glucophage 500mg	8	474.3	152.05	3794.41
	Glucophage Forte 850mg	35	504.13	138.99	17644.47
	Glycomin	3	463.09	0	1389.27
	Humalog Mix 25 Cartridges	1	1062.61	0	1062.61
	Lantus 300IU 3ml	5	1697.21	378.36	8486.03
	Novomix 30 Flexpen 3ml Injection	4	1061.13	15.07	4244.5
	Novonorm 1.0mg	2	466.41	91.27	932.81
	Protaphane HM Penfill 3ml	2	965.54	0	1931.08
	Rolab-Metformin HCl 500mg	2	396.67	0.16	793.34
	Rolab-Metformin FC 500mg	2	381.39	5.64	762.77
	Rolab-Metformin FC 850mg	5	398.16	40.55	1990.78
	Rolab-Metformin HCL 850mg	4	427.67	8.21	1710.67
Daonil	Glucobay 50mg	6	709.67	290.24	4258.02
	Glucophage 500mg	75	545.91	194.66	40943.05
	Glucophage Forte 850mg	51	630.86	179.05	32173.8
	Merck-Metformin 500	1	693.27	0	693.27
	Rolab-Metformin HCl 500mg	33	714.24	168.56	23570.06
	Rolab-Metformin FC 500mg	15	583.3	219.24	8749.5
	Rolab-Metformin FC 850mg	9	437.23	96.27	3935.04
	Rolab-Metformin HCL 850mg	5	561.43	174.02	2807.15
Diacare 5mg	Glycron	1	136.79	0	136.79
	Rolab-Metformin HCl 500mg	1	125.17	0	125.17
	Rolab-Metformin FC 500mg	1	93.4	0	93.4
Diaglucide 80mg	Glucophage 500mg	25	182.26	77.65	4556.61
	Glucophage Forte 850mg	27	238.9	81.05	6450.23
	Glycomin	1	160.5	0	160.5
	Merck-Metformin 500	3	224.35	70.73	673.05
	Merck-Metformin 850	2	263.49	0	526.98
	Rolab-Metformin HCl 500mg	5	199.44	48.35	997.22

Table E1: (Continue) Utilisation of combination of two antidiabetic agents for the time January to April

Agents in combination		No of Rx	Average cost	Std deviation	Total cost
	Rolab-Metformin FC 500mg	3	154.14	60.21	462.43
	Rolab-Metformin FC 850mg	10	238.77	48.85	2387.73
	Rolab-Metformin HCL 850mg	6	217.12	44.32	1302.73
Diamicron 80mg	Glucophage 500mg	160	203.86	78.68	32617.68
	Glucophage Forte 850mg	290	231.66	68.39	67182.64
	Glycomin	1	270.02	0	270.02
	Humalog Mix 25 Cartridges	1	739.41	0	739.41
	Merck-Metformin 500	1	235.41	0	235.43
	Merck-Metformin 850	8	249.9	85.77	1999.18
	Monotard HM 10ml Ampoules	2	471.68	0	943.36
	Novomix 30 Flexpen 3ml Injection	4	656.84	258.3	2627.34
	Protaphane HM Penfill 3ml	1	770.36	0	770.36
	Rolab-Metformin HCl 500mg	40	226.69	65.26	9067.62
	Rolab-Metformin FC 500mg	36	210.87	62.72	7591.29
	Rolab-Metformin FC 850mg	35	228	90.12	7980.02
	Rolab-Metformin HCL 850mg	30	206.44	80.76	6193.27
Diamicron MR 30mg	Glucobay 50mg	1	415.5	0	415.5
	Glucophage 500mg	30	194.69	54.62	5840.83
	Glucophage Forte 850mg	63	258.58	110.83	16290.5
	Lantus 300IU 3ml	1	1037.3	0	1037.3
	Merck-Metformin 500	8	164.32	71.59	1314.59
	Merck-Metformin 850	10	194.42	32.61	1944.19
	Novomix 30 Flexpen 3ml Injection	3	892.31	20.3	2676.93
	Novorapid 3ml Penfill	2	883.48	0.04	1766.95
	Rolab-Metformin HCl 500mg	6	303.89	149.54	1823.32
	Rolab-Metformin FC 500mg	9	176.47	53.36	1588.23
	Rolab-Metformin FC 850mg	16	210.31	44.14	3365.02
	Rolab-Metformin HCL 850mg	21	243.8	50.78	5119.7
Euglycon 5mg	Glucophage Forte 850mg	3	941.58	91.52	2824.74
Glucobay 100mg	Glucomed	10	394.74	72.23	3947.44
	Glucophage 500mg	1	330.62	0	330.62
	Glucophage Forte 850mg	1	462.29	0	462.29
	Glycomin	5	521.32	31.73	2606.61
	Glygard	1	452.22	0	452.22

Table E1: (Continue) Utilisation of combination of two antidiabetic agents for the time January to April

Agents in combination		No of Rx	Average cost	Std deviation	Total cost
	Protaphane HM Penset 3ml	1	1050.53	0	1050.53
Glucobay 50mg	Glucomed	7	352.13	73.95	2464.89
	Glucophage 500mg	3	315.55	39.16	946.65
	Glyben	3	384.06	12.99	1152.18
	Glycomin	5	424.03	35.89	2120.16
	Norton-Glibenclamide	2	284.86	0	569.72
	Rolab-Gliclazide	1	268.1	0	268.1
Glucomed 80mg	Glucophage 500mg	360	181.28	63.3	65261.48
	Glucophage Forte 850mg	549	209.17	67.29	114836.03
	Glyben	2	172.18	0	344.36
	Glycomin	7	218	39.66	1526.04
	Humalog Mix 25 Penset	1	886.45	0	886.45
	Humalog Mix 25 Cartridges	1	888.63	0	888.63
	Humulin 30/70 3ml Cartridges	4	841.11	293.78	3364.42
	Humulin L 10ml Vial	1	441.09	0	441.09
	Humulin N 10ml Vial	4	402.09	0	1608.36
	Humulin N 3ml Penset	3	755.83	132.65	2267.5
	Lantus 300IU/3ml O/T	1	1916.88	0	1916.88
	Merck-Metformin 500	23	167.47	48.19	3851.84
	Merck-Metformin 850	43	238.67	50.04	10271.4
	Novomix 30 Flexpen 3ml Injection	1	771.34	0	771.34
	Novonorm 1.0mg	2	292.97	0	585.94
	Novonorm 2.0mg	4	741.1	0	2964.4
	Protaphane HM Penfill 3ml	1	735.65	0	735.65
	Rolab-Metformin HCl 500mg	135	164.43	53.99	22197.77
	Rolab-Metformin FC 500mg	183	160.11	60.94	29300.71
	Rolab-Metformin FC 850mg	247	205.69	62.43	50804.55
	Rolab-Metformin HCL 850mg	131	215.56	60.46	28237.74
Glucophage 500mg	Glucophage Forte 850mg	17	102.61	29.98	1744.39
	Glucovance 500/2.5mg	1	131.52	0	131.52
	Glyben	35	207.95	103.46	7278.25
	Glycomin	518	233.65	96.71	121028.85
	Glycron	8	159.52	62.16	1276.16
	Humalog 3ml Penset/Prefill	5	1394.03	632.79	6970.15

Table E1: (Continue) Utilisation of combination of two antidiabetic agents for the time January to April

Agents in combination		No of Rx	Average cost	Std deviation	Total cost
	Humalog Mix 25 Injection	1	468.97	0	468.97
	Humalog Mix 25 Penset	37	673.95	408.6	24936.08
	Humulin L 10ml Vial	4	467.67	28.08	1870.68
	Humulin N 10ml Vial	2	417.14	0	834.28
	Lantus 1000IU 10ml	3	1178.54	415.88	8535.63
	Lantus 300IU 3ml	4	1187.83	442.24	4751.31
	Lantus 300IU/3ml O/T	2	980.22	0.01	1960.43
	Merck-Gliclazide	4	226.01	0	904.04
	Minidiab	20	264.51	108.47	5290.13
	Mixtard 20/80 Penfill	3	1159.86	380.94	3479.57
	Monotard HM 10ml Ampoules	7	419.62	21.61	2937.32
	Norton-Glibenclamide	2	115.45	104.84	230.9
	Novomix 30 Flexpen 3ml Injection	24	930.99	338.54	22343.71
	Novonorm 0.5mg	6	210.18	18.61	1261.1
	Novonorm 1.0mg	4	328.87	72.85	1315.46
	Novonorm 2.0mg	3	446.16	8.2	1338.48
	Novorapid 3ml Penfill	1	777.05	0	777.05
	Protaphane HM Penset 3ml	17	719.98	128.31	12239.66
	Protaphane HM 10ml Ampoules	2	776.04	0	1552.08
	Rolab-Gliclazide	41	180.68	68.09	7407.82
	Rolab-Metformin FC 850mg	1	109.85	0	109.85
	Starlix FCT 120mg	7	524.46	15.9	3671.23
Glucophage Forte 850mg	Glucovance 250/1.25mg	1	164.85	0	164.85
	Glucovance 500/2.5mg	3	254.87	0	764.61
	Glyben	29	212.9	64.69	6174.04
	Glycomin	379	270.58	85.96	102549
	Glycron	16	147.13	89.1	2354.02
	Glygard	4	167.14	36.41	668.55
	Humalog 3ml Penset/Prefill	3	1613.16	739.98	4839.47
	Humalog Mix 25 Injection	1	873.1	0	873.1
	Humalog Mix 25 Penset	63	1037.68	648.75	65374.07
	Humalog Mix 25 Cartridges	7	1138.97	397.76	7972.81
	Humulin 30/70 3ml Cartridges	6	734.15	0.01	4404.88
	Humulin L 10ml Vial	8	385.36	133.03	3082.9

Table E1: (Continue) Utilisation of combination of two antidiabetic agents for the time January to April

Agents in combination		No of Rx	Average cost	Std deviation	Total cost
	Humulin N 3ml Penset	6	739.14	108.69	4434.86
	Hypomide	6	199.97	15.19	1199.83
	Lantus 1000IU 10ml	2	678.77	10.3	1357.54
	Lantus 300IU 3ml	14	1202.78	430.88	16838.88
	Lantus 300IU/3ml O/T	8	1002.89	175.19	8023.14
	Merck-Gliclazide	4	135.73	25.2	542.92
	Minidiab	25	421.89	203.23	10547.14
	Mixtard 20/80 Penfill	2	758.39	0	1516.78
	Novomix 30 Flexpen 3ml Injection	53	962.91	387.76	51034.21
	Novomix 30 Penfill 3ml Injection	10	1313.64	333	13136.39
	Novonorm 0.5mg	9	243.25	26.31	2189.29
	Novonorm 1.0mg	10	314.9	22.28	3148.96
	Novonorm 2.0mg	13	448.02	39.75	5824.3
	Novorapid 3ml Penfill	1	1532.5	0	1532.5
	Protaphane HM Penfill 3ml	3	622.88	110.04	1868.64
	Protaphane HM Penset 3ml	20	790.22	276.16	15804.33
	Protaphane HM 10ml Ampoules	1	495.83	0	495.83
	Rolab-Gliclazide	94	196.55	59.45	18476.03
	Rolab-Metformin HCl 500mg	1	145.73	0	145.73
	Starlix FCT 120mg	1	547.2	0	547.2
Glucovance 250/1.25mg	Glucovance 500/2.5mg	3	155.94	0	467.82
	Merck-Metformin 850	1	192.2	0	192.2
Glucovance 500/2.5mg	Lantus 300IU 3ml	1	1070.31	0	1070.31
	Novomix 30 Flexpen 3ml Injection	1	729.2	0	729.2
	Protaphane HM Penset 3ml	1	666.85	0	666.85
Glucovance 500/5mg	Humalog Mix 25 Penset	1	932.37	0	932.37
	Lantus 300IU/3ml O/T	2	1268.3	0	2536.6
	Protaphane HM Penset 3ml	2	1427.66	485.65	2855.31
	Rolab-Metformin FC 850mg	1	150.35	0	150.35
Glyben 5mg	Humalog Mix 25 Penset	1	869.94	0	869.94
	Merck-Metformin 500	5	208.7	97.51	1043.52
	Merck-Metformin 850	1	208.82	0	208.82
	Protaphane HM Penset 3ml	1	670.25	0	670.25
	Rolab-Metformin HCl 500mg	30	210.56	101.82	6316.89

Table E1: (Continue) Utilisation of combination of two antidiabetic agents for the time January to April

Agents in combination		No of Rx	Average cost	Std deviation	Total cost
	Rolab-Metformin FC 500mg	33	185.08	65.81	6107.65
	Rolab-Metformin FC 850mg	42	268.94	92.68	11295.46
	Rolab-Metformin HCL 850mg	38	217.43	82	8262.27
Glycomin 5mg	Glycron	1	287.18	0	287.18
	Glygard	1	160.91	0	160.91
	Humalog Mix 25 Penset	1	88.4	0	88.4
	Lantus 300IU 3ml	2	1150.42	0	2300.84
	Lantus 300IU/3ml O/T	1	606.24	0	606.24
	Merck-Gliclazide	1	100.46	0	100.46
	Merck-Metformin 500	20	194.02	67.15	3880.36
	Merck-Metformin 850	17	179.32	116.25	3048.36
	Novomix 30 Flexpen 3ml Injection	4	951.81	0	3807.24
	Novonorm 1.0mg	1	281.5	0	281.5
	Novonorm 2.0mg	1	565.33	0	565.33
	Protaphane HM Penset 3ml	8	1068.64	321.4	8549.13
	Protaphane HM 10ml Ampoules	2	358.33	0	716.66
	Rolab-Gliclazide	2	273.08	0	546.16
	Rolab-Metformin HCl 500mg	231	243.55	93.43	56260.37
	Rolab-Metformin FC 500mg	230	214.01	88.04	49222.08
	Rolab-Metformin FC 850mg	123	256.69	90.66	31573.26
	Rolab-Metformin HCL 850mg	100	270.29	86.59	27028.91
Glycron 80mg	Merck-Metformin 850	3	166.05	10.6	498.16
	Protaphane HM 10ml Ampoules	1	526.65	0	526.65
	Rolab-Metformin HCl 500mg	6	182.34	47.71	1094.06
	Rolab-Metformin FC 500mg	21	188.16	62.16	3951.44
	Rolab-Metformin FC 850mg	12	184.65	63.16	2215.85
	Rolab-Metformin HCL 850mg	6	163.11	22.24	978.68
Glygard	Merck-Metformin 850	1	225.82	0	225.82
	Rolab-Metformin HCl 500mg	1	48.45	0	48.45
	Rolab-Metformin FC 500mg	4	111.09	6.32	444.35
	Rolab-Metformin FC 850mg	12	220.5	50.8	2646.03
	Rolab-Metformin HCL 850mg	1	176.27	0	176.27
Humulin 30/70 Humaject Injection	Rolab-Metformin HCL 850mg	2	2917.98	0	5835.96

Table E1: (Continue) Utilisation of combination of two antidiabetic agents for the time January to April

Agents in combination		No of Rx	Average cost	Std deviation	Total cost
Humulin R Humaject Pen 5ml	Humulin N 3ml Penset	2	639.98	648.46	1279.96
Humalog 10ml Ampoules	Humulin L 10ml Vial	6	831.01	166.32	4986.06
	Humulin N 10ml Vial	10	877.56	324.3	8775.55
	Lantus 1000IU 10ml	1	989.43	0	989.43
	Lantus 300IU 3ml	1	1279.7	0	1279.7
	Rolab-Metformin FC 850mg	1	955.15	0	955.15
Humalog 3ml Cartridges Injection	Humalog Mix 25 Cartridges	3	1468.28	0	4404.84
	Humulin L 10ml Vial	3	1085.9	0.85	3257.7
	Humulin N 3ml Cartridges	15	2284.14	516.3	34262.11
	Humulin N 3ml Penset	5	1442	149.71	7209.98
	Lantus 1000IU 10ml	1	1324.73	0	1324.73
	Lantus 300IU 3ml	13	1604.57	3.9	20859.43
	Lantus 300IU/3ml O/T	1	1603.49	0	1603.49
	Protaphane HM Penfill 3ml	2	1370.55	13.33	2741.09
	Protaphane HM Penset 3ml	6	1327.79	142.01	7966.71
	Ultratard HM 10ml Ampoules	1	1432.83	0	1432.83
Humalog 3ml Penset/Prefill	Humalog Mix 25 Injection	1	1163.31	0	1163.31
	Humulin L 10ml Vial	55	1259.29	366.51	69261.18
	Humulin N 10ml Vial	6	1067.8	0.01	6406.8
	Humulin N 3ml Cartridges	3	1465.84	450.14	4397.51
	Humulin N 3ml Penset	130	1506.86	537.51	195892.06
	Lantus 1000IU 10ml	3	1759.88	762.05	5279.64
	Lantus 300IU 3ml	43	2201.41	1009.36	94660.7
	Lantus 300IU/3ml O/T	27	1871.77	876.85	50537.87
	Monotard HM 10ml Ampoules	2	1089.98	0	2179.96
	Protaphane HM Penfill 3ml	10	1527.71	437.68	15277.14
	Protaphane HM Penset 3ml	69	1633.76	426.14	112729.5
	Protaphane HM 10ml Ampoules	1	1741.38	0	1741.38
	Rolab-Metformin HCl 500mg	1	657.49	0	657.49
	Rolab-Metformin FC 500mg	2	1588.09	0	3176.18
	Rolab-Metformin HCL 850mg	4	989.57	396.73	3958.29
Humalog Mix 25 Penset	Humulin N 3ml Penset	6	1307.39	393.64	7844.36
	Lantus 300IU 3ml	1	1683.97	0	1683.97

Table E1: (Continue) Utilisation of combination of two antidiabetic agents for the time January to April

Agents in combination		No of Rx	Average cost	Std deviation	Total cost
	Merck-Metformin 500	2	1654.75	0	3309.5
	Merck-Metformin 850	1	1364.12	0	1364.12
	Novonorm 2.0mg	2	1053.24	0	2106.48
	Novorapid 3ml Penfill	1	1515.46	0	1515.46
	Protaphane HM Penset 3ml	4	1115.98	324.29	4463.91
	Rolab-Gliclazide	2	883.11	0	1766.22
	Rolab-Metformin HCl 500mg	14	506.85	404.46	7095.85
	Rolab-Metformin FC 500mg	19	778.81	347.34	14797.38
	Rolab-Metformin FC 850mg	12	503.96	416.55	6047.53
	Rolab-Metformin HCL 850mg	14	805.92	492.7	11282.92
Humalog Mix 25 Cartridges	Humalog Mix 25 Cartridges	1	1483.94	0	1483.94
	Lantus 300IU 3ml	6	1551.52	127.3	9309.13
	Protaphane HM Penset 3ml	3	1663.67	423	4991.01
	Rolab-Metformin HCl 500mg	3	800.82	10.48	2402.47
	Rolab-Metformin HCL 850mg	3	967.96	245.25	2903.87
Humulin 30/70 3ml Cartridges	Rolab-Metformin FC 850mg	1	587.27	0	587.27
	Rolab-Metformin HCL 850mg	2	1364.92	6.82	2729.84
Humulin L 10ml Vial	Humulin R 10ml Vial	1	708.44	0	708.44
	Humulin R 3ml Cartridges	2	864.02	192.16	1728.04
	Merck-Metformin 850	1	794.77	0	794.77
	Novorapid 3ml Flexpen	1	1827.75	0	1827.75
	Rolab-Gliclazide	2	481.79	0	963.58
	Rolab-Metformin HCl 500mg	4	410.69	3.45	1642.75
	Rolab-Metformin FC 500mg	2	409.93	4.1	819.86
	Rolab-Metformin HCL 850mg	2	623.06	256.57	1246.12
Humulin N 10ml Vial	Humulin R 10ml Vial	16	763.42	147.09	12214.68
Humulin N 3ml Cartridges	Humulin R 3ml Cartridges	2	1249.68	0.01	2499.35
Humulin N 3ml Penset	Humulin R 10ml Vial	1	2420.39	0	2420.39
	Humulin R 3ml Cartridges	4	2378.19	1414.66	9512.75
	Novorapid 3ml Flexpen	3	978.37	15.69	2935.11
	Rolab-Gliclazide	4	664.53	141.98	2658.12
	Rolab-Metformin FC 850mg	2	762.87	0	1525.74
	Rolab-Metformin HCL 850mg	2	755.24	0	1510.48
Humulin R 3ml Cartridges	Lantus 300IU 3ml	1	1406.28	0	1406.28

Table E1: (Continue) Utilisation of combination of two antidiabetic agents for the time January to April

Agents in combination		No of Rx	Average cost	Std deviation	Total cost
	Lantus 300IU/3ml O/T	1	1536.29	0	1536.29
	Ultratard HM 10ml Ampoules	4	997.24	0	3988.96
Hypomide 250mg	Merck-Metformin 500	1	102.68	0	102.68
	Rolab-Metformin HCl 500mg	2	104.78	0	209.56
	Rolab-Metformin HCL 850mg	1	328.57	0	328.57
Lantus 1000Iu 10ml	Novorapid 3ml Flexpen	2	1307.52	34.75	2615.03
	Rolab-Metformin HCl 500mg	3	636.8	3.33	1910.4
	Rolab-Metformin FC 500mg	3	499.26	10.74	1497.77
	Rolab-Metformin FC 850mg	1	1259.63	0	1259.63
Lantus 300IU 3ml	Novorapid 3ml Flexpen	50	1633.12	181.61	81656.24
	Novorapid 3ml Penfill	7	1584.31	8.71	11090.15
	Rolab-Metformin HCl 500mg	2	955.61	6.15	1911.22
	Rolab-Metformin FC 500mg	1	980.27	0	980.27
Lantus 300IU/3ml O/T	Novomix 30 Flexpen 3ml Injection	1	1608.31	0	1608.31
	Novorapid 3ml Flexpen	24	1353.19	467.82	32476.54
	Novorapid 3ml Penfill	2	1351.96	303.94	2703.91
Merck-Gliclazide	Merck-Metformin 500	3	92.94	75.06	278.81
	Merck-Metformin 850	5	128.08	73.66	640.38
	Rolab-Metformin FC 500mg	1	168.42	0	168.42
	Rolab-Metformin FC 850mg	3	187.01	0	561.03
	Rolab-Metformin HCL 850mg	2	128.85	74.88	257.7
Merck-Metformin 500mg	Novomix 30 Flexpen 3ml Injection	2	836.17	0	1672.34
	Novonorm 1.0mg	1	158.27	0	158.27
	Protaphane HM Penset 3ml	2	629.06	2.23	1258.11
	Rolab-Gliclazide	11	172.42	99.61	1896.62
Merck-Metformin 850mg	Minidiab	5	319.64	6.39	1598.18
	Novomix 30 Flexpen 3ml Injection	2	828.46	11.41	1656.92
	Novonorm 2.0mg	4	435.03	0	1740.12
	Protaphane HM Penset 3ml	2	775.61	0	1551.12
	Rolab-Gliclazide	9	227	33.83	2043.03
Minidiab 5mg	Protaphane HM Penset 3ml	2	1120.72	0	2241.44
	Rolab-Metformin HCl 500mg	19	291.12	122.63	5531.31
	Rolab-Metformin FC 500mg	6	348.69	40.64	2092.16
	Rolab-Metformin FC 850mg	2	248.94	0	497.88

Table E1: (Continue) Utilisation of combination of two antidiabetic agents for the time January to April

Agents in combination		No of Rx	Average cost	Std deviation	Total cost
	Rolab-Metformin HCL 850mg	10	440.26	249.52	4402.56
Mixtard 20/80 Penfill	Rolab-Metformin HCL 850mg	2	695.85	49.51	1391.7
Monotard 10ml Ampoules	Novorapid 3ml Flexpen	1	1087.61	0	1087.61
Norton-Glibenclamide	Rolab-Metformin HCl 500mg	6	99.33	14.04	595.98
	Rolab-Metformin HCL 850mg	1	107.57	0	107.57
Novomix 30 Flexpen 3ml Injection	Novorapid 3ml Flexpen	2	1474.98	0	2949.96
	Rolab-Metformin HCl 500mg	4	862.25	481.48	3449.01
	Rolab-Metformin FC 500mg	8	654.93	101.33	5239.45
	Rolab-Metformin FC 850mg	16	771.49	99.19	12343.76
	Rolab-Metformin HCL 850mg	2	714.11	103.78	1428.21
Novomix 30 Penfill 3ml Injection	Rolab-Metformin FC 850mg	3	889.35	127.91	2668.04
	Rolab-Metformin HCL 850mg	4	1566.9	28.14	6267.6
Novonorm 0.5mg	Rolab-Metformin FC 500mg	2	165.58	4.1	331.16
	Rolab-Metformin FC 850mg	1	197.27	0	197.27
	Rolab-Metformin HCL 850mg	4	184.49	64.18	737.95
Novonorm 1.0mg	Rolab-Metformin HCl 500mg	5	302.94	19.4	1514.69
	Rolab-Metformin FC 500mg	2	288.97	6.12	577.94
	Rolab-Metformin FC 850mg	1	208.97	0	208.97
	Rolab-Metformin HCL 850mg	5	307.08	25.29	1535.38
Novonorm 2.0mg	Rolab-Metformin HCl 500mg	6	403.39	3.17	2420.36
	Rolab-Metformin FC 850mg	3	276.9	103.36	830.69
Novorapid 3ml Flexpen	Protaphane HM Penfill 3ml	3	1249.6	244.75	3748.81
	Protaphane HM Penset 3ml	29	1471.93	438.39	42685.91
	Protaphane HM 10ml Ampoules	2	1083.9	0	2167.8
	Rolab-Metformin FC 500mg	1	487.09	0	487.09
Novorapid 3ml Penfill	Protaphane HM Penfill 3ml	8	1317.29	102.12	10538.29
	Protaphane HM Penset 3ml	5	1694.14	389.47	8470.72
	Protaphane HM 10ml Ampoules	3	1763.35	24.09	5290.05
Protaphane HM Penfill 3ml	Rolab-Metformin FC 500mg	3	710.4	8.13	2131.21
Protaphane HM Penset 3ml	Protaphane HM Penset 3ml	1	607.36	0	607.36
	Rolab-Gliclazide	3	705.71	24.92	2117.12
	Rolab-Metformin HCl 500mg	3	770.67	25.63	2312.01
	Rolab-Metformin FC 500mg	5	662.22	112.96	3311.12

Table E1: (Continue) Utilisation of combination of two antidiabetic agents for the time January to April

Agents in combination		No of Rx	Average cost	Std deviation	Total cost
	Rolab-Metformin FC 850mg	6	673.63	106.46	4041.76
	Rolab-Metformin HCL 850mg	6	758.32	79.44	4549.91
Protaphane HM 10ml Ampoules	Rolab-Metformin FC 500mg	3	422.3	13.25	1266.9
	Rolab-Metformin FC 850mg	1	558.58	0	558.58
Rolab-Gliclazide	Rolab-Metformin HCl 500mg	48	204.07	62.7	9795.57
	Rolab-Metformin FC 500mg	67	159.41	56.72	10680.54
	Rolab-Metformin FC 850mg	92	196.64	60.83	18091.06
	Rolab-Metformin HCL 850mg	93	191.38	58.33	17798.06
Rolab-Metformin HCl 500mg	Rolab-Metformin HCl 500mg	1	66.02	0	66.02
	Rolab-Metformin FC 500mg	2	136.05	22.33	272.1
	Rolab-Metformin FC 850mg	1	78.2	0	78.2
	Rolab-Metformin HCL 850mg	6	116.4	36.02	698.41
Rolab-Metformin FC 500mg	Starlix FCT 120mg	2	458.72	55.82	917.43
Rolab-Metformin HCL 850mg	Ultratard HM 10ml Ampoules	1	847.31	0	847.31

Table E2: Utilisation of the combination of three antidiabetic agents for the time January to April

Agents in combination			No of Rx	Average cost	Std deviation	Total cost
Actos 15mg	Actos 30mg	Amaryl 1mg	5	1073.03	0	5365.3
		Amaryl 2mg	1	1179.77	0	1179.77
		Rolab-Metformin HCl 850mg	3	1118.49	8.34	3355.48
	Actraphane HM Penset 3ml	Amaryl 4mg	1	1531.26	0	1531.26
	Actrapid HM 10ml Ampoules	Protaphane HM 10ml Ampoules	2	1120.75	0	2241.5
	Amaryl 1mg	Glucophage Forte 850mg	1	597.43	0	597.43
	Amaryl 4mg	Glucophage 500mg	2	817.48	0	1634.96
		Rolab-Metformin HCl 500mg	1	846.81	0	846.81
		Rolab-Metformin FC 500mg	2	822.66	7.32	1645.31
		Rolab-Metformin HCl 850mg	2	877.14	0	1754.28
	Diamicron 80mg	Glucophage Forte 850mg	1	614	0	614
	Glucomed 80mg	Rolab-Metformin HCl 500mg	1	575.35	0	575.35
		Rolab-Metformin FC 850mg	3	652.03	15.84	1956.08
	Glucophage 500mg	Humalog Mix 25 Penset	3	2861.26	102.17	8583.77
	Glucophage Forte 850mg	Glycron 80mg	1	580.45	0	580.45
	Glycomin 5mg	Protaphane HM Penset 3ml	4	1973.46	0	7893.84
	Humalog 3ml Penset Prefill	Lantus 300IU 3ml	2	2735.07	0	5470.14
	Humalog Mix 25 Penset	Rolab-Metformin FC 500mg	1	1256.8	0	1256.8
Actos 30mg	Amaryl 4mg	Glycomin	1	1029.43	0	1029.43
		Protaphane HM 10ml Ampoules	1	1298.57	0	1298.57
		Rolab-Metformin HCl 500mg	1	1061.94	0	1061.94
	Diamicron 80mg	Glucobay 50	2	1063.94	0	2127.88
		Glucophage 500mg	1	977.38	0	977.38
	Glucomed 80mg	Glucophage 500mg	1	876.13	0	876.13
	Glucophage 500mg	Humalog mix 25 Cartridges	3	1828.72	372.97	5486.17
		Lantus 300IU 3ml	2	1579.67	0	3159.34
		Lantus 300IU/3ml O/T	1	1529.92	0	1529.92
	Glycron 80mg	Rolab-Metformin FC 850mg	1	781.24	0	781.24
	Humalog 3ml Penset Prefill	Humulin N 3ml Penset	1	4771.65	0	4771.65
	Lantus 300IU 3ml	Rolab-Metformin HCl 500mg	1	1598.77	0	1598.77
Actraphane HM Penfill 3ml	Actrapid HM Penfill 3ml	Protaphane HM Penfill 3ml	2	1754.01	301.04	3508.01

Table E2: (Continue) Utilisation of the combination of three antidiabetic agents for the time January to April

Agents in combination			No of Rx	Average cost	Std deviation	Total cost
Actraphane HM Penset 1.5ml	Glucomed 80mg	Merck-Metformin 850mg	1	486.44	0	486.44
Actraphane HM Penset 3ml	Actrapid Penset 3ml	Glucophage 500mg	2	1078.59	0	2157.18
		Glucophage Forte 850mg	1	1498.82	0	1498.82
	Amaryl 2mg	Avandia 4mg	1	1278.75	0	1278.75
	Diaglucide 80mg	Merck-Metformin 500mg	1	775.39	0	775.39
	Diamicron 80mg	Glucophage Forte 850mg	1	463.38	0	463.38
		Rolab-Metformin HCl 500mg	3	901.08	20.27	2703.25
	Glucomed 80mg	Glucophage 500mg	6	826.27	178.92	4957.61
		Glucophage Forte 850mg	3	840.49	112.29	2521.47
		Rolab-Metformin FC 500mg	1	676.78	0	676.78
	Glucophage Forte 850mg	Glycomin	1	791.65	0	791.65
		Rolab-Gliclazide	1	918.3	0	918.3
	Glycron 80mg	Rolab-Metformin HCl 500mg	2	734.74	0	1469.48
	Lantus 300IU/3ml O/T	Rolab-Metformin HCl 850mg	1	1616.15	0	1616.15
	Rolab-Gliclazide	Rolab-Metformin FC 850mg	2	1144.3	0	2288.6
Actraphane HM 10ml Ampoules	Actrapid 10ml Ampoules	Glucophage Forte 850mg	2	672.68	102.3	1345.35
	Glycomin 5mg	Rolab-Metformin FC 850mg	1	695.31	0	695.31
Actrapid HM 10ml Ampoules	Diamicron 80mg	Glucophage Forte 850mg	2	600.27	0	1200.54
	Glycomin 5mg	Rolab-Metformin HCl 500mg	1	254.7	0	254.7
Actrapid HM Penfill 3ml	Glucophage 500mg	Protaphane HM Penset 3ml	1	1651.21	0	1651.21
	Protaphane HM Penset 3ml	Rolab-Metformin HCl 850mg	2	2770.14	40.74	5540.27
Actrapid HM Pensets 3ml	Glucomed 80mg	Rolab-Metformin HCl 500mg	1	848.58	0	848.58
	Glucophage 500mg	Lantus 300IU 3ml	1	1695.52	0	1685.52
		Protaphane HM Penset 3ml	4	1396.93	284.37	5587.73
		Humulin L 10ml Vial	2	3009.93	0	6019.86
		Protaphane HM Penset 3ml	2	1459.98	35.9	2919.95
		Rolab-Gliclazide	1	1181.92	0	1181.92
		Merck-Metformin 500mg	1	1670.46	0	1670.46
		Rolab-Metformin FC 850mg	1	2309.04	0	2309.04
		Rolab-Metformin HCl 850mg	3	2151.98	691.23	6455.94
Amaryl 1mg	Amaryl 2mg	Avandia 4mg	1	1250.74	0	1250.74

Table E2: (Continue) Utilisation of the combination of three antidiabetic agents for the time January to April

Agents in combination			No of Rx	Average cost	Std deviation	Total cost
		Glucophage 500mg	13	361.83	29.93	4703.73
		Glucophage Forte 850mg	7	358.24	70.3	2507.65
		Rolab-Metformin HCl 500mg	4	350.23	42.23	1400.92
		Rolab-Metformin FC 500mg	13	356.95	24.26	4640.4
	Amaryl 4mg	Glucophage 500mg	3	522.69	1.39	1568.06
	Glucomed 80mg	Rolab-Metformin HCl 500mg	2	307.67	0.01	615.34
Amaryl 2mg	Amaryl 4mg	Glucophage 500mg	6	547	173.03	3282
		Glucophage Forte 850mg	15	667.97	32.88	10019.62
		Rolab-Metformin HCl 500mg	4	333.29	208.33	1333.16
		Rolab-Metformin FC 500mg	4	613.84	3.35	2455.36
	Avandia 2mg	Rolab-Metformin FC 850mg	6	639.7	22.24	3838.19
		Rolab-Metformin HCl 850mg	1	645.55	0	645.55
	Avandia 4mg	Glucophage Forte 850mg	2	477.04	0	954.08
	Glucobay 100mg	Rolab-Metformin HCl 850mg	1	463.43	0	463.43
	Glucobay 50mg	Glucophage Forte 850mg	3	614.61	0	1843.83
	Glucophage 500mg	Glucophage Forte 850mg	10	649.93	14.02	6499.31
		Merck-Metformin 500mg	1	499.18	0	499.18
		Glycomin	3	435.9	0	1307.7
Amaryl 4mg	Avandia 2mg	Avandia 4mg	1	1027.52	0	1027.52
		Glucophage Forte 850mg	2	794.45	0	1588.9
	Avandia 4mg	Glucophage Forte 850mg	2	702.75	0	1405.5
	Diamicron 80mg	Rolab-Metformin FC 850mg	4	578.01	4.84	2312.04
	Glucobay 50mg	Glucophage Forte 850mg	3	1042.57	714.23	3127.72
		Protaphane HM Penset 3ml	4	1296.1	0	5184.4
		Rolab-Metformin FC 500mg	3	669.1	0.27	2007.29
	Glucomed 80mg	Glucophage Forte 850mg	2	687.92	0	1375.84
	Glucophage 500mg	Glucophage Forte 850mg	4	518.97	0	2075.88
	Glucophage Forte 850mg	Humulin N 3ml Penset	2	1115.54	0	2231.08
		Protaphane HM Penset 3ml	1	932.02	0	932.02
	Glycomin 5mg	Rolab-Metformin FC 850mg	1	721.49	0	721.49
	Rolab-Gliclazide	Rolab-Metformin FC 850mg	1	436.8	0	436.8
Avandia 2mg	Glucophage 500mg	Minidiab 5mg	3	464.52	0	1393.56
Avandia 4mg	Diamicron 80mg	Glucophage 500mg	5	650.64	76.54	3253.2

