PRESCRIBING PATTERNS AND DRUG COST IMPLICATIONS FOR DIABETIC PATIENTS IN EASTERN PROVINCE, KENYA

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Prescribing Patterns and Drug Cost Implications for Diabetic Patients in Eastern Province, Kenya

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DECLARATION

This thesis is my original work and has not been presented for a degree in any other University.

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DEDICATION

I dedicate this thesis to my dear wife Rosemary for her outstanding patience and holistic support and my son Victor, my parents and all the members of my family for their love, support and encouragement during this process.

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LIST OF ABBREVIATIONS

ACE	Angiotensin-Converting Enzyme
ADA	American Diabetes Association
BMI	Body Mass Index
BP	Blood Pressure
CPHR	Center for Public Health Research
DCCT	Diabetes Complications and Control Trials
DM	Diabetes Mellitus
DNCD	Division of Non Communicable Disease
GDM	Gestational Diabetes Mellitus
HbA1c	Glycosylated hemoglobin
HIV/AIDS	Human Immunodeficiency Virus/Acquired Immunodeficiency Syndrome
IDF	International Diabetes Federation
IDF-Africa	International Diabetes Federation Africa Region
IEC	Information, Education and Communication
IGT	Impaired Glucose Tolerance
KEMRI	Kenya Medical Research Institute
KSH	Kenya Shilling
MOH	Ministry of Health
NSAID	Non Steroidal Anti-Inflammatory Drug
OGTT	Oral Glucose Tolerance Test

RPSGB	Royal Pharmaceutical Society of Great Britain
UKPDS	United Kingdom Prospective Diabetes Study Group
US$	United States dollar
WHO	World Health Organization
WHO-AFRO	World Health Organization Regional Office for Africa

ABSTRACT

Achieving best practice in management of chronic diseases such as diabetes, which requires long duration of treatment and multiple therapies, remains a major challenge in primary health care settings worldwide. As healthcare costs continue to rise, much attention has been placed on ensuring good prescribing practice to optimize patient care within available resources. An essential component of evaluating and improving diabetic care is the assessment of drug prescribing standards and quality of care. It is in this context that this study was conducted. The main objective was to establish the prescribing patterns and drug cost implications for diabetic patients in Eastern Province, Kenya. A cross-sectional study design was used in which data was collected retrospectively in Machakos District and Embu Provincial General Hospitals between July 1st and 5th of August 2008. Data collection tools included a pre-tested data abstraction form and selection of study subjects done by systematic random sampling technique. Data were entered, cleaned and analyzed using Statistical Package for Social Sciences (SPSS) version 12.0. A total of 218 diabetic patients were selected for the study. The study findings revealed that 59.6% were females while the mean (±SD) age for women was 55.60 (15.19) years and that of men was 54.57(18.58) years. The age ranges were 63 years (25-88) and 79 years (19-98) for females and males respectively. Majority of the study population (90%) had type 2 diabetes. Those with a duration of diabetes of >20 years were mainly in age older than 60 years. Among the oral hypoglycemic agents (OHA), sulfonylurea class was widely prescribed (39%) while antihypertensive drugs were the most prescribed (57.8%) among the non-antidiabetic

category. The major co morbid condition was Hypertension (50.2%). Prescription by brand name dominated with 56.1% for antidiabetic drugs while for non-diabetic category generic prescribing scored 53.4%. Overall females were more likely to be treated with sulfonylurea compared to males though this was not statistically significant, P >0.05. Men had 22% less likelihood to be treated with biguanide OR=0.78 compared to females. The use of biguanide among the age group 31-40 years was statistically significant P<0.05, compared to age group >60 years. Men were more likely to have insulin prescriptions compared to females, P >0.05. The mean number of drugs per prescription was 3.4 with females being prescribed more drugs than males. Majority, 27% (n=59) were prescribed >4 drugs per prescription. Insulin was the most expensive among antidiabetic drugs costing 10 Ksh (0.13 US$) per day and for non-diabetic drugs, multivitamins were more costly dispensing at 13 Ksh (0.18 US$) per day. In review of the prescribing patterns and drug cost implications among the diabetic patients, there may be significant contribution by the clinicians to the relatively costly diabetic treatment. This study suggests an urgent need for the review of current prescribing guidelines for diabetic patient's management.

CHAPTER ONE

INTRODUCTION

1.1 Background

Diabetes mellitus (DM) accounts for a significant proportion of morbidity and mortality in all age groups and therefore emerging as an important global public health problem (Wild *et al*., 2004). The clinical definition of diabetes is a metabolic disease mainly characterized by chronic hyperglycemia resulting from defects in insulin secretion, insulin action or both and affects metabolism of carbohydrates, proteins and fats (ADA, 2003 (a). The result of insufficient action of insulin is an increase in blood glucose concentration (hyperglycemia). Many other metabolic abnormalities occur, notably an increase in ketone bodies in the blood when there is a severe lack of insulin (Ward *et al*., 1986). If not diagnosed early or properly treated and controlled, it can lead to devastating irreversible complications. The disease is classified as type 1, type 2 and gestational diabetes (Alberti *et al*., 1998).

Diabetes management in developing countries is a great challenge from both the providers and patients' perspective and evidence exists that levels of care are suboptimal (Glasgow *et al.,* 2000, Peters *et al.,* 1996). Of particular challenge to clinicians is the management of complications which often requires multiple medications to adequately and appropriately treat the associated co morbidities. Thus, concerns for polypharmacy must be balanced against the need to adequately treat diabetes as well as associated co morbidities (Grant *et al*., 2002, Stephen *et al*., 2001, Ary., 1986).

The management of type-1 diabetes depends mainly on insulin, whereas type-2 diabetes is through diet and exercise in combination with oral hypoglycemic agents (OHAs) (Evans *et al*., 1999, Pan *et al*., 1997). Proper control of blood glucose, blood pressure and lipids can potentially prevent many of the major complications that make the economic cost of diabetes so high, such as hypertension, heart attack, limb amputation, diabetic nephropathy, diabetic neuropathy, peripheral vascular disease and blindness (Gray *et al*., 2000). The epidemic of Diabetes is particularly serious in developing countries like Kenya where living conditions are changing dramatically and urbanization and demographic changes are the greatest (King *et al*., 1998). Diabetics are at a higher risk of numerous medications and are more vulnerable to irrational prescription (Yuen *et al*., 1998, Chiang *et al*., 2006, Upadhyay *et al*., 2006). An essential component of evaluating and improving diabetic care is the assessment of drug prescribing standards and quality of care. Given the limited resources within the health care sector in the country it is important to evaluate the prescribing patterns and cost of drugs among diabetic patients. A study on prescribing patterns identifies drug use patterns, prescribing behavior and factors responsible for polypharmacy.

1.1.1 Basic Concept of Glucose Metabolism.

Glucose is the primary source of energy for human body. After absorption in the small intestine it is metabolized and converted to energy, amino acids and proteins and also stored as glycogen. Metabolism of glucose is regulated by complex orchestration of hormones activities. Dietary sugars are broken down into various carbohydrates. The

most important is glucose, metabolized in nearly all body cells. Glucose enters the cell by facilitated diffusion (glucose transport proteins). This facilitated transport is stimulated very rapidly and effectively by an insulin signal. After glucose is transported into the cytoplasm, insulin then directs the disposition of it; conversion to glycogen, to pyruvate and lactate, and fatty acids (Kahn, 1992).

1.1.2 A Brief History of Diabetes.

The oldest description of diabetes as a polyuric state dates back to 1550 BC in ancient Egypt. The word diabetes, derived from Greek meaning siphon or pass through, was first used by Aretaeus of Cappadocia in the 2nd century AD when he gave a clinical description of the disease. In the 5th and 6th centuries, Indian physicians recognized the sweet, honey-like taste of urine from polyuric patients, which attracted ants and insects. The Indian descriptions of diabetes mellitus also recognized the distinction between two forms of diabetes: one in older, fatter people, and the other in thin people who rapidly succumbed to their illness.