Table E2: (Continue) Utilisation of the combination of three antidiabetic agents for the time January to April

Agents in combination			No of Rx	Average cost	Std deviation	Total cost
		Glucophage Forte 850mg	2	668.11	0	1336.22
	Glucomed 80mg	Glucophage Forte 850mg	1	532.08	0	532.08
		Rolab-Metformin FC 500mg	2	565.57	62.89	1131.14
	Glucophage Forte 850mg	Glyben 5mg	4	629.63	0	2518.52
		Humalog Mix 25 Penset	2	1212.87	5.49	2425.74
		Humalog mix 25 Cartridges	2	1159.87	5.54	2319.73
	Glycron 80mg	Rolab-Metformin HCl 850mg	1	562.94	0	562.94
	Rolab-Gliclazide	Rolab-Metformin HCl 850mg	2	493.2	0	986.4
Daonil 5mg	Glucophage 500mg	Glucophage Forte 850mg	4	311.14	0	1244.56
Diaglucide 80mg	Glucophage Forte 850mg	Humulin L 10ml Vial	2	593.2	0	1186.4
	Protaphane HM Penset 3ml	Rolab-Metformin FC 850mg	1	633.08	0	633.08
Diamicron 80mg	Glucobay 100mg	Glucophage Forte 850mg	1	1080.03	0	1080.03
	Glucobay 50mg	Glucophage Forte 850mg	3	536.7	116.56	1610.09
	Glucophage Forte 850mg	Lantus 300IU 3ml	1	1265.45	0	1265.45
		Lantus 300IU/3ml O/T	2	1125.53	0	2251.06
		Novonorm 0.5mg	1	343.73	0	343.73
	Humulin N 3ml Penset	Rolab-Metformin FC 500mg	1	930.45	0	930.45
	Novonorm 2mg	Rolab-Metformin FC 850mg	2	615.41	6.86	1230.82
		Rolab-Metformin HCl 850mg	1	620.24	0	620.24
	Novorapid 3ml Flexpen	Rolab-Metformin FC 500mg	1	941.56	0	941.56
	Protaphane HM Penset 3ml	Rolab-Metformin FC 850mg	2	906.91	0	1813.82
	Rolab-Metformin FC 500mg	Rolab-Metformin FC 850mg	1	226.01	0	226.01
Diamicron MR 30mg	Glucophage Forte 850mg	Lantus 300IU 3ml	2	1551.35	587.62	3102.7
		Novonorm 1.0mg	1	402.56	0	402.56
	Lantus 300IU 3ml	Rolab-Metformin HCl 850mg	1	1135.85	0	1135.85
	Novomix 30 Flexpen 3ml Injection	Rolab-Metformin FC 500mg	2	1013.42	0	2026.84
	Rolab-Metformin FC 500mg	Rolab-Metformin FC 850mg	1	253.31	0	253.31
Glucobay 100mg	Glucomed 80mg	Glucophage 500mg	7	524.66	108.5	3672.63
		Glucophage Forte 850mg	5	547.69	152.28	2738.43
	Glucophage Forte 850mg	Glycomin	3	730.47	0	2191.41
	Glycomin 5mg	Protaphane HM Penset 3ml	1	1264.87	0	1264.87
		Rolab-Metformin FC 500mg	1	395.83	0	395.83
	Rolab-Gliclazide	Rolab-Metformin FC 850mg	1	475.17	0	475.17

Table E2: (Continue) Utilisation of the combination of three antidiabetic agents for the time January to April

Agents in combination			No of Rx	Average cost	Std deviation	Total cost
Glucobay 50mg	Glucomed 80mg	Glucophage 500mg	1	354.7	0	354.7
		Glucophage Forte 850mg	3	357.4	57.87	1072.21
		Merck-Metformin 850mg	6	528.99	0.11	3173.94
		Rolab-Metformin FC 850mg	2	424.23	0	848.46
		Rolab-Metformin HCl 850mg	2	517.96	6.82	1035.92
	Glucophage 500mg	Rolab-Gliclazide	2	422.77	0	845.54
	Glucophage Forte 850mg	Novonorm 0.5mg	1	396.91	0	396.91
		Rolab-Gliclazide	1	335.18	0	335.18
	Glycomin 5mg	Protaphane HM Penset 3ml	1	1084.61	0	1084.61
	Merck-Gliclazide	Merck-Metformin 850mg	2	409.34	0	818.68
		Rolab-Metformin FC 850mg	1	424.35	0	424.35
	Merck-Metformin 850mg	Rolab-Gliclazide	2	388.97	23.3	777.93
	Rolab-Gliclazide	Rolab-Metformin HCl 500mg	1	285.67	0	285.67
Glucomed 80mg	Glucophage 500mg	Humalog 3ml Penset Prefill	2	2500.81	2.02	5001.61
		Humulin N 10ml Vial	1	507.41	0	507.41
		Humulin N 3ml Penset	1	832.38	0	832.38
		Protaphane HM Penset 3ml	5	954.03	38.85	4770.13
	Glucophage Forte 850mg	Humalog Mix 25 Penset	2	1126.1	0	2252.2
		Humulin N 3ml Cartridges	1	711.98	0	711.98
		Lantus 1000IU 10ml	3	1363.23	0	4089.69
		Lantus 300IU 3ml	2	1111.6	0	2223.2
		Protaphane HM Penfill 3ml	1	921.06	0	921.06
		Protaphane HM Penset 3ml	6	897.29	108.06	5383.73
	Glyben	Rolab-Metformin HCl 500mg	2	452.33	0	904.66
	Glycomin 5mg	Rolab-Metformin FC 850mg	1	346.19	0	346.19
	Humulin 30/70 3ml Cartridges	Rolab-Metformin FC 850mg	2	758.29	10.41	1516.58
	Humulin N 3ml Penset	Rolab-Metformin FC 500mg	1	941.36	0	941.36
		Rolab-Metformin FC 850mg	2	747.58	0	1495.16
		Rolab-Metformin HCl 850mg	2	877.61	61.09	1755.21
	Lantus 300IU 3ml	Rolab-Metformin FC 500mg	1	160.98	0	160.98
		Rolab-Metformin HCl 850mg	1	1033.03	0	1033.03
	Protaphane HM Penfill 3ml	Rolab-Metformin FC 850mg	1	832.29	0	832.29
	Protaphane HM Penset 3ml	Rolab-Metformin FC 500mg	6	920.46	72.53	5522.77

Table E2: (Continue) Utilisation of the combination of three antidiabetic agents for the time January to April

Agents in combination			No of Rx	Average cost	Std deviation	Total cost
		Rolab-Metformin FC 850mg	2	717.91	27.16	1435.81
	Rolab-Metformin HCl 500mg	Rolab-Metformin HCl 850mg	3	168.53	6.45	505.58
Glucophage 500mg	Glucophage Forte 850mg	Glycomin	2	409.17	0	818.34
		Humalog Mix 25 Penset	1	884.88	0	884.88
	Glycomin 5mg	Humulin L 10ml Vial	1	556.21	0	556.21
		Novomix 30 Flexpen 3ml Injection	1	731.04	0	731.04
		Novonorm 1.0mg	3	265.12	0	795.36
		Protaphane HM Penset 3ml	4	975.42	84.9	3901.65
	Glygard	Humulin L 10ml Vial	2	431.17	0	862.34
	Humalog 3ml Penset Prefill	Humulin L 10ml Vial	2	1181.24	0	2362.48
		Humulin N 3ml Penset	4	2224.58	0	8898.32
		Lantus 1000IU 10ml	2	5547.79	0	11095.58
		Protaphane HM Penfill 3ml	2	3553.88	0	7107.76
		Protaphane HM Penset 3ml	3	1515.29	0	4545.87
	Lantus 300IU 3ml	Novorapid 3ml Penfill	2	1647.87	0	3295.74
	Lantus 300IU/3ml O/T	Novorapid 3ml Flexpen	2	1717.7	0	3435.4
	Novorapid 3ml Flexpen	Protaphane HM Penset 3ml	4	1475.59	17.56	5902.37
Glucophage Forte 850mg	Glycomin 5mg	Humulin N 3ml Penset	5	978.55	119.81	4892.77
		Protaphane HM Penset 3ml	6	988.65	141.97	5931.91
	Glycron 80mg	Lantus 300IU 3ml	1	1111.54	0	1111.54
	Humalog 3ml Cartridge Injection	Protaphane HM Penfill 3ml	2	2885.39	998.05	5770.78
	Humalog 3ml Penset Prefill	Humalog Mix 25 Penset	1	907.76	0	907.76
		Humulin N 3ml Penset	3	2725.6	379.16	8176.81
		Protaphane HM Penfill 3ml	1	1442	0	1442
		Protaphane HM Penset 3ml	1	1578.6	0	1578.6
	Lantus 300IU 3ml	Merck-Gliclazide	2	601.24	610.83	1202.41
		Novorapid 3ml Flexpen	1	1725.58	0	1725.58
		Novorapid 3ml Penfill	1	3274.12	0	3274.12
		Rolab-Gliclazide	1	770.06	0	770.06
	Lantus 300IU/3ml O/T	Novorapid 3ml Flexpen	1	1700.15	0	1700.15
	Minidiab 5mg	Protaphane HM Penset 3ml	2	842.34	0	1684.68
	Novonorm 1mg	Novonorm 2mg	1	479.44	0	479.44
	Novonorm 2mg	Protaphane HM Penset 3ml	1	1131.53	0	1131.53

Table E2: (Continue) **Utilisation of the combination of three antidiabetic agents for the time January to April**

Agents in combination			No of Rx	Average cost	Std deviation	Total cost
	Novorapid 3ml Flexpen	Protaphane HM Penset 3ml	1	1049.3	0	1049.3
	Protaphane HM Penfill 3ml	Rolab-Gliclazide	1	913.58	0	913.58
	Protaphane HM Penset 3ml	Rolab-Gliclazide	2	871.86	2.72	1743.72
	Rolab-Gliclazide	Rolab-Metformin FC 850mg	1	600.53	0	600.53
Glyben 5mg	Humulin N 3ml Penset	Rolab-Metformin HCl 500mg	1	1105.59	0	1105.59
	Lantus 300IU/3ml O/T	Rolab-Metformin HCl 850mg	1	1009.81	0	1009.81
	Merck-Metformin 500mg	Protaphane HM 10ml Ampoules	2	723.4	0	1446.8
	Protaphane HM Penset 3ml	Rolab-Metformin FC 850mg	2	854.75	2.53	1709.5
	Rolab-Gliclazide	Rolab-Metformin FC 500mg	3	281.43	98.53	844.28
Glycomin 5mg	Humalog Mix 25 Penset	Rolab-Metformin HCl 500mg	3	940.9	3.35	2822.69
	Humulin N 3ml Cartridges	Rolab-Metformin FC 850mg	1	744.95	0	744.95
	Novonorm 1mg	Rolab-Metformin FC 500mg	1	612.03	0	612.03
		Rolab-Metformin HCl 850mg	3	451.36	5.57	1354.07
	Novonorm 2mg	Rolab-Metformin HCl 850mg	1	700.35	0	700.35
	Protaphane HM Penset 3ml	Rolab-Metformin HCl 500mg	1	1010.51	0	1010.51
		Rolab-Metformin FC 500mg	2	838.34	0	1676.68
		Rolab-Metformin FC 850mg	2	1113.48	3.99	2226.96
	Rolab-Metformin FC 500mg	Rolab-Metformin HCl 850mg	4	202.83	38.22	811.33
Glycron 80mg	Protaphane HM Penfill 3ml	Rolab-Metformin HCl 850mg	1	754.67	0	754.67
Humulin R Humaject Pen 5ml	Humulin N 10ml Vial	Humulin R 10ml Vial	2	1386.52	0	2773.04
Humalog 10ml Ampoules	Humulin N 10ml Vial	Rolab-Metformin HCl 500mg	3	1943.62	0.01	5830.85
Humalog 3ml Penset Prefill	Humulin N 3ml Penset	Rolab-Metformin HCl 500mg	1	1450.39	0	1450.39
	Lantus 300IU 3ml	Rolab-Metformin HCl 500mg	4	1851.48	362.42	7405.92
	Novonorm 2mg	Rolab-Metformin FC 500mg	1	2950.1	0	2950.1
	Protaphane HM Penset 3ml	Rolab-Metformin FC 500mg	3	3060.92	9.51	9182.77
		Rolab-Metformin FC 850mg	1	1571.78	0	1571.78
Humalog Mix 25 Penset	Protaphane HM Penset 3ml	Rolab-Metformin FC 500mg	1	1709.05	0	1709.05
	Rolab-Gliclazide	Rolab-Metformin FC 500mg	1	680.66	0	680.66
Humulin N 3ml Penset	Rolab-Gliclazide	Rolab-Metformin HCl 850mg	2	927.33	10.22	1854.66
Merck-Metformin 850mg	Novorapid 3ml Flexpen	Protaphane Penset 3ml	2	1503.81	13.15	3007.61
Novonorm 1.0mg	Novonorm 2mg	Rolab-Metformin FC 500mg	1	292.58	0	292.58
		Rolab-Metformin HCl 850mg	3	646.15	5.57	1938.44

Table E2: (Continue) Utilisation of the combination of three antidiabetic agents for the time January to April

Agents in combination			No of Rx	Average cost	Std deviation	Total cost
Novorapid 3ml Flexpen	Protaphane HM Penfill 3ml	Rolab-Metformin FC 500mg	2	1097.03	0	2194.06
	Protaphane HM Penset 3ml	Rolab-Metformin FC 850mg	2	1142.39	474.67	2284.77
		Rolab-Metformin HCl 850mg	1	2180.43	0	2180.43
Protaphane HM Penset 3ml	Rolab-Gliclazide	Rolab-Metformin FC 850mg	2	864.67	0	1729.34
		Rolab-Metformin HCl 850mg	1	906.04	0	906.04
Protaphane HM 10ml Ampoules	Rolab-Gliclazide	Rolab-Metformin FC 500mg	1	927.48	0	927.48

Table E3: Utilisation of the combination of four antidiabetic agents for the time January to April

Agents in combination				No of Rx	Average cost	Std dev	Total cost
Amaryl 2mg	Amaryl 2mg	Glucophage 500mg	Glucophage 500mg	1	363.72	0	363.72
	Amaryl 4mg	Glucobay 100mg	Glucophage Forte 850	1	1031.89	0	1031.89
Avandia 4mg	Glucomed 80mg	Novomix 30 Flexpen 3ml Injection	Rolab-Metformin FC 850mg	1	1293.12	0	1293.12
	Glucophage Forte 850mg	Humalog 3ml Cartridge Injection	Humulin N 3ml Cartridge	1	3142.48	0	3142.48
Humalog 3ml Cartridge Injection	Humalog 3ml Cartridge Injection	Humulin N 3ml Cartridge	Humulin N 3ml Cartridge	1	4135.68	0	4135.68
Novomix 30 Flexpen 3ml Injection	Novonorm 1.0mg	Novonorm 2.0mg	Rolab-Metformin HCl 850mg	1	1377.2	0	1377.2

Appendix F

Table F1: Utilisation of two antidiabetic agents in combination for the time May to August

Agents in combination		No of Rx	Average cost	Std deviation	Total cost
Actos 15mg	Actos 15mg	1	1024.46	0	1024.46
	Actraphane HM Penfill 3ml	1	1055.57	0	1055.57
	Actraphane HM Penset 3ml	7	981.61	135.52	6871.3
	Amaryl 1mg	8	493.13	5.47	3945
	Amaryl 2mg	14	584.7	8.42	8185.79
	Amaryl 4mg	13	853.16	292.89	11091.06
	Daonil 5mg	5	667.05	176.4	3335.27
	Diamicron 80mg	9	567.44	63.86	5106.95
	Diamicron MR 30mg	5	452.89	160.88	2264.47
	Glucomed 80mg	1	304.18	0	304.18
	Glucophage 500mg	16	466.86	16.15	7469.8
	Glucophage Forte 850mg	5	477.41	101.41	2387.03
	Glucovance 500/5mg	1	585.04	0	585.04
	Glyben 5mg	2	437.95	35.41	875.9
	Glycomin 5mg	3	564.87	74.5	1694.61
	Humalog 3ml Cartridge Injection	1	1162.63	0	1162.63
	Humalog Mix 25 Cartridge	1	1855.08	0	1855.08
	Humulin 30/70 3ml Cartridge	4	1619.11	107.75	6476.43
	Lantus 1000IU 10ml	1	975.58	0	975.58
	Rolab-Metformin FC 500mg	1	482.9	0	482.9
Actos 30mg	Actraphane HM Penset 3ml	7	1332.99	1.69	9330.9
	Actraphane HM 10ml Ampoules	6	976.01	417.77	5856.03
	Amaryl 1mg	2	695.56	0	1391.12
	Amaryl 2mg	16	739.6	87.94	11833.6
	Amaryl 4mg	22	1015.55	142.25	22342
	Avandia 4mg	4	1219.25	0.01	4876.99
	Diamicron 80mg	14	793.3	189.93	11106.17

Table F1 (Continue): Utilisation of two antidiabetic agents in combination for the time May to August

Agents in combination		No of Rx	Average cost	Std deviation	Total cost
	Diamicron MR 30mg	12	732.78	41.93	8793.3
	Glucomed 80mg	9	595.25	84.24	5357.22
	Glucophage 500mg	15	642.75	40.59	9641.26
	Glucophage Forte 850mg	10	661.24	142.38	6612.38
	Glucovance 500/5mg	1	797.74	0	797.74
	Glycomin 5mg	7	658.66	153.03	4610.6
	Glycron 80mg	1	767.3	0	767.3
	Humalog 3ml Penset Prefill	1	1384.78	0	1384.78
	Humalog Mix 25 Penset	3	1333.65	112.09	4000.94
	Lantus 300IU 3ml	4	1382.78	170.58	5531.12
	Novomix 30 Flexpen 3ml Injection	3	1243.33	101.76	3729.98
	Protaphane HM Penset 3ml	1	1282.43	0	1282.43
	Rolab-Gliclazide	1	514.47	0	514.47
	Rolab-Metformin FC 500mg	3	661.52	17.43	1984.57
	Rolab-Metformin FC 850mg	1	684.07	0	684.07
	Rolab-Metformin HCl 850mg	1	690.73	0	690.73
Actraphane HM Penfill 3ml	Actraphane HM Penfill 3ml	1	1345.12	0	1345.12
	Actrapid HM Penfill 3ml	4	1194.62	158.63	4778.46
	Actrapid HM Pensets 3ml	1	1151.28	0	1151.28
	Avandia 4mg	2	1657.3	0	3314.6
	Glucophage 500mg	10	742.18	12.67	7421.8
	Glucophage Forte 850mg	13	712.44	73.77	9261.78
	Merck-Metformin 850mg	1	578.73	0	578.73
	Protaphane HM Penset 3ml	1	1104.36	0	1104.36
	Rolab-Metformin HCl 500mg	5	766	238.97	3830
	Rolab-Metformin FC 500mg	3	550.8	2.57	1652.41
	Rolab-Metformin FC 850mg	2	573.81	1.73	1147.61
	Rolab-Metformin FC 850mg	2	546	0	1092
Actraphane HM Penset 3ml	Actraphane HM Penset 3ml	29	1525.6	454.57	44242.28
	Actraphane HM 10ml Ampoules	1	1094.8	0	1094.8
	Actrapid HM Pensets 3ml	4	1375.43	268.21	5501.72
	Amaryl 2mg	2	1139.76	0	2279.52
	Amaryl 4mg	5	1520.43	449.99	7602.17

Table F1: (Continue) Utilisation of two antidiabetic agents in combination for the time May to August

Agents in combination		No of Rx	Average cost	Std deviation	Total cost
	Avandia 4mg	3	1458.48	133.31	4375.44
	Diaglucide 80mg	1	611.33	0	611.33
	Diamicron 80mg	1	865.26	0	865.26
	Glucobay 100mg	1	1834.04	0	1834.04
	Glucomed 80mg	6	664.05	14.51	3984.28
	Glucophage 500mg	64	873.52	274.41	55905
	Glucophage Forte 850mg	105	995.01	487.15	104476.01
	Glucovance 500/5mg	1	691.03	0	691.03
	Glycomin 5mg	8	1035.22	617.09	8281.73
	Glycron 80mg	2	1095.74	11.03	2191.48
	Humalog 3ml Penset Prefill	3	1195.7	153.59	3587.1
	Lantus 300IU 3ml	1	1070.65	0	1070.65
	Merck-Metformin 500mg	4	595.71	8.91	2382.84
	Merck-Metformin 850mg	2	423.18	312.73	846.35
	Monotard HM 10ml Ampoules	1	931.61	0	931.61
	Novonorm 1.0mg	1	752.1	0	752.1
	Protaphane HM Penfill 3ml	1	1638.31	0	1638.31
	Protaphane HM Penset 3ml	2	2338.87	0	4677.74
	Rolab-Gliclazide	4	628.54	44.21	2514.14
	Rolab-Metformin HCl 500mg	23	1007.26	292.26	23166.92
	Rolab-Metformin FC 500mg	26	890.99	312.74	23165.69
	Rolab-Metformin FC 850mg	20	981.92	423.37	19638.35
	Rolab-Metformin HCl 850mg	17	1024.45	351.48	17415.57
Actraphane HM 10ml Ampoules	Actraphane HM 10ml Ampoules	2	524.03	148.22	1048.06
	Actrapid HM 10ml Ampoules	2	943.23	0	1886.48
	Amaryl 2mg	1	549.3	0	549.3
	Amaryl 4mg	1	715.13	0	715.13
	Avandia 2mg	2	963.27	120.41	1926.53
	Avandia 4mg	3	954.97	348.69	2864.91
	Diamicron 80mg	1	477.25	0	477.25
	Diamicron MR 30mg	1	448.48	0	448.48
	Glucomed 80mg	1	743.01	0	743.01
	Glucophage 500mg	13	606.55	172.91	7885.11

Table F1: (Continue) Utilisation of two antidiabetic agents in combination for the time May to August

Agents in combination		No of Rx	Average cost	Std deviation	Total cost
	Glucophage Forte 850mg	16	518.38	175.99	8294.03
	Glycomin 5mg	1	989.7	0	989.7
	Merck-Metformin 850mg	4	395.53	33.12	1582.11
	Metforal 850mg	1	376.59	0	376.59
	Monotard HM 10ml Ampoules	5	1699.3	160.18	8496.48
	Novonorm 1.0mg	3	559.83	1.37	1679.48
	Rolab-Gliclazide	1	622.73	0	622.73
	Rolab-Metformin HCl 500mg	5	325.69	37.28	1628.44
Actrapid HM 10ml Ampoules	Actrapid HM Pensets 3ml	1	1099.78	0	1099.78
	Humulin N 10ml Vial	3	638.62	33.19	1915.86
	Lantus 1000IU 10ml	8	1215.33	477.58	9722.63
	Lantus 300IU 3ml	1	549.65	0	549.68
	Monotard HM 10ml Ampoules	29	746.51	342.36	21648.68
	Protaphane HM 10ml Ampoules	24	879.8	319.97	21115.21
	Ultratard HM 10ml Ampoules	1	484.24	0	484.24
Actrapid HM Penfill 3ml	Glucophage Forte 850mg	2	1232.42	0	2464.84
	Humulin L 10ml Vial	3	941.78	65.65	2825.33
	Humulin N 3ml Penset	1	1641.1	0	1641.1
	Monotard HM 10ml Ampoules	5	1053.45	282.12	5267.27
	Novorapid 3ml Penfill	1	1165.42	0	1165.42
	Protaphane HM Penfill 3ml	15	1419.68	563.47	21295.23
	Protaphane HM Penset 3ml	2	1688.58	188.97	3377.15
Actrapid HM Pensets 3ml	Actrapid HM Pensets 3ml	3	1260.57	378.88	3781.7
	Glucophage 500mg	6	807.52	335.38	4845.12
	Glucophage Forte 850mg	9	832.85	369.22	7495.69
	Glycomin 5mg	1	716.18	0	716.18
	Humulin L 10ml Vial	3	914.86	283.79	2744.58
	Humulin N 3ml Penset	4	1257.1	129.4	5028.41
	Lantus 1000IU 10ml	2	1521.94	29.16	3043.88
	Lantus 300IU 3ml	13	1591.46	461.2	20688.96
	Lantus 300IU/3ml O/T	4	1824.22	561.31	7296.88
	Monotard HM 10ml Ampoules	12	1178.27	494.25	14139.28
	Protaphane HM Penfill 3ml	4	2087.42	391.46	8349.68

Table F1: (Continue) Utilisation of two antidiabetic agents in combination for the time May to August

Agents in combination		No of Rx	Average cost	Std deviation	Total cost
	Protaphane HM Penset 3ml	42	1364.39	312.27	57304.44
	Protaphane HM 10ml Ampoules	1	885.48	0	885.48
	Rolab-Metformin FC 500mg	1	630.95	0	630.95
	Rolab-Metformin FC 850mg	1	1561.29	0	1561.29
	Rolab-Metformin HCl 850mg	3	1016.19	419.73	3048.57
Amaryl 1mg	Amaryl 1mg	6	176.35	26.79	1058.12
	Amaryl 2mg	29	266.56	57.42	7730.2
	Amaryl 4mg	4	117.14	0.01	468.57
	Avandia 2mg	1	160.99	0	160.99
	Diamicron 80mg	5	200.77	26.49	1003.86
	Glucophage 500mg	78	155.58	55.8	12135.08
	Glucophage Forte 850mg	78	177.4	54.82	13837.01
	Glycomin 5mg	2	180.44	47.77	360.87
	Merck-Metformin 500mg	1	203.85	0	203.85
	Merck-Metformin 850mg	6	158.54	28.21	951.21
	Metforal 850mg	1	144.17	0	144.17
	Novonorm 1.0mg	1	314.07	0	314.07
	Rolab-Gliclazide	2	155.32	0	310.64
	Rolab-Metformin HCl 500mg	23	125.57	24.86	2888.11
	Rolab-Metformin FC 500mg	22	175.43	50.39	3859.52
	Rolab-Metformin FC 850mg	12	141.64	40.78	1699.71
	Rolab-Metformin HCl 850mg	13	136.82	17.09	1778.63
Amaryl 2mg	Amaryl 2mg	5	428.66	80.87	2143.32
	Amaryl 4mg	22	437.53	149.73	9625.6
	Avandia 4mg	4	271.17	15.06	1084.69
	Diaglucide 80mg	1	211.75	0	211.75
	Diamicron MR 30mg	4	418.74	83.28	1674.97
	Glucomed 80mg	4	228.6	24.06	914.4
	Glucophage 500mg	154	219.32	73.31	33775.69
	Glucophage Forte 850mg	228	254.14	98.59	57944.25
	Glucovance 500/2.5mg	3	339.66	30.34	1018.97
	Glucovance 500/5mg	1	48.96	0	48.96
	Glycomin 5mg	1	429.57	0	429.57

Table F1: (Continue) Utilisation of two antidiabetic agents in combination for the time May to August

Agents in combination		No of Rx	Average cost	Std deviation	Total cost
	Humalog Mix 25 Penset	8	720.62	321.68	5764.97
	Merck-Metformin 500mg	8	204.31	38.99	1634.49
	Novonorm 0.5mg	2	309.43	0	618.86
	Novonorm 1.0mg	2	404.75	2.48	809.49
	Novonorm 2.0mg	1	549.33	0	549.33
	Rolab-Metformin HCl 500mg	38	207.56	55.07	7887.15
	Rolab-Metformin FC 500mg	45	219.38	105.48	9872.01
	Rolab-Metformin FC 850mg	28	226.29	67.1	6336.25
	Rolab-Metformin HCl 850mg	19	230.41	43.12	4377.82
Amaryl 4mg	Amaryl 4mg	7	607.79	80.47	4254.56
	Avandia 2mg	10	492.95	94.72	4929.48
	Avandia 4mg	24	732.58	138.71	17581.91
	Daonil 5mg	6	764.46	219.99	4586.76
	Diamicron 80mg	4	434.3	0	1737.2
	Diamicron MR 30mg	1	533.47	0	533.47
	Glucobay 100mg	4	1017.29	0	4069.16
	Glucobay 50mg	5	531.41	48.14	2657.06
	Glucomed 80mg	10	384.85	32.56	3848.54
	Glucophage 500mg	112	381.79	106.79	42760.51
	Glucophage Forte 850mg	250	418.86	120.64	104713.8
	Glucovance 250/1.25mg	3	307.4	8.61	922.21
	Glucovance 500/2.5mg	4	441.04	138.18	1764.14
	Glucovance 500/5mg	5	889.48	618.01	4447.38
	Glyben 5mg	3	484.58	40.75	1453.75
	Glycomin 5mg	5	544.79	45.8	2723.94
	Humulin N 3ml Cartridges	2	802.34	8.94	1604.67
	Humulin N 3ml Penset	2	1004.1	35.8	2008.19
	Lantus 300IU 3ml	5	1245.57	0.34	6227.86
	Lantus 300IU/3ml O/T	2	889.83	10.54	1779.65
	Merck-Metformin 500mg	7	373.51	56.76	2614.57
	Merck-Metformin 850mg	9	380.5	21.36	3424.46
	Metforal 850mg	1	352.28	0	352.28
	Novomix 30 Flexpen 3ml Injection	2	574.31	439.02	1148.61

Table F1: (Continue) Utilisation of two antidiabetic agents in combination for the time May to August

Agents in combination		No of Rx	Average cost	Std deviation	Total cost
	Novonorm 0.5mg	1	474.81	0	474.81
	Novonorm 1.0mg	6	571.88	0	3431.28
	Novonorm 2.0mg	2	714.71	0	1429.42
	Rolab-Gliclazide	3	352.14	12.94	1056.43
	Rolab-Metformin HCl 500mg	48	363.62	69.67	17453.74
	Rolab-Metformin FC 500mg	27	415.57	68.08	11220.44
	Rolab-Metformin FC 850mg	39	384.51	118.43	14995.95
	Rolab-Metformin HCl 850mg	32	374.71	83.25	11990.77
Avandia 2mg	Avandia 2mg	5	391.46	251.06	1957.28
	Glucomed 80mg	5	236.53	56.08	1182.64
	Glucophage 500mg	8	237.11	108.8	1986.9
	Glucophage Forte 850mg	7	183.72	63.89	1286.05
	Humalog Mix 25 Penset	2	979.78	0	1959.56
	Rolab-Metformin HCl 500mg	1	283.84	0	283.84
Avandia 4mg	Avandia 4mg	3	648.52	100.32	1945.56
	Daonil 5mg	1	521.95	0	521.95
	Diamicron 80mg	2	390.79	6.2	781.57
	Diamicron MR 30mg	18	502.46	93.67	9044.3
	Glucomed 80mg	13	354.89	32.43	4613.53
	Glucophage 500mg	28	404.23	75.79	11318.32
	Glucophage Forte 850mg	38	385.44	119.07	14646.56
	Glycomin 5mg	9	355.91	92.07	3203.15
	Glycron 80mg	3	708.82	22.35	2126.47
	Humulin 30/70 Humaject Injection	2	1022.34	0	2044.68
	Humalog Mix 25 Penset	3	1315.51	344.54	3946.54
	Humalog Mix 25 Cartridge	5	948.03	256.43	4740.14
	Lantus 300IU 3ml	5	1442.84	205.34	7214.18
	Lantus 300IU/3ml O/T	3	981.35	469.7	2944.06
	Merck-Metformin 500mg	1	305.11	0	305.11
	Novomix 30 Flexpen 3ml Injection	5	851.43	58.4	4257.15
	Novonorm 1.0mg	4	522.97	9.2	2091.86
	Novonorm 2.0mg	1	646.72	0	646.72
	Novorapid 3ml Flexpen	2	1063.74	0	2127.48

Table F1: (Continue) **Utilisation of two antidiabetic agents in combination for the time May to August**

Agents in combination		No of Rx	Average cost	Std deviation	Total cost
	Protaphane HM Penset 3ml	2	1011.78	0	2023.56
	Rolab-Metformin HCl 500mg	3	327.78	50.73	983.35
	Rolab-Metformin FC 500mg	10	373.24	27.23	3732.44
	Rolab-Metformin FC 850mg	4	519.73	261.83	2078.92
	Rolab-Metformin HCl 850mg	5	422.1	182.72	2110.51
Daonil 5mg	Glucobay 50mg	4	784.06	265.09	3136.24
	Glucophage 500mg	134	436.2	180.84	58450.24
	Glucophage Forte 850mg	57	538.07	176.58	30669.83
	Merck-Metformin 500mg	1	379.03	0	379.03
	Rolab-Metformin HCl 500mg	24	561.33	209.87	13472
	Rolab-Metformin FC 500mg	26	543.63	162.94	14134.28
	Rolab-Metformin FC 850mg	8	420.88	43.37	3367.02
	Rolab-Metformin HCl 850mg	7	333.06	31.74	2331.45
Diacare 5mg	Merck-Metformin 500mg	4	73.01	47.05	292.03
	Rolab-Metformin FC 500mg	2	94.75	4.07	189.49
Diaglucide 80mg	Diaglucide 80mg	1	108.34	0	108.34
	Glucophage 500mg	45	114.09	37.41	5134
	Glucophage Forte 850mg	86	154.83	54.25	13315.28
	Glyben 5mg	1	92.3	0	92.3
	Glycomin 5mg	1	87.09	0	87.09
	Merck-Metformin 500mg	17	157.34	39.43	2674.76
	Merck-Metformin 850mg	13	151.31	35.44	1967
	Protaphane HM Penfill 3ml	1	625.37	0	625.37
	Rolab-Metformin HCl 500mg	20	118.31	27.86	2366.17
	Rolab-Metformin FC 500mg	9	175.49	68.67	1579.45
	Rolab-Metformin FC 850mg	39	152.56	42.17	5949.93
	Rolab-Metformin HCl 850mg	25	130.16	44.26	3253.91
Diamicron 80mg	Diamicron 80mg	13	255.96	115.63	3327.54
	Glucobay 100mg	1	491.6	0	491.6
	Glucobay 50mg	2	258.63	0	517.26
	Glucophage 500mg	166	202.03	85.47	33537.27
	Glucophage Forte 850mg	261	200.13	67.98	52233.45
	Glycomin 5mg	4	246.6	46.84	986.41

Table F1: (Continue) Utilisation of two antidiabetic agents in combination for the time May to August

Agents in combination		No of Rx	Average cost	Std deviation	Total cost
	Merck-Metformin 500mg	7	171.46	45.72	1200.25
	Merck-Metformin 850mg	5	275.6	48.52	1377.99
	Novomix 30 Flexpen 3ml Injection	4	775.19	15.92	3100.77
	Rolab-Metformin HCl 500mg	38	204.17	82.72	7758.5
	Rolab-Metformin FC 500mg	28	156.78	63.88	4389.9
	Rolab-Metformin FC 850mg	35	197.82	72.54	6923.73
	Rolab-Metformin HCl 850mg	26	208.63	67.23	5424.37
Diamicron MR 30mg	Diamicron MR 30mg	2	239.12	80.84	478.24
	Glucobay 50mg	3	324.05	0	972.15
	Glucophage 500mg	51	173.49	58.25	8847.83
	Glucophage Forte 850mg	149	224.24	86.39	33411.69
	Glygard	1	190.82	0	190.82
	Lantus 300IU/3ml O/T	2	964.45	120.86	1928.9
	Merck-Metformin 500mg	4	242.67	44.16	970.67
	Merck-Metformin 850mg	13	188.36	43.03	2448.65
	Metforal 850mg	3	160.89	37.91	482.66
	Novomix 30 Flexpen 3ml Injection	1	747.17	0	747.17
	Protaphane HM Penset 3ml	1	1031.46	0	1031.46
	Protaphane HM 10ml Ampoules	3	495.95	16.9	1487.84
	Rolab-Metformin HCl 500mg	27	209.72	99.73	5662.39
	Rolab-Metformin FC 500mg	24	190.87	56.47	4580.9
	Rolab-Metformin FC 850mg	24	201.66	80.03	4839.87
	Rolab-Metformin HCl 850mg	24	239.12	75.49	5738.9
Euglycon 5mg	Glucophage Forte 850mg	2	564.7	0	1129.4
Glucobay 100mg	Glucobay 100mg	1	678.72	0	678.72
	Glucomed 80mg	1	331.52	0	331.52
	Glucophage 500mg	3	303.69	46.65	911.06
	Glucophage Forte 850mg	1	468.35	0	468.35
	Glucovance 250/1.25mg	2	313.83	39.55	627.65
	Glycomin 5mg	7	412	13.46	2884.01
	Glygard	1	319.2	0	319.2
Glucobay 50mg	Glucomed 80mg	8	293.89	58.38	2351.08
	Glucophage 500mg	3	256.44	22.56	769.31

Table F1: (Continue) Utilisation of two antidiabetic agents in combination for the time May to August

Agents in combination		No of Rx	Average cost	Std deviation	Total cost
	Glucophage Forte 850mg	6	287.88	39.28	1727.25
	Glucovance 500/5mg	3	470.97	0.16	1412.9
	Glyben 5mg	5	246.77	34.33	1233.86
	Glycomin 5mg	8	285.3	42.38	2282.36
	Lantus 300IU 3ml	1	836.77	0	836.77
	Protaphane HM Penset 3ml	1	790.5	0	790.5
	Rolab-Gliclazide	1	239.19	0	239.19
	Rolab-Metformin FC 500mg	2	343.37	0.01	686.74
Glucomed 80mg	Glucomed 80mg	5	177.72	83.58	888.58
	Glucophage 500mg	392	148.6	60.17	58252.49
	Glucophage Forte 850mg	609	170.09	56.29	103583.34
	Glucovance 250/1.25mg	1	172.58	0	172.58
	Glyben 5mg	1	85.87	0	85.87
	Glycomin 5mg	6	156.17	78.11	937.02
	Humulin 30/70 10ml Vials	1	736.86	0	736.86
	Humulin 30/70 3ml Cartridges	2	1106.28	0	2212.56
	Humulin L 10ml Vial	2	296.24	0.33	592.48
	Humulin N 3ml Penset	1	683.06	0	683.06
	Lantus 300IU/3ml O/T	5	1388.12	593.14	6940.58
	Merck-Metformin 500mg	22	144.24	53.7	3173.32
	Merck-Metformin 850mg	28	181.16	50.17	5072.34
	Novomix 30 Flexpen 3ml Injection	4	489.64	272.48	1958.57
	Novonorm 1.0mg	4	211.38	8.63	845.52
	Novonorm 2.0mg	3	609.93	14.77	1829.79
	Protaphane HM Penset 3ml	4	676.11	37.11	2704.43
	Rolab-Gliclazide	1	200.05	0	200.05
	Rolab-Metformin HCl 500mg	188	139.28	48.75	26184.27
	Rolab-Metformin FC 500mg	223	147.9	53.08	32981.56
	Rolab-Metformin FC 850mg	286	171.2	53.55	48962.87
	Rolab-Metformin HCl 850mg	130	158.73	53.02	20635.13
Glucophage 500mg	Glucophage 500mg	55	73.47	39.37	4040.8
	Glucophage Forte 850mg	7	79.4	34.62	555.79
	Glucovance 500/2.5mg	4	92.27	18.39	369.06

Table F1: (Continue) Utilisation of two antidiabetic agents in combination for the time May to August

Agents in combination		No of Rx	Average cost	Std deviation	Total cost
	Glucovance 500/5mg	1	173.9	0	173.9
	Glyben 5mg	65	119.44	86.73	7763.83
	Glycomin 5mg	628	133.17	61.47	83632.71
	Glycron 80mg	17	139.97	102.37	2379.45
	Glygard	4	151.58	12.49	606.3
	Humulin 30/70 Humaject Injection	4	1143.51	368.11	4574.05
	Humalog 3ml Cartridge Injection	2	1099.35	11.84	2198.69
	Humalog 3ml Penset Prefill	7	962.93	262.79	6740.51
	Humalog Mix 25 Penset	56	1017.61	470.07	56986.1
	Humalog Mix 25 Cartridge	3	721.44	142.02	2164.33
	Humulin 30/70 3ml Cartridges	11	640.31	254.15	7043.43
	Humulin L 10ml Vial	7	414.6	41.54	2902.19
	Humulin N 10ml Vial	1	385.5	0	385.5
	Humulin N 3ml Penset	2	655.35	78.43	1310.69
	Lantus 1000IU 10ml	2	1019.81	484.83	2039.61
	Lantus 300IU 3ml	3	830	114.28	2490
	Lantus 300IU/3ml O/T	5	809.48	131.63	4047.42
	Merck-Gliclazide	12	119.9	53.97	1438.81
	Minidiab 5mg	15	267.79	130.87	4016.8
	Mixtard 20/80 Penfill	3	583.46	118.21	1750.37
	Monotard HM 10ml Ampoules	7	402.21	79.39	2815.49
	Norton-Glibenclamide	3	98.18	3.29	294.54
	Novomix 30 Flexpen 3ml Injection	41	778.79	262.99	31930.47
	Novonorm 0.5mg	15	163.09	15.12	2446.28
	Novonorm 1.0mg	13	282.49	63.96	3672.41
	Novonorm 2.0mg	17	427.39	14.89	7265.7
	Novorapid 3ml Flexpen	3	720.91	92.87	2162.72
	Protaphane HM Penfill 3ml	5	1041.48	364.61	5207.38
	Protaphane HM Penset 3ml	7	729.04	56.11	5103.26
	Protaphane HM 10ml Ampoules	2	403.32	10.59	806.64
	Rolab-Gliclazide	79	114.36	50.86	9034.69
	Rolab-Metformin FC 850mg	2	130.39	8.9	240.77
	Starlix FCT 120mg	5	408.17	150.43	2040.83

Table F1: (Continue) Utilisation of two antidiabetic agents in combination for the time May to August

Agents in combination		No of Rx	Average cost	Std deviation	Total cost
Glucophage Forte 850mg	Glucophage Forte 850mg	40	126.3	71.53	5051.92
	Glucovance 500/2.5mg	5	180.09	22.71	900.44
	Glyben 5mg	32	104.03	63.91	3328.98
	Glycomin 5mg	485	157	58.97	76147.36
	Glycron 80mg	24	175.86	58.38	4220.72
	Glygard	9	164.3	42.67	1478.71
	Humulin 30/70 Humaject Injection	4	799.7	484.8	3198.78
	Humulin N Humaject 3ml Injection	1	679.51	0	679.51
	Humalog 10ml Ampoules	1	433.89	0	433.89
	Humalog 3ml Cartridge Injection	2	1400.66	618.52	2801.32
	Humalog 3ml Penset Prefill	6	1233.03	768.73	7398.16
	Humalog Mix 25 Penset	87	1070.62	513.45	93143.92
	Humalog Mix 25 Cartridge	4	953.25	233.37	3812.98
	Humulin 30/70 3ml Cartridges	9	823.52	256.98	7411.67
	Humulin L 10ml Vial	12	392.32	103.53	4707.88
	Humulin N 3ml Penset	19	752.26	228.6	14293.01
	Hypomide 250mg	4	121.95	42.87	487.78
	Lantus 300IU 3ml	20	1092.82	375.92	21856.34
	Lantus 300IU/3ml O/T	9	764.08	151.22	6876.72
	Merck-Gliclazide	21	141.62	51.81	2974.1
	Minidiab 5mg	26	309.55	153.42	8048.36
	Norton-Glibenclamide	2	102.16	7.84	204.31
	Novomix 30 Flexpen 3ml Injection	61	840.9	382.78	51294.81
	Novomix 30 Penfill 3ml Injection	10	1218.52	307.52	12185.21
	Novonorm 0.5mg	4	148.82	19.5	595.27
	Novonorm 1.0mg	18	280.3	41.89	5045.41
	Novonorm 2.0mg	20	406.63	62.72	8132.54
	Novorapid 3ml Flexpen	6	954.73	299.5	5728.39
	Novorapid 3ml Penfill	1	1337.74	0	1337.74
	Protaphane HM Penset 3ml	10	704.67	241.58	7046.74
	Rolab-Gliclazide	160	142.3	45.55	22768.2
	Rolab-Metformin HCl 850mg	1	201.2	0	201.2
	Ultratard HM 10ml Ampoules	2	362.78	4.79	725.56

Table F1: (Continue) **Utilisation of two antidiabetic agents in combination for the time May to August**

Agents in combination		No of Rx	Average cost	Std deviation	Total cost
Glucovance 250/1.25mg	Glucovance 250/1.25mg	3	104.83	35.53	314.48
	Glucovance 500/2.5mg	5	118.15	21.35	590.73
	Glucovance 500/5mg	1	254.96	0	254.96
Glucovance 500/2.5	Glucovance 500/2.5mg	5	370.27	190.69	1851.36
	Humulin 30/70 3ml Cartridges	2	580.58	0	1161.16
	Lantus 300IU 3ml	1	947.15	0	947.15
	Novomix 30 Flexpen 3ml Injection	3	683.45	0	2050.35
	Rolab-Metformin HCl 500mg	1	84.92	0	84.92
	Rolab-Metformin FC 850mg	3	224.14	29.68	672.43
Glucovance 500/5mg	Glucovance 500/5mg	6	368.97	206.81	2213.82
	Humalog Mix 25 Penset	2	944.25	0	1888.5
	Lantus 300IU/3ml O/T	6	1066.54	105.33	6399.25
	Protaphane HM Penset 3ml	2	1084.22	0.03	2168.44
	Rolab-Metformin FC 500mg	1	41.9	0	41.9
Glyben 5mg	Glyben 5mg	2	11.86	0.82	23.72
	Glycron 80mg	1	316.88	0	316.88
	Merck-Metformin 500mg	7	113.73	82.5	796.14
	Merck-Metformin 850mg	4	77.17	27.43	308.66
	Metforal 850mg	1	67.4	0	67.4
	Novomix 30 Flexpen 3ml Injection	1	1173.66	0	1173.66
	Rolab-Gliclazide	1	60.51	0	60.51
	Rolab-Metformin HCl 500mg	35	96.13	66.47	3364.66
	Rolab-Metformin FC 500mg	58	100.71	79.24	5841.04
	Rolab-Metformin FC 850mg	45	127.39	76.03	5732.61
	Rolab-Metformin HCl 850mg	27	106.77	52.18	2882.9
Glycomin 5mg	Glycomin 5mg	8	53.51	37.9	428.06
	Glycron 80mg	1	195.48	0	195.48
	Humalog Mix 25 Penset	8	1123.35	228.57	8986.78
	Lantus 1000IU 10ml	1	728.15	0	728.15
	Lantus 300IU 3ml	2	840.55	9.55	1681.1
	Merck-Gliclazide	2	114.5	0	229
	Merck-Metformin 500mg	34	116.19	40.36	3950.49
	Merck-Metformin 850mg	9	133.24	36.32	1199.19

Table F1: (Continue) Utilisation of two antidiabetic agents in combination for the time May to August

Agents in combination		No of Rx	Average cost	Std deviation	Total cost
	Metforal 850mg	8	114.35	20.32	914.8
	Novomix 30 Flexpen 3ml Injection	2	751.12	87.14	1502.23
	Novonorm 1.0mg	2	152.43	0	304.86
	Novonorm 2.0mg	2	424.33	0	848.66
	Protaphane HM Penfill 3ml	1	556.61	0	556.61
	Protaphane HM Penset 3ml	4	1262.13	403.28	5048.5
	Rolab-Gliclazide	5	187.14	59.63	935.69
	Rolab-Metformin HCl 500mg	274	124.04	70.07	33987.29
	Rolab-Metformin FC 500mg	291	128.13	58.33	37284.74
	Rolab-Metformin FC 850mg	177	143.9	57.64	25469.53
	Rolab-Metformin HCl 850mg	113	132.28	48.19	14947.1
Glycron 80mg	Merck-Metformin 500mg	1	27.9	0	27.9
	Merck-Metformin 850mg	7	158.14	38.53	1106.98
	Metforal 500mg	1	89.33	0	89.33
	Protaphane HM 10ml Ampoules	1	522.83	0	522.83
	Rolab-Metformin HCl 500mg	13	136.79	45.41	1778.22
	Rolab-Metformin FC 500mg	21	143.22	45.67	3007.56
	Rolab-Metformin FC 850mg	18	167.81	43.96	3020.69
	Rolab-Metformin HCl 850mg	10	178.11	72.78	1781.1
Glygard	Merck-Metformin 850mg	3	164.24	36.74	492.71
	Rolab-Metformin HCl 500mg	5	104.83	19.12	524.13
	Rolab-Metformin FC 500mg	1	82.68	0	82.68
	Rolab-Metformin FC 850mg	2	117.95	33.21	235.89
	Rolab-Metformin HCl 850mg	9	141.78	27.97	1272.4
Humulin 30/70 Humaject Injection	Humulin 30/70 Humaject Injection	4	1765.15	1338.66	7060.58
	Rolab-Metformin HCl 850mg	1	850.68	0	850.68
Humulin R Humaject Pen 5ml Injection	Humulin L 10ml Vial	3	897.66	0	2692.98
	Humulin N 3ml Penset	4	1505.04	252.16	6020.16
Humalog 10ml Ampoules	Humalog 10ml Ampoules	1	697.86	0	697.86
	Humulin N 10ml Vial	8	809.02	171.81	6472.12
	Lantus 1000IU 10ml	1	818.56	0	818.56
	Lantus 300IU/3ml O/T	1	1199.74	0	1199.74
Humalog 3ml Cartridge Injection	Humulin L 10ml Vial	11	941.58	105.47	10357.4

Table F1: (Continue) Utilisation of two antidiabetic agents in combination for the time May to August

Agents in combination		No of Rx	Average cost	Std deviation	Total cost
	Humulin N 3ml Cartridges	14	1672.18	519.61	23410.53
	Humulin N 3ml Penset	4	1194	54.47	4775.99
	Lantus 1000IU 10ml	1	1203.84	0	1203.84
	Lantus 300IU 3ml	16	1477.48	167.02	23639.75
	Lantus 300IU/3ml O/T	2	1314.29	21.64	2628.57
	Protaphane HM Penfill 3ml	3	1490.99	412.79	4472.97
	Ultratard HM 10ml Ampoules	2	1189.1	28.59	2378.19
	Humalog 3ml Penset Prefill	3	1344.56	6.72	4033.68
	Humalog Mix 25 Penset	6	1274.91	97.96	7649.44
	Humulin L 10ml Vial	45	1033.47	275.83	46506.23
	Humulin N 10ml Vial	7	891.87	53.96	6243.12
	Humulin N 3ml Cartridges	5	1598.34	331.5	7991.71
	Humulin N 3ml Penset	111	1390.05	486.06	154295.72
	Lantus 1000IU 10ml	11	1414.68	405.52	15561.49
	Lantus 300IU 3ml	81	1638.79	545.84	132742.2
	Lantus 300IU/3ml O/T	44	1491.98	494.43	65647.11
	Protaphane HM Penfill 3ml	4	890.97	471.7	3563.86
	Protaphane HM Penset 3ml	27	1547.69	464.88	41787.7
	Rolab-Metformin HCl 500mg	2	642.94	0	1285.88
	Rolab-Metformin FC 500mg	9	841.95	281.54	7577.53
	Rolab-Metformin HCl 850mg	3	881.78	300.65	2645.33
	Ultratard HM 10ml Ampoules	1	876.79	0	876.79
Humalog Mix 25 Penset	Humalog Mix 25 Penset	8	1923.91	642.46	15391.3
	Humalog Mix 25 Cartridge	2	1147.14	562.1	2294.27
	Humulin N 3ml Penset	10	1229.64	3.61	12296.4
	Lantus 300IU 3ml	4	1468.28	145.3	5873.1
	Merck-Metformin 500mg	2	1105.45	516.95	2210.9
	Merck-Metformin 850mg	4	1403.15	26.17	5612.6
	Protaphane HM Penset 3ml	6	1253.78	53.94	7522.69
	Rolab-Gliclazide	2	789.34	0	1578.68
	Rolab-Metformin HCl 500mg	20	876.31	410.69	17526.17
	Rolab-Metformin FC 500mg	17	920.73	363.48	15652.36
	Rolab-Metformin FC 850mg	20	1035.58	469.34	20711.59

Table F1: (Continue) **Utilisation of two antidiabetic agents in combination for the time May to August**

Agents in combination		No of Rx	Average cost	Std deviation	Total cost
	Rolab-Metformin HCl 850mg	22	883.05	328.72	19427.08
Humalog Mix 25 Cartridges	Humulin N 3ml Cartridges	1	1720.67	0	1720.67
	Lantus 300IU 3ml	2	1477.45	198.14	2954.89
	Lantus 300IU/3ml O/T	2	1355.83	0	2711.66
	Protaphane HM Penfill 3ml	1	1142.92	0	1142.92
	Rolab-Metformin HCl 500mg	2	707.62	131.97	1415.24
	Rolab-Metformin FC 500mg	6	1292.99	303.28	7757.93
Humulin 30/70 3ml Cartridges	Humulin 30/70 3ml Cartridges	3	1359.81	179.5	4079.42
	Merck-Metformin 500mg	1	1059.21	0	1059.21
	Rolab-Metformin FC 850mg	2	574.14	15.92	1148.28
Humulin L 10ml Vial	Humulin R 10ml Vial	2	778.85	395.74	1557.7
	Humulin R 3ml Cartridges	2	848.8	0	1697.6
	Merck-Metformin 850mg	4	732.66	71.73	2930.62
	Novorapid 3ml Flexpen	2	1555.92	384.43	3111.83
	Rolab-Gliclazide	2	377.71	74	755.41
	Rolab-Metformin HCl 500mg	2	392.65	2.36	785.3
	Rolab-Metformin FC 500mg	2	609.5	478.49	1219
	Rolab-Metformin HCl 850mg	1	323.78	0	323.78
Humulin N 10ml Vial	Humulin R 10ml Vial	19	641.46	140.48	12187.83
Humulin N 3ml Cartridges	Humulin N 3ml Cartridges	1	4017.08	0	4017.08
	Humulin R 3ml Cartridges	1	803.24	0	803.24
	Novorapid 3ml Flexpen	1	1089.37	0	1089.37
Humulin N 3ml Penset	Humulin R 3ml Cartridges	4	1113.87	27.69	4455.49
	Lantus 300IU/3ml O/T	1	1291.01	0	1291.01
	Merck-Metformin 850mg	1	630.59	0	630.59
	Novorapid 3ml Flexpen	4	1105.16	59.64	4420.59
	Rolab-Gliclazide	1	610.14	0	610.14
	Rolab-Metformin HCl 500mg	1	730.79	0	730.79
	Rolab-Metformin FC 850mg	8	702.39	64.71	5619.15
	Rolab-Metformin HCl 850mg	3	611.2	0	1833.6
Humulin R 3ml Cartridges	Lantus 300IU 3ml	1	1406.28	0	1406.28
	Lantus 300IU/3ml O/T	1	1536.29	0	1536.29
	Ultratard HM 10ml Ampoules	5	707.72	51.45	3538.59

Table F1: (Continue) Utilisation of two antidiabetic agents in combination for the time May to August

Agents in combination		No of Rx	Average cost	Std deviation	Total cost
Hypomide 250mg	Merck-Metformin 500mg	1	137.35	0	137.35
	Rolab-Metformin FC 850mg	3	81.6	35.22	244.79
Lantus 1000IU 10ml	Lantus 1000IU 10ml	2	1369.67	841.92	2739.34
	Lantus 300IU/3ml O/T	1	2052.24	0	2052.24
	Rolab-Metformin HCl 500mg	4	474.23	90.6	1896.91
	Rolab-Metformin FC 500mg	2	561.8	0	1123.6
	Rolab-Metformin FC 850mg	1	686.05	0	686.05
Lantus 300IU 3ml	Lantus 300IU 3ml	1	1458.72	0	1458.72
	Merck-Metformin 500mg	2	775.05	103.49	1550.1
	Novomix 30 Penfill 3ml Injection	2	1601.71	0	3203.42
	Novorapid 3ml Flexpen	41	1321.33	219.96	54174.72
	Novorapid 3ml Penfill	4	1565.25	371.43	6261.01
Lantus 300IU/3ml O/T	Lantus 300IU/3ml O/T	2	1236.55	231.86	2473.1
	Novorapid 3ml Flexpen	36	1301.71	260.22	46861.68
	Novorapid 3ml Penfill	1	1312.8	0	1312.8
	Rolab-Metformin FC 500mg	1	780.34	0	780.34
	Rolab-Metformin FC 850mg	1	2298.33	0	2298.33
	Rolab-Metformin HCl 850mg	1	865.21	0	865.21
Merck-Gliclazide	Merck-Gliclazide	1	114.24	0	114.24
	Merck-Metformin 500mg	7	125.84	21.57	880.86
	Merck-Metformin 850mg	4	141.8	67.66	567.2
	Rolab-Metformin HCl 500mg	2	166.77	50.59	333.54
	Rolab-Metformin FC 500mg	2	120.81	56.12	241.61
	Rolab-Metformin FC 850mg	2	136.06	25.65	272.11
	Rolab-Metformin HCl 850mg	6	135.45	52.37	812.69
Merck-Metformin 500mg	Merck-Metformin 850mg	1	47.95	0	47.95
	Novomix 30 Flexpen 3ml Injection	1	672.78	0	672.78
	Novonorm 1.0mg	4	210.33	38.62	841.31
	Protaphane HM Penset 3ml	3	652.39	0	1957.17
	Rolab-Gliclazide	14	148.46	69.86	2078.44
Merck-Metformin 850mg	Minidiab 5mg	6	272.91	24.63	1637.46
	Novomix 30 Flexpen 3ml Injection	6	779.3	213.51	4675.81
	Novonorm 1.0mg	1	239.76	0	239.76

Table F1: (Continue) Utilisation of two antidiabetic agents in combination for the time May to August

Agents in combination		No of Rx	Average cost	Std deviation	Total cost
	Novonorm 2.0mg	2	363.22	21.5	726.44
	Rolab-Gliclazide	10	147.68	57.19	1476.76
Metforal 500mg	Rolab-Gliclazide	1	104.32	0	104.32
Metforal 850mg	Novomix 30 Flexpen 3ml Injection	1	640.14	0	640.14
	Rolab-Gliclazide	1	109.07	0	109.07
Minidiab 5mg	Rolab-Metformin HCl 500mg	14	205.11	115.58	2871.5
	Rolab-Metformin FC 500mg	11	363.15	187.73	3994.62
	Rolab-Metformin FC 850mg	3	234.83	16.22	704.48
	Rolab-Metformin HCl 850mg	10	315.96	225.9	3159.56
Monotard HM 10ml Ampoules	Monotard HM 10ml Ampoules	1	628.84	0	628.84
Norton-Glibenclamide	Rolab-Metformin FC 500mg	1	103.36	0	103.36
	Rolab-Metformin HCl 850mg	1	122.88	0	122.88
Novomix 30 Flexpen 3ml Injection	Novomix 30 Flexpen 3ml Injection	9	1288.98	508.44	11600.84
	Novomix 30 Penfill 3ml Injection	1	1472.19	0	1472.19
	Novonorm 1.0mg	1	840.66	0	840.66
	Novorapid 3ml Flexpen	2	1430.53	324.27	2861.06
	Rolab-Metformin HCl 500mg	14	689.2	207.49	9648.83
	Rolab-Metformin FC 500mg	21	850.66	395.89	17863.84
	Rolab-Metformin FC 850mg	26	890.28	443.14	23147.24
	Rolab-Metformin HCl 850mg	16	862.88	335.28	13806.12
Novomix 30 Penfill 3ml Injection	Novomix 30 Penfill 3ml Injection	1	191.46	0	191.46
	Rolab-Metformin FC 850mg	2	893.1	356.78	1786.19
	Rolab-Metformin HCl 850mg	1	1521.57	0	1521.57
Novonorm 0.5mg	Rolab-Metformin FC 500mg	1	138.5	0	138.5
	Rolab-Metformin HCl 850mg	6	199.61	50.27	1197.68
Novonorm 1.0mg	Novonorm 1.0mg	2	360.29	24.93	720.58
	Novonorm 2.0mg	1	557.64	0	557.64
	Rolab-Metformin HCl 500mg	6	244.17	15.25	1465
	Rolab-Metformin FC 500mg	3	264.47	49.4	793.4
	Rolab-Metformin FC 850mg	3	227.84	0	683.52
	Rolab-Metformin HCl 850mg	2	218.29	25.72	436.57
Novonorm 2.0mg	Rolab-Metformin HCl 500mg	9	359.88	27.85	3238.91
Novorapid 3ml Flexpen	Novorapid 3ml Flexpen	1	1166.9	0	1166.9

Table F1: (Continue) **Utilisation of two antidiabetic agents in combination for the time May to August**

Agents in combination		No of Rx	Average cost	Std deviation	Total cost
	Protaphane HM Penfill 3ml	6	1023.52	290.75	6141.13
	Protaphane HM Penset 3ml	13	1549.39	588.69	20142.09
	Rolab-Metformin FC 500mg	1	708.3	0	708.3
	Rolab-Metformin HCl 850mg	1	2093.98	0	2093.98
Novorapid 3ml Penfill	Protaphane HM Penfill 3ml	6	1130.86	69.95	6785.14
	Protaphane HM Penset 3ml	3	1612.19	418.45	4836.57
	Protaphane HM 10ml Ampoules	3	1281	186.83	3842.99
Protaphane HM Penfill 3ml	Rolab-Gliclazide	1	692.28	0	692.28
Protaphane HM Penset 3ml	Protaphane HM Penset 3ml	1	1248.34	0	1248.34
	Rolab-Gliclazide	1	726.33	0	726.33
	Rolab-Metformin FC 500mg	3	658.61	34.41	1975.82
	Rolab-Metformin FC 850mg	3	768.76	20.12	2306.29
Protaphane HM 10ml Ampoules	Rolab-Metformin HCl 500mg	1	399.34	0	399.34
	Rolab-Metformin FC 500mg	4	439.17	4.97	1756.66
	Rolab-Metformin FC 850mg	1	681.66	0	681.66
Rolab-Gliclazide	Rolab-Gliclazide	2	110.47	7.31	220.94
	Rolab-Metformin HCl 500mg	82	103.61	39.63	8496.25
	Rolab-Metformin FC 500mg	85	118.71	52.53	10090.26
	Rolab-Metformin FC 850mg	111	139.62	41.23	15497.67
	Rolab-Metformin HCl 850mg	96	127.77	33.97	12265.76
Rolab-Metformin HCL 500mg	Rolab-Metformin HCl 500mg	9	63.88	24.26	574.94
	Rolab-Metformin FC 850mg	1	37.48	0	37.48
	Rolab-Metformin HCl 850mg	3	79.61	3.7	238.83
Rolab-Metformin FC 500mg	Rolab-Metformin FC 500mg	12	109.54	99.59	1314.46
	Rolab-Metformin FC 850mg	4	77.68	34.28	310.72
	Starlix FCT 120mg	3	394.12	23.16	1182.36
Rolab-Metformin FC 850mg	Rolab-Metformin FC 850mg	6	169.71	80.95	1018.26
	Starlix FCT 120mg	4	593.8	0	2375.2
Rolab-Metformin HCl 850mg	Rolab-Metformin HCl 850mg	2	138.93	61.02	277.86
	Ultratard HM 10ml Ampoules	4	554.14	39.74	2216.56

Table F2: Utilisation of three antidiabetic agents in combination

Agents in combination			No of Rx	Average cost	Std deviation	Total cost
Actos 15mg	Actos 30mg	Amaryl 1mg	3	1130.15	480.23	3390.45
		Amaryl 2mg	2	1179.76	0.01	2359.51
	Actraphane HM Penfill 3ml	Glucophage 500mg	4	1118.37	0.01	4473.46
	Actraphane HM Penset 3ml	Amaryl 4mg	2	1441.02	127.58	2882.03
	Actrapid HM 10ml Ampules	Protaphane HM 10ml Ampules	7	1118.72	2.53	7831.06
	Amaryl 1mg	Rolab-Metformin HCl 500mg	3	748.5	30.37	2245.49
	Amaryl 2mg	Amaryl 4mg	4	908.34	30.09	3633.37
		Glucophage Forte 850mg	4	676.75	56.93	2707.01
	Amaryl 4mg	Glucophage 500mg	1	846.81	0	846.81
		Glucophage Forte 850mg	1	932.42	0	932.42
		Rolab-Metformin HCl 500mg	3	846.81	0	2540.43
		Rolab-Metformin FC 500mg	2	813.75	6.41	1627.49
	Diaglucide 80mg	Glucophage 500mg	1	425.92	0	425.92
	Diamicron 80mg	Glucophage Forte 850mg	1	614	0	614
	Diamicron MR 30mg	Rolab-Metformin FC 500mg	1	650.04	0	650.04
	Glucomed 80mg	Glucophage Forte 850mg	1	572.07	0	572.07
		Rolab-Metformin HCl 500mg	3	575.35	0	1726.05
		Rolab-Metformin FC 850mg	7	614.76	23.48	4303.33
	Glucophage 500mg	Glycomin 5mg	1	892.75	0	892.75
		Glycron 80mg	1	632.46	0	632.46
		Humalog Mix 25 Penset	4	2673.58	175.55	10694.32
	Glucophage Forte 850mg	Glycomin 5mg	2	613.02	5.08	1226.04
		Glycron 80mg	4	577.53	5.84	2310.12
		Rolab-Gliclazide	1	497.4	0	497.4
	Glycomin 5mg	Rolab-Metformin HCl 500mg	2	412.22	1.56	824.44
		Rolab-Metformin FC 500mg	2	387.67	40.88	775.33
		Rolab-Metformin FC 850mg	2	577.37	0	1154.74
	Glycron 80mg	Rolab-Metformin HCl 500mg	3	630.19	0	1890.57
	Humalog 3ml Penset Prefill	Lantus 300IU 3ml	1	2611.15	0	2611.15
	Humalog Mix 25 Penset	Rolab-Metformin FC 500mg	1	1248.4	0	1248.4
	Novorapid 3ml Flexpen	Protaphane HM Penset 3ml	2	3268.45	0	6536.9
Actos 30mg	Actraphane HM Penfill 3ml	Actraphane HM 10ml Ampules	1	1608.83	0	1608.83

Table F2: (Continue) Utilisation of three antidiabetic agents in combination

Agents in combination			No of Rx	Average cost	Std deviation	Total cost
		Glucobay 50mg	3	1509.96	0	4529.88
	Actrapid HM 10ml Ampules	Protaphane HM 10ml Ampules	1	1336.1	0	1336.1
	Amaryl 4mg	Glycomin 5mg	2	1029.43	0	2058.86
		Lantus 300IU/3ml O/T	1	1836.16	0	1836.16
		Rolab-Metformin HCl 500mg	3	1038.58	7.13	3115.74
	Diamicron 80mg	Glucobay 50mg	1	942.78	0	942.78
		Glucophage 500mg	5	942.79	77.34	4713.96
	Diamicron MR 30mg	Glucophage 500mg	1	659.05	0	659.05
	Glucomed 80mg	Glucophage 500mg	1	876.79	0	876.79
		Lantus 300IU 3ml	1	1645.83	0	1645.83
	Glucophage 500mg	Humalog Mix 25 Cartridges	2	1489.69	321.78	2979.37
	Glucophage Forte 850mg	Glycomin 5mg	1	836.38	0	836.38
		Lantus 300IU 3ml	1	1691.66	0	1691.66
		Novomix 30 Flexpen 3ml	1	1437.6	0	1437.6
	Glycron 80mg	Rolab-Metformin FC 500mg	1	880.77	0	880.77
		Rolab-Metformin FC 850mg	3	778.77	4.28	2336.31
	Lantus 300IU 3ml	Rolab-Metformin HCl 500mg	4	1579.67	0	6318.68
	Lantus 300IU/3ml O/T	Rolab-Gliclazide	1	1202.46	0	1202.46
Actraphane HM Penset 1.5ml	Glucomed 80mg	Glucophage Forte 850mg	2	548.99	37.9	1097.98
Actraphane HM Penset 3ml	Actrapid HM Penset 3ml	Glucophage 500mg	1	1169.19	0	1169.19
		Glucophage Forte 850mg	1	1255.35	0	1255.35
	Amaryl 2mg	Glucophage Forte 850mg	1	922.1	0	922.1
	Amaryl 4mg	Glucophage Forte 850mg	2	1146.98	84.14	2293.95
	Diaglucide 80mg	Merck-Metformin 500mg	1	781.26	0	781.26
	Diamicron 80mg	Rolab-Metformin HCl 500mg	3	656.4	40.87	1969.2
		Rolab-Metformin FC 500mg	1	702.35	0	702.35
	Diamicron MR 30mg	Rolab-Metformin HCl 500mg	1	976.14	0	976.14
	Glucomed 80mg	Glucophage 500mg	7	783.74	104.19	5486.16
		Glucophage Forte 850mg	3	742.53	26.35	2227.59
		Rolab-Metformin HCl 500mg	1	726.34	0	726.34
		Rolab-Metformin FC 500mg	1	726.91	0	726.91
	Glucophage 500mg	Glycomin 5mg	2	1105.62	450.19	2211.23
	Glucophage Forte 850mg	Glycomin 5mg	3	805.04	4.83	2415.11