The sweetness in the urine was rediscovered by the Englishman Thomas Willis, physician to King Charles II in the 17th century, who also noted the importance of lifestyle when he remarked that the prevalence of diabetes was increasing because of good fellowship and guslig down chiefly of unalloyed wine. A century later, Mathew Dobson in 1776 showed that urinary sweetness was caused by sugar and was associated with a rise in blood sugar. At the turn of the 18th century, John Rollo was the first person to use the term diabetes mellitus (honey) to distinguish the condition from diabetes insipidus (tasteless).Claude Bernard, a French physiologist, made several

important advances in the 19th century when he discovered that sugar was stored in the liver in the form of glucogen, and that transfixion of the medulla in conscious rabbits caused hyperglycaemia. Paul Langerhans, also working in the 19th century, discovered the pancreatic islets that now bear his name, although it was Edouard Laguesse in 1893 who suggested that they were the endocrine tissue of the pancreas. In 1889, Joseph Von Mering and Oskar Minkowski removed the pancreas from a dog and discovered that the animal developed diabetes, demonstrating the important link between the pancreas and diabetes. Several workers in different institutions followed this observation by attempting to isolate the blood glucose lowering agent from the pancreas, culminating in the discovery of insulin in 1921 by a team based at the University of Toronto, comprising Fredrick Banting, Charles Best, James Collip and J.R Macleod. In 1922, Leonard Thompson was the first person to receive insulin thus transforming the management of diabetes forever.

Although insulin has major actions on lipid and protein metabolism, this historical perspective explains why the focus of diabetic management has been the normalization of blood glucose levels and why the diagnosis is based on the finding of chronic hyperglycemia (Richard *et al*., 2004).

1.1.3 Clinical Features of Diabetes

Type 2 diabetes usually affects overweight individuals and most cases are diagnosed in those over 40 years old (Jonsson, 2002). However, the demographics of diabetes are changing and it is now becoming increasingly common in children and young adults (ADA, 2000). Approximately half of patients with type 2 are diagnosed as a result of

typical diabetic symptoms of polyuria, nocturia, thirst, tiredness and blurred vision. A further 16% of patients are diagnosed after presenting with an infection (UKPDS, 1988). Micro vascular diabetic complications are frequently present at the time of diagnosis, but account for 2% of all presentations. The classical risk factors for developing gestational diabetes are the following : a previous diagnosis of diabetes or pre diabetes, impaired glucose tolerance or impaired fasting glycaemia, a family history revealing a first degree relative with type 2 diabetes, maternal age- a woman's risk factor increases as she gets older (especially for women over 35 years of age), ethnic background (those with higher risk factors include: African-Americans, Afrocaribeans, Native Americans, Hispanics, Pacific Islanders and people originating from the Indian subcontinent),being overweight, obese or severely obese, a previous pregnancy which resulted in a child with a high birth weight (>90^{th} centile, or >4000g), a previous poor obstetric history (Ross,2006). Frequently women with gestational diabetes exhibit no symptoms. However, possible symptoms include increased thirst, increased urination, fatigue, nausea and vomiting, bladder infection, yeast infections and blurred vision.

1.1.4 Classification and Diagnosis of Diabetes mellitus

The World Health Organization recognizes three main forms of Diabetes mellitus: Type 1, type 2, and gestational diabetes. All have similar signs, symptoms and consequences but different causes and population distributions (WHO, 1999). The three major forms are due to the beta cells of the pancreas being unable to produce sufficient insulin to prevent hyperglycemia. Type 1 is usually due to autoimmune destruction of the pancreatic beta cells which produce insulin. Type 2 is characterized by insulin

resistance, but impairment of beta cell function is necessary for its development. Gestational diabetes is similar to type 2 diabetes in that it involves insulin resistance; the hormones of pregnancy cause insulin resistance in women genetically predisposed to developing this condition. Gestational diabetes usually resolves after pregnancy but in some cases could lead to type 2 diabetes.

Criteria for diagnosis of diabetes mellitus:

The three major criteria's for diagnosis of Diabetes mellitus are:

1) Symptoms of diabetes plus causal plasma glucose concentration $\geq$11.1mmol/l.Causal is defined as any time of the day without regard to time since last meal.

2) Fasting blood glucose $\geq$7.0 mmol/l. Fasting is defined as no caloric intake at least eight hours.