Table F2: (Continue) Utilisation of three antidiabetic agents in combination

Agents in combination			No of Rx	Average cost	Std deviation	Total cost
	Glycron 80mg	Rolab-Metformin HCl 500mg	2	742.82	28.21	1485.64
	Rolab-Gliclazide	Rolab-Metformin FC 850mg	2	1305.31	0	2610.62
Actraphane HM 10ml Ampules	Actrapid HM 10ml Ampules	Glucophage Forte 850mg	1	1008.64	0	1008.64
	Avandia 4mg	Diamicron MR 30mg	3	803.47	48.1	2410.42
		Novonorm 1.0mg	1	1239.79	0	1239.79
	Diaglucide 80mg	Rolab-Metformin FC 850mg	2	479.16	0	958.32
	Diamicron MR 30mg	Glucophage 500mg	1	616.23	0	616.23
	Glucomed 80mg	Rolab-Metformin FC 850mg	2	572.63	64.56	1145.26
	Glucophage Forte 850mg	Glycomin 5mg	1	583.06	0	583.06
Actrapid HM 10ml Ampules	Diaglucide 80mg	Glucophage Forte 850mg	1	393.3	0	393.3
	Diamicron 80mg	Glucophage Forte 850mg	1	600.27	0	600.27
Actrapid HM Penfill 3ml	Daonil 5mg	Glucophage 500mg	2	960.71	34.11	1921.42
	Protaphane HM Penset 3ml	Rolab-Metformin HCl 850mg	1	2813.41	0	2813.41
Actrapid HM Penset 3ml	Glucophage 500mg	Protaphane HM Penset 3ml	4	1202.39	23.47	4809.54
	Glucophage Forte 850mg	Humulin L 10ml Vial	3	2735.6	244.18	8206.79
	Humalog 3ml Penset Prefill	Lantus 300IU/3ml O/T	1	1679.48	0	1679.48
	Humulin L 10ml Vial	Rolab-Gliclazide	1	819.14	0	819.14
		Rolab-Metformin FC 500mg	1	1420.07	0	1420.07
	Lantus 300IU 3ml	Merck-Metformin 500mg	2	1516.34	42.72	3032.68
	Protaphane HM Penset 3ml	Rolab-Metformin FC 850mg	1	2011.72	0	2011.72
Amaryl 1mg	Amaryl 2mg	Avandia 4mg	2	1181.57	97.83	2363.13
		Glucophage 500mg	16	229.69	92.05	3675.08
		Glucophage Forte 850mg	13	300.3	84.97	3903.86
		Glycomin 5mg	1	535.52	0	535.52
		Rolab-Metformin FC 500mg	10	345.23	51.33	3452.33
	Amaryl 4mg	Glucophage 500mg	4	405.66	18.86	1622.64
	Diamicron 80mg	Glucophage 500mg	3	322	0.03	966
	Glucobay 50mg	Rolab-Gliclazide	4	563.8	0	2255.2
	Glucomed 80mg	Rolab-Metformin HCl 500mg	4	307.66	0	1230.64
	Glucophage 500mg	Novonorm 2.0mg	4	525.38	14.65	2101.5
		Starlix FCT 120mg	1	623.96	0	623.96
	Glycomin 5mg	Rolab-Metformin FC 500mg	2	208.51	0	417.02
	Novonorm 0.5mg	Novonorm 1.0mg	3	423.72	0	1271.16

Table F2: (Continue) Utilisation of three antidiabetic agents in combination

Agents in combination			No of Rx	Average cost	Std deviation	Total cost
Amaryl 2mg	Amaryl 4mg	Avandia 4mg	1	887.06	0	887.06
		Glucophage 500mg	1	592.88	0	592.88
		Glucophage Forte 850mg	20	550.73	58.93	11014.68
		Rolab-Metformin HCl 500mg	6	318.72	145.77	1912.29
	Avandia 2mg	Glucophage Forte 850mg	4	349.09	8.69	1396.37
		Rolab-Metformin HCl 850mg	4	362.01	26.77	1448.02
	Avandia 4mg	Novorapid 3ml Flexpen	1	789	0	789
		Rolab-Metformin HCl 850mg	1	495.63	0	495.63
	Diamicron MR 30mg	Glucophage Forte 850mg	1	375.28	0	375.28
	Glucobay 100mg	Glucophage Forte 850mg	7	526.56	12.72	3685.89
		Glucovance 500/2.5mg	3	530.31	3.48	1590.94
	Glucophage 500mg	Glycomin 5mg	1	507.46	0	507.46
	Glucophage Forte 850mg	Lantus 300IU 3ml	1	1181.59	0	1181.59
		Merck-Metformin 500mg	1	410.06	0	410.06
		Rolab-Metformin FC 850mg	1	399.9	0	399.9
	Glycomin 5mg	Glycron 80mg	1	506.36	0	506.36
		Rolab-Metformin FC 850mg	1	240.19	0	240.19
	Merck-Metformin 500mg	Merck-Metformin 850mg	1	426.2	0	426.2
Amaryl 4mg	Avandia 2mg	Diamicron 80mg	1	948.82	0	948.82
	Avandia 4mg	Diamicron MR 30mg	1	1271	0	1271
		Glucophage Forte 850mg	7	747.7	128.92	5233.93
		Rolab-Metformin FC 850mg	3	589.7	10.54	1769.09
		Rolab-Metformin HCl 850mg	4	808.34	380.67	3233.34
	Diamicron 80mg	Rolab-Metformin FC 850mg	2	500.51	9.94	1001.02
	Glucobay 100mg	Glucophage Forte 850mg	3	833.58	0.66	2500.73
	Glucobay 50mg	Glucophage Forte 850mg	7	604.69	23.85	4232.8
		Protaphane HM Penset 3ml	2	1070.34	90.53	2140.67
		Rolab-Metformin FC 500mg	1	527.71	0	527.71
	Glucomed 80mg	Glucophage Forte 850mg	3	450.47	64.69	1351.4
	Glucophage 500mg	Glucophage Forte 850mg	5	456.19	53.37	2280.94
		Lantus 300IU 3ml	1	1418.1	0	1418.1
		Lantus 300IU/3ml O/T	4	1099.23	40.67	4396.92
		Novonorm 1.0mg	1	663.73	0	633.73

Table F2: (Continue) Utilisation of three antidiabetic agents in combination

Agents in combination			No of Rx	Average cost	Std deviation	Total cost
		Novonorm 2.0mg	5	776.56	0	3882.8
	Glucophage Forte 850mg	Lantus 300IU 3ml	2	1346.97	0	2693.94
		Protaphane HM Penset 3ml	1	973.16	0	973.16
		Rolab-Gliclazide	1	450.26	0	450.26
	Glycomin 5mg	Rolab-Metformin FC 850mg	3	554.33	49.99	1662.99
	Rolab-Gliclazide	Rolab-Metformin FC 500mg	3	403.51	27.06	1210.53
Avandia 2mg	Daonil 5mg	Glucophage Forte 850mg	4	666.92	0	2667.68
	Diamicron MR 30mg	Glucophage Forte 850mg	1	625.5	0	626.5
	Glucophage 500mg	Glyben 5mg	1	376.52	0	376.52
		Glycomin 5mg	1	370.02	0	370.02
Avandia 4mg	Diamicron 80mg	Glucophage 500mg	3	453.93	100.59	1361.79
		Glucophage Forte 850mg	4	1142.58	993.17	4570.31
		Rolab-Metformin HCl 850mg	1	487.19	0	487.19
	Diamicron MR 30mg	Glucophage 500mg	5	521.77	57.5	2608.84
		Glucophage Forte 850mg	1	820.52	0	820.52
		Glycron 80mg	1	903.58	0	903.58
	Glucomed 80mg	Glucophage 500mg	1	409.87	0	409.87
		Glucophage Forte 850mg	7	433.55	20.54	3034.86
	Glucophage 500mg	Glycomin 5mg	5	565.35	94.53	2826.74
		Novonorm 1.0mg	5	600.62	25.01	3003.11
	Glucophage Forte 850mg	Glyben 5mg	1	355.33	0	355.33
		Glycomin 5mg	4	411.11	21	1644.45
		Humalog Mix 25 Penset	2	1062.41	236.22	2124.81
		Humalog Mix 25 Cartridges	4	1163.4	0.44	4653.6
		Rolab-Metformin FC 850mg	1	951.55	0	951.55
	Glycomin 5mg	Rolab-Metformin FC 500mg	3	480.78	6.51	1442.35
	Humalog 3ml Penset Prefill	Lantus 300IU/3ml O/T	4	4597.56	178.67	18390.22
	Humalog Mix 25 Penset	Novonorm 1.0mg	1	1201.23	0	1201.23
		Rolab-Metformin HCl 850mg	3	1786.21	49.34	5358.62
	Humulin N 3ml Cartridges	Humulin R 3ml Cartridges	1	1584.16	0	1584.16
	Novorapid 3ml Flexpen	Protaphane HM Penset 3ml	1	1447.69	0	1447.69
Daonil 5mg	Glucophage 500mg	Glucophage Forte 850mg	5	267.15	29.83	1335.73
	Glucophage Forte 850mg	Glycomin 5mg	1	939.86	0	939.86

Table F2: (Continue) Utilisation of three antidiabetic agents in combination

Agents in combination			No of Rx	Average cost	Std deviation	Total cost
Diaglucide 80mg	Glucobay 100mg	Glucophage Forte 850mg	1	259.55	0	259.55
	Glucobay 50mg	Glucophage Forte 850mg	4	296.63	1.94	1186.5
		Rolab-Metformin FC 850mg	1	264.1	0	264.1
	Glucophage 500mg	Glycomin 5mg	1	270.74	0	270.74
	Glucophage Forte 850mg	Humulin L 10ml Vial	4	423.1	65.27	1692.41
	Humulin N 3ml Penset	Rolab-Metformin HCl 850mg	1	452.96	0	452.96
	Merck-Metformin 850mg	Novomix 30 Flexpen 3ml	2	1389	0	2778
Diamicron 80mg	Glucobay 100mg	Glucophage Forte 850mg	3	1080.03	0	3240.09
	Glucobay 50mg	Glucophage Forte 850mg	2	624.43	27.2	1248.86
	Glucophage 500mg	Lantus 300IU 3ml	1	1495.78	0	1495.78
	Glucophage Forte 850mg	Lantus 300IU/3ml O/T	1	1125.53	0	1125.53
		Novonorm 0.5mg	9	313.7	72.28	2823.3
		Rolab-Metformin FC 850mg	1	586.96	0	586.96
		Starlix FCT 120mg	1	428.47	0	428.47
	Rolab-Metformin FC 500mg	Rolab-Metformin FC 850mg	1	156.23	0	156.23
Diamicron MR 30mg	Glucophage Forte 850mg	Lantus 300IU 3ml	3	1010.32	19.65	3030.95
	Novomix 30 Flexpen 3ml	Rolab-Metformin FC 500mg	3	795	0.14	2385
	Rolab-Metformin FC 500mg	Rolab-Metformin FC 850mg	2	304.61	11.14	609.22
Glucobay 100mg	Glucomed 80mg	Glucophage 500mg	5	494.29	58.73	2471.45
		Glucophage Forte 850mg	1	244.19	0	244.19
		Rolab-Metformin FC 500mg	3	583.48	0	1750.44
	Glucophage Forte 850mg	Glycomin 5mg	3	468.23	31.78	1404.7
		Novonorm 0.5mg	1	446.62	0	446.62
	Glycomin 5mg	Protaphane HM Penset 3ml	1	1019.11	0	1019.11
Glucobay 50mg	Glucomed 80mg	Glucophage Forte 850mg	7	477.35	350.6	3341.47
		Merck-Metformin 850mg	3	423.81	89.49	1271.43
		Rolab-Metformin FC 500mg	3	308.93	54.21	926.78
		Rolab-Metformin HCl 850mg	1	284	0	284
	Glucophage 500mg	Rolab-Gliclazide	1	323.71	0	323.71
	Glucophage Forte 850mg	Glycomin 5mg	1	216.69	0	216.69
	Glycomin 5mg	Rolab-Metformin HCl 500mg	1	283.03	0	283.03
	Rolab-Gliclazide	Rolab-Metformin HCl 500mg	2	331.05	0	662.1
		Rolab-Metformin FC 500mg	2	277.87	69.4	555.73

Table F2: (Continue) Utilisation of three antidiabetic agents in combination

Agents in combination			No of Rx	Average cost	Std deviation	Total cost
		Rolab-Metformin FC 850mg	2	317.22	78.58	634.43
		Rolab-Metformin HCl 850mg	1	370.87	0	370.87
Glucomed 80mg	Glucophage 500mg	Humalog 3ml Penset Prefill	4	1290.49	51.71	5161.97
		Humalog Mix 25 Penset	1	758.11	0	758.11
		Humulin N 3ml Penset	1	685.89	0	685.89
		Novomix 30 Flexpen 3ml	3	1472.71	130.74	4418.12
		Protaphane HM Penset 3ml	2	875.98	134.95	1751.95
	Glucophage Forte 850mg	Humalog Mix 25 Penset	1	814.77	0	814.77
		Humulin L 10ml Vial	1	515.4	0	515.4
		Humulin N 3ml Penset	4	800.7	279.86	3202.81
		Lantus 1000IU 10ml	2	840.85	175.57	1681.7
		Lantus 300IU 3ml	3	900.88	63.99	2702.65
		Lantus 300IU/3ml O/T	2	1057.52	67.85	2115.03
		Protaphane HM Penset 3ml	1	970.99	0	970.99
	Glycomin 5mg	Rolab-Metformin HCl 850mg	1	209.3	0	209.3
	Humulin L 10ml Vial	Rolab-Metformin FC 850mg	1	339.09	0	339.09
	Humulin N 3ml Penset	Rolab-Metformin FC 500mg	2	852	74.05	1704
		Rolab-Metformin FC 850mg	2	751.49	10.3	1502.98
		Rolab-Metformin HCl 850mg	3	760.46	11.04	2281.37
	Lantus 300IU/3ml O/T	Rolab-Metformin FC 500mg	2	1025.01	4.91	2050.02
	Merck-Metformin 850mg	Novomix 30 Flexpen 3ml	1	907.43	0	907.43
	Novomix 30 Flexpen 3ml	Rolab-Metformin HCl 500mg	2	732.31	66.79	1464.61
		Rolab-Metformin HCl 850mg	1	642.85	0	642.85
	Protaphane HM Penfill 3ml	Rolab-Metformin FC 850mg	2	832.29	0	1664.58
	Protaphane HM Penset 3ml	Rolab-Metformin HCl 500mg	1	796.32	0	796.32
		Rolab-Metformin FC 500mg	3	928.34	9.67	2785.01
	Rolab-Metformin HCl 500mg	Rolab-Metformin HCl 850mg	3	124.34	6.19	373.01
Glucophage 500mg	Glucophage Forte 850mg	Glycomin 5mg	3	199.36	10.03	598.09
	Glycomin 5mg	Glycron 80mg	2	178.61	48.86	357.22
		Humulin L 10ml Vial	1	460.31	0	460.31
		Humulin N 3ml Penset	4	558.29	29.71	2233.14
		Lantus 300IU 3ml	1	938.65	0	938.65
		Lantus 300IU/3ml O/T	1	976.29	0	976.29

Table F2: (Continue) Utilisation of three antidiabetic agents in combination

Agents in combination			No of Rx	Average cost	Std deviation	Total cost
		Novonorm 1.0mg	3	248.31	2.2	744.94
	Glycron 80mg	Lantus 1000IU 10ml	1	678.37	0	678.37
	Glygard	Humulin L 10ml Vial	2	454.5	47.77	909
	Humalog 3ml Cartridges	Protaphane HM Penfill 3ml	3	1951.65	426.71	5854.94
	Humalog 3ml Penset Prefill	Humalog Mix 25 Penset	1	2206.08	0	2206.08
		Humulin L 10ml Vial	1	922.16	0	922.16
		Humulin N 3ml Penset	8	1744.06	401.14	13952.44
		Lantus 1000IU 10ml	3	4025.62	36.44	12076.87
		Lantus 300IU 3ml	2	1721.1	40.59	3442.2
		Protaphane HM Penfill 3ml	2	3191.81	0	6383.62
	Lantus 300IU 3ml	Novorapid 3ml Flexpen	1	1593.78	0	1593.78
		Novorapid 3ml Penfill	1	1516.71	0	1516.71
		Rolab-Gliclazide	2	1409.04	45.86	2818.08
	Novonorm 1.0mg	Novonorm 2.0mg	5	631.96	15.38	3159.81
	Novorapid 3ml Flexpen	Protaphane HM Penset 3ml	2	1437.4	66.43	2874.79
Glucophage Forte 850mg	Glyben 5mg	Protaphane HM Penset 3ml	2	711.34	3.3	1422.68
	Glycomin 5mg	Humalog Mix 25 Penset	1	815.87	0	815.87
		Humulin N 3ml Penset	4	720.92	32.17	2883.66
		Lantus 300IU 3ml	2	1409.35	66.3	2818.7
		Lantus 300IU/3ml O/T	2	847.71	2.35	1695.41
		Protaphane HM Penset 3ml	1	915.22	0	915.22
		Protaphane HM 10ml Ampules	1	399.73	0	399.73
	Glycron 80mg	Humalog 3ml Penset Prefill	1	808.44	0	808.44
	Humalog 3ml Cartridges	Humulin N 3ml Cartridges	1	1340.83	0	1340.83
		Lantus 300IU 3ml	1	2325.03	0	2325.03
		Protaphane HM Penfill 3ml	2	2867.27	9.84	5734.53
	Humalog 3ml Penset Prefill	Humalog Mix 25 Penset	1	2222	0	2222
		Humulin N 3ml Penset	5	1935.94	334.43	9679.72
		Protaphane HM Penfill 3ml	1	2934.9	0	2934.9
		Protaphane HM Penset 3ml	1	3057.28	0	3057.28
		Ultratard HM 10ml Ampules	1	984.9	0	984.9
	Humulin N 3ml Penset	Rolab-Gliclazide	2	747.26	164.11	1494.51
	Lantus 1000IU 10ml	Rolab-Gliclazide	2	946.99	29.8	1893.97

Table F2: (Continue) Utilisation of three antidiabetic agents in combination

Agents in combination			No of Rx	Average cost	Std deviation	Total cost
	Lantus 300IU 3ml	Novorapid 3ml Flexpen	2	2339.51	39.88	4679.02
		Novorapid 3ml Penfill	1	3026.28	0	3026.28
	Lantus 300IU/3ml O/T	Novonorm 1.0mg	1	1087.43	0	1087.43
		Novorapid 3ml Flexpen	1	1412.14	0	1412.14
	Novomix 30 Flexpen 3ml	Novorapid 3ml Flexpen	1	2048.65	0	2048.65
	Novonorm 1.0mg	Novonorm 2.0mg	4	569.91	104.02	2279.62
Glyben 5mg	Glycomin 5mg	Rolab-Metformin FC 850mg	1	129.27	0	129.27
	Humulin N 3ml Penset	Rolab-Metformin HCl 500mg	1	758.11	0	758.11
	Lantus 300IU 3ml	Rolab-Metformin FC 500mg	1	965.55	0	965.55
	Lantus 300IU/3ml O/T	Rolab-Metformin HCl 850mg	1	820.66	0	820.66
	Novomix 30 Flexpen 3ml	Rolab-Metformin FC 850mg	1	1228.69	0	1228.69
	Protaphane HM Penset 3ml	Rolab-Metformin FC 850mg	2	898.68	0	1797.36
	Protaphane HM 10ml Ampules	Rolab-Metformin HCl 500mg	1	414.61	0	414.61
	Rolab-Gliclazide	Rolab-Metformin FC 500mg	2	201.94	24.59	403.88
		Rolab-Metformin FC 850mg	1	188.62	0	188.62
Glycomin 5mg	Humalog MIx 25 Penset	Rolab-Metformin HCl 500mg	2	1476.67	145.85	2953.33
		Rolab-Metformin FC 500mg	1	847.76	0	847.76
	Humulin L 10ml Vial	Rolab-Metformin HCl 500mg	2	398.11	20	796.21
	Humulin N 3ml Cartridges	Rolab-Metformin FC 850mg	1	623.17	0	623.17
	Lantus 1000IU 10ml	Rolab-Metformin FC 500mg	1	562.19	0	562.19
	Lanrus 300IU	Rolab-Metformin FC 500mg	1	814.8	0	814.8
	Novonorm 1.0mg	Rolab-Metformin HCl 850mg	3	217.03	0	651.09
	Protaphane HM Penfill 3ml	Rolab-Metformin HCl 500mg	2	727.69	16.23	1455.37
		Rolab-Metformin FC 850mg	1	630.72	0	630.72
	Protaphane HM Penset 3ml	Rolab-Metformin HCl 500mg	1	834.48	0	834.48
		Rolab-Metformin FC 850mg	2	1013.12	352.9	2026.23
	Protaphane HM 10ml Ampules	Rolab-Metformin FC 500mg	2	1054.28	0	2108.56
		Rolab-Metformin FC 850mg	1	398.21	0	398.21
	Rolab-Gliclazide	Rolab-Metformin FC 850mg	1	248.18	0	248.18
		Rolab-Metformin HCl 850mg	1	144.2	0	144.22
	Rolab-Metformin FC 500mg	Rolab-Metformin HCl 850mg	3	103.35	2.5	310.06
Glycron 80mg	Rolab-Gliclazide	Rolab-Metformin FC 500mg	1	518.17	0	518.17
Glygard	Novorapid 3ml Flexpen	Protaphane HM Penset 3ml	1	1389.93	0	1389.93

Table F2: (Continue) Utilisation of three antidiabetic agents in combination

Agents in combination			No of Rx	Average cost	Std deviation	Total cost
Humulin R Humaject Penset 5ml	Humalog 3ml Penset Prefill	Humulin N 3ml Penset	1	1521.26	0	1521.26
Humaject/Humalog 3ml	Humalog Mix 25 Penset	Rolab-Metformin HCl 500mg	1	3051.28	0	3051.28
Humalog 10ml Ampules	Humulin N 10ml Vial	Rolab-Metformin HCl 500mg	3	1615.39	66.89	4846.17
Humalog 3ml Cartridges	Humulin N 3ml Cartridges	Rolab-Metformin HCl 500mg	1	2290.25	0	2290.25
	Lantus 300IU 3ml	Rolab-Metformin HCl 850mg	1	1766.93	0	1766.93
Humalog 3ml Penset Prefill	Humulin N 3ml Cartridges	Rolab-Metformin HCl 850mg	1	1446.75	0	1446.75
	Humulin N 3ml Penset	Rolab-Metformin FC 500mg	2	1859.52	0	3719.04
	Lantus 1000IU 10ml	Lantus 300IU 3ml	1	2395.49	0	2395.49
	Lantus 300IU 3ml	Rolab-Metformin HCl 500mg	1	1384.08	0	1384.08
	Novonorm 2.0mg	Rolab-Metformin FC 500mg	5	2628.13	409.26	13140.67
Humalog Mix 25 Penset	Rolab-Gliclazide	Rolab-Metformin FC 500mg	3	792.11	36.38	2376.33
		Rolab-Metformin HCl 850mg	1	967.82	0	967.82
Humulin L 10ml Vial	Rolab-Gliclazide	Rolab-Metformin FC 850mg	1	341.04	0	341.04
Humulin N 3ml Penset	Rolab-Gliclazide	Rolab-Metformin FC 850mg	1	701.58	0	701.58
Lantus 1000IU 10ml	Lantus 300IU/3ml O/T	Novonorm 2.0mg	1	1132.34	0	1132.34
Lantus 300IU 3ml	Lantus 300IU/3ml O/T	Rolab-Metformin HCl 850mg	1	1851.01	0	1851.01
	Novorapid 3ml Flexpen	Protaphane HM Penfill 3ml	1	1610.62	0	1610.62
		Rolab-Metformin FC 500mg	1	1156.81	0	1156.81
Novonorm 1.0mg	Novonorm 2.0mg	Rolab-Metformin FC5	4	261.34	21.94	1047.75
		Rolab-Metformin HCl 850mg	1	609.74	0	609.74
Novonorm 2.0mg	Rolab-Gliclazide	Rolab-Metformin FC 850mg	1	508.69	0	508.69
Novorapid 3ml Flexpen	Protaphane HM Penfill 3ml	Rolab-Metformin FC 500mg	3	1649.5	392.27	4948.5
Protaphane HM Penset 3ml	Rolab-Gliclazide	Rolab-Metformin HCl 850mg	2	644.7	0	1289.4
Protaphane HM 10ml Ampules	Rolab-Gliclazide	Rolab-Metformin FC 850mg	1	411.64	0	411.64
		Rolab-Metformin HCl 850mg	1	410.4	0	410.4

Table F3: Utilisation of four antidiabetic agents in combination

Agents in combination				No of Rx	Average cost	Std. deviation	Total cost
Actos 15mg	Actos 30mg	Amaryl 4mg	Protaphane HM 10ml Ampules	1	2049.48	0	2049.48
Actos 30mg	Actos 30mg	Glucophage Forte 850mg	Glucophage Forte 850mg	1	902.86	0	902.86
		Humalog Mix 25 Cartridges	Humalog Mix 25 Cartridges	1	2924.48	0	2924.48
		Rolab-Metformin HCl 500mg	Rolab-Metformin HCl 500mg	2	1862.77	142.43	3725.54
	Amaryl 4mg	Avandia 4mg	Glucophage Forte 850mg	1	1264.23	0	1264.23
	Glucophage 500mg	Humalog 3ml Penset Prefill	Lantus 300IU/3ml O/T	1	2275.76	0	2275.76
Actraphane HM Penset 3ml	Actraphane HM Penset 3ml	Actrapid HM Pensets 3ml	Actrapid HM Pensets 3ml	1	1798.5	0	1798.5
		Amaryl 2mg	Amaryl 2mg	2	1536.62	85.08	3073.24
	Amaryl 2mg	Amaryl 4mg	Glucophage Forte 850mg	3	1256.55	118.01	3769.66
		Glucophage 500mg		1	1102.94	0	1102.94
Actrapid HM Pensets 3ml	Actrapid HM Pensets 3ml	Humulin 30/70 3ml Cartridges	Humulin 30/70 3ml Cartridges	1	3430.52	0	3430.52
Amaryl 1mg	Amaryl 1mg	Amaryl 2mg	Amaryl 2mg	1	366	0	366
		Glucophage 500mg	Glucophage 500mg	2	679.59	25.39	1359.18
	Amaryl 2mg	Avandia 2mg	Glucophage Forte 850mg	2	180.8	1.05	361.6
Amaryl 2mg	Amaryl 2mg	Glucophage Forte 850mg	Glucophage Forte 850mg	6	470.31	89.44	2821.88
		Humalog Mix 25 Penset	Humalog Mix 25 Penset	1	1942.06	0	1942.06
		Rolab-Metformin FC 500mg	Rolab-Metformin FC 500mg	2	412.61	38.25	825.22
	Amaryl 4mg	Glucobay 100mg	Glucophage Forte 850mg	1	1031.89	0	1031.89
		Glucophage Forte 850mg	Protaphane HM Penfill 3ml	1	1026.71	0	1026.71
		Protaphane HM Penset 3ml	Rolab-Metformin FC 850mg	1	1125.99	0	1125.99
	Avandia 4mg	Lantus 300IU 3ml	Novorapid 3ml Flexpen	1	2080.04	0	2080.04
Amaryl 4mg	Amaryl 4mg	Glucophage Forte 850mg	Glucophage Forte 850mg	10	724.63	233.11	7246.3
		Humulin N 3ml Penset	Humulin N 3ml Penset	1	1893.5	0	1893.5
Avandia 2mg	Avandia 4mg	Glucophage Forte 850mg	Glycomin 5mg	1	516.64	0	516.64
Avandia 4mg	Avandia 4mg	Glucophage Forte 850mg	Glucophage Forte 850mg	6	666.93	86.77	4001.56
	Diamicron MR 30mg		Humalog Mix 25 Penset	1	1249.39	0	1249.39
Diaglucide 80mg	Diaglucide 80mg	Glucophage Forte 850mg	Glucophage Forte 850mg	1	227.68	0	227.68
Diamicron 80mg	Diamicron 80mg	Glucophage 500mg	Glucophage 500mg	8	250.15	59.07	2001.16
		Glucophage Forte 850mg	Glucophage Forte 850mg	16	345.01	96.88	5520.2
		Rolab-Metformin FC 500mg	Rolab-Metformin FC 500mg	3	276.52	23	829.56

Table F3: (Continue) Utilisation of four antidiabetic agents in combination

Agents in combination				No of Rx	Average cost	Std. deviation	Total cost
Diamicron MR 30mg	Diamicron MR 30mg	Glucophage 500mg	Glucophage 500mg	1	269.3	0	269.3
	Protaphane HM Penfill 3ml	Protaphane HM Penset 3ml	Rolab-Metformin FC 850mg	1	1652.69	0	1652.69
Glucobay 100mg	Glucophage Forte 850mg	Glycomin 5mg	Humalog Mix 25 Penset	1	1153.64	0	1153.64
Glucobay 50mg	Glucobay 50mg	Glucovance 500/5mg	Glucovance 500/5mg	1	629.58	0	629.58
	Glucomed 80mg	Glyben 5mg	Rolab-Metformin HCl 500mg	1	491.69	0	491.69
Glucomed 80mg	Glucomed 80mg	Glucophage 500mg	Glucophage 500mg	2	421.05	23.86	842.1
		Glucophage Forte 850mg	Glucophage Forte 850mg	3	304.21	53.69	912.62
		Metforal 850mg	Metforal 850mg	2	446.88	0.2	893.76
		Rolab-Metformin HCl 500mg	Rolab-Metformin HCl 500mg	2	420.8	29.47	841.6
		Rolab-Metformin FC 500mg	Rolab-Metformin FC 500mg	2	450.74	120.66	901.48
Glucophage 500mg	Glucophage 500mg	Glucophage Forte 850mg	Glucophage Forte 850mg	2	66.09	1.32	132.18
		Glyben 5mg	Glyben 5mg	1	353.38	0	353.38
		Glycomin 5mg	Glycomin 5mg	5	236.2	36.67	1181.02
		Humalog Mix 25 Penset	Humalog Mix 25 Penset	1	1441.82	0	1441.82
Glucophage Forte 850mg	Glucophage Forte 850mg	Glycomin 5mg	Glycomin 5mg	5	341.24	49.75	1706.2
		Humalog Mix 25 Penset	Humalog Mix 25 Penset	1	3058.82	0	3058.82
		Lantus 300IU/3ml O/T	Lantus 300IU/3ml O/T	1	1200.08	0	1200.08
		Rolab-Gliclazide	Rolab-Gliclazide	1	218.14	0	218.14
	Novomix 30 Flexpen 3ml Injection	Novonorm 1.0mg	Novonorm 2.0mg	1	1216.96	0	1216.96
Glyben 5mg	Glyben 5mg	Rolab-Metformin FC 500mg	Rolab-Metformin FC 500mg	1	131.68	0	131.68
		Rolab-Metformin FC 850mg	Rolab-Metformin FC 850mg	2	396.35	316.03	792.7
Glycomin 5mg	Glycomin 5mg	Merck-Metformin 850mg	Merck-Metformin 850mg	1	176.5	0	176.5
		Metforal 850mg	Metforal 850mg	1	255.56	0	255.56
		Rolab-Metformin HCl 500mg	Rolab-Metformin HCl 500mg	2	328.2	49.75	656.4
		Rolab-Metformin FC 500mg	Rolab-Metformin FC 500mg	2	406.83	371.27	813.66
		Rolab-Metformin HCl 850mg	Rolab-Metformin HCl 850mg	1	379.54	0	379.54
	Humalog 3ml Penset Prefill	Humulin N 3ml Penset	Rolab-Metformin FC 850mg	1	1393.47	0	1393.47
Humulin R Humaject Pen 5ml	Humulin N 10ml Vial	Humulin R 10ml Vial	Humulin R 3ml Cartridges	1	1141.33	0	1141.33
Humalog 3ml Penset Prefill	Humalog 3ml Penset Prefill	Humalog Mix 25 Penset	Humalog Mix 25 Penset	1	1879.72	0	1879.72
		Humulin N 3ml Penset	Humulin N 3ml Penset	2	2492.08	121.93	4984.16

Table F3: (Continue) Utilisation of four antidiabetic agents in combination

Agents in combination				No of Rx	Average cost	Std. deviation	Total cost
Lantus 300IU/3ml O/T	Lantus 300IU/3ml O/T	Novorapid 3ml Penfill	Novorapid 3ml Penfill	1	4491.32	0	4491.32
Novomix 30 Flexpen 3ml Injection	Novonorm 1.0mg	Novonorm 2.0mg	Rolab-Metformin HCl 850mg	1	1386.84	0	1386.84

Table F4: Utilisation of five antidiabetic agents in combination

Agents in combination					No of Rx	Average cost	Std dev	Total cost
Actos 15mg	Actos 30mg	Glucophage 500mg	Glycron 80mg	Rolab-Metformin FC 500mg	1	1335.47	0	1335.47

Table F5: Utilisation of six antidiabetic agents in combination for the time May tot August

Agents in combination						No of Rx	Average cost (R)	Std dev (R)	Total cost (R)
Actos 30mg	Actos 30mg	Glucophage 500mg	Glucophage 500mg	Humalog Mix 25 Cartridges	Humalog Mix 25 Cartridges	1	3326.68	0	3326.68
Amaryl 1mg	Amaryl 1mg	Amaryl 2mg	Amaryl 2mg	Glucophage Forte 850mg	Glucophage Forte 850	1	439.6	0	439.6
Amaryl 4mg	Amaryl 4mg	Avandia 4mg	Avandia 4mg	Glucophage Forte 850mg	Glucophage Forte 850	2	1854.26	0	3708.52
		Diamicron 80mg	Diamicron 80mg	Rolab-Metformin FC 850mg	Rolab-Metformin FC 850mg	2	955.9	84.88	1911.8
Diamicron 80mg	Diamicron 80mg	Glucobay 50mg	Glucobay 50mg	Glucophage Forte 850mg	Glucophage Forte 850	2	930.91	870.63	1861.82
Glucobay 100mg	Glucobay 100mg	Glucomed 80mg	Glucomed 80mg	Glucophage Forte 850mg	Glucophage Forte 850	2	1034.83	11.5	2069.66
Glucophage Forte 850mg	Glucophage Forte 850mg	Glycomin 5mg	Glycomin 5mg	Lantus 300IU/3ml O/T	Lantus 300IU/3ml O/T	1	1206.4	0	1206.4
Glucophage Forte 850mg		Humalog 3ml Penset Prefill	Humalog 3ml Penset Prefill	Lantus 300IU/3ml O/T	Lantus 300IU/3ml O/T	1	3045.68	0	3045.68

Appendix G

Table G1: Utilisation of two antidiabetic agents in combination for the time September to December

Agents in combination (Trade name ®)		No of Rx	Average cost (R)	Std deviation (R)	Total cost (R)
Actos 15mg	Actos 15mg	5	728.54	401.46	3642.70
	Actos 30mg	2	793.77	0.54	1587.54
	Actraphane HM Penfill 3ml	3	893.76	0	2681.28
	Actraphane HM Penset 3ml	9	974.85	245.15	8773.64
	Amaryl 1mg	9	412.34	8081.00	3711.02
	Amaryl 2mg	12	492.35	0.30	5908.25
	Amaryl 4mg	14	588.23	101.95	8235.19
	Daonil 5mg	4	478.16	8.14	1912.64
	Diamicron 80mg	2	363.36	19.75	726.71
	Diamicron MR 30mg	8	440.01	75.84	3520.04
	Glucomed 80mg	4	357.30	60.84	1429.20
	Glucophage 500mg	15	389.61	78.63	5844.17
	Glucophage Forte 850mg	11	380.73	13.89	4187.99
	Glyben 5mg	1	326.15	0	326.15
	Glycomin 5mg	4	398.01	93.08	1592.03
	Glycron 80mg	6	416.39	30.26	2498.32
	Humulin 30/70 3ml Cartridges	4	1199.78	166.43	4799.13
	Rolab-Metformin HCl 500mg	1	279.46	0	279.46
	Rolab-Metformin FC 500mg	2	378.68	30.38	757.36
	Sandoz-Metformin HCl 500mg	1	487.70	0	487.70
	Sandoz-Metformin FC 500mg	5	336.19	95.79	1680.95
Actos 30mg	Actraphane HM Penfill 3ml	3	1057.54	0.44	3172.63
	Actraphane HM Penset 3ml	7	1101.00	1.49	7707.03
	Actraphane HM 10ml Ampoules	8	1276.55	390.31	10212.42
	Amaryl 1mg	5	568.96	2.97	2844.80
	Amaryl 2mg	11	585.66	86.17	6442.24
	Amaryl 4mg	21	844.32	150.05	17730.71

Table G1: (Continue) Utilisation of two antidiabetic agents in combination for the time September to December

Agents in combination (Trade name ®)		No of Rx	Average cost (R)	Std deviation (R)	Total cost (R)
	Avandia 4mg	4	1014.47	0.46	4057.86
	Diamicron 80mg	2	565.16	37.35	1130.32
	Diamicron MR 30mg	12	614.99	97.77	7379.84
	Glucobay 50mg	1	710.77	0	710.77
	Glucomed 80mg	2	477.05	60.95	954.10
	Glucophage 500mg	22	502.56	49.35	11056.29
	Glucophage Forte 850mg	9	496.27	70.10	4466.41
	Glucovance 500/5mg	5	594.10	16.89	2970.52
	Glyben 5mg	1	368.32	0	368.32
	Glycomin 5mg	10	527.51	92.21	5275.06
	Glycron 80mg	7	565.28	29.95	3956.96
	Glygard	3	475.41	105.32	1426.22
	Humalog Mix 25 Penset	1	1161.84	0	1161.84
	Humalog Mix 25 Cartridges	1	1156.17	0	1156.17
	Lantus 300IU 3ml	4	1005.33	293.00	4021.33
	Merck-Gliclazide	2	412.19	0	824.38
	Novomix 30 Flexpen 3ml	4	1177.70	61.75	4710.80
	Novonorm 1.0mg	1	653.66	0	653.66
	Protaphane HM Penset 3ml	2	1170.04	0	2340.08
	Rolab-Metformin FC 500mg	1	517.39	0	517.39
	Rolab-Metformin HCl 850mg	1	477.85	0	477.85
	Sandoz-Gliclazide	1	413.10	0	413.10
	Sandoz-Metformin FC 500mg	2	281.78	333.78	562.75
	Sandoz-Metformin HCl 850mg	1	477.85	0	477.85
Actraphane HM Penfill 3ml	Actraphane HM Penfill 3ml	2	2353.96	475.57	4707.92
	Actraphane HM 10ml Ampoules	1	894.77	0	894.77
	Actrapid HM Penfill 3ml	1	822.70	0	822.70
	Actrapid HM Pensets 3ml	3	852.44	0	2557.32
	Glucophage 500mg	7	578.22	95.04	4047.53
	Glucophage Forte 850mg	22	568.93	150.78	12561.55
	Protaphane HM Penfill 3ml	1	822.70	0	822.70
	Rolab-Metformin FC 500mg	2	494.32	77.79	988.63
	Sandoz-Metformin FC 500mg	3	439.31	0.01	1317.94

Table G1: (Continue) Utilisation of two antidiabetic agents in combination for the time September to December

Agents in combination (Trade name ®)		No of Rx	Average cost (R)	Std deviation (R)	Total cost (R)
	Sandoz-Metformin HCl 850mg	1	436.25	0	436.25
Actraphane HM Penset 3ml	Actraphane HM Penset 3ml	55	1306.04	524.59	71832.34
	Actraphane HM 10ml Ampoules	1	2209.21	0	2209.21
	Actrapid HM Pensets 3ml	3	1705.08	0	5115.24
	Amaryl 2mg	4	791.50	159.52	316599.00
	Amaryl 4mg	6	1308.86	416.15	7853.17
	Avandia 4mg	7	1872.48	1280.35	13107.33
	Diamicron 80mg	1	658.55	0	658.55
	Glucomed 80mg	7	535.31	65.11	3747.18
	Glucophage 500mg	74	655.02	256.55	48471.43
	Glucophage Forte 850mg	126	773.18	288.89	97421.02
	Glucovance 500/5mg	1	561.54	0	561.51
	Glycomin 5mg	17	753.89	213.54	12816.05
	Glycron 80mg	3	915.50	409.33	2746.50
	Humulin N 3ml Pensets	1	879.19	0	879.19
	Merck-Gliclazide	1	487.52	0	487.52
	Merck-Metformin 500mg	4	495.90	23.05	1983.61
	Metforal 500mg	1	483.04	0	483.04
	Novomix 30 Flexpen 3ml	1	899.76	0	899.76
	Novonorm 0.5mg	1	125.51	0	125.51
	Novorapid 3ml Flexpen	3	899.76	0.01	2699.27
	Novorapid 3ml Penfill	1	894.89	0	894.89
	Protaphane HM Penset 3ml	7	1392.56	335.07	9747.90
	Rolab-Gliclazide	3	481.21	13.67	1443.63
	Rolab-Metformin HCl 500mg	7	713.91	233.89	4997.37
	Rolab-Metformin FC 500mg	5	822.17	33.42	4110.83
	Rolab-Metformin FC 850mg	6	756.85	415.44	4541.10
	Rolab-Metformin HCl 850mg	4	703.38	245.61	2813.51
	Sandoz-Gliclazide	6	476.58	12.95	2859.45
	Sandoz-Metformin HCl 500mg	27	687.72	210.68	18568.36
	Sandoz-Metformin FC 500mg	22	693.64	282.27	15260.16
	Sandoz-Metformin FC 850mg	19	690.33	251.65	13116.19
	Sandoz-Metformin HCl 850mg	11	702.63	213.41	7728.91

Table G1: (Continue) Utilisation of two antidiabetic agents in combination for the time September to December

Agents in combination (Trade name ®)		No of Rx	Average cost (R)	Std deviation (R)	Total cost (R)
Actraphane HM 10ml Ampoules	Actraphane HM 10ml Ampoules	6	1019.98	808.61	6119.90
	Actrapid HM 10ml Ampoules	3	642.21	79.45	1926.62
	Avandia 4mg	7	771.97	165.80	5403.80
	Diaglucide 80mg	1	546.46	0	546.46
	Diamicron 80mg	2	298.47	28.02	596.93
	Glucomed 80mg	1	743.01	0	743.01
	Glucophage 500mg	13	567.00	158.67	7370.95
	Glucophage Forte 850mg	17	466.44	110.01	7929.48
	Glycomin 5mg	1	764.91	0	764.910
	Monotard HM 10ml Ampoules	4	1590.85	0	6363.40
	Protaphane HM 10ml Ampoules	1	478.50	0	478.50
	Rolab-Gliclazide	1	496.20	0	496.20
	Rolab-Metformin HCl 500mg	1	266.97	0	266.97
	Rolab-Metformin FC 500mg	1	375.83	0	375.83
	Rolab-Metformin FC 850mg	1	501.30	0	501.30
	Sandoz-Gliclazide	4	460.65	71.00	1842.60
	Sandoz-Metformin HCl 500mg	5	566.55	228.42	2832.74
	Sandoz-Metformin FC 500mg	5	498.84	162.67	2494.21
	Sandoz-Metformin FC 850mg	1	698.79	0	698.79
Actrapid HM 10ml Ampoules	Glucophage 500mg	2	359.90	0	719.80
	Humulin L 10ml Vials	3	476.81	0	1430.43
	Humulin N 10ml Ampoules	2	476.81	0	953.62
	Lantus 1000IU 10ml	7	104.92	434.21	7454.41
	Lantus 300IU 3ml	3	1094.64	0	3283.92
	Monotard HM 10ml Ampoules	39	602.13	227.41	23483.21
	Protaphane HM 10ml Ampoules	19	657.26	204	12487.92
	Ultratard HM 10ml Ampoules	3	462.82	0	1388.46
Actrapid HM Penfill 3ml	Glucophage Forte 850mg	3	869.54	0	2608.62
	Humulin L 10ml Vials	3	648.91	0	1946.73
	Monotard HM 10ml Ampoules	4	808.91	263.35	3235.64
	Protaphane HM Penfill 3ml	25	1105.51	334.03	27637.87
	Protaphane HM Penset 3ml	1	1200.44	0	1200.44
Actrapid HM Pensets 3ml	Actrapid HM Pensets 3ml	4	882.20	0	3528.80

Table G1: (Continue) Utilisation of two antidiabetic agents in combination for the time September to December

Agents in combination (Trade name ®)		No of Rx	Average cost (R)	Std deviation (R)	Total cost (R)
	Glucophage 500mg	10	571.02	183.17	5710.23
	Glucophage Forte 850mg	4	709.06	250.57	2836.25
	Glycomin 5mg	3	494.90	0	1484.70
	Humalog Mix 25 Penset	2	1860.36	0	3720.72
	Humulin L 10ml Vials	11	697.56	62.69	7673.18
	Humulin N 3ml Pensets	4	835.25	87.93	3340.98
	Lantus 1000IU 10ml	3	1162.86	0	3488.58
	Lantus 300IU 3ml	11	1360.03	191.41	14960.36
	Lantus 300IU/3ml O/T	5	1073.89	187.49	5369.47
	Merck-Metformin 500mg	1	904.79	0	904.79
	Monotard HM 10ml Ampoules	9	1032.09	394.81	9288.83
	Novorapid 3ml Flexpen	1	899.76	0	899.76
	Protaphane HM Penfill 3ml	3	1263.91	0	3791.73
	Protaphane HM Penset 3ml	54	992.60	179.66	53600.13
	Rolab-Metformin HCl 850mg	1	902.32	0	902.32
	Sandoz-Metformin HCl 500mg	1	894.14	0	894.14
	Sandoz-Metformin FC 500mg	1	866.53	0	866.53
	Sandoz-Metformin FC 850mg	1	929.04	0	929.04
	Sandoz-Metformin HCl 850mg	3	902.32	0	2706.96
	Ultratard HM 10ml Ampoules	1	664.66	0	664.66
Amaryl 1mg	Amaryl 1mg	13	208.93	105.38	2716.13
	Amaryl 2mg	39	237.80	53.67	9274.11
	Amaryl 4mg	4	200.92	135.18	803.66
	Avandia 2mg	1	142.14	0	142.14
	Diamicron 80mg	1	149.39	0	149.39
	Diamicron MR 30mg	1	211.99	0	211.99
	Glucomed 80mg	1	155.91	0	155.91
	Glucophage 500mg	59	118.68	47.63	7002.38
	Glucophage Forte 850mg	63	134.02	46.91	8443.45
	Glycomin 5mg	4	130.87	1.89	523.49
	Novomix 30 Flexpen 3ml	3	745.58	0	2236.74
	Rolab-Gliclazide	1	128.38	0	128.38
	Rolab-Metformin HCl 500mg	6	91.72	37.28	550.34

Table G1: (Continue) Utilisation of two antidiabetic agents in combination for the time September to December

Agents in combination (Trade name ®)		No of Rx	Average cost (R)	Std deviation (R)	Total cost (R)
	Rolab-Metformin FC 500mg	4	143.08	77.61	572.30
	Rolab-Metformin FC 850mg	3	107.32	57.74	321.97
	Rolab-Metformin HCl 850mg	3	118.14	23.77	354.42
	Sandoz-Gliclazide	4	134.59	12.43	538.37
	Sandoz-Metformin HCl 500mg	25	93.73	28.55	2343.25
	Sandoz-Metformin FC 500mg	7	140.92	56.41	986.45
	Sandoz-Metformin FC 850mg	20	121.56	37.10	2431.16
	Sandoz-Metformin HCl 850mg	4	108.68	19.88	434.72
Amaryl 2mg	Amaryl 2mg	20	334.39	90.66	6687.82
	Amaryl 4mg	22	391.16	106.80	8606.08
	Avandia 2mg	2	183.27	34.44	366.53
	Diaglucide 80mg	4	193.24	0	772.96
	Diamicron MR 30mg	10	348.98	77.02	3489.78
	Glucobay 50mg	2	368.25	58.66	736.50
	Glucophage 500mg	173	183.09	61.40	31674.47
	Glucophage Forte 850mg	207	197.12	66.80	40803.13
	Glucovance 500/2.5mg	1	264.85	0	264.85
	Glycomin 5mg	3	283.05	0.60	849.14
	Humalog Mix 25 Penset	4	663.15	0	2652.60
	Humulin N 3ml Pensets	1	582.54	0	582.54
	Lantus 300IU 3ml	1	687.87	0	687.87
	Merck-Metformin 500mg	4	146.04	58.46	584.14
	Metforal 500mg	1	228.36	0	228.36
	Novonorm 1.0mg	4	367.66	0	1470.64
	Rolab-Metformin HCl 500mg	9	191.42	26.07	1722.78
	Rolab-Metformin FC 500mg	14	183.69	92.45	2571.67
	Rolab-Metformin FC 850mg	6	176.26	46.91	1057.55
	Rolab-Metformin HCl 850mg	6	166.49	84.07	998.92
	Sandoz-Gliclazide	1	210.66	0	210.66
	Sandoz-Metformin HCl 500mg	30	198.85	82.20	5965.36
	Sandoz-Metformin FC 500mg	26	172.73	76.30	4490.90
	Sandoz-Metformin FC 850mg	24	185.58	95.46	4453.85
	Sandoz-Metformin HCl 850mg	13	183.44	29.22	2384.70

Table G1: (Continue)   Utilisation of two antidiabetic agents in combination for the time September to December

Agents in combination (Trade name ®)		No of Rx	Average cost (R)	Std deviation (R)	Total cost (R)
Amaryl 4mg	Amaryl 4mg	13	474.60	22.26	6169.80
	Avandia 2mg	8	412.10	135.43	3296.78
	Avandia 4mg	33	652.68	205.84	21538.57
	Daonil 5mg	1	844.21	0	844.21
	Diamicron 80mg	5	355.69	191.07	1778.47
	Diamicron MR 30mg	4	452.94	42.00	1811.76
	Glucobay 100mg	4	988.08	0	3952.32
	Glucobay 50mg	3	468.53	76.79	1405.60
	Glucomed 80mg	6	324.28	61.55	1945.69
	Glucophage 500mg	120	288.46	110.29	34615.41
	Glucophage Forte 850mg	253	343.63	117.83	86937.43
	Glucovance 500/5mg	5	951.90	329.61	4759.48
	Glyben 5mg	2	333.60	0	667.20
	Glycomin 5mg	6	388.17	45.98	2328.99
	Humulin N 3ml Cartridges	2	613.84	22.57	1227.68
	Humulin N 3ml Pensets	1	505.19	0	505.19
	Lantus 300IU 3ml	2	783.57	0	1567.14
	Merck-Metformin 500mg	1	272.79	0	272.79
	Merck-Metformin 850mg	4	290.79	7.38	1163.17
	Metforal 850mg	3	267.93	139.09	803.78
	Novomix 30 Flexpen 3ml	2	806.62	150.06	1613.23
	Novonorm 0.5mg	1	425.84	0	425.84
	Novonorm 1.0mg	2	455.62	84.13	911.24
	Novonorm 2.0mg	3	825.95	0	2477.85
	Protaphane HM Penset 3ml	2	729.34	0	1458.68
	Rolab-Gliclazide	1	290.55	0	290.55
	Rolab-Metformin HCl 500mg	13	330.28	68.46	4293.68
	Rolab-Metformin FC 500mg	5	271.06	137.41	1355.29
	Rolab-Metformin FC 850mg	12	299.78	163.77	3597.30
	Rolab-Metformin HCl 850mg	7	313.32	48.82	2193.26
	Sandoz-Gliclazide	5	324.55	24.40	1622.77
	Sandoz-Metformin HCl 500mg	25	315.03	109.29	7875.76
	Sandoz-Metformin FC 500mg	35	329.62	116.39	11536.71

Table G1: (Continue) Utilisation of two antidiabetic agents in combination for the time September to December

Agents in combination (Trade name ®)		No of Rx	Average cost (R)	Std deviation (R)	Total cost (R)
	Sandoz-Metformin FC 850mg	29	297.79	31.62	8635.93
	Sandoz-Metformin HCl 850mg	29	320.56	54.00	9296.32
Avandia 2mg	Avandia 2mg	5	311.92	136.99	1559.62
	Avandia 4mg	1	323.18	0	323.18
	Diamicron MR 30mg	1	613.72	0	613.72
	Glucomed 80mg	2	179.10	18.80	358.19
	Glucophage 500mg	2	150.21	46.61	300.42
	Glucophage Forte 850mg	7	189.78	29.12	1328.47
	Glucovance 500/2.5mg	2	290.84	0	581.68
	Glycomin 5mg	1	170.80	0	170.80
	Humalog Mix 25 Penset	1	886.27	0	886.27
	Novomix 30 Flexpen 3ml	1	583.99	0	583.99
	Sandoz-Gliclazide	1	259.85	0	259.85
Avandia 4mg	Avandia 4mg	8	751.68	308.21	6013.42
	Daonil 5mg	1	427.61	0	427.610
	Diamicron MR 30mg	17	486.82	175.88	8275.90
	Glucomed 80mg	15	294.80	35.31	4421.99
	Glucophage 500mg	25	297.43	54.91	7435.66
	Glucophage Forte 850mg	42	330.66	90.87	13887.56
	Glucovance 500/2.5mg	5	416.95	0.34	2084.74
	Glucovance 500/5mg	7	378.64	47.58	2650.48
	Glycomin 5mg	9	288.17	38.83	2593.57
	Glycron 80mg	2	572.30	0	1144.60
	Humulin 30/70 Humaject Injection	4	887.78	0	3551.12
	Humalog 3ml Penset Prefill	2	951.78	0	1903.56
	Humalog Mix 25 Penset	5	1006.36	195.47	5031.80
	Humalog Mix 25 Cartridges	2	946.15	0	1892.30
	Humulin L 10ml Vials	2	828.26	0.02	1656.51
	Lantus 1000IU 10ml	1	793.33	0	793.33
	Lantus 300IU 3ml	1	1068.86	0	1068.86
	Lantus 300IU/3ml O/T	6	1068.04	256.19	6408.21
	Merck-Metformin 500mg	3	234.50	0.27	703.49
	Novomix 30 Flexpen 3ml	8	847.52	159.12	6780.19

Table G1: (Continue) Utilisation of two antidiabetic agents in combination for the time September to December

Agents in combination (Trade name ®)		No of Rx	Average cost (R)	Std deviation (R)	Total cost (R)
	Novonorm 1.0mg	2	461.16	0.02	922.31
	Novonorm 2.0mg	2	592.89	0	1185.78
	Protaphane HM Penset 3ml	3	974.29	14.76	2922.87
	Rolab-Metformin FC 500mg	1	309.85	0	309.85
	Rolab-Metformin FC 850mg	1	238.93	0	238.93
	Rolab-Metformin HCl 850mg	1	332.75	0	332.75
	Sandoz-Gliclazide	3	796.19	175.43	2388.57
	Sandoz-Metformin HCl 500mg	2	290.20	406.13	580.40
	Sandoz-Metformin FC 500mg	5	290.22	26.88	1451.11
	Sandoz-Metformin FC 850mg	6	249.41	103.96	1496.45
	Sandoz-Metformin HCl 850mg	9	334.95	62.18	3014.54
Daonil 5mg	Daonil 5mg	1	652.76	0	652.76
	Diamicron 80mg	1	45.63	0	45.63
	Glucobay 100mg	1	656.69	0	656.69
	Glucobay 50mg	2	622.88	0	1245.76
	Glucophage 500mg	124	300.55	112.22	37268.81
	Glucophage Forte 850mg	64	389.83	132.31	24949.22
	Humalog Mix 25 Penset	2	1137.21	0	2274.42
	Minidiab 5mg	5	151.78	0	758.90
	Novonorm 1.0mg	1	349.40	0	349.40
	Rolab-Metformin HCl 500mg	8	327.02	131.76	2616.16
	Rolab-Metformin FC 500mg	6	369.20	111.54	2215.17
	Rolab-Metformin FC 850mg	3	255.63	52.67	766.89
	Sandoz-Metformin HCl 500mg	21	298.07	96.26	6259.45
	Sandoz-Metformin FC 500mg	16	389.66	113.91	6234.51
	Sandoz-Metformin FC 850mg	5	306.58	45.92	1532.89
	Sandoz-Metformin HCl 850mg	7	305.79	102.95	2140.51
Diacare 5mg	Diacare 5mg	1	30.28	0	30.28
	Glucophage 500mg	2	24.59	9.19	49.17
	Glucophage Forte 850mg	1	63.48	0	63.48
	Rolab-Metformin FC 500mg	1	88.73	0	88.73
	Rolab-Metformin FC 850mg	1	108.22	0	108.22
	Sandoz-Metformin FC 500mg	2	39.29	0	78.58

Table G1: (Continue) Utilisation of two antidiabetic agents in combination for the time September to December

Agents in combination (Trade name ®)		No of Rx	Average cost (R)	Std deviation (R)	Total cost (R)
	Sandoz-Metformin FC 850mg	1	84.96	0	84.96
Diaglucide 80mg	Glucophage 500mg	95	95.60	38.12	9081.91
	Glucophage Forte 850mg	184	129.55	36.53	23836.97
	Glucovance 500/5mg	3	146.61	65.12	439.84
	Humalog 3ml Penset Prefill	1	529.21	0	529.21
	Humalog Mix 25 Penset	5	557.75	13.36	2788.77
	Humulin N 3ml Pensets	1	486.92	0	486.92
	Merck-Metformin 500mg	13	134.72	62.45	1751.33
	Merck-Metformin 850mg	15	137.57	29.14	2063.54
	Metforal 850mg	4	113.37	41.56	45.47
	Protaphane HM Penfill 3ml	1	460.15	0	460.15
	Protaphane HM Penset 3ml	1	536.29	0	536.29
	Rolab-Metformin HCl 500mg	12	109.40	44.55	1312.80
	Rolab-Metformin FC 500mg	6	136.39	40.43	818.34
	Rolab-Metformin FC 850mg	16	133.10	27.87	2129.62
	Rolab-Metformin HCl 850mg	7	106.53	21.22	745.73
	Sandoz-Metformin HCl 500mg	29	124.85	46.60	3620.70
	Sandoz-Metformin FC 500mg	36	103.78	36.98	3735.97
	Sandoz-Metformin FC 850mg	53	115.68	30.19	6131.18
	Sandoz-Metformin HCl 850mg	22	118.52	19.41	2607.51
Diamicron 80mg	Diamicron 80mg	35	220.08	85.46	7702.94
	Diamicron MR 30mg	1	226.84	0	226.84
	Glucobay 50mg	5	201.75	2.77	1008.76
	Glucomed 80mg	1	200.90	0	200.90
	Glucophage 500mg	148	126.02	56.50	18651.42
	Glucophage Forte 850mg	235	137.43	41.03	32294.98
	Glucovance 250/1.25mg	1	134.98	0	134.98
	Glucovance 500/2.5mg	2	157.85	0	315.70
	Glycomin 5mg	2	137.98	61.48	275.96
	Merck-Metformin 500mg	6	122.07	37.67	732.43
	Merck-Metformin 850mg	2	157.29	43.09	314.58
	Metforal 850mg	2	191.36	43.49	382.71
	Rolab-Metformin HCl 500mg	5	148.33	59.01	741.67

Table G1: (Continue) **Utilisation of two antidiabetic agents in combination for the time September to December**

Agents in combination (Trade name ®)		No of Rx	Average cost (R)	Std deviation (R)	Total cost (R)
	Rolab-Metformin FC 500mg	4	87.51	16.54	350.02
	Rolab-Metformin FC 850mg	8	154.94	54.54	1239.48
	Rolab-Metformin HCl 850mg	7	174.53	54.77	1221.74
	Sandoz-Gliclazide	1	154.77	0	154.77
	Sandoz-Metformin HCl 500mg	13	99.42	52.65	1292.49
	Sandoz-Metformin FC 500mg	11	102.51	10.04	1127.63
	Sandoz-Metformin FC 850mg	24	150.62	48.64	3614.87
	Sandoz-Metformin HCl 850mg	16	150.17	23.34	2402.74
Diamicron MR 30mg	Diamicron MR 30mg	8	214.20	127.46	1713.58
	Glucobay 50mg	1	251.56	0	251.56
	Glucophage 500mg	105	146.49	55.86	15381.91
	Glucophage Forte 850mg	207	201.77	83.65	41766.24
	Glyben 5mg	1	110.42	0	110.42
	Glycomin 5mg	2	233.55	0	467.10
	Lantus 300IU 3ml	1	611.39	0	611.39
	Lantus 300IU/3ml O/T	4	696.69	34.74	2786.75
	Merck-Metformin 500mg	2	150.93	77.18	301.85
	Merck-Metformin 850mg	5	134.97	19.04	674.86
	Metforal 500mg	1	96.40	0	96.40
	Metforal 850mg	7	211.66	106.01	1481.63
	Novomix 30 Flexpen 3ml	3	594.54	0.01	1783.61
	Protaphane HM Penfill 3ml	3	743.28	0	2229.84
	Protaphane HM 10ml Ampoules	3	644.05	158.99	1932.16
	Rolab-Metformin HCl 500mg	4	202.42	72.38	809.68
	Rolab-Metformin FC 500mg	10	149.18	78.04	1491.75
	Rolab-Metformin FC 850mg	6	216.05	69.75	1269.28
	Rolab-Metformin HCl 850mg	14	189.78	64.93	2656.87
	Sandoz-Metformin HCl 500mg	16	183.48	62.58	2935.74
	Sandoz-Metformin FC 500mg	34	158.88	74.53	5401.76
	Sandoz-Metformin FC 850mg	22	159.26	44.05	3503.81
	Sandoz-Metformin HCl 850mg	43	204.17	97.94	8779.46
Euglucon 5mg	Euglucon 5mg	1	437.14	0	437.14
	Glucophage Forte 850mg	2	389.52	0	779.04

Table G1: (Continue) Utilisation of two antidiabetic agents in combination for the time September to December

Agents in combination (Trade name ®)		No of Rx	Average cost (R)	Std deviation (R)	Total cost (R)
Glucobay 100mg	Glucophage 500mg	2	180.08	0	360.16
	Glucovance 250/1.25mg	2	284.98	0	569.96
	Glycomin 5mg	9	323.67	14.18	2913.03
Glucobay 50mg	Glucomed 80mg	10	215.49	18.40	2154.89
	Glucophage 500mg	4	203.47	13.81	813.89
	Glucophage Forte 850mg	3	258.82	0	776.46
	Glucovance 500/5mg	3	403.10	0.01	1209.31
	Glyben 5mg	3	188.58	0	565.74
	Glycomin 5mg	6	227.03	27.92	1362.20
	Glycron 80mg	4	352.34	2.70	1409.37
	Metforal 850mg	1	309.70	0	309.70
	Rolab-Metformin FC 500mg	1	292.18	0	292.18
	Sandoz-Metformin FC 500mg	2	292.18	0	584.36
Glucomed 80mg	Glucomed 80mg	16	146.05	63.05	2336.80
	Glucophage 500mg	395	107.92	46.68	42628.21
	Glucophage Forte 850mg	694	133.97	43.37	92974.82
	Glycomin 5mg	7	108.53	32.98	759.71
	Humalog Mix 25 Penset	2	655.01	97.89	1310.02
	Humulin 30/70 10ml Vials	1	371.71	0	371.71
	Humulin 30/70ml Cartridges	4	828.32	1.76	3313.29
	Humulin L 10ml Vials	2	286.39	0	572.78
	Humulin N 3ml Pensets	3	572.92	1.13	1718.76
	Lantus 300IU/3ml O/T	6	605.52	27.92	3633.09
	Merck-Metformin 500mg	9	110.82	49.83	997.37
	Merck-Metformin 850mg	14	147.91	73.17	2070.72
	Metforal 500mg	1	218.06	0	218.06
	Metforal 850mg	7	99.64	51.74	697.45
	Novomix 30 Flexpen 3ml	6	491.20	4.17	2947.21
	Novonorm 1.0mg	4	203.36	0	813.44
	Novonorm 2.0mg	2	502.34	34.52	1004.68
	Protaphane HM Penfill 3ml	1	478.43	0	478.43
	Protaphane HM Penset 3ml	5	556.14	2.56	2780.68
	Rolab-Metformin HCl 500mg	51	103.71	35.94	5289.29

Table G1: (Continue) Utilisation of two antidiabetic agents in combination for the time September to December

Agents in combination (Trade name ®)		No of Rx	Average cost (R)	Std deviation (R)	Total cost (R)
	Rolab-Metformin FC 500mg	71	117.62	43.32	8351.19
	Rolab-Metformin FC 850mg	51	146.53	37.64	7473.25
	Rolab-Metformin HCl 850mg	39	126.47	42.71	4932.36
	Sandoz-Metformin HCl 500mg	144	106.39	34.16	15320.60
	Sandoz-Metformin FC 500mg	162	121.44	46.77	19672.47
	Sandoz-Metformin FC 850mg	161	132.57	40.24	21343.69
	Sandoz-Metformin HCl 850mg	106	136.28	41.38	14446.00
Glucophage 500mg	Glucophage 500mg	139	47.71	43.70	6632.32
	Glucophage Forte 850mg	13	55.18	15.70	717.38
	Glucovance 500/2.5mg	1	74.27	0	74.27
	Glucovance 500/5mg	3	224.29	42.43	672.86
	Glyben 5mg	97	46.67	25.09	4527.13
	Glycomin 5mg	778	98.90	42.49	76943.19
	Glycron 80mg	50	100.15	43.93	5007.45
	Glygard	22	107.32	35.62	2361.06
	Humulin 30/70 Humaject Injection	3	738.44	235.81	2215.32
	Humalog 3ml Cartridges	2	940.33	0.05	1880.65
	Humalog 3ml Penset Prefill	7	970.18	450.83	6791.25
	Humalog Mix 25 Penset	89	814.84	364.10	72520.84
	Humalog Mix 25 Cartridges	15	567.85	128.92	8517.81
	Humulin 30/70 3ml Cartridges	10	486.98	163.61	4869.81
	Humulin L 10ml Vials	11	331.35	135.34	3644.87
	Humulin N 10ml Ampoules	1	279.54	0	279.54
	Humulin N 3ml Pensets	3	475.45	8.11	1426.34
	Hypomide 250mg	1	56.78	0	56.78
	Lantus 1000IU 10ml	2	722.04	0	1444.08
	Lantus 300IU 3ml	9	717.55	129.10	6457.98
	Lantus 300IU/3ml O/T	9	548.59	108.15	4937.27
	Merck-Gliclazide	36	82.73	41.07	2978.11
	Metforal 850mg	1	78.96	0	78.96
	Minidiab 5mg	18	178.83	107.81	3218.87
	Mixtard 20/80 Penfill	2	411.63	0	823.26
	Monotard HM 10ml Ampoules	4	344.56	53.59	1378.24

Table G1: (Continue) Utilisation of two antidiabetic agents in combination for the time September to December

Agents in combination (Trade name ®)		No of Rx	Average cost (R)	Std deviation (R)	Total cost (R)
	Norton-Glibenclamide	4	37.91	20.77	151.62
	Novomix 30 Flexpen 3ml	64	626.01	207.30	40064.54
	Novomix 30 Penfill 3ml Injection	1	678.39	0	678.39
	Novonorm 0.5mg	16	144.59	28.41	2313.36
	Novonorm 1.0mg	21	231.32	58.92	4870.31
	Novonorm 2.0mg	12	374.30	9.63	4491.60
	Novorapid 3ml Flexpen	7	476.98	23.91	3338.89
	Protaphane HM Penset 3ml	8	595.92	161.78	4767.39
	Protaphane HM 10ml Ampoules	3	365.19	9.25	1095.58
	Rolab-Gliclazide	40	84.89	32.71	3395.58
	Sandoz-Gliclazide	173	94.07	47.52	16273.81
	Sandoz-Metformin HCl 850mg	1	54.09	0	54.09
	Starlix FCT 120mg	4	369.26	122.49	1477.04
Glucophage Forte 850mg	Glucophage Forte 850mg	107	111.27	57.40	11906.01
	Glucovance 500/2.5mg	1	145.94	0	145.94
	Glyben 5mg	88	69.17	23.15	6087.08
	Glycomin 5mg	574	122.73	38.83	70446.05
	Glycron 80mg	83	126.92	34.95	10534.19
	Glygard	41	133.30	42.17	5465.37
	Humalog 3ml Cartridges	1	963.30	0	963.30
	Humalog 3ml Penset Prefill	5	982.16	328.13	4910.80
	Humalog Mix 25 Penset	114	821.35	306.33	93634.21
	Humalog Mix 25 Cartridges	8	827.62	401.11	6620.99
	Humulin 30/70 3ml Cartridges	13	554.06	189.43	7202.77
	Humulin L 10ml Vials	15	371.54	105.23	5573.08
	Humulin N 10ml Ampoules	3	496.95	0.86	1490.84
	Humulin N 3ml Pensets	24	523.24	63.45	12557.84
	Hypomide 250mg	2	106.18	12.66	212.36
	Lantus 1000IU 10ml	3	725.95	120.05	2177.86
	Lantus 300IU 3ml	11	710.85	127.27	7819.38
	Lantus 300IU/3ml O/T	22	625.58	58.48	13762.82
	Merck-Gliclazide	42	117.30	32.48	4926.53
	Minidiab 5mg	29	251.36	139.98	7289.41

Table G1: (Continue) Utilisation of two antidiabetic agents in combination for the time September to December

Agents in combination (Trade name ®)		No of Rx	Average cost (R)	Std deviation (R)	Total cost (R)
	Monotard HM 10ml Ampoules	4	316.27	1.11	1265.06
	Novomix 30 Flexpen 3ml	146	641.12	229.01	93603.29
	Novomix 30 Penfill 3ml Injection	5	849.50	178.46	4247.52
	Novonorm 0.5mg	8	160.15	27.48	1281.22
	Novonorm 1.0mg	23	258.60	81.84	5947.80
	Novonorm 2.0mg	17	411.05	156.30	6987.93
	Novorapid 3ml Flexpen	13	771.51	216.15	10029.65
	Protaphane HM Penfill 3ml	3	402.98	105.91	1208.95
	Protaphane HM Penset 3ml	8	682.84	233.83	5462.74
	Rolab-Gliclazide	87	125.52	40.61	10920.42
	Sandoz-Gliclazide	270	124.60	38.21	33643.29
	Sandoz-Metformin HCl 500mg	1	90.32	0	90.32
	Sandoz-Metformin FC 500mg	1	39.49	0	39.49
	Sandoz-Metformin HCl 850mg	2	95.17	43.57	190.34
Glucovance 250/1.25mg	Glucovance 250/1.25mg	2	148.47	45.50	296.94
	Glucovance 500/2.5mg	5	96.34	13.46	481.70
Glucovance 500/2.5mg	Glucovance 500/2.5mg	6	197.51	132.81	1185.08
	Glucovance 500/5mg	1	294.24	0	294.24
	Humulin 30/70 3ml Cartridges	3	425.90	53.13	1277.71
	Humulin L 10ml Vials	1	458.34	0	458.34
	Lantus 300IU 3ml	4	660.06	65.12	2640.22
	Novomix 30 Flexpen 3ml	5	567.04	26.93	2835.20
Glucovance 500/5mg	Glucovance 500/5mg	11	318.55	237.51	3504.02
	Humalog Mix 25 Penset	5	885.99	218.58	4429.93
	Lantus 300IU/3ml O/T	10	744.15	42.31	7441.50
	Metforal 850mg	1	145.91	0	145.91
	Novomix 30 Flexpen 3ml	2	629.25	70.97	1258.50
	Glyben 5mg	5	7.29	2.34	36.44
	Glycomin 5mg	1	33.13	0	33.13
	Merck-Metformin 850mg	6	102.59	39.12	615.51
	Novomix 30 Flexpen 3ml	2	893.92	0	1787.84
	Rolab-Metformin HCl 500mg	13	73.32	57.95	953.10
	Rolab-Metformin FC 500mg	21	64.04	55.40	1344.76

Table G1: (Continue) Utilisation of two antidiabetic agents in combination for the time September to December