3) Two hour plasma glucose $\geq$11.1mmol/l during an Oral Glucose Tolerance Test (OGTT). The test is performed according to WHO 1985, by using a glucose load containing the equivalent of 75g anhydrous glucose dissolved in water. OGTT is not usually recommended for routine clinical use but can be used for epidemiological field studies (Gilberti *et al.*, 1998).

1.1.5 Epidemiology and Etiology of Diabetes

The number of people with diabetes worldwide is set to double in the next 20 years as result of increasing obesity and longevity. Once considered primarily a risk factor for heart disease, diabetes has become a high profile public health concern in its own right,

due to the escalating epidemic of diabetes in older people and the emergence of type 2 diabetes in children.

Type 1 diabetes is caused by an absolute deficiency of insulin, and it represents around 10% of all cases of diabetes affecting approximately 20 million people worldwide (ADA, 2001). Although type 1 diabetes affects all age groups, the majority diagnosed are either at around the ages of 4-5 years, or in their teens and early adulthood (Bloom *et al*., 1975). The etiology of type 1 diabetes remains poorly understood, but is likely that an environmental factor triggers an autoimmune process in a predisposed individual. Although the genetic susceptibility to type 1 diabetes is inherited, only 12-15% of type 1 diabetes occurs in families. Twin studies have shown that the concordance rate for type 1 diabetes in monozygotic twins is around 20-30% (Barnett *et al.*, 1981). Studies indicate that genetic factors do not account entirely for the development of type 1 diabetes, and several environmental triggers, including viral infections, nutritional factors, parental age and low birth weight, have been implicated (Akerblom *et al*.,2000).

Type 2 Diabetes is a heterogeneous disorder that results from an interaction between a genetic predisposition and environmental factors. It accounts for around 90% of all cases of diabetes. A marked geographical variation in the prevalence of type 2 diabetes exists (Zimmet, 1982). The etiology of type 2 diabetes is multifactorial and probably genetically based, but it also has strong behavioral components. This is the most common form of diabetes mellitus and is highly associated with a family history of diabetes, older age, obesity and lack of exercise. Defective beta cells become exhausted, further fuelling the cycle of glucose intolerance and hyperglycemia. Gestational diabetes

is a condition in which women without previously diagnosed diabetes exhibit high blood glucose levels during pregnancy. It is generally diagnosed during pregnancy. The frequency of gestational diabetes varies widely by study depending on the population studied .It occurs in between 5 and 10% of all pregnancies (1-14% in various studies) (ADA, 2004). Etiology: There is no specific cause which has been identified, but it is believed that hormones produced during pregnancy reduce a woman's sensitivity to insulin, resulting in high blood sugar levels.

1.1.6 Pathogenesis of Diabetes

Under normal physiological conditions, plasma glucose concentration is maintained within a narrow range, despite fluctuations in supply and demand, through a tightly regulated and dynamic interaction between tissue sensitivity to insulin (DeFronzo, 1988).

Type 2 diabetes results from an imbalance between insulin sensitivity and insulin secretion. Both longitudinal and cross-sectional studies have demonstrated that the earliest detectable abnormality of type 2 is impairment in the body's ability to appropriately augment its secretion of insulin to offset the insulin resistance, glucose tolerance remains normal. With time, however, the beta –cell fails to maintain its high rate of insulin secretion. Although the mechanisms underlying the beta cell dysfunction remain unclear, they are likely to be multifactorial as well as genetic factors (Pratley *et al*., 2001). A number of environmental factors (including early-life malnutrition and

obesity) and hyperglycemia and hyperlipidemia per se may accelerate the decline in beta-cell function (Hales, *et al*., 1991).

1.1.7 Pathophysiology of Diabetes Mellitus

Diabetes involves poor control of blood glucose and is thought to play a role in the development of a number of abnormalities. One of the major adverse effects of diabetes is the greatly increased risk for macro vascular and micro vascular diseases such as coronary heart disease and retinal damage. People with type 2 diabetes have a much higher risk for developing heart disease, kidney disease, eye problems, poor circulation, and have much higher rate of limb amputation (Colwell *et al*.,1991). The pathophysiology of type 2 diabetes mellitus is characterized by peripheral insulin resistance, impaired regulation of hepatic glucose production, and declining beta cell function, eventually leading to beta cell failure. The primary events are believed to be an initial deficit in insulin secretion and, in many patients, relative insulin deficiency in association with peripheral insulin resistance (Reaven, 1998).