Agents in combination (Trade name ®)		No of Rx	Average cost (R)	Std deviation (R)	Total cost (R)
	Rolab-Metformin FC 850mg	9	67.83	14.41	610.47
	Rolab-Metformin HCl 850mg	12	67.26	20.98	807.15
	Sandoz-Metformin HCl 500mg	38	54.80	21.41	2082.50
	Sandoz-Metformin FC 500mg	51	58.02	22.96	2959.16
	Sandoz-Metformin FC 850mg	24	64.45	22.72	1546.68
	Sandoz-Metformin HCl 850mg	33	68.36	23.23	2255.80
Glycomin 5mg	Glycomin 5mg	13	117.57	135.17	1528.44
	Glycron 80mg	4	115.57	58.38	462.27
	Glygard	2	101.66	39.46	203.32
	Humalog Mix 25 Penset	3	774.65	226.25	2323.96
	Humulin L 10ml Vials	2	264.47	0	528.94
	Lantus 1000IU 10ml	1	480.03	0	480.03
	Lantus 300IU/3ml O/T	1	647.77	0	647.77
	Merck-Metformin 500mg	19	107.40	35.52	2040.56
	Merck-Metformin 850mg	6	146.94	30.75	881.61
	Metforal 500mg	4	78.30	13.39	313.18
	Metforal 850mg	14	102.48	28.35	1434.66
	Monotard HM 10ml Ampoules	1	34.35	0	34.35
	Novomix 30 Flexpen 3ml	1	512.47	0	512.47
	Protaphane HM Penset 3ml	4	764.70	202.33	3058.79
	Rolab-Gliclazide	1	101.16	0	101.16
	Rolab-Metformin HCl 500mg	84	97.24	40.05	8168.43
	Rolab-Metformin FC 500mg	95	102.80	41.29	9766.18
	Rolab-Metformin FC 850mg	49	133.14	39.80	6524.06
	Rolab-Metformin HCl 850mg	39	119.87	29.51	4675.00
	Sandoz-Gliclazide	6	100.33	18.61	60.96
	Sandoz-Metformin HCl 500mg	220	92.44	36.24	20337.08
	Sandoz-Metformin FC 500mg	281	100.58	38.65	28261.91
	Sandoz-Metformin FC 850mg	134	122.00	35.58	16347.56
	Sandoz-Metformin HCl 850mg	120	117.56	34.00	14107.49
Glycron 80mg	Merck-Metformin 500mg	1	79.75	0	79.75
	Merck-Metformin 850mg	2	98.31	5.74	196.62
	Metforal 850mg	1	199.61	0	199.61

Table G1: (Continue) **Utilisation of two antidiabetic agents in combination for the time September to December**

Agents in combination (Trade name ®)		No of Rx	Average cost (R)	Std deviation (R)	Total cost (R)
	Rolab-Metformin HCl 500mg	5	131.89	53.46	659.44
	Rolab-Metformin FC 500mg	2	141.61	52.09	283.21
	Rolab-Metformin FC 850mg	6	142.54	49.55	855.26
	Rolab-Metformin HCl 850mg	5	167.03	29.51	835.13
	Sandoz-Metformin HCl 500mg	15	101.77	31.14	1526.62
	Sandoz-Metformin FC 500mg	13	107.31	45.83	1395.05
	Sandoz-Metformin FC 850mg	24	133.31	38.19	3199.38
	Sandoz-Metformin HCl 850mg	13	155.47	35.07	2021.12
Glygard	Glygard	1	97.74	0	97.74
	Merck-Metformin 500mg	3	124.76	48.33	374.28
	Novorapid 3ml Flexpen	2	507.49	0	1014.98
	Rolab-Metformin FC 500mg	3	88.14	33.89	264.42
	Rolab-Metformin FC 850mg	5	105.19	43.67	525.96
	Rolab-Metformin HCl 850mg	3	87.35	19.52	262.05
	Sandoz-Metformin HCl 500mg	6	104.43	51.80	626.57
	Sandoz-Metformin FC 500mg	7	85.61	28.72	599.27
	Sandoz-Metformin FC 850mg	12	107.17	47.74	1285.98
	Sandoz-Metformin HCl 850mg	9	132.30	57.59	1190.71
Humulin Humaject 30/70 Injection	Humulin 30/70 Humaject Injection	2	1273.28	593.80	2546.56
	Sandoz-Metformin FC 850mg	4	691.79	405.42	2767.15
Humaject R Penfill 5ml Injection	Humulin L 10ml Vials	4	675.66	0.01	2702.62
	Humulin N 3ml Cartridges	1	1185.93	0	1185.93
	Humulin N 3ml Pensets	1	1241.14	0	1241.14
	Humulin R 10ml Vials	1	675.67	0	675.67
	Merck-Gliclazide	2	688.74	288.82	1377.48
Humaject/Humalog 3ml	Humalog Mix 25 Penset	1	2449.99	0	2449.99
Humalog 10ml Ampoules	Humalog 10ml Ampoules	4	700.71	256.57	2802.82
	Humulin N 10ml Ampoules	18	848.79	397.78	15278.27
	Lantus 1000IU 10ml	3	661.91	0	1985.73
	Novorapid 3ml Flexpen	2	744.87	0	1489.74
Humalog 3ml Cartridges	Humulin L 10ml Vials	9	708.54	0	6376.86
	Humulin N 3ml Cartridges	7	1024.34	196.59	7170.41
	Humulin N 3ml Pensets	2	1538.23	889.75	3076.45

Table G1: (Continue) Utilisation of two antidiabetic agents in combination for the time September to December

Agents in combination (Trade name ®)		No of Rx	Average cost (R)	Std deviation (R)	Total cost (R)
	Lantus 300IU 3ml	12	1122.14	194.86	13465.62
	Lantus 300IU/3ml O/T	6	173.61	389.93	7041.66
	Protaphane HM Penfill 3ml	6	953.80	153.15	5722.80
	Protaphane HM Penset 3ml	1	878.36	0	878.36
	Ultratard HM 10ml Ampoules	4	888.48	0	3553.92
Humalog 3ml Penset Prefill	Humalog 3ml Penset Prefill	6	1328.55	442.00	7971.32
	Humalog Mix 25 Penset	4	1356.35	714.45	5425.41
	Humulin 30/70 3ml Cartridges	1	875.91	0	875.91
	Humulin L 10ml Vials	40	887.84	210.50	35513.57
	Humulin N 10ml Ampoules	3	717.97	0	2153.91
	Humulin N 3ml Cartridges	5	1622.67	414.03	8113.34
	Humulin N 3ml Pensets	159	1082.11	350.44	172055.31
	Lantus 1000IU 10ml	9	1315.16	277.14	11836.46
	Lantus 300IU 3ml	66	1226.50	330.07	80948.94
	Lantus 300IU/3ml O/T	72	1186.54	294.54	85430.57
	Novomix 30 Flexpen 3ml	1	939.07	0	939.07
	Protaphane HM Penfill 3ml	11	1309.89	537.75	14408.74
	Protaphane HM Penset 3ml	34	1039.16	277.80	35331.31
	Rolab-Metformin HCl 500mg	2	740.16	328.95	1480.32
	Rolab-Metformin FC 500mg	1	508.38	0	508.38
	Rolab-Metformin HCl 850mg	1	980.98	0	980.98
	Sandoz-Metformin HCl 500mg	4	849.67	228.07	3398.69
	Sandoz-Metformin FC 500mg	5	702.67	246.89	3513.35
	Ultratard HM 10ml Ampoules	3	703.99	0.01	2111.96
Humalog Mix 25 Penset	Humalog Mix 25 Penset	13	1345.94	406.95	17497.20
	Humulin N 3ml Pensets	13	1007.98	128.00	13103.71
	Lantus 300IU/3ml O/T	6	1112.03	214.39	6672.15
	Metforal 850mg	2	569.70	0.01	1139.39
	Novonorm 0.5mg	1	844.76	0	844.76
	Protaphane HM Penset 3ml	8	1013.12	107.76	8104.93
	Rolab-Gliclazide	1	566.05	0	566.05
	Rolab-Metformin HCl 500mg	5	688.05	212.16	3440.24
	Rolab-Metformin FC 500mg	5	755.96	205.75	3779.79

Table G1: (Continue) Utilisation of two antidiabetic agents in combination for the time September to December

Agents in combination (Trade name ®)		No of Rx	Average cost (R)	Std deviation (R)	Total cost (R)
	Rolab-Metformin FC 850mg	5	878.04	249.27	4390.18
	Rolab-Metformin HCl 850mg	6	825.02	254.22	4950.13
	Sandoz-Gliclazide	2	566.05	0	1132.10
	Sandoz-Metformin HCl 500mg	13	573.31	138.00	7453.03
	Sandoz-Metformin FC 500mg	11	701.53	225.74	7716.79
	Sandoz-Metformin FC 850mg	37	745.89	260.90	27598.11
	Sandoz-Metformin HCl 850mg	13	733.01	223.80	9529.14
Humalog Mix 25 Cartridges	Humalog Mix 25 Cartridges	1	1847.48	0	1847.48
	Humulin N 3ml Pensets	2	1770.32	0	3540.64
	Lantus 300IU 3ml	1	1020.13	0	1020.13
	Lantus 300IU/3ml O/T	3	1042.61	0	3127.83
	Protaphane HM Penfill 3ml	1	888.03	0	888.03
	Protaphane HM Penset 3ml	4	1823.61	52.47	7294.44
	Rolab-Metformin FC 500mg	2	1121.40	200.12	2242.79
	Sandoz-Metformin FC 500mg	6	903.61	181.79	5421.63
	Sandoz-Metformin HCl 850mg	1	973.50	0	973.50
Humulin 30/70 3ml Cartridges	Humulin 30/70 3ml Cartridges	6	1127.22	368.31	6763.32
	Rolab-Metformin FC 500mg	1	391.20	0	391.20
	Sandoz-Metformin FC 500mg	2	437.44	19.78	874.87
	Sandoz-Metformin FC 850mg	1	649.85	0	649.85
Humulin L 10ml Vials	Humulin R 10ml Vials	2	475.10	0	950.20
	Humulin R 3ml Cartridges	4	660.13	41.95	2640.53
	Merck-Metformin 850mg	1	525.87	0	525.87
	Sandoz-Metformin HCl 850mg	1	287.36	0	287.36
Humulin N 10ml Vials	Humulin N 3ml Pensets	1	340.49	0	340.49
	Humulin R 10ml Vials	7	653.33	222.27	4573.30
Humulin N 3ml Cartridges	Humulin N 3ml Cartridges	3	1914.47	1563.46	5743.40
	Humulin R 3ml Cartridges	2	964.49	228.04	1928.98
	Sandoz-Metformin HCl 850mg	1	476.27	0	476.27
Humulin N 3ml Pensets	Humulin N 3ml Pensets	1	876.22	0	876.22
	Humulin R 3ml Cartridges	3	1099.87	450.60	3299.62
	Novorapid 3ml Flexpen	4	896.77	0.01	3587.06
	Rolab-Metformin FC 850mg	1	618.54	0	618.54

Table G1: (Continue) Utilisation of two antidiabetic agents in combination for the time September to December

Agents in combination (Trade name ®)		No of Rx	Average cost (R)	Std deviation (R)	Total cost (R)
	Rolab-Metformin HCl 850mg	1	487.91	0	487.91
	Sandoz-Gliclazide	1	485.41	0	485.41
	Sandoz-Metformin HCl 500mg	1	493.49	0	493.49
	Sandoz-Metformin FC 500mg	2	340.05	168.36	680.09
	Sandoz-Metformin FC 850mg	7	582.61	93.24	4078.24
	Sandoz-Metformin HCl 850mg	2	487.91	0	975.82
Humulin R 3ml Cartridges	Lantus 300IU/3ml O/T	1	1345.69	0	1345.69
	Ultratard HM 10ml Ampoules	3	625.19	0	1875.57
Hypomide 250mg	Rolab-Metformin HCl 850mg	1	203.02	0	203.02
	Sandoz-Metformin HCl 500mg	1	59.53	0	59.53
	Sandoz-Metformin FC 850mg	2	42.28	0	84.56
Lantus 1000IU 10ml	Lantus 1000IU 10ml	2	1082.98	509.88	2165.96
	Novorapid 3ml Flexpen	4	834.36	0	3337.44
	Rolab-Metformin HCl 500mg	1	403.42	0	403.42
	Rolab-Metformin FC 500mg	2	452.02	48.59	904.03
	Sandoz-Metformin HCl 500mg	1	403.42	0	403.42
	Sandoz-Metformin FC 500mg	7	447.17	60.00	3130.17
Lantus 300IU 3ml	Lantus 300IU 3ml	1	2114.48	0	2114.48
	Novorapid 3ml Flexpen	42	1114.26	279.70	46799.08
	Novorapid 3ml Penfill	11	1172.23	344.17	12894.49
	Rolab-Metformin HCl 850mg	2	763.90	107.29	1527.79
	Sandoz-Gliclazide	2	1151.89	0	2303.78
	Sandoz-Metformin FC 500mg	3	571.41	0	1714.23
	Sandoz-Metformin FC 850mg	3	594.42	0	1783.26
	Sandoz-Metformin HCl 850mg	2	716.50	174.32	432.99
Lantus 300IU/3ml O/T	Lantus 300IU/3ml O/T	1	2055.20	0	2055.20
	Merck-Gliclazide	1	636.28	0	636.28
	Novomix 30 Flexpen 3ml	5	837.68	171.95	4188.42
	Novomix 30 Penfill 3ml Injection	2	1424.28	0	2848.56
	Novorapid 3ml Flexpen	48	1076.88	217.00	51690.19
	Novorapid 3ml Penfill	1	1019.73	0	1019.73
	Rolab-Gliclazide	1	586.27	0	586.27
	Sandoz-Gliclazide	1	590.77	0	590.77

Table G1: (Continue) Utilisation of two antidiabetic agents in combination for the time September to December

Agents in combination (Trade name ®)		No of Rx	Average cost (R)	Std deviation (R)	Total cost (R)
	Sandoz-Metformin FC 500mg	4	592.69	7.74	2370.77
	Sandoz-Metformin FC 850mg	3	625.40	14.72	1876.20
	Sandoz-Metformin HCl 850mg	1	593.23	0	593.23
Merck-Gliclazide	Merck-Metformin 500mg	6	94.99	17.94	569.94
	Merck-Metformin 850mg	6	110.23	43.83	661.38
	Metforal 500mg	3	79.05	8.07	237.14
	Metforal 850mg	5	164.22	27.92	821.11
	Rolab-Metformin HCl 500mg	5	99.63	23.03	498.14
	Rolab-Metformin FC 500mg	2	74.40	0.01	148.79
	Rolab-Metformin FC 850mg	4	142.61	23.88	570.43
	Rolab-Metformin HCl 850mg	1	142.19	0	142.19
	Sandoz-Metformin HCl 500mg	21	92.62	26.45	1945.05
	Sandoz-Metformin FC 500mg	14	103.44	38.92	1448.13
	Sandoz-Metformin FC 850mg	16	116.25	30.35	1860.04
	Sandoz-Metformin HCl 850mg	10	119.57	24.82	1195.66
Merck-Metformin 500mg	Merck-Metformin 500mg	3	104.40	0	313.20
	Protaphane HM Penset 3ml	4	554.10	0	2216.40
	Rolab-Gliclazide	4	108.01	26.51	432.02
	Sandoz-Gliclazide	9	12.74	28.14	924.63
Merck-Metformin 850mg	Merck-Metformin 850mg	1	108.90	0	108.90
	Minidiab 5mg	3	212.24	58.98	636.73
	Novonorm 0.5mg	2	129.88	2.90	259.76
	Rolab-Gliclazide	3	78.89	31.11	236.68
	Sandoz-Gliclazide	2	108.92	11.37	217.84
Metforal 500mg	Rolab-Gliclazide	1	136.61	0	136.61
	Sandoz-Gliclazide	2	75.27	0	150.54
Metforal 850mg	Metforal 850mg	2	92.15	13.87	184.30
	Norton-Glibenclamide	1	64.53	0	64.53
	Novomix 30 Flexpen 3ml	1	509.64	0	509.64
	Novonorm 0.5mg	4	134.00	0	536.00
	Sandoz-Gliclazide	2	98.31	0	196.62
Minidiab 5mg	Rolab-Metformin HCl 500mg	3	96.69	30.59	290.06
	Rolab-Metformin FC 500mg	3	116.72	91.03	350.17

Table G1: (Continue) Utilisation of two antidiabetic agents in combination for the time September to December

Agents in combination (Trade name ®)		No of Rx	Average cost (R)	Std deviation (R)	Total cost (R)
	Rolab-Metformin FC 850mg	1	199.24	0	199.24
	Rolab-Metformin HCl 850mg	2	298.78	186.80	597.56
	Sandoz-Metformin HCl 500mg	8	202.99	129.42	1623.91
	Sandoz-Metformin FC 500mg	7	246.63	88.79	1726.43
	Sandoz-Metformin FC 850mg	5	221.20	52.39	1105.99
	Sandoz-Metformin HCl 850mg	5	315.24	158.34	1576.19
Mixtard 20/80 Penfill	Novomix 30 Flexpen 3ml	1	870.01	0	870.01
Monotard HM 10ml Ampoules	Novorapid 3ml Flexpen	1	697.91	0	697.91
Norton-Glibenclamide	Rolab-Metformin FC 500mg	1	69.06	0	69.06
	Sandoz-Metformin HCl 500mg	8	62.72	21.26	501.74
	Sandoz-Metformin FC 500mg	3	69.06	0	207.18
Novomix 30 Flexpen 3ml Injection	Novomix 30 Flexpen 3ml	20	1143.06	415.11	22861.18
	Novorapid 3ml Flexpen	6	1131.83	234.98	6790.95
	Rolab-Gliclazide	1	935.00	0	935.00
	Rolab-Metformin HCl 500mg	4	540.53	98.73	2162.10
	Rolab-Metformin FC 500mg	5	835.03	521.74	4175.15
	Rolab-Metformin FC 850mg	9	903.24	480.65	8129.18
	Rolab-Metformin HCl 850mg	9	546.25	75.72	4916.26
	Sandoz-Gliclazide	1	482.32	0	482.32
	Sandoz-Metformin HCl 500mg	19	578.20	270.31	10985.75
	Sandoz-Metformin FC 500mg	23	757.76	272.30	17428.55
	Sandoz-Metformin FC 850mg	51	657.27	307.99	33520.93
	Sandoz-Metformin HCl 850mg	22	624.68	175.83	13742.96
Novomix 30 Penfill 3ml Injection	Novomix 30 Penfill 3ml Injection	1	907.62	0	907.62
	Sandoz-Metformin FC 850mg	1	504.78	0	504.78
Novonorm 0.5mg	Novonorm 0.5mg	1	166.04	0	166.04
	Novonorm 1.0mg	2	293.68	0	587.36
	Rolab-Metformin HCl 850mg	2	159.36	63.23	318.72
	Sandoz-Metformin FC 850mg	1	131.86	0	131.86
	Sandoz-Metformin HCl 850mg	3	204.07	0	612.21
Novonorm 1.0mg	Novonorm 2.0mg	4	485.20	59.39	1940.79
	Rolab-Metformin HCl 500mg	1	209.97	0	209.97
	Sandoz-Metformin HCl 500mg	5	222.12	17.83	1110.60

Table G1: (Continue) **Utilisation of two antidiabetic agents in combination for the time September to December**

Agents in combination (Trade name ®)		No of Rx	Average cost (R)	Std deviation (R)	Total cost (R)
	Sandoz-Metformin FC 500mg	1	183.31	0	183.31
	Sandoz-Metformin HCl 850mg	2	204.33	0	408.66
Novonorm 2.0mg	Rolab-Metformin HCl 500mg	2	269.30	0	538.60
	Rolab-Metformin HCl 850mg	1	138.82	0	138.82
	Sandoz-Metformin HCl 500mg	3	269.30	0	807.90
Novorapid 3ml Flexpen	Novorapid 3ml Flexpen	3	1489.33	495.38	4468.00
	Protaphane HM Penfill 3ml	5	838.96	33.18	4194.82
	Protaphane HM Penset 3ml	10	1373.78	528.82	13737.83
	Protaphane HM 10ml Ampoules	1	907.52	0	907.52
	Rolab-Metformin FC 500mg	1	472.65	0	472.65
	Sandoz-Metformin HCl 500mg	3	943.06	0	2829.18
	Sandoz-Metformin FC 500mg	4	499.21	17.91	1996.83
	Sandoz-Metformin HCl 850mg	1	508.44	0	508.44
Novorapid 3ml Penfill	Protaphane HM Penfill 3ml	10	1014.43	193.71	10144.31
	Protaphane HM Penset 3ml	2	861.19	0	1722.38
	Protaphane HM 10ml Ampoules	1	959.02	0	959.02
	Rolab-Metformin FC 500mg	2	481.78	0	963.56
Protaphane HM Penfill 3ml	Rolab-Gliclazide	2	483.72	35.40	967.43
	Sandoz-Metformin HCl 850mg	1	486.02	0	486.02
Protaphane HM Penset 3ml	Rolab-Gliclazide	1	502.03	0	502.03
	Rolab-Metformin HCl 500mg	1	515.18	0	515.18
	Rolab-Metformin FC 500mg	1	463.33	0	463.33
	Rolab-Metformin FC 850mg	1	756.53	0	756.53
	Sandoz-Gliclazide	2	336.38	209.64	672.76
	Sandoz-Metformin HCl 500mg	2	475.14	56.63	950.28
	Sandoz-Metformin FC 500mg	1	463.32	0	463.32
	Sandoz-Metformin FC 850mg	1	538.47	0	538.47
Protaphane HM 10ml Ampoules	Rolab-Metformin FC 500mg	1	384.36	0	384.36
	Sandoz-Metformin HCl 500mg	1	359.45	0	359.45
	Sandoz-Metformin FC 500mg	2	267.20	0	534.40
Rolab-Gliclazide	Rolab-Metformin HCl 500mg	33	86.28	32.85	2847.14
	Rolab-Metformin FC 500mg	35	111.49	44.62	3902.27

Table G1: (Continue) Utilisation of two antidiabetic agents in combination for the time September to December

Agents in combination (Trade name ®)		No of Rx	Average cost (R)	Std deviation (R)	Total cost (R)
	Rolab-Metformin FC 850mg	22	119.82	33.64	2636.08
	Rolab-Metformin HCl 850mg	32	112.65	37.23	3604.78
Rolab-Metformin HCl 500mg	Rolab-Metformin HCl 500mg	2	69.23	19.59	138.46
Rolab-Metformin FC 500mg	Rolab-Metformin FC 500mg	5	61.55	12.51	307.74
	Rolab-Metformin FC 850mg	3	98.345	6.07	295.36
Rolab-Metformin HCl 850mg	Rolab-Metformin HCl 850mg	1	99.58	0	99.58
	Ultratard HM 10ml Ampoules	1	492.19	0	492.19
Sandoz-Gliclazide	Sandoz-Metformin HCl 500mg	88	82.50	31.41	7259.6.
	Sandoz-Metformin FC 500mg	152	102.27	41.69	15544.90
	Sandoz-Metformin FC 850mg	130	121.88	33.01	15844.78
	Sandoz-Metformin HCl 850mg	92	106.53	27.09	9800.36
Sandoz-Metformin HCl 500mg	Sandoz-Metformin HCl 500mg	13	39.12	18.80	508.62
	Sandoz-Metformin HCl 850mg	1	77.49	0	77.49
	Starlix FCT 120mg	4	499.74	0	1998.96
Sandoz-Metformin FC 500mg	Sandoz-Metformin FC 500mg	10	55.51	18.70	555.12
	Sandoz-Metformin FC 850mg	4	55.72	19.60	222.87
	Starlix FCT 120mg	2	483.67	0	967.34
Sandoz-Metformin FC 850mg	Sandoz-Metformin FC 850mg	2	97.91	5.73	195.82
Sandoz-Metformin HCl 850mg	Sandoz-Metformin HCl 850mg	4	124.46	49.79	497.82
	Ultratard HM 10ml Ampoules	1	492.19	0	492.19

Table G2: Utilisation of three antidiabetic agents in combination for the time September to December

Agents in combination (Trade name ®)			No of Rx	Average cost (R)	Std deviation (R)	Total cost (R)
Actos 15mg	Actos 30mg	Amaryl 1mg	3	693.63	0	2080.89
		Amaryl 4mg	3	1117.01	0	3351.03
	Actraphane HM Penfill 3ml	Glucophage 500mg	5	934.8	0.01	4674.02
	Actraphane HM Penset 3ml	Amaryl 4mg	2	1283.05	10.19	2566.09
	Amaryl 1mg	Sandoz-Metformin HCl 500mg	2	563.82	0	1127.64
	Amaryl 2mg	Glucophage Forte 850mg	1	583.01	0	583.01
	Amaryl 2mg	Glucophage 500mg	3	426.5	82.36	1279.49
		Glucophage Forte 850mg	1	763.22	0	763.22
	Diamicron 80mg	Glucophage Forte 850mg	1	475.45	0	475.45
	Diamicron MR 30mg	Glucophage Forte 850mg	1	472.83	0	472.83
	Glucomed 80mg	Glucophage 500mg	3	375.32	15.85	1125.95
	Glucomed 80mg	Rolab-Metformin HCl 500mg	1	466.66	0	466.66
		Rolab- Metformin FC 850mg	1	561.19	0	561.19
		Sandoz-Metformin FC 850mg	3	514.92	77.13	1544.76
	Glucophage 500mg	Glyben 5mg	4	334.19	0.03	1336.74
		Glycron 80mg	4	476.85	0	1907.40
		Humalog Mix 25 Penset	2	1804.63	0	3609.26
	Glucophage Forte 850mg	Glycron 80mg	5	452.59	25.84	2262.97
		Sandoz-Gliclazide	1	522.1	0	522.10
	Glycomin 5mg	Rolab-Metformin HCl 500mg	1	306.82	0	306.80
		Rolab-Metformin FC 500mg	1	348.58	0	348.58
		Rolab-Metformin FC 850mg	2	517.83	0	1035.66
		Sandoz-Metformin HCl 500mg	5	312.19	7.38	1560.96
		Sandoz-Metformin FC 500mg	3	348.58	0	1045.74
		Sandoz-Metformin FC 850mg	2	514.79	4.31	1029.57
	Humalog 3ml Penset Prefill	Lantus 300IU/3ml O/T	2	1260.79	0	2521.58
Actos 30mg	Actraphane HM Penfill 3ml	Glucobay 50mg	2	1290.84	0	2581.68
		Glucophage 500mg	1	1098.76	0	1098.76
		Glucophage Forte 850mg	1	1129.12	0	1129.12
	Amaryl 2mg	Daonil 5mg	3	822.41	9	2467.22
		Glycomin 5mg	1	763.49	0	763.49

Table G2: (Continue) Utilisation of three antidiabetic agents in combination for the time September to December

Agents in combination (Trade name ®)			No of Rx	Average cost (R)	Std deviation (R)	Total cost (R)
		Sandoz-Metformin HCl 850mg	1	654.05	0	654.05
	Amaryl 4mg	Rolab-Metformin FC 500mg	1	859.48	0	859.48
	Diamicron 80mg	Glucophage Forte 850mg	1	443.17	0	443.17
		Sandoz-Metformin HCl 500mg	1	571.39	0	571.39
	Diamicron MR 30mg	Glucophage Forte 850mg	1	552.63	0	552.63
	Glucomed 80mg	Glucophage 500mg	3	669.2	1	2007.60
		Lantus 300IU 3ml	3	1375.06	1	4125.18
	Glucophage 500mg	Glygard	1	597.06	0	597.06
		Rolab-Gliclazide	1	460.71	0	460.71
	Glucophage Forte 850mg	Glycomin 5mg	2	879.97	377.53	1759.93
		Novomix 30 Flexpen 3ml	1	1193.73	0	1193.73
	Glycomin 5mg	Rolab-Metformin FC 850mg	1	550.88	0	550.88
		Sandoz-Metformin FC 850mg	1	550.4	0	550.40
		Sandoz-Metformin HCl 850mg	2	545.71	0	1091.42
	Glycron 80mg	Sandoz-Metformin HCl 500mg	1	688.12	0	688.12
		Sandoz-Metformin FC 500mg	3	289.99	213.68	869.98
	Humalog 3ml Penset Prefill	Lantus 300IU/3ml O/T	1	1934.27	0	1934.27
	Lantus 300IU 3ml	Rolab-Metformin HCl 500mg	1	1325.53	0	1325.53
		Sandoz-Metformin HCl 500mg	1	1325.53	0	1325.53
	Novonorm 0.5mg	Sandoz-Gliclazide	1	696.76	0	696.76
Actraphane HM Penfill 3ml	Actrapid HM Penfill 3ml	Novorapid 3ml Penfill	1	1797.02	0	1797.02
	Avandia 4mg	Glucophage 500mg	4	1467.6	0	5870.40
	Diamicron 80mg	Glucophage 500mg	1	678.92	0	678.92
Actraphane HM Penset 3ml	Actrapid HM Pensets 3ml	Glucophage Forte 850mg	1	929.17	0	929.17
	Diaglucide 80mg	Merck-Metformin 500mg	3	605.32	0	1815.96
		Sandoz-Metformin FC 500mg	3	531.84	0	1595.52
	Diamicron MR 30mg	Rolab-Metformin HCl 500mg	1	831.84	0	831.84
		Sandoz-Metformin HCl 500mg	1	831.84	0	831.84
	Glucomed 80mg	Glucophage 500mg	4	600.05	6.51	2400.18
		Glucophage Forte 850mg	5	691.79	168.11	3458.96
		Rolab-Metformin FC 500mg	1	553.33	0	553.33
		Sandoz-Metformin FC 850mg	1	565.32	0	565.32

Table G2: (Continue) Utilisation of three antidiabetic agents in combination for the time September to December

Agents in combination (Trade name ®)			No of Rx	Average cost (R)	Std deviation (R)	Total cost (R)
	Glucophage 500mg	Glygard	1	566.87	0	566.87
	Glycomin 5mg	Sandoz-Metformin FC 500mg	1	522.86	0	522.86
	Glycron 80mg	Rolab-Metformin FC 850mg	1	595.11	0	595.11
		Sandoz-Metformin HCl 500mg	1	684.21	0	684.21
		Sandoz-Metformin FC 850mg	1	590.81	0	590.81
	Glygard	Sandoz-Metformin FC 850mg	1	952.37	0	952.37
	Novomix 30 Flexpen 3ml	Rolab-Metformin HCl 850mg	1	1814.93	0	1814.93
		Sandoz-Metformin FC 850mg	2	1610.99	290.95	3221.98
		Sandoz-Metformin HCl 850mg	2	974.45	0	1948.90
	Rolab-Gliclazide	Rolab-Metformin HCl 850mg	2	1246.22	197.74	2492.44
	Sandoz-Gliclazide	Sandoz-Metformin FC 850mg	3	950.83	0	2852.49
Actraphane HM 10ml Ampoules	Avandia 4mg	Diamicron 80mg	1	1020.11	0	1020.11
		Glucophage Forte 850mg	1	693.57	0	693.57
	Diaglucide 80mg	Rolab-Metformin FC 850mg	1	413.33	0	413.33
		Sandoz-Metformin FC 850mg	2	518.13	148.21	1036.26
	Diamicron MR 30mg	Glucophage Forte 850mg	1	641.36	0	641.36
	Glucomed 80mg	Rolab-Metformin HCl 850mg	1	381	0	381.00
		Sandoz-Metformin HCl 850mg	3	381	0	1143.00
	Glucophage 500mg	Glycomin 5mg	2	399.56	0.05	799.11
	Glucophage Forte 850mg	Glyben 5mg	1	445.05	0	445.05
	Glycomin 5mg	Sandoz-Metformin HCl 850mg	1	420.51	0	420.51
Actrapid HM 10ml Ampoules	Diamicron 80mg	Glucophage Forte 850mg	2	640.71	0	1281.42
Actrapid HM Penfill 3ml	Daonil 5mg	Glucophage 500mg	3	688.41	0.03	2065.23
Actrapid HM Pensets 3ml	Glucomed 80mg	Glucophage Forte 850mg	2	626.23	0	1252.46
	Glucophage 500mg	Protaphane HM Penset 3ml	4	952.28	46.84	3809.11
	Glucophage Forte 850mg	Glycomin 5mg	1	381.3	0	381.30
		Protaphane HM Penfill 3ml	3	1751.85	0	5255.55
	Humulin L 10ml Vial	Rolab-Gliclazide	1	679.37	0	679.37
		Sandoz-Gliclazide	3	724	38.65	2172.01
		Sandoz-Metformin FC 500mg	1	1104.11	0	1104.11
	Lantus 300IU 3ml	Merck-Metformin 500mg	1	1448.23	0	1448.23
		Rolab-Metformin HCl 850mg	1	1487.99	0	1487.99

Table G2: (Continue) Utilisation of three antidiabetic agents in combination for the time September to December

Agents in combination (Trade name ®)			No of Rx	Average cost (R)	Std deviation (R)	Total cost (R)
		Sandoz-Metformin FC 500mg	2	998.53	0	1997.06
	Merck-Gliclazide	Sandoz-Metformin FC 500mg	1	515.49	0	515.49
	Protaphane HM Penset 3ml	Rolab-Metformin FC 850mg	2	1088.49	154.04	2176.97
Amaryl 1mg	Amaryl 2mg	Avandia 4mg	3	1116.03	0.41	3348.10
		Glucophage 500mg	17	246.84	34.36	4196.24
		Glucophage Forte 850mg	5	203.43	93.24	1017.17
		Rolab-Metformin FC 500mg	3	295.83	42	887.48
		Sandoz-Metformin HCl 500mg	2	309.91	0	619.82
		Sandoz-Metformin FC 500mg	7	289.07	38.68	2023.52
	Amaryl 4mg	Glucophage 500mg	3	346	0.04	1037.99
	Diamicron MR 30mg	Glucophage 500mg	2	240.75	37.69	481.50
	Glucobay 50mg	Rolab-Gliclazide	1	475.6	0	475.60
		Sandoz-Gliclazide	2	475.6	0	951.20
	Glucomed 80mg	Sandoz-Metformin HCl 500mg	2	225.87	0	451.74
	Glucophage 500mg	Sandoz-Gliclazide	1	212.92	0	212.92
	Glycomin 5mg	Sandoz-Metformin HCl 500mg	2	200.87	0	401.74
Amaryl 2mg	Amaryl 4mg	Glucophage Forte 850mg	18	438.36	76.81	7890.49
		Rolab-Metformin HCl 500mg	1	429.03	0	429.03
		Sandoz-Metformin HCl 500mg	3	427.83	0	1283.49
		Sandoz-Metformin FC 500mg	1	414.26	0	414.26
	Avandia 2mg	Glucophage Forte 850mg	1	312.38	0	312.38
		Sandoz-Metformin FC 850mg	2	312.38	0	624.76
	Avandia 4mg	Novorapid 3ml Flexpen	3	711.02	0	2133.06
	Diaglucide 80mg	Glucophage Forte 850mg	1	293.03	0	293.03
	Diamicron MR 30mg	Glucophage Forte 850mg	3	358.04	2.21	1074.13
	Glucobay 100mg	Glucophage Forte 850mg	3	450.3	0	1350.90
		Glucovance 500/2.5mg	3	523.22	0	1569.66
	Glucomed 80mg	Glucophage Forte 850mg	2	220.54	0	441.08
	Glucophage Forte 850mg	Humalog Mix 25 Penset	1	714.13	0	714.13
		Merck-Metformin 500mg	1	297.95	0	297.95
	Glyben 5mg	Rolab-Metformin FC 500mg	1	194.02	0	194.02
Amaryl 4mg	Avandia 4mg	Diamicron Mr 30mg	1	758.98	0	758.98

Table G2: (Continue) Utilisation of three antidiabetic agents in combination for the time September to December