1.1.8 Complications in Diabetes

Since the introduction of effective treatment that allows patients with diabetes to live through acute metabolic consequences of the illness, it has become apparent that diabetes is associated with a number of chronic micro vascular complications which affect the eyes, kidneys and nervous system and macro vascular complications which lead to an increased risk of myocardial infarction, stroke and peripheral vascular disease. Micro vascular complications are frequently present at diagnosis in patients with type 2 diabetes. Retinopathy, nephropathy and neuropathy are the most common micro

vascular complications in individuals with type 2 diabetes (UKPDS, 1988). Foot ulcer and amputation also cause considerable morbidity and mortality (Boulton *et al*., 1998). Mortality following myocardial infarction is far greater in people with diabetes. Majority, 60-75% of all people with diabetes die from cardiovascular disease (Stamler *et al*., 1993).

Gestational diabetes poses a risk to the mother and child. This risk is largely related to high blood glucose levels and its consequences. The risk increases with higher blood glucose levels. The two main risks for gestational diabetes on the baby are growth abnormalities and chemical imbalances after birth, which may require admission to a neonatal intensive care unit (HSCRG, 2008). Studies have also documented periodontal conditions such as plague, supra- and sub gingival calculus, gingivitis to be common among insulin- dependent diabetics (Hugoson *et al*, 2005). The results of a population-based study (Carsene *et al*, 2002) support an association between poorly controlled type 2 diabetes mellitus and severe complications.

1.2 Problem Statement

Management of diabetes mellitus and its complications presents an increasing challenge to healthcare systems throughout the world (RPSGB, 2001). Although substantial resources have been invested in Diabetes mellitus in several developed and developing countries (Fitzsimons *et al*., 2002, Jayed *et al*., 2002), management and outcomes remain unsatisfactory and Kenya as a developing country is not an exception. There is a recognized need to improve prescribing in chronic diseases particularly in diabetes.

Similar studies in various countries have been used in various clinical settings and the results have identified inappropriate drug therapy and gaps in adherence to clinical guidelines (Elliot *et al*., 2003). However, there is uncertainty regarding the extent to which these guidelines are adhered to. As the Ministry of Health (MOH) plans to raise standards of diabetes care through optimizing interventions according to evidence-based guidelines and best practices to improve outcomes of diabetic patients, it is important to conduct this study to identify both met and unmet standards.

1.3 Justification

Diabetes Mellitus (DM) is a widespread disease which has affected both young and the old worldwide and is a major cause of morbidity and mortality. Its chronic nature and constantly increasing prevalence as well as its complications, remains a major medical and social problem. It puts a heavy burden on the individuals affected, their families and society as a whole, not only financially but also in psychological and social terms. The goals of diabetes management are to extend the periods of wellness that patients experience, improve the overall quality of their lives and prevent occurrence of complications. Clinical guidelines are therefore an important element in the management of diabetics for it provides a basis for screening, treatment, evaluation, and pharmacological management of patients with diabetes. Consistent review of drug prescribing pattern is needed to ensure that the guidelines reflect the latest research. The cost of irrational drug prescribing is enormous in terms of both scarce resources and the adverse clinical consequences of therapies that may have real risks but no objective

benefits. Despite the existence of evidence -based prescribing guidelines, the patterns of drug prescribing are often inappropriate (Stanton *et al*., 1994, Lesar *et al*., 1994). Studies have suggested the need for evaluation of these patterns in an effort to improve prescribing standards (Figueirus *et al*., 2001). According to previous studies from the literature, polypharmacy is associated with a higher cost, increased risk of side effects, drug interactions and non compliance (Ebbessen *et al*.,2000,Good,2002). It is important to assess the prescribing patterns to obtain information about usage and cost of drugs, which are of economic interest in a resource limited setting. There is no existing data on prescribing patterns of drugs used to manage diabetes mellitus in Kenya. The study provides information concerning prescribing patterns and cost of drugs which may be useful to policy makers in development of protocols governing prescribing for diabetics.

1.4 Broad Objective

To establish the prescribing patterns and drug cost implications for diabetic patients in Eastern Province, Kenya.

1.5 Specific Objectives

- To establish the various type of drugs prescribed among diabetic patients
- To determine the cost of drugs prescribed among diabetic patients

1.6 Research Hypothesis

The relatively high costs of diabetic treatment are largely attributed to the prescribing patterns by clinicians.

1.7 Limitations of the Study

- The diabetic patients who never bought their medicines from the hospital pharmacy were excluded. Such patients could have vital information which could contribute to our findings.

CHAPTER TWO

LITERATURE REVIEW

2.1 Global Burden of Diabetes

Worldwide, diabetes is expected to result to 3.8 million deaths (or 10% of world mortality in 2007), the same figure as HIV/AIDS. An estimated 380 million people globally will have diabetes by 2025, with the largest increase occurring in developing countries (IDF, 2003). Recent projections by World Health Organization suggest that at least 194 million people suffer from diabetes worldwide (WHO, 2004).

Diabetes Mellitus (DM) is major cause of morbidity, mortality, and economic consequences (both direct and indirect).

Table 2.1 Estimated Numbers of People Age 20 to 79 with Diabetes, as well as Mortality and Direct Medical Costs Attributable to Diabetes, by Regions.

Region	**No. of people(thousands)**		**Prevalence (%)**		**Direct medical costs,2003(US$ million)**		**Deaths, 2001 (thousands)**
	2003	2025	2003	2025	Low est.	High est.	
Developing countries	**140,849**	**264,405**	**4.5**	**5.9**	**12,304**	**23,127**	**757**
East Asia and the pacific	31,363	60,762	2.6	3.9	1,368	2,656	234
Europe and Central Asia	25,764	33,141	7.6	9	2,884	5,336	51
Latin America and the Caribbean	19,026	36,064	6	7.8	4,592	8,676	163
Middle East and North Africa	10,792	23,391	6.4	7.9	2,347	4,340	31
South Asia	46,309	94,848	5.9	7.7	840	1,589	196
Sub Saharan Africa	7,595	16,199	2.4	2.8	273	530	82
Developed countries	**53,337**	**68,345**	**7.8**	**9.2**	**116,365**	**217,760**	**202**
World	194,186	332,750	5.1	6.3	128,669	240,887	959

Source: Number of persons with diabetes, prevalence of diabetes, and direct medical costs of diabetes, International Diabetes Federation 2003,WHO 2004.

2.2 Diabetes in Africa

Diabetes in Africa is increasingly becoming a major health problem. Ageing populations, urbanization, rapid industrialization and rising levels of obesity associated with dietary changes and decrease in physical activity are all contributing factors. Although the prevalence of Type 2 diabetes is predicted to increase globally by 55% by 2025, in Africa the rate is expected to rise by 80 % (Table 2.2 (Lefebvre 2006).

Table 2.2 Predicted prevalence rates of Type 2 Diabetes in Africa 2007-2025

African parameters	**2007**	**2025**
Total population	747 million	1088 million
Adult population (20-79)	336 million	537 million
Prevalence of diabetes	3.10%	3.50%
Number of diabetics	10.4 million	18.7 million (+80%)
Prevalence impaired glucose tolerance	7.20%	7.50%
Number with impaired glucose tolerance	24.2 million	40.3 million (+66%)

There is evidence that complications resulting from late diagnosis, late presentation, lack of access to essential medications and services, and poor management of diabetes are common and combine to create a heavy socio-economic burden for Africa. A recent study suggested that direct costs such as medical care and treatment of diabetes are usually met by the patients, family and healthy sector (Motala, 2000).

However, it is estimated that African countries use less than ten percent of their public health budgets on preventing and treating non-communicable diseases.