Agents in combination (Trade name ®)			No of Rx	Average cost (R)	Std deviation (R)	Total cost (R)
		Glucophage Forte 850mg	7	638.58	68.82	4470.07
		Rolab-Metformin HCl 850mg	1	1544.06	0	1544.06
		Sandoz-Metformin FC 850mg	2	545.16	65.21	1090.32
		Sandoz-Metformin HCl 850mg	3	1543.81	0.22	4631.42
	Diamicron MR 30mg	Glucophage Forte 850mg	2	526.22	0	1052.44
	Glucobay 50mg	Glucophage Forte 850mg	8	553.06	89.5	4424.45
	Glucomed 80mg	Glucophage 500mg	1	395.52	0	395.52
	Glucophage 500mg	Glucophage Forte 850mg	4	320.86	0.04	1283.45
		Humalog Mix 25 Penset	2	760.84	0	1521.68
		Lantus 300IU 3ml	1	1222.23	0	1222.23
		Lantus 300IU/3ml O/T	4	1045.44	250.98	4181.77
	Glucophage Forte 850mg	Glycomin 5mg	2	346.64	0	693.28
		Glygard	1	341.65	0	341.65
		Lantus 300IU 3ml	2	847.66	0	1695.32
		Novonorm 1.0mg	1	578.84	0	578.84
		Novonorm 2.0mg	5	710.56	0	3552.80
		Protaphane HM Penset 3ml	1	780.32	0	780.32
		Rolab-Gliclazide	1	449.98	0	449.98
	Glycomin 5mg	Rolab-Metformin FC 850mg	1	521.27	0	521.27
		Sandoz-Metformin FC 850mg	5	416.49	95.65	2082.46
	Lantus 300IU 3ml	Sandoz-Metformin FC 850mg	1	836.28	0	836.28
	Novonorm 2.0mg	Sandoz-Metformin HCl 850mg	1	1211.83	0	1211.83
	Rolab-Gliclazide	Rolab-Metformin FC 850mg	1	340.14	0	340.14
	Sandoz-Gliclazide	Sandoz-Metformin FC 850mg	2	340.14	0	680.28
Avandia 2mg	Daonil 5mg	Glucophage Forte 850mg	3	521.15	0	1563.45
	Diamicron 80mg	Glucophage 500mg	1	305.36	0	305.36
	Glucomed 80mg	Glucophage Forte 850mg	3	242.28	0	726.84
	Glucophage 500mg	Glyben 5mg	1	200.66	0	200.66
	Glucophage Forte 850mg	Glycomin 5mg	1	233.08	0	233.08
		Sandoz-Gliclazide	2	357.3	0	714.60
Avandia 4mg	Daonil 5mg	Glucophage 500mg	1	797.12	0	797.12
		Lantus 300IU 3ml	1	1205.07	0	1205.07

Table G2: (Continue) Utilisation of three antidiabetic agents in combination for the time September to December

Agents in combination (Trade name ®)			No of Rx	Average cost (R)	Std deviation (R)	Total cost (R)
	Diamicron 80mg	Glucophage 500mg	3	295.65	0.05	886.95
		Glucophage Forte 850mg	1	398.98	0	398.98
	Diamicron MR 30mg	Glucophage 500mg	11	501.51	91.03	5516.56
		Glucophage Forte 850mg	5	500.72	3.61	2503.62
		Lantus 300IU 3ml	3	1990.21	1.37	5970.62
		Rolab-Metformin HCl 500mg	1	475.18	0	475.18
		Rolab-Metformin HCl 850mg	1	766.25	0	766.25
		Sandoz-Metformin HCl 500mg	1	966.5	0	966.50
		Sandoz-Metformin FC 850mg	2	633.05	0	1266.09
	Glucomed 80mg	Glucophage Forte 850mg	5	401.07	21.75	2005.34
	Glucophage 500mg	Glycomin 5mg	1	416.43	0	416.43
		Novonorm 1.0mg	3	501.37	0.01	1504.12
	Glucophage Forte 850mg	Glycomin 5mg	4	325.79	17.18	1303.14
		Humalog Mix 25 Penset	6	978.23	156.77	5869.35
		Humalog Mix 25 Cartridges	1	1010.64	0	1010.64
		Novomix 30 Flexpen 3ml	1	1004.31	0	1004.31
		Sandoz-Gliclazide	1	661.08	0	661.08
	Glycomin 5mg	Rolab-Metformin FC 500mg	2	379.1	0.01	758.20
	Glycron 80mg	Rolab-Metformin HCl 850mg	1	414.93	0	414.93
		Sandoz-Metformin FC 850mg	2	354.82	0	709.64
	Humalog 3ml Penset Prefill	Lantus 300IU/3ml O/T	5	2552.73	772.98	12763.64
	Humalog Mix 25 Penset	Sandoz-Metformin HCl 850mg	1	1276.42	0	1276.42
	Merck-Gliclazide	Sandoz-Metformin HCl 500mg	3	354.49	0	1063.47
	Novonorm 1.0mg	Rolab-Metformin HCl 500mg	1	531.96	0	531.96
	Novorapid 3ml Flexpen	Protaphane HM Penset 3ml	1	1072.25	0	1072.25
Daonil 5mg	Glucophage 500mg	Glucophage Forte 850mg	1	237.71	0	237.71
		Lantus 300IU 3ml	1	1067.98	0	1067.98
	Lantus 300IU 3ml	Sandoz-Metformin FC 850mg	1	829.48	0	829.48
	Protaphane HM Penset 3ml	Sandoz-Metformin FC 850mg	2	914.45	0	1828.90
Diaglucide 80mg	Glucobay 100mg	Glucophage Forte 850mg	3	219.88	0	659.64
	Glucobay 50mg	Glucophage Forte 850mg	8	253.04	1.41	2024.34
		Merck-Metformin 850mg	3	359.02	2.19	1077.05

Table G2: (Continue) Utilisation of three antidiabetic agents in combination for the time September to December

Agents in combination (Trade name ®)			No of Rx	Average cost (R)	Std deviation (R)	Total cost (R)
	Glucophage 500mg	Glycomin 5mg	1	168.27	0	168.27
	Glucophage Forte 850mg	Humulin L 10ml Vial	2	362.85	0	725.70
		Protaphane HM Penset 3ml	1	551.12	0	551.12
	Lantus 300IU 3ml	Sandoz-Metformin FC 850mg	1	643.22	0	643.22
	Merck-Metformin 850	Novomix 30 Flexpen 3ml	4	1018.35	0.71	4073.38
	Protaphane HM Penset 3ml	Sandoz-Metformin FC 500mg	1	641.04	0	641.04
Diamicron 80mg	Glucophage 500mg	Rolab-Gliclazide	1	413.65	0	413.65
	Glucophage Forte 850mg	Glycron 80mg	1	338.81	0	338.81
		Lantus 300IU 3ml	1	668.75	0	668.75
		Novonorm 0.5mg	1	425.74	0	425.74
		Sandoz-Metformin FC 500mg	1	185.14	0	185.14
	Protaphane HM Penset 3ml	Sandoz-Metformin FC 850mg	1	738.38	0	438.38
Diamicron MR 30mg	Glucophage Forte 850mg	Glucovance 500/5mg	1	298.05	0	298.05
		Lantus 300IU 3ml	2	730.3	0	1460.60
		Lantus 300IU/3ml O/T	1	752.78	0	752.78
		Protaphane HM Penset 3ml	1	960.34	0	960.34
		Protaphane HM 10ml Ampoules	1	746.67	0	746.67
	Novomix 30 Flexpen 3ml	Sandoz-Metformin FC 500mg	3	650.49	0	1951.47
	Rolab-Metformin HCl 500mg	Rolab-Metformin FC 850mg	1	270.05	0	270.05
	Sandoz-Metformin FC 500mg	Sandoz-Metformin FC 850mg	2	270.33	0	540.66
Glucobay 100mg	Glucomed 80mg	Glucophage 500mg	7	361.89	99.31	2533.23
		Rolab-Metformin FC 500mg	1	477.35	0	477.35
		Sandoz-Metformin FC 500mg	3	472.94	0	1418.82
	Glucophage Forte 850mg	Glycomin 5mg	2	414.37	3.2	828.73
		Sandoz-Gliclazide	2	466.42	0	932.84
	Protaphane HM Penset 3ml	Sandoz-Metformin FC 500mg	1	1097.25	0	1097.25
Glucobay 50mg	Glucomed 80mg	Glucophage Forte 850mg	7	317.22	30.72	2220.51
	Glucophage 500mg	Sandoz-Gliclazide	5	255.03	22.76	1275.13
	Glucophage Forte 850mg	Glycomin 5mg	2	314.02	0	628.04
	Glyben 5mg	Sandoz-Metformin HCl 500mg	1	290.33	0	290.33
	Glycomin 5mg	Sandoz-Metformin HCl 500mg	1	236.73	0	236.73
	Rolab-Gliclazide	Rolab-Metformin HCl 500mg	1	257.33	0	257.33

Table G2: (Continue) **Utilisation of three antidiabetic agents in combination for the time September to December**

Agents in combination (Trade name ®)			No of Rx	Average cost (R)	Std deviation (R)	Total cost (R)
		Rolab-Metformin FC 500mg	2	244.59	38.24	489.18
		Rolab-Metformin FC 850mg	1	275.64	0	275.64
	Sandoz-Gliclazide	Sandoz-Metformin HCl 500mg	3	257.33	0	771.99
		Sandoz-Metformin FC 500mg	4	231.07	27.04	924.28
		Sandoz-Metformin FC 850mg	1	275.64	0	275.64
Glucomed 80mg	Glucophage 500mg	Humalog 3ml Penset Prefill	2	1060.41	34.54	2120.81
		Humulin N 3ml Penset	1	528.9	0	528.90
		Lantus 300IU/3ml O/T	3	697.08	0.04	2091.23
		Novomix 30 Flexpen 3ml	1	567.73	0	567.73
		Protaphane HM Penset 3ml	1	597.55	0	597.55
	Glucophage Forte 850mg	Glyben 5mg	1	205.85	0	205.85
		Humalog Mix 25 Penset	4	653.54	33.54	2614.16
		Humulin 30/70 3ml Cartridges	1	610.3	0	610.30
		Humulin N 3ml Penset	2	537.92	0	1075.84
		Lantus 300IU 3ml	2	763.41	151.07	1526.82
		Lantus 300IU/3ml O/T	2	704.82	18.03	1409.64
		Novomix 30 Flexpen 3ml	3	616.5	50.29	1849.50
		Novonorm 0.5mg	1	364.68	0	364.68
		Protaphane HM Penfill 3ml	4	554.9	0	2219.60
		Protaphane HM Penset 3ml	1	508.6	0	508.60
	Glyben 5mg	Sandoz-Metformin HCl 500mg	1	242.16	0	242.16
	Glycomin 5mg	Rolab-Metformin HCl 850mg	1	178.61	0	178.61
	Lantus 1000IU 10 ml	Sandoz-Metformin FC 500mg	1	428.11	0	428.11
	Lantus 300IU 3ml	Sandoz-Metformin FC 850mg	2	838.01	45.57	1676.01
	Lantus 300IU/3ml O/T	Rolab-Metformin FC 500mg	1	752.38	0	752.38
		Sandoz-Metformin FC 850mg	1	643.24	0	643.24
	Merck-Gliclazide	Metforal 500mg	1	89.61	0	89.61
	Metforal 500mg	Sandoz-Gliclazide	1	90.09	0	90.09
	Novomix 30 Flexpen 3ml	Rolab-Metformin HCl 500mg	1	538.47	0	538.47
	Novomix 30 Flexpen 3ml	Rolab-Metformin HCl 850mg	1	692.41	0	692.41
		Sandoz-Metformin FC 850mg	2	559.88	0	1119.76
		Sandoz-Metformin HCl 850mg	1	692.4	0	692.40

Table G2: (Continue) Utilisation of three antidiabetic agents in combination for the time September to December

Agents in combination (Trade name ®)			No of Rx	Average cost (R)	Std deviation (R)	Total cost (R)
	Protaphane HM Penfill 3ml	Rolab-Metformin FC 850mg	1	762.86	0	762.86
		Sandoz-Metformin HCl 850mg	3	789.59	0	2368.77
	Protaphane HM Penset 3ml	Sandoz-Metformin FC 500mg	2	565.24	45.59	1130.48
	Rolab-Metformin HCl 500mg	Rolab-Metformin HCl 850mg	1	105.84	0	105.84
	Rolab-Metformin FC 500mg	Rolab-Metformin HCl 850mg	1	2.82	0	2.82
	Sandoz-Metformin HCl 500mg	Sandoz-Metformin HCl 850mg	1	105.84	0	105.84
Glucophage 500mg	Glucophage Forte 850mg	Glycomin 5mg	9	135.21	32.67	1216.89
		Novonorm 1.0mg	1	675.38	0	675.38
		Rolab-Gliclazide	1	101.37	0	101.37
		Sandoz-Gliclazide	2	96.62	0	193.24
	Glycomin 5mg	Glycron 80mg	2	121.23	0	242.46
		Glygard	4	127.36	0.01	509.42
		Humulin N 3ml Penset	4	475.83	20.77	1903.30
		Lantus 300IU 3ml	3	670.07	29.14	2010.20
		Lantus 300IU/3ml O/T	4	598.93	0.03	2395.70
		Monotard HM 10ml Ampoules	2	347.98	0	695.96
		Novonorm 1.0mg	2	196.05	0	392.10
		Protaphane HM 10ml Ampoules	1	640.43	0	640.43
	Glycron 80mg	Humulin L 10ml Vial	1	425.81	0	425.81
		Lantus 1000IU 10ml	2	676.27	0	1352.54
	Glygard	Humulin L 10ml Vial	3	427.23	62.35	1281.69
	Humalog 3ml Cartridges	Humulin L 10ml Vial	4	1365	13.85	5460.01
		Humulin N 3ml Cartridges	1	901.39	0	901.39
		Protaphane HM Penfill 3ml	2	1291.03	0.59	2582.05
	Humalog 3ml Penset Prefill	Humulin N 3ml Penset	14	1095.49	247.87	15336.87
		Lantus 1000IU 10ml	2	3407.28	0.04	6814.55
		Lantus 300IU 3ml	4	1495.61	0.01	5982.42
		Protaphane HM Penset 3ml	3	929.81	0	2789.43
		Sandoz-Gliclazide	1	1081.76	0	1081.76
	Humalog Mix 25 Penset	Humulin N 3ml Penset	1	2611.43	0	2611.43
	Lantus 300IU 3ml	Novorapid 3ml Flexpen	1	1471.84	0	1471.84
	Novomix 30 Flexpen 3ml	Sandoz-Gliclazide	1	510.3	0	510.30

Table G2: (Continue) Utilisation of three antidiabetic agents in combination for the time September to December

Agents in combination (Trade name ®)			No of Rx	Average cost (R)	Std deviation (R)	Total cost (R)
	Novonorm 1.0mg	Novonorm 2.0mg	1	573.16	0	573.16
Glucophage Forte 850mg	Glyben 5mg	Protaphane HM Penset 3ml	3	588.89	0	1766.67
	Glycomin 5mg	Humulin N 3ml Penset	4	563.77	30.22	2255.09
		Lantus 300IU 3ml	2	1188.96	0	2377.92
		Novomix 30 Flexpen 3ml	2	981.37	0	1962.74
		Protaphane HM Penset 3ml	6	980.25	195.33	5881.48
		Protaphane HM 10ml Ampoules	4	346.23	1.55	1384.90
		Rolab-Metformin HCl 850mg	2	148.39	22.86	296.77
	Glycron 80mg	Novonorm 1.0mg	1	410.11	0	410.11
	Humalog 10ml Ampoules	Humulin N 10ml Vials	1	1993.71	0	1993.71
	Humalog 3ml Cartridges	Lantus 300IU 3ml	2	1579.19	0	3158.38
	Humalog 3ml Penset Prefill	Humulin N 3ml Cartridges	1	958.48	0	958.48
		Humulin N 3ml Penset	4	1445.77	0	5783.08
		Lantus 300IU 3ml	9	3100.19	2086.69	27901.70
		Protaphane HM Penset 3ml	2	1865.8	0	3731.60
		Ultratard HM 10ml Ampoules	3	754.96	0	2264.88
	Humulin L 10ml Vial	Rolab-Gliclazide	1	385	0	385.00
	Humulin N 3ml Penset	Rolab-Gliclazide	1	515.3	0	515.30
		Sandoz-Gliclazide	3	515.3	0	1545.90
	Lantus 1000IU 10 ml	Sandoz-Gliclazide	2	821.89	0	1643.78
	Lantus 300IU 3ml	Novonorm 1.0mg	1	1032.67	0	1032.67
		Novorapid 3ml Flexpen	4	2595.76	1070.24	10383.04
		Sandoz-Gliclazide	1	1253.85	0	1253.85
	Lantus 300IU/3ml O/T	Novorapid 3ml Flexpen	1	1029.8	0	1029.80
		Novorapid 3ml Penfill	1	1073.72	0	1073.72
	Novomix 30 Flexpen 3ml	Novorapid 3ml Flexpen	3	2242.67	732.1	6728.01
		Sandoz-Gliclazide	1	556.95	0	556.95
	Novonorm 0.5mg	Sandoz-Gliclazide	1	317.24	0	317.24
	Novonorm 1.0mg	Novonorm 2.0mg	2	447.09	0	894.18
Glyben 5mg	Merck-Metformin 850	Protaphane HM Penset 3ml	3	593.94	0	1781.82
	Protaphane HM 10ml Ampoules	Sandoz-Metformin HCl 500mg	1	319.64	0	319.64
	Rolab-Gliclazide	Rolab-Metformin HCl 500mg	1	177.8	0	177.80

Table G2: (Continue) Utilisation of three antidiabetic agents in combination for the time September to December

Agents in combination (Trade name ®)			No of Rx	Average cost (R)	Std deviation (R)	Total cost (R)
	Sandoz-Gliclazide	Sandoz-Metformin HCl 500mg	3	172.76	0	518.28
Glycomin 5mg	Humalog Mix 25 Penset	Rolab-Metformin HCl 500mg	1	1089.35	0	1089.35
		Sandoz-Metformin HCl 500mg	2	1089.35	0	2178.70
		Sandoz-Metformin FC 500mg	2	1168.07	0	2336.14
	Humulin L 10ml Vial	Sandoz-Metformin HCl 500mg	2	373.69	0	747.38
	Humulin N 3ml Cartridges	Sandoz-Metformin FC 850mg	1	506.43	0	506.43
	Lantus 300IU/3ml O/T	Sandoz-Metformin FC 500mg	1	612.86	0	612.86
	Merck-Gliclazide	Merck-Metformin 850mg	1	123.47	0	123.47
	Novomix 30 Flexpen 3ml	Sandoz-Metformin HCl 500mg	1	240.1	0	20.10
	Novonorm 1.0mg	Rolab-Metformin HCl 500mg	1	334.37	0	334.37
		Rolab-Metformin HCl 850mg	1	187.63	0	187.63
		Sandoz-Metformin HCl 500mg	1	348.9	0	348.90
		Sandoz-Metformin HCl 850mg	3	190.76	27.4	572.27
	Protaphane HM Penfill 3ml	Rolab-Metformin HCl 500mg	1	547.53	0	547.53
		Sandoz-Metformin HCl 500mg	3	547.53	0	1642.59
	Protaphane HM Penset 3ml	Sandoz-Metformin FC 850mg	2	565.95	0	1131.96
	Rolab-Gliclazide	Rolab-Metformin HCl 850mg	1	159.97	0	159.97
	Sandoz-Gliclazide	Sandoz-Metformin FC 500mg	2	155.99	0	311.98
		Sandoz-Metformin HCl 850mg	1	177.8	0	177.80
	Sandoz-Metformin HCl 500mg	Sandoz-Metformin HCl 850mg	1	122.94	0	122.94
Glycron 80mg	Novomix 30 Flexpen 3ml	Rolab-Metformin FC 850mg	1	816.18	0	816.18
		Sandoz-Metformin FC 850mg	4	608.38	0	2433.52
Glygard	Novorapid 3ml Flexpen	Protaphane HM Penset 3ml	2	914.89	0.02	1829.77
Humalog 3ml Cartridges	Humulin N 3ml Cartridges	Rolab-Metformin HCl 500mg	1	1342.45	0	1342.45
		Sandoz-Metformin HCl 500mg	1	900.28	0	900.28
Humalog 3ml Penset Prefill	Humulin L 10ml Vial	Sandoz-Metformin HCl 850mg	1	1218.54	0	1218.54
	Humulin N 3ml Penset	Rolab-Metformin HCl 500mg	1	925.18	0	925.18
		Sandoz-Metformin HCl 500mg	1	1131.89	0	1131.89
		Sandoz-Metformin FC 500mg	3	1387.59	40.93	4162.77
		Sandoz-Metformin FC 850mg	1	969.48	0	969.48
	Lantus 300IU 3ml	Rolab-Metformin HCl 850mg	1	1525.8	0	1525.80
		Sandoz-Metformin HCl 850mg	1	1551.75	0	1551.75

Table G2: (Continue) Utilisation of three antidiabetic agents in combination for the time September to December

Agents in combination (Trade name ®)			No of Rx	Average cost (R)	Std deviation (R)	Total cost (R)
	Lantus 300IU/3ml O/T	Rolab-Metformin FC 500mg	1	1051.81	0	1051.81
		Sandoz-Metformin HCl 500mg	2	1290.82	318.74	2581.63
		Sandoz-Metformin FC 500mg	1	2002.41	0	2002.41
	Novonorm 2.0mg	Sandoz-Metformin HCl 500mg	3	1918.57	0	5755.71
Humalog Mix 25 Penset	Sandoz-Gliclazide	Sandoz-Metformin FC 500mg	2	527.06	73.36	1054.12
Humulin L 10ml Vials	Sandoz-Gliclazide	Sandoz-Metformin FC 850mg	1	325.86	0	325.86
		Sandoz-Metformin HCl 850mg	1	324.08	0	324.08
Humulin N 3ml Penset	Rolab-Gliclazide	Rolab-Metformin FC 500mg	2	564.32	34.48	1128.64
	Sandoz-Gliclazide	Sandoz-Metformin FC 500mg	3	537.04	0	1611.12
		Sandoz-Metformin FC 850mg	2	583.71	0	1167.42
Lantus 300IU 3ml	Merck-Gliclazide	Merck-Metformin 500mg	2	669.06	0	1338.12
Lantus 300IU/3ml O/T	Merck-Gliclazide	Sandoz-Metformin FC 500mg	1	720.2	0	720.20
	Novorapid 3ml Penfill	Sandoz-Metformin HCl 500mg	1	1024.94	0	1024.94
		Sandoz-Metformin FC 500mg	2	1025.22	0	2050.44
Novonorm 1.0mg	Novonorm 2.0mg	Rolab-Metformin FC 500mg	1	183.46	0	183.46
		Sandoz-Metformin FC 500mg	3	183.46	0	550.38
Novorapid 3ml Flexpen	Protaphane HM Penfill 3ml	Rolab-Metformin FC 500mg	1	1356.6	0	1356.60
Protaphane HM Penset 3ml	Rolab-Gliclazide	Rolab-Metformin HCl 500mg	1	564.68	0	564.68
	Sandoz-Gliclazide	Sandoz-Metformin HCl 500mg	1	562.49	0	562.49
		Sandoz-Metformin FC 850mg	1	553.01	0	553.01
Protaphane HM 10ml Ampoules	Rolab-Gliclazide	Rolab-Metformin HCl 850mg	1	467.85	0	467.85
	Sandoz-Gliclazide	Sandoz-Metformin HCl 850mg	1	383.65	0	383.65

Table G3: Utilisation of four anti-diabetic agents in combination for the time September to December

Agents in combination				No of Rx	Average cost (R)	Std dev (R)	Total cost (R)
Actos 30mg	Actos 30mg	Glucophage Forte 850mg	Glucophage Forte 850mg	3	2056.49	431.72	6169.46
		Rolab-Metformin HCl 500mg	Rolab-Metformin HCL 500mg	1	1314.64	0	1314.64
		Sandoz-Metformin HCl 500mg	Sandoz-Metformin HCl 500mg	2	1369.58	0	2739.16
	Actrapid HM 10ml Ampoules	Protaphane HM 10ml Ampoules	Sandoz-Gliclazide	1	1228.46	0	1228.46
	Glucophage Forte 850mg	Humalog 3ml Penset Prefill	Lantus 300IU 3ml	1	6271.81	0	6271.81
Actraphane HM Penset 3ml	Actraphane HM Penset 3ml	Actrapid HM Penset 3ml	Actrapid HM Penset 3ml	1	2528.04	0	2528.04
		Glucophage 500mg	Glucophage 500mg	1	882.76	0	882.76
		Glucophage Forte 850mg	Glucophage Forte 850mg	1	1812.65	0	1812.65
	Amaryl 2mg	Amaryl 4mg	Glucophage Forte 850mg	3	903.87	0	2711.61
	Diamicron MR 30mg	Glucophage 500mg	Sandoz-Metformin HCl 500mg	1	872.55	0	872.55
Actrapid HM 10ml Ampoules	Protaphane HM 10ml Ampoules	Sandoz-Metformin FC 500mg	Starlix FCT 60mg	1	1083.29	0	1083.29
Actrapid HM Pensets 3ml	Diamicron 80mg	Glucophage Forte 850mg	Lantus 300IU/3ml O/T	1	1189.91	0	1189.91
	Glucophage 500mg	Glycomin 5mg	Protaphane HM Penset 3ml	1	903.36	0	903.36
Amaryl 1mg	Amaryl 1mg	Amaryl 2mg	Amaryl 2mg	1	700.80	0	700.80
		Glucophage 500mg	Glucophage 500mg	2	515.04	0	1030.08
		Glucophage Forte 850mg	Glucophage Forte 850mg	3	802.63	822.38	2407.90
Amaryl 2mg	Amaryl 2mg	Glucophage 500mg	Glucophage 500mg	1	630.40	0	630.40
		Glucophage Forte 850mg	Glucophage Forte 850mg	9	539.96	221.26	4859.66
		Humalog Mix 25 Penset	Humalog Mix 25 Penset	1	1521.92	0	1521.92
		Rolab-Metformin FC 500mg	Rolab-Metformin FC 500mg	1	344.82	0	344.82
		Sandoz-Metformin FC 500mg	Sandoz-Metformin FC 500mg	2	344.82	0	689.64
	Amaryl 4mg	Avandia 2mg	Glygard	1	878.38	0	878.38
		Diamicron MR 30mg	Sandoz-Metformin FC 850mg	1	698.13	0	698.13
		Glucophage Forte 850mg	Protaphane HM Penset 3ml	1	844.65	0	844.65
	Avandia 4mg	Lantus 300IU 3ml	Novorapid 3ml Flexpen	1	1768.26	0	1768.26
Amaryl 4mg	Amaryl 4mg	Glucophage Forte 850mg	Glucophage Forte 850mg	10	658.66	388.21	6586.60
Avandia 2mg	Avandia 4mg	Glucophage Forte 850mg	Glycomin 5mg	1	453.49	0	453.49
Avandia 4mg	Avandia 4mg	Glucophage 500mg	Glucophage 500mg	1	816.54	0	816.54
		Glucophage Forte 850mg	Glucophage Forte 850mg	7	634.52	123.2	4441.64

Table G3: (Continue) Utilisation of four anti-diabetic agents in combination for the time September to December

Agents in combination				No of Rx	Average cost (R)	Std dev (R)	Total cost (R)
	Diamicron MR 30mg		Humalog Mix 25 Penset	2	1981.68	0	3963.36
	Glucophage 500mg		Sandoz-Gliclazide	1	273.02	0	273.02
	Humalog 3ml Penset Prefill	Lantus 300IU/3ml O/T	Rolab-Metformin FC 850mg	1	1281.04	0	1281.04
Daonil 5mg	Daonil 5mg	Glucophage 500mg	Glucophage 500mg	1	470.68	0	470.68
		Glucophage Forte 850mg	Glucophage Forte 850mg	1	699.70	0	699.70
		Sandoz-Metformin HCl 500mg	Sandoz-Metformin HCl 500mg	1	351.14	0	351.14
Diacare 5mg	Diacare 5mg	Metforal 850mg	Metforal 850mg	1	102.52	0	102.52
Diamicron 80mg	Diamicron 80mg	Glucophage 500mg	Glucophage 500mg	23	274.51	179.27	6313.82
		Glucophage Forte 850mg	Glucophage Forte 850mg	28	385.80	234.48	10802.48
		Merck-Metformin 850mg	Merck-Metformin 850mg	4	552.50	73.04	2210.00
		Rolab-Metformin FC 500mg	Rolab-Metformin FC 500mg	2	251.28	30.86	502.56
		Sandoz-Metformin FC 500mg	Sandoz-Metformin FC 500mg	6	236.60	5.66	1419.58
Glucobay 100mg	Glucobay 100mg	Glycomin 5mg	Glycomin 5mg	1	671.28	0	671.28
Glucobay 50mg	Glucobay 50mg	Glucovance 500/5mg	Glucovance 500/5mg	1	497.36	0	497.36
	Glucomed 80mg	Glyben 5mg	Sandoz-Metformin HCl 500mg	1	424.49	0	424.49
Glucomed 80mg	Glucomed 80mg	Glucophage	Glucophage	2	380.36	0	760.72
		Glucophage 500mg	Glucophage 500mg	5	406.46	382.2	2032.30
		Glucophage Forte 850mg	Glucophage Forte 850mg	9	310.48	136.3	2794.32
		Merck-Metformin 850mg	Merck-Metformin 850mg	1	273.62	0	273.62
		Metforal 850mg	Metforal 850mg	2	317.30	74.93	634.60
		Rolab-Metformin HCl 500mg	Rolab-Metformin HCL 500mg	2	289.04	162.78	578.08
		Sandoz-Metformin FC 500mg	Sandoz-Metformin FC 500mg	3	436.18	0	1308.54
	Glucophage Forte 850mg	Lantus 300IU/3ml O/T	Novorapid 3ml Flexpen	2	2928.27	0	5856.54
Glucophage 500mg	Glucophage 500mg	Glucophage Forte 850mg	Glucophage Forte 850mg	3	74.77	31.08	224.30
		Glycomin 5mg	Glycomin 5mg	14	163.81	132.37	2293.30
		Humalog Mix 25 Penset	Humalog Mix 25 Penset	2	1038.00	0	2076.00
		Novonorm 1.0mg	Novonorm 1.0mg	3	399.27	164.12	1197.80
Glucophage Forte 850mg	Glucophage Forte 850mg	Glycomin 5mg	Glycomin 5mg	13	214.94	85.32	2794.16
		Lantus 1000IU 10ml	Lantus 1000IU 10ml	1	1545.48	0	1545.48
		Lantus 300IU 3ml	Lantus 300IU 3ml	1	1239.82	0	1239.82
		Novomix 30 Flexpen 3ml	Novomix 30 Flexpen 3ml	1	938.86	0	938.96

Table G3: (Continue) **Utilisation of four anti-diabetic agents in combination for the time September to December**

Agents in combination				No of Rx	Average cost (R)	Std dev (R)	Total cost (R)
	Novomix 30 Flexpen 3ml	Novonorm 1.0mg	Novonorm 2.0mg	2	905.75	0	1811.50
Glyben 5mg	Glyben 5mg	Rolab-Metformin FC 850mg	Rolab-Metformin FC 850mg	1	171.88	0	171.88
		Sandoz-Gliclazide	Sandoz-Gliclazide	1	110.06	0	110.06
		Sandoz-Metformin FC 850mg	Sandoz-Metformin FC 850mg	3	139.36	0	418.08
Glycomin 5mg	Glycomin 5mg	Lantus 300IU/3ml O/T	Lantus 300IU/3ml O/T	1	1056.52	0	1056.52
		Rolab-Metformin HCl 500mg	Rolab-Metformin HCl 500mg	1	352.66	0	352.66
		Sandoz-Metformin HCl 500mg	Sandoz-Metformin HCl 500mg	3	171.13	134.42	513.38
		Sandoz-Metformin FC 500mg	Sandoz-Metformin FC 500mg	3	161.37	89.33	484.12
		Sandoz-Metformin HCl 850mg	Sandoz-Metformin HCl 850mg	1	141.22	0	141.22
Humalog 3ml Penset Prefill	Humalog 3ml Penset Prefill	Humulin N 3ml Penset	Humulin N 3ml Penset	5	1837.04	0	9158.20
		Lantus 1000IU 10ml		1	2495.20	0	2495.20
		Lantus 300IU 3ml		2	4822.85	1364.11	9645.70
		Lantus 300IU/3ml O/T		2	3909.38	1202.7	7818.76
Lantus 300IU 3ml	Lantus 300IU 3ml	Novorapid 3ml Flexpen	Novorapid 3ml Flexpen	2	3889.82	0	7779.64
Novonorm 0.5mg	Novonorm 0.5mg	Rolab-Metformin HCl 500mg	Rolab-Metformin HCL 500mg	1	377.30	0	377.30
Novorapid 3ml Flexpen	Novorapid 3ml Flexpen	Sandoz-Metformin FC 500mg	Sandoz-Metformin FC 500mg	1	1859.26	0	1859.26

Table G4: Utilisation of five antidiabetic agents in combination for the time September to December

Agents in combination (Trade name ®					No of Rx	Average cost (R)	Std dev (R)	Total cost (R)
Actos 15mg	Glucophage 500mg	Glycomin 5mg	Humalog 3ml Penset Prefill	Lantus 300IU/3ml O/T	1	1398.47	0	1398.47

Table G5: Utilisation of six antidiabetic agents in combination

Agents in combination (Trade name ®)						No of Rx	Average cost (R)	Std dev (R)	Total cost (R)
Actos 30mg	Actos 30mg	Glucophage Forte 850mg	Glucophage Forte 850mg	Humalog 3ml Cartridges	Humalog 3ml Cartridges	1	2658.14	0	2658.14
				Humalog Mix 25 Cartridges	Humalog Mix 25 Cartridges	3	1786.88	0	5360.64
Amaryl 1mg	Amaryl 1mg	Amaryl 2mg	Amaryl 2mg	Glucophage Forte 850mg	Glucophage Forte 850mg	2	728.72	347.16	1457.44
Amaryl 4mg	Amaryl 4mg	Avandia 4mg	Avandia 4mg	Glucophage Forte 850mg	Glucophage Forte 850mg	4	1351.26	0	5405.04
		Diamicron 80mg	Diamicron 80mg			1	695.90	0	695.90
				Rolab-Metformin FC 850mg	Rolab-Metformin FC 850mg	1	770.68	0	770.68
				Sandoz-Metformin FC 850mg	Sandoz-Metformin FC 850mg	1	752.64	0	752.64
Diamicron 80mg	Diamicron 80mg	Glucophage Forte 850mg	Glucophage Forte 850mg	Glycomin 5mg	Glycomin 5mg	2	272.23	43.29	544.46
Diamicron MR 30mg	Diamicron MR 30mg	Glucobay 50mg	Glucobay 50mg	Glucophage Forte 850mg	Glucophage Forte 850mg	2	1609.09	528.62	3218.18
Glucobay 100mg	Glucobay 100mg	Glucomed 80mg	Glucomed 80mg	Glucophage Forte 850mg	Glucophage Forte 850mg	1	751.30	0	751.30
				Metforal 850mg	Metforal 850mg	1	751.30	0	751.30
Glucomed 80mg	Glucomed 80mg	Glycomin 5mg	Glycomin 5mg	Humulin N 3ml Penset	Humulin N 3ml Penset	1	1318.52	0	1318.52
Glucophage Forte 850mg	Glucophage Forte 850mg	Glycomin 5mg	Glycomin 5mg		Lantus 300IU/3ml O/T	1	1216.54	0	1216.54
		Humalog 3ml Penset Prefill	Humalog 3ml Penset Prefill			2	4018.87	1298.35	8037.74