2.3 Diabetes in Sub-Saharan Africa

Although there is limited available evidence regarding the burden of non-communicable diseases, what is available suggest that diabetes is "substantial" (Unwin *et al.*, 1999). According to a study done by Murray et al, sub-Saharan Africa is suffering the double impact of communicable and non-communicable diseases (Murray *et al.*, 1997). Despite the lack of costing data for sub-Saharan Africa, it is clear that the potential damage from Diabetes to national economies is huge in both direct and indirect costs.

2.4 Diabetes in Kenya

Kenya, like other developing countries is experiencing an increase in diabetes and other non-communicable diseases. The true prevalence of diabetes in the country is unknown due to lack of population-based studies. According to the Ministry of health, division of non-communicable diseases (DNCD) current prevalence is estimated to be 10% (DNCD, 2007) which the World Diabetes Foundation (WDF) claims to be an underestimate.

2.5 Management of Diabetes

Although lifestyle modifications play an important role in diabetes management, drugs become unavoidable in many patients (Elis *et al.*, 2000). Modern approaches to diabetes primarily rely upon dietary and lifestyle management, often combined with regular ongoing blood glucose level monitoring (Tuomilehto *et al.*, 2001). Treatment of diabetes

is aimed at reducing elevated blood glucose levels. The goals of management are to extend the periods of wellness that patients experience, improve overall quality of their lives and prevent occurrence of complications.

2.6 The Costs of Diabetes Management.

Despite such an alarming prediction of the prevalence of diabetes in Kenya, there have been few studies on the status and economic burden of diabetes. Health resources in Kenya and other developing countries are very limited with only 5% of countries GDP (gross domestic income), being spent on healthcare. The costs of diabetes is differentiated between direct costs (consultation, Investigation, Treatment e.g. for drugs, costs of treating complications), indirect costs (man days lost, disability payments, social security and tax rebates) and intangible costs (pain, anxiety, depression and loss of enjoyment of life) (Gluber *et a*l., 1997).

2.7 Polypharmacy

The term polypharmacy is defined as a concurrent use of several different drugs. For patients suffering from multiple diseases, and for certain conditions associated with a need for multiple drug treatment e.g. congestive heart failure, hypertension, chronic obstructive lung disease, some psychiatric disorders, some infections and neoplastic diseases, polypharmacy may, from a clinical pharmacological point of view, be rational and necessary (Reus,1993). Even if a multiple drug regimen is clinically appropriate, however, individuals exposed to multiple drugs deserve attention because of quality of care issues related to higher risk of adverse drug reactions, interactions, poor compliance

and cost control issues. The distribution of drug exposures has important cost and quality of care implications. Polypharmacy may be responsible for unnecessary health expenditures directly due to the cost of superfluous medication, but also indirectly due to increased number of hospitalization caused by drug-related complications. The beneficial effect of the occurrence of polpharmacy has been addressed in order to cut down on expenditures for both physician and hospital services (Famuyiwa, 1988).

2.8 Current Diabetes Management

The current diabetes pandemic threatens to be rapidly expanding burden in the future for both developed and developing countries (King *et al*, 1995). Several interventions now exist that can vastly improve diabetes care and reduce needless human suffering. New interventions that prevent diabetes among those at high risk also now hold much promise and need to be implemented. Despite this promise, suboptimal diabetes care is common throughout the world, and considerable health benefit is needlessly foregone. Development and implementation of standard diabetes care quality measures can help track progress and guide improvement effort. Several efficacious treatments that can substantially reduce or prevent diabetes-related complications have been established. These treatments include glycemic and Blood Pressure control to reduce micro vascular complications (UKPDS,1998 a); eye examination with timely follow-up, and laser treatment to prevent vision loss; foot care to decrease serious foot disease (Littzelman *et al*.,1993); BP, lipid control, and aspirin use to prevent cardiovascular disease (UKPDS,1998 a), angiotensin -converting enzymes inhibitors to reduce nephropathy and

cardiovascular disease (Ravid *et al*.,1998); and influenza and pneumococcal vaccines in the elderly to reduce hospitalizations, respiratory conditions, and death (Nichol *et al*.,1998).