Appendix H

Table H1: Summary of the total average cost, standard deviation and prevalence of the oral antidiabetic agents as single agent or in combination for the time January to April

January-April			
Agent (Trade name)	Average cost (Total prevalence)	Average cost (One alone)	Average cost (Combination)
Actos 15mg	400.32 ± 58.32 (200)	403.63 ± 80.94 (101)	396.94 (99)
Actos 30mg	582.41 ± 88.96 (135)	592.91 ± 16.33 (55)	575.19 (80)
Amaryl 1mg	103.92 ± 32.51 (1001)	102.05 ± 29.40 (678)	107.85 (323)
Amaryl 2mg	194.97 ± 65.07 (1513)	194.79 ± 61.37 (817)	195.19 (696)
Amaryl 4mg	366.20 ± 125.90 (1085)	365.96 ± 113.69 (495)	366.41 (590)
Avandia 2mg	206.42 ± 73.43 (119)	200.07 ± 65.02 (77)	218.05 (42)
Avandia 4mg	372.41 ± 116.69 (287)	376.44 ± 123.95 (144)	170.75 (143)
Daonil 5mg	432.64 ± 194.08 (372)	356.68 ± 167.46 (170)	496.58 (202)
Diabinese 250mg	46.51 ± 0.00 (1)	46.51 ± 0.00 (1)	0
Diacare 5mg	55.70 ± 4.16 (3)	0	55.70 (3)
Diaglucide 80mg	108.33± 47.88 (147)	88.69 ± 38.80 (61)	122.27 (86)
Diamicron 80mg	116.95 ± 59.61 (1291)	98.11 ± 52.85 (631)	134.97 (660)
Diamicron MR 30mg	135.43 ± 61.96 (424)	131.92 ± 57.46 (243)	140.13 (181)
Euglucon 5mg	573.93 ± 360.66 (6)	358.23 ± 421.00 (3)	789.62 (3)
Glucobay 100mg	336.50 ± 74.28 (87)	347.63 ± 38.98 (36)	328.64 (51)
Glucobay 50mg	231.83 ± 68.12 (153)	231.62 ± 83.74 (82)	232.07 (71)
Glucomed 80mg	97.75 ± 44.78 (3512)	84.79 ± 40.80 (1642)	109.13 (1870)
Glucophage 500mg	64.73 ± 29.30 (4286)	60.64 ± 27.94 (2319)	69.56 (1967)
Glucophage Forte 850mg	101.69 ± 33.37 (4243)	100.92 ± 31.98 (1681)	102.19 (2562)
Glucovance 250/1.25mg	73.86 ± 27.62 (77)	74.91 ± 27.99 (68)	65.92 (9)
Glucovance 500/2.5mg	187.88 ± 70.42 (188)	189.08 ± 72.70 (170)	176.53 (18)
Glucovance 500/5mg	237.92 ± 111.72 (124)	234.12 ± 111.04 (115)	286.44 (9)
Glyben 5mg	128.39 ± 71.79 (402)	108.87 ± 64.18 (167)	142.26 (235)
Glycomin 5mg	147.75 ± 76.82 (2943)	123.78 ± 67.77 (1200)	164.46 (1743)
Glycron 80mg	93.98 ± 41.90 (138)	90.67 ± 43.09 (54)	96.11 (84)
Glygard	99.14 ± 41.74 (57)	94.28 ± 36.84 (30)	104.54 (27)

Table H1: (Continue) **Summary of the total average cost, standard deviation and prevalence of the oral antidiabetic agents as single agent or in combination for the time January to April**

January-April			
Agent (Trade name)	Average cost (Total prevalence)	Average cost (One alone)	Average cost (Combination)
Hypomide 250mg	100.57 ± 54.02 (20)	108.46 ± 65.29 (10)	92.67 (10)
Merck-Gliclazide 80mg	63.19 ± 47.12 (39)	40.08 ± 43.54 (11)	72.27 (28)
Merck-Metformin 500mg	58.11 ± 27.86 (234)	54.66 ± 26.53 (128)	62.29 (106)
Merck-Metformin 850mg	87.52 ± 25.80 (231)	82.67 ± 23.47 (89)	90.56 (142)
Minidiab 5mg	241.04 ± 148.63 (193)	214.08 ± 139.63 (99)	269.42 (94)
Norton-Glibenclamide	30.43 ± 20.12 (19)	22.91 ± 4.20 (8)	35.91 (11)
Novonorm 0.5mg	99.93 ± 20.30 (101)	98.76 ± 21.14 (72)	102.84 (29)
Novonorm 1.0mg	196.50 ± 45.35 (98)	199.84 ± 42.45 (49)	193.16 (49)
Novonorm 2.0mg	356.92 ± 122.51 (69)	356.22 ± 124.02 (21)	357.23 (48)
Rolab-Gliclazide	92.93 ± 39.97 (833)	81.10 ± 37.77 (332)	100.76 (501)
Rolab-Metformin HCL 500mg	63.46 ± 28.78 (1799)	57.49 ± 26.47 (1034)	71.53 (765)
Rolab-Metformin FC 500mg	61.24 ± 27.88 (1732)	57.46 ± 26.80 (889)	65.22 (843)
Rolab-Metformin FC 850mg	93.66 ± 30.40 (1382)	90.38 ± 29.09 (566)	95.95 (816)
Rolab-Metformin HCl 850mg	94.14 ± 29.63 (1074)	92.60 ± 27.32 (427)	95.16 (647)
Starlix FCT 120mg	426.69 ± 60.22 (25)	418.81 ± 71.59 (15)	438.50 (10)
Starlix FCT 60mg	208.23 ± 0.00 (1)	208.23 ± 0.00 (1)	0
Ziclin 80mg	136.79 ± 0.00 (4)	136.79 ± 0.00 (4)	0

Table H2: Summary of the total average cost, standard deviation and prevalence of the oral antidiabetic agents as single agent or in combination for the time May to August

May-August			
Agent (Trade name)	Average cost (Total prevalence)	Average cost (One alone)	Average cost (Combination)
Actos 15mg	390.06 ± 70.63 (382)	387.02 ± 78.21 (204)	393.54 (178)
Actos 30mg	578.66 ± 78.37 (352)	574.67 ± 62.11 (155)	581.79 (197)
Amaryl 1mg	88.28 ± 33.49 (1126)	85.36 ± 28.15 (743)	93.95 (383)
Amaryl 2mg	170.76 ± 62.96 (1719)	169.95 ± 56.88 (929)	171.70 (790)
Amaryl 4mg	337.14 ± 114.17 (1462)	341.40 ± 120.93 (596)	334.40 (866)
Avandia 2mg	167.30 ± 65.41 (144)	168.33 ± 52.45 (79)	166.05 (65)
Avandia 4mg	340.36 ± 130.79 (530)	346.95 ± 132.56 (215)	335.86 (315)
Daonil 5mg	360.11 ± 169.53 (474)	291.16 ± 136.34 (189)	405.83 (285)
Diabetix 250mg	15.20 ± 0.00 (1)	15.20 ± 0.00 (1)	0
Diacare 5mg	46.16 ± 32.43 (8)	75.17 ± 60.05 (2)	36.49 (6)
Diaglucide 80mg	71.85 ± 32.91 (436)	62.59 ± 32.71 (154)	76.91 (383)
Diamicron 80mg	118.78 ± 66.18 (1288)	99.66 ± 59.65 (542)	132.67 (746)
Diamicron MR 30mg	136.60 ± 58.93 (882)	131.20 ± 56.36 (478)	143.00 (404)
Euglucon 5mg	300.59 ± 184.27 (6)	216.34 ± 167.91 (4)	469.11 (2)
Glucobay 100mg	318.99 ± 100.92 (95)	299.59 ± 77.08 (35)	330.30 (60)
Glucobay 50mg	207.28 ± 63.74 (171)	203.62 ± 57.38 (63)	209.41 (108)
Glucomed 80mg	88.38 ± 41.55 (3822)	79.32 ± 39.90 (1698)	95.62 (2124)
Glucophage 500mg	52.40 ± 24.97 (5531)	49.20 ± 22.87 (2838)	55.78 (2693)
Glucophage Forte 850mg	74.88 ± 31.90 (5618)	72.93 ± 29.94 (2139)	76.08 (3479)
Glucovance 250/1.25mg	55.86 ± 22.84 (113)	57.64 ± 23.35 (95)	46.45 (18)
Glucovance 500/2.5mg	134.16 ± 63.95 (268)	133.30 ± 63.99 (224)	138.53 (44)
Glucovance 500/5mg	197.40 ± 93.24 (228)	193.17 ± 89.15 (189)	217.89 (39)
Glyben 5mg	50.10 ± 59.97 (510)	43.09 ± 49.74 (193)	54.36 (317)
Glycomin 5mg	74.42 ± 51.67 (3645)	64.95 ± 51.03 (1377)	80.17 (2268)
Glycron 80mg	89.90 ± 48.62 (213)	78.29 ± 48.21 (70)	95.59 (143)
Glygard	73.41 ± 29.12 (83)	71.62 ± 32.31 (45)	75.53 (38)
Hypomide 250mg	73.54 ± 47.71 (14)	108.12 ± 47.79 (6)	47.61 (8)
Merck-Gliclazide 80mg	63.59 ± 29.49 (91)	54.19 ± 22.22 (31)	68.44 (60)
Merck-Metformin 500mg	55.59 ± 25.05 (361)	54.17 ± 25.04 (202)	57.39 (159)
Merck-Metformin 850mg	79.46 ± 20.35 (238)	80.23 ± 18.80 (86)	79.02 (152)

Table H2: (Continue) Summary of the total average cost, standard deviation and prevalence of the oral antidiabetic agents as single agent or in combination for the time May to August

May-August			
Agent (Trade name)	Average cost (Total prevalence)	Average cost (One alone)	Average cost (Combination)
Metforal 500mg	38.63 ± 21.19 (8)	37.02 ± 24.27 (6)	43.46 (2)
Metforal 850mg	57.13 ± 16.71 (36)	51.26 ± 26.59 (13)	60.44 (23)
Minidiab 5mg	202.73 ± 141.21 (161)	171.31 ± 122.77 (76)	230.54 (85)
Norton-Glibenclamide	19.83 ± 11.58 (20)	12.86 ± 6.23 (13)	32.78 (7)
Novonorm 0.5mg	89.83 ± 33.21 (111)	86.71 ± 38.17 (69)	94.95 (42)
Novonorm 1.0mg	190.60 ± 92.29 (168)	202.51 ± 149.56 (55)	184.80 (113)
Novonorm 2.0mg	336.24 ± 99.36 (117)	312.03 ± 130.94 (27)	343.50 (90)
Rolab-Gliclazide	64.21 ± 31.61 (1151)	56.67 ± 28.66 (436)	68.80 (715)
Rolab-Metformin HCL 500mg	43.84 ± 20.96 (2166)	39.99 ± 19.09 (1139)	46.09 (1027)
Rolab-Metformin FC 500mg	47.83 ± 24.29 (2273)	43.75 ± 22.32 (1151)	52.01 (1122)
Rolab-Metformin FC 850mg	66.23 ± 25.51 (1696)	63.84 ± 25.03 (672)	67.80 (1024)
Rolab-Metformin HCl 850mg	64.10 ± 23.51 (1208)	61.50 ± 22.61 (519)	66.05 (689)
Starlix FCT 120mg	393.82 ± 100.37 (31)	403.82 ± 78.91 (17)	381.67 (14)

Table H3: Summary of the total average cost, standard deviation and prevalence of the oral antidiabetic agents as single agent or in combination for the time September to December

September-December			
Agent (Trade name)	Average cost (Total prevalence)	Average cost (One alone)	Average cost (Combination)
Actos 15mg	314.36 ± 57.60 (366)	317.68 ± 50.87 (176)	311.30 (190)
Actos 30mg	467.58 ± 91.25 (380)	468.08 ± 46.08 (160)	467.21 (220)
Amaryl 1mg	78.14 ± 43.46 (1081)	73.22 ± 28.73 (717)	87.82 (364)
Amaryl 2mg	148.78 ± 56.10 (1680)	146.62 ± 52.57 (878)	151.13 (802)
Amaryl 4mg	275.48 ± 115.78 (1454)	273.06 ± 115.67 (591)	277.14 (863)
Avandia 2mg	149.23 ± 48.06 (136)	154.99 ± 51.71 (80)	140.99 (56)
Avandia 4mg	287.77 ± 124.52 (614)	274.45 ± 93.91 (230)	295.75 (384)
Daonil 5mg	252.47 ± 111.77 (514)	218.77 ± 99.37 (218)	277.28 (296)
Diacare 5mg	13.55 ± 10.56 (17)	9.94 ± 4.63 (5)	15.06 (12)
Diaglucide 80mg	62.84 ± 26.31 (838)	56.30 ± 26.58 (295)	66.40 (543)
Diamicron 80mg	83.74 ± 48.12 (1136)	66.72 ± 38.23 (401)	93.03 (735)
Diamicron MR 30mg	130.48 ± 65.00 (1237)	123.75 ± 59.55 (618)	137.19 (619)
Euglucon 5mg	181.61 ± 86.90 (9)	114.26 ± 10.64 (5)	265.81 (4)
Glucobay 100mg	250.53 ± 65.45 (86)	256.48 ± 61.66 (37)	246.04 (49)
Glucobay 50mg	177.05 ± 48.19 (185)	170.60 ± 39.95 (75)	181.44 (110)
Glucomed 80mg	72.05 ± 35.63 (3817)	63.99 ± 33.16 (1617)	77.97 (2200)
Glucophage	56.02 ± 0.00 (6)	56.02 ± 0.00 (2)	56.02 (4)
Glucophage 500mg	30.83 ± 20.36 (7135)	27.97 ± 18.36 (3601)	33.75 (3534)
Glucophage Forte 850mg	30.83 ± 18.75 (7214)	55.57 ± 16.25 (2659)	58.48 (4555)
Glucovance 250/1.25mg	49.13 ± 18.17 (138)	48.95 ± 17.61 (126)	50.97 (12)
Glucovance 500/2.5mg	110.14 ± 42.53 (434)	110.68 ± 41.58 (388)	105.58 (46)
Glucovance 500/5mg	150.96 ± 59.34 (339)	145.75 ± 52.51 (268)	170.64 (71)
Glyben 5mg	15.02 ± 14.51 (685)	13.79 ± 12.98 (240)	15.68 (445)
Glycomin 5mg	58.78 ± 30.68 (4408)	49.47 ± 27.10 (1638)	64.29 (2770)
Glycron 80mg	69.06 ± 29.14 (424)	61.58 ± 29.43 (147)	73.03 (277)
Glygard	58.61 ± 26.30 (229)	51.24 ± 22.96 (95)	63.83 (134)
Hypomide 250mg	46.00 ± 38.48 (20)	46.48 ± 38.89 (13)	45.11 (7)
Merck-Gliclazide 80mg	53.66 ± 23.83 (318)	44.36 ± 21.43 (132)	60.25 (186)
Merck-Metformin 500mg	45.31 ± 23.83 (164)	41.28 ± 27.58 (65)	47.95 (99)
Merck-Metformin 850mg	65.58 ± 24.63 (116)	46.20 ± 21.83 (19)	69.38 (97)

Table H3: (Continue) **Summary of the total average cost, standard deviation and prevalence of the oral antidiabetic agents as single agent or in combination for the time September to December**

September-December			
Agent (Trade name)	Average cost (Total prevalence)	Average cost (One alone)	Average cost (Combination)
Metforal 500mg	35.32 ± 18.24 (42)	33.05 ± 17.13 (26)	39.01 (16)
Metforal 850mg	54.83 ± 19.22 (128)	52.69 ± 17.94 (60)	56.71 (68)
Minidiab 5mg	152.91 ± 118.96 (157)	133.52 ± 113.66 (68)	167.73 (89)
Norton-Glibenclamide	20.62 ± 30.68 (24)	13.58 ± 6.75 (7)	23.52 (17)
Novonorm 0.5mg	87.41 ± 33.23 (117)	83.53 ± 35.63 (68)	92.79 (49)
Novonorm 1.0mg	185.01 ± 180.47 (156)	201.34 ± 297.03 (52)	176.85 (104)
Novonorm 2.0mg	303.94 ± 117.53 (81)	277.45 ± 111.86 (17)	310.98 (64)
Rolab-Gliclazide	56.48 ± 28.18 (496)	50.44 ± 27.73 (204)	60.69 (202)
Rolab-Metformin HCL 500mg	33.72 ± 16.62 (639)	30.82 ± 14.26 (331)	36.84 (308)
Rolab-Metformin FC 500mg	36.48 ± 16.58 (715)	33.15 ± 15.15 (362)	39.89 (353)
Rolab-Metformin FC 850mg	57.22 ± 18.93 (434)	56.29 ± 20.79 (183)	57.91 (251)
Rolab-Metformin HCl 850mg	54.26 ± 20.06 (376)	52.08 ± 19.52 (148)	55.67 (228)
Sandoz-Gliclazide	55.72 ± 28.37 (1660)	49.47 ± 27.66 (633)	59.58 (1027)
Sandoz-Metformin HCl 500mg	33.45 ± 15.48 (1751)	30.81 ± 14.37 (854)	35.96 (897)
Sandoz-Metformin FC 500mg	35.64 ± 16.54 (2251)	32.16 ± 14.73 (1158)	39.33 (1093)
Sandoz-Metformin FC 850mg	54.96 ± 15.54 (1445)	53.47 ± 14.02 (551)	55.88 (894)
Sandoz-Metformin HCl 850mg	53.46 ± 17.22 (1040)	52.79 ± 17.54 (398)	53.88 (642)
Starlix FCT 120mg	390.10 ± 77.19 (20)	378.61 ± 60.01 (10)	401.60 (10)
Starlix FCT 60mg	337.43 ± 0.00 (1)	0	0

Table H4: Summary of the total average cost, standard deviation and prevalence of the insulins as single agent or in combination for the time January to April

Active ingredient	Agent	Average cost (Total prevalence)	Average cost (One alone)	Average cost (Combination)
January-April				
Insulin Lispro	Humalog Mix 25 Penset	767.81 ± 561.73 (791)	775.31 ± 569.77 (584)	746.66 (207)
	Humalog Mix 25 Cartridges	866.32 ± 313.37 (79)	862.12 ± 344.21 (43)	871.34 (36)
	Humalog Mix 25 Injection	861.31 ± 637.34 (16)	933.79 ± 684.28 (13)	547.21 (3)
	Humalog 10ml Ampules	581.57 ± 282.38 (38)	575.18 ± 251.40 (16)	586.23 (22)
	Humalog 3ml Penset/Prefill	917.43 ± 459.34 (640)	825.08 ± 325.73 (239)	972.47 (401)
	Humalog 3ml Cartridge injection	860.54 ± 331.76 (92)	728.14 ± 139.74 (37)	949.60 (55)
Insulin aspartame	Novorapid 3ml FlexPen	754.65 ± 271.44 (289)	767.03 ± 297.79 (150)	741.29 (139)
	Novorapid 3ml Penfill	825.50 ± 312.80 (57)	786.29 ± 324.70 (24)	854.02 (33)
Biosynthetic human insulin	Humulin R 10ml vial	414.29 ± 285.17 (25)	377.98 ± 114.47 (5)	423.36 (20)
	Humulin R 3ml cartridges	794.53 ± 515.92 (20)	647.16 ± 0.01 (6)	857.70 (14)
	Humulin R Humaject Pen 5ml	415.33 ± 340.86 (5)	3.43 ± 0.00 (1)	518.30 (4)
Biosynthetic human soluble insulin	Actrapid HM Pensets 1,5ml	786.16 ± 0.00 (1)	786.00 ± 0.00 (1)	0
	Actrapid HM Pensets 3ml	827.56 ± 359.45 (333)	806.96 ± 331.79 (165)	847.80 (168)
	Actrapid HM Penfill 3ml	839.05 ± 385.17 (44)	776.89 ± 319.63 (17)	878.18 (27)
	Actrapid HM 10ml Ampules	456.02 ± 268.32 (115)	371.89 ± 109.61 (33)	489.88 (82)
Soluble insulin and isophane	Actraphane HM Penset 1,5ml	285.83 ± 0.00 (1)	0	285.83 (1)
	Actraphane HM Penset 3ml	845.14 ± 355.05 (1594)	829.32 ± 329.72 (1310)	918.11 (284)
	Actraphane HM Penfill 3ml	809.07 ± 434.68 (143)	823.09 ± 454.73 (123)	722.90 (20)
	Actraphane HM 10ml Ampules	526.19 ± 278.62 (287)	534.24 ± 283.97 (260)	448.70 (27)
Biosynthetic human isophane	Humulin 30/70 3ml Cartridges	741.33 ± 280.38 (64)	744.52 ± 285.25 (49)	730.89 (15)
	Humulin 30/70 10ml vial	657.11 ± 243.92 (21)	657.11 ± 243.92 (21)	0
	Humulin 30/70 Humaject Inj	837.67 ± 580.05 (42)	725.15 ± 386.22 (38)	1906.57 (4)
	Humulin N 3ml Penset	645.09 ± 205.18 (269)	606.15 ± 197.99 (64)	657.25 (205)
	Humulin N 3ml Cartridges	765.11 ± 408.21 (41)	617.82 ± 503.09 (16)	859.37 (25)
	Humulin N Humaject 3ml Inj	459.06 ± 0.00 (1)	459.06 ± 0.00 (1)	0
	Humulin N 10ml vial	378.70 ± 122.58 (62)	330.87 ± 57.04 (17)	396.77 (45)
Biphasic biosynthetic human insulin 20/80	Mixtard 20/80 Penfill	836.32 ± 310.56 (11)	820.02 ± 333.25 (4)	845.63 (7)
Soluble insulin aspartame, protamine	Novomix 30 Flexpen 3ml Inj.	771.28 ± 287.47 (451)	765.78 ± 278.33 (315)	784.03 (136)

Table H4: (Continue) Summary of the total average cost, standard deviation and prevalence of the insulins as single agent or in combination for the time January to April

Active ingredient	Agent	Average cost (Total prevalence)	Average cost (One alone)	Average cost (Combination)
January-April				
	Novomix 30 Penfill 3ml Inj.	996.23 ± 358.93 (37)	840.02 ± 322.58 (20)	1180.00 (17)
Zinc biosynthetic human insulin	Humulin L 10ml vial	395.18 ± 131.90 (173)	399.02 ± 139.59 (61)	393.08 (112)
Biosynthetic human insulin zinc susp	Monotard HM 10ml Ampules	445.90 ± 200.34 (104)	449.00 ± 163.22 (51)	442.92 (53)
Biosynthetic monocomponent isophane	Protaphane HM Penset 1,5ml	393.08 ± 0.00 (1)	393.08 ± 0.00 (1)	0
	Protaphane HM Penset 3ml	664.28 ± 195.84 (605)	641.69 ± 186.04 (213)	676.55 (392)
	Protaphane HM Penfill 3ml	694.09 ± 268.25 (79)	663.08 ± 347.04 (19)	703.92 (60)
	Protaphane HM 10ml Ampules	417.15 ± 158.78 (95)	385.13 ± 147.67 (39)	439.46 (56)
Biosynthetic human insulin zinc suspension monocomponent crystals	Ultratard HM 10ml Ampules	360.14 ± 107.50 (25)	330.22 ± 36.32 (16)	413.33 (9)
Insulin Glargine	Lantus 300IU/3ml	907.18 ± 287.65 (308)	819.50 ± 223.20 (119)	962.38 (189)
	Lantus 300IU/3ml O/T	830.68 ± 256.13 (139)	792.25 ± 198.27 (56)	856.50 (83)
	Lantus 1000IU/10ml	757.14 ± 334.43 (60)	722.17 ± 274.88 (32)	797.10 (28)

Table H5: Summary of the total average cost, standard deviation and prevalence of the insulins as single agent or in combination for the time May to August

Active ingredient	Agent	Average cost (Total prevalence)	Average cost (One alone)	Average cost (Combination)
May-August				
Insulin Lispro	Humalog Mix 25 Penset	872.45 ± 438.40 (1086)	847.51 ± 431.83 (752)	928.60 (334)
	Humalog Mix 25 Cartridges	853.49 ± 341.65 (136)	855.48 ± 361.96 (97)	848.54 (39)
	Humalog Mix 25 Injection	901.80 ± 587.04 (25)	901.80 ± 587.04 (25)	0
	Humalog 10ml Ampules	445.65 ± 227.69 (40)	385.07 ± 176.84 (24)	536.52 (16)
	Humalog 3ml Penset/Prefill	828.68 ± 424.02 (762)	796.91 ± 390.56 (325)	852.32 (437)
	Humalog 3ml Cartridge injection	753.8 ± 279.24 (110)	624.47 ± 65.04 (43)	838.21 (67)
	Humaject/Humalog 3ml	1004.52 ± 0.00 (1)	0	1004.52 (1)
Insulin aspartame	Novorapid 3ml FlexPen	680.39 ± 277.00 (346)	680.92 ± 271.38 (210)	679.58 (136)
	Novorapid 3ml Penfill	719.02 ± 295.04 (57)	668.26 ± 285.80 (32)	783.99 (25)
Biosynthetic human insulin	Humulin R 10ml vial	300.24 ± 31.83 (24)	308.10 ± 65.22 (2)	299.52 (22)
	Humulin R 3ml cartridges	479.78 ± 168.18 (19)	526.30 ± 106.46 (3)	471.06 (16)
	Humulin R Humaject Pen 5ml	663.01 ± 222.00 (11)	532.52 ± 55.64 (2)	692.01 (9)
Biosynthetic human soluble insulin	Actrapid HM Pensets 1,5ml	54.21 ± 0.00 (1)	54.21 ± 0.00 (1)	0
	Actrapid HM Pensets 3ml	734.61 ± 375.28 (430)	720.52 ± 388.98 (293)	764.75 (137)
	Actrapid HM Penfill 3ml	722.45 ± 329.88 (63)	638.39 ± 292.70 (27)	785.50 (36)
	Actrapid HM 10ml Ampules	386.66 ± 162.18 (113)	370.61 ± 132.71 (33)	393.29 (80)
Soluble insulin and isophane	Actraphane HM Penset 1,5ml	334.64 ± 0.00 (2)	0	334.64 (2)
	Actraphane HM Penset 3ml	762.82 ± 349.85 (2025)	744.43 ± 346.37 (1600)	832.05 (425)
	Actraphane HM Penfill 3ml	711.37 ± 292.97 (244)	727.24 ± 319.68 (189)	656.83 (55)
	Actraphane HM 10ml Ampules	472.17 ± 211.69 (447)	478.59 ± 213.74 (363)	444.44 (84)
Biosynthetic human isophane	Humulin 30/70 3ml Cartridges	732.23 ± 279.13 (104)	713.86 ± 276.28 (65)	762.85 (39)
	Humulin 30/70 10ml vial	762.05 ± 607.05 (16)	773.76 ± 626.49 (15)	586.47 (1)
	Humulin 30/70 Humaject Inj	790.74 ± 479.81 (55)	753.76 ± 477.75 (36)	860.80 (19)
	Humulin N 3ml Penset	609.72 ± 158.89 (329)	636.96 ± 191.10 (100)	597.87 (229)
	Humulin N 3ml Cartridges	655.21 ± 409.74 (43)	427.94 ± 206.32 (12)	743.18 (31)
	Humulin N Humaject 3ml Inj	524.02 ± 0.00 (1)	0	524.02 (1)
	Humulin N 10ml vial	334.76 ± 103.57 (61)	321.09 ± 69.56 (19)	340.94 (42)
Biphasic biosynthetic human insulin 20/80	Mixtard 20/80 Penfill	757.19 ± 260.20 (9)	865.00 ± 249.58 (6)	541.57 (3)

Table H5: (Continue) Summary of the total average cost, standard deviation and prevalence of the insulins as single agent or in combination for the time May to August

Active ingredient	Agent	Average cost (Total prevalence)	Average cost (One alone)	Average cost (Combination)
May-August				
Soluble insulin aspartame, protamine	Novomix 30 Flexpen 3ml Inj.	693.89 ± 305.50 (715)	667.91 ± 288.01 (464)	741.91 (251)
	Novomix 30 Penfill 3ml Inj.	862.15 ± 374.15 (30)	763.44 ± 269.96 (12)	927.95 (18)
Zinc biosynthetic human insulin	Humulin L 10ml vial	353.28 ± 143.21 (198)	378.11 ± 168.73 (77)	337.48 (121)
Biosynthetic human insulin zinc susp	Monotard HM 10ml Ampules	426.00 ± 219.68 (106)	411.06 ± 164.22 (45)	437.02 (61)
Biosynthetic monocomponent isophane	Protaphane HM Penset 1,5ml	0	0	0
	Protaphane HM Penset 3ml	672.11 ± 218.48 (257)	681.29 ± 248.37 (81)	667.88 (176)
	Protaphane HM Penfill 3ml	622.35 ± 228.01 (112)	563.31 ± 166.60 (45)	662.00 (67)
	Protaphane HM 10ml Ampules	372.83 ± 137.44 (126)	377.91 ± 155.43 (70)	366.49 (56)
Biosynthetic human insulin zinc suspension monocomponent crystals	Ultratard HM 10ml Ampules	339.50 ± 119.72 (19)	282.50 ± 9.95 (3)	350.19 (16)
Insulin Glargine	Lantus 300IU/3ml	816.16 ± 222.08 (432)	771.82 ± 178.08 (179)	847.53 (253)
	Lantus 300IU/3ml O/T	761.87 ± 257.55 (266)	747.23 ± 203.12 (101)	770.82 (165)
	Lantus 1000IU/10ml	636.75 ± 265.69 (88)	562.79 ± 225.44 (38)	692.96 (50)

Table H6: Summary of the total average cost, standard deviation and prevalence of the insulins as single agent or in combination for the time September to December

Active ingredient	Agent	Average cost (Total prevalence)	Average cost (One alone)	Average cost (Combination)
September-December				
Insulin Lispro	Humalog Mix 25 Penset	698.32 ± 265.81 (1325)	684.49 ± 247.54 (901)	727.71 (424)
	Humalog Mix 25 Cartridges	666.80 ± 261.66 (161)	650.31 ± 251.07 (106)	698.58 (55)
	Humalog Mix 25 Injection	696.75 ± 406.89 (22)	696.75 ± 406.89 (22)	0
	Humalog 10ml Ampules	393.99 ± 202.33 (53)	341.04 ± 93.95 (21)	428.74 (32)
	Humalog 3ml Penset/Prefill	642.59 ± 338.54 (916)	594.67 ± 260.99 (372)	675.35 (544)
	Humalog 3ml Cartridge injection	561.61 ± 162.77 (116)	534.95 ± 138.02 (53)	584.03 (63)
	Humaject/Humalog 3ml	823.35 ± 0.00 (1)	0	823.35 (1)
Insulin aspartame	Novorapid 3ml FlexPen	559.16 ± 236.32 (431)	539.60 ± 222.18 (242)	584.20 (189)
	Novorapid 3ml Penfill	561.94 ± 182.90 (71)	581.52 ± 184.96 (38)	539.38 (33)
Biosynthetic human insulin	Humulin R 10ml vial	272.21 ± 79.73 (18)	237.56 ± 0.00 (8)	299.93 (10)
	Humulin R 3ml cartridges	448.89 ± 102.94 (16)	401.62 ± 0.00 (3)	459.80 (13)
	Humulin R Humaject Pen 5ml	508.41 ± 133.81 (11)	438.11 ± 0.00 (2)	524.04 (9)
Biosynthetic human soluble insulin	Actrapid HM Pensets 1,5ml	44.86 ± 0.00 (1)	44.86 ± 0.00 (1)	0
	Actrapid HM Pensets 3ml	555.03 ± 260.83 (503)	560.69 ± 289.58 (333)	543.94 (170)
	Actrapid HM Penfill 3ml	533.20 ± 186.83 (68)	492.29 ± 194.54 (27)	560.14 (41)
	Actrapid HM 10ml Ampules	299.01 ± 110.42 (124)	299.74 ± 110.74 (39)	298.68 (85)
Soluble insulin and isophane	Actraphane HM Penset 1,5ml	0	0	0
	Actraphane HM Penset 3ml	585.56 ± 233.43 (2559)	562.50 ± 203.36 (2005)	669.02 (554)
	Actraphane HM Penfill 3ml	595.62 ± 252.71 (262)	594.85 ± 257.36 (196)	597.93 (66)
	Actraphane HM 10ml Ampules	422.92 ± 194.61 (530)	408.47 ± 173.74 (425)	481.41 (105)
Biosynthetic human isophane	Humulin 30/70 3ml Cartridges	567.18 ± 211.56 (121)	584.95 ± 222.31 (69)	543.60 (52)
	Humulin 30/70 10ml vial	357.74 ± 147.71 (23)	363.21 ± 148.79 (22)	237.45 (1)
	Humulin 30/70 Humaject Inj	553.65 ± 211.35 (56)	519.61 ± 193.52 (41)	692.91 (14)
	Humulin N 3ml Penset	482.01 ± 139.72 (409)	521.68 ± 184.00 (110)	467.42 (299)
	Humulin N 3ml Cartridges	544.43 ± 631.25 (45)	378.40 ± 104.92 (16)	636.04 (29)
	Humulin N Humaject 3ml Inj	485.42 ± 0.00 (2)	485.42 ± 0.00 (2)	0
	Humulin N 10ml vial	339.82 ± 145.99 (50)	285.37 ± 73.66 (14)	360.99 (36)
Biphasic biosynthetic human insulin 20/80	Mixtard 20/80 Penfill	564.03 ± 209.07 (5)	793.06 ± 0.00 (2)	411.35 (3)
Soluble insulin aspartame, protamine	Novomix 30 Flexpen 3ml Inj.	558.49 ± 207.86 (1307)	537.58 ± 182.96 (823)	594.06 (484)

Table H6: (Continue) Summary of the total average cost, standard deviation and prevalence of the insulins as single agent or in combination for the time September to December

Active ingredient	Agent	Average cost (Total prevalence)	Average cost (One alone)	Average cost (Combination)
September-December				
	Novomix 30 Penfill 3ml Inj.	564.91 ± 178.53 (43)	509.25 ± 142.61 (30)	693.35 (13)
Zinc biosynthetic human insulin	Humulin L 10ml vial	285.95 ± 109.51 (203)	296.13 ± 141.38 (71)	280.48 (132)
Biosynthetic human insulin zinc susp	Monotard HM 10ml Ampules	363.54 ± 189.33 (113)	364.84 ± 153.20 (45)	362.68 (68)
Biosynthetic monocomponent isophane	Protaphane HM Penset 1,5ml	0	0	0
	Protaphane HM Penset 3ml	513.53 ± 163.50 (269)	526.75 ± 160.38 (56)	510.05 (213)
	Protaphane HM Penfill 3ml	482.12 ± 134.06 (125)	463.49 ± 120.47 (34)	489.09 (91)
	Protaphane HM 10ml Ampules	334.58 ± 120.02 (112)	348.74 ± 135.87 (69)	311.86 (43)
Biosynthetic human insulin zinc suspension monocomponent crystals	Ultratard HM 10ml Ampules	294.09 ± 95.48 (22)	352.85 ± 111.96 (3)	284.81 (19)
Insulin Glargine	Lantus 300IU/3ml	686.62 ± 283.62 (438)	631.22 ± 178.80 (175)	723.48 (263)
	Lantus 300IU/3ml O/T	596.36 ± 160.40 (435)	601.95 ± 159.75 (163)	341.74 (472)
	Lantus 1000IU/10ml	537.44 ± 186.88 (96)	501.33 ± 155.02 (37)	560.09 (59)