2.9 Insulin and Other Drug-Based Approaches

Patients with type-1 diabetes mellitus require direct injection of insulin as their bodies cannot produce enough insulin. For type-2 diabetics, diabetes management consists of a combination of diet, exercise and weight loss, in any achievable combination depending on the patient. Insulin is used in type 2 diabetic patients whose pancreas produces little or no insulin or whose oral medications do not control their blood sugar. Studies have shown that obesity in type 2 diabetes is common and contributes greatly to insulin resistance (DCCT,1993).Weight reduction and exercise improve tissue sensitivity to insulin and allows proper use by target tissues (Cantrill *et al*.,2003). Patients that have poor diabetic control after lifestyle modifications are typically placed on oral hypoglycemic drugs. For type 2, combination therapy using insulin, metformin, pioglitazone can be used. There is now a wealth of evidence from literature which demonstrates that diabetes complications can be prevented or significantly minimized with early detection and access to appropriate medical treatment and care. Two landmark studies have suggested the effectiveness of good glycemic and metabolic control in reducing micro vascular complications in both type 1 and type 2 (DCCT 1993, UKPDS 1988).

2.10 Oral Hypoglycemic Agents

Oral hypoglycemic agents are the group of drugs that may be taken singly or in combination to lower blood glucose in type 2 diabetes. They are not usually used in type 1 diabetes but metformin may be of use in the overweight type 2 diabetics (Moon *et al*., 2007). The following groups of oral hypoglycemic agents are currently available: Biguanides, sulfonylurea, meglitinides, Glitazones, alpha glycosidase inhibitors. The table below is a summary of their risks and benefits.

Table 2.3 Summary of the benefits and risks of Oral Hypoglycemic Agents (OHA).

Drug	Benefits	Risks
Biguanides e.g. Metformin	Used as a first-line drug in overweight patients when strict dieting has failed. Reduces macro vascular complications and death. Does not cause overweight gain	Known to cause lactic acidosis,gastro-intensital side-effects
Sulphonylurea e.g.chlopropamide	Known to reduce glycosylated haemoglobin (HbA1c)	Known to cause hypoglycaemia,weight gain, liver dysfunction and gastrointestinal disturbance
Thiazolidinediones e.g. pioglitazone	Used in combination with metformin and sulphonylyurea.May reduce the development of diabetes in patients with impaired fasting glycaemia	Not used in patients with history of heart failure, symptoms of coronary ischemia.
Alpha-glycosidase inhibitors e.g. Acarbose	Used in patients who cannot use other oral hypoglycemic drugs	Known to cause gastro-intestinal adverse effects e.g. flatulence,diarrhoea
Meglitinides e.g. Exenatide	Can be considered as a third line therapy in combination with metformin or glitazone	Hypersensitivity reactions known to occur(anaphylaxis,angiodema)

Newer treatment options like the use of exenatide have been licensed for use in combination with metformin and/or sulphonyureas. It can be considered as an alternative to insulin therapy in obese patients who have failed to achieve adequate glycaemic control on maximal doses of established oral treatment regimens. A strategy for type 2 diabetes management based on currently available guidance has been suggested (Campbell, 2007; Nathan *et al*., 2006).

The table below illustrates the scheme for the pharmacotherapy of glucose lowering in diabetes. It shows a guideline on actions to take e.g. when lifestyle changes it would be advisable to measure Hb1c at 6-monthly intervals and when lifestyle changes are not sufficient metformin is given unless contraindicated. Measurement of glycoslyated hemoglobin (HbA1c) at 1-6 monthly intervals and setting target HbA1c level based on risk of macro vascular and micro vascular complications is considered critical.

Table 2.4 Scheme for the pharmacotherapy of glucose lowering in diabetes.

Lifestyle changes	Measure HbA1c at 6 monthly intervals
Lifestyle changes not sufficient	Institute metformin unless contraindicated in which case start a sulfonylurea. If both contraindicated consider a thiazolidinedione,meglitinide or acarbose
Glucose control remains unsatisfactory or deteriorates. Consider dual therapy,; Metformin+sulfonylurea Metformin+Thiazolidinedione Metformin+basal insulin Acarbose+metformin or sulfonylurea Choice depends on individual patient circumstances, co-existing pathology,etc	Although not in the 2003 NICE guidance, increasingly metformin+Thiazolidenediones are being used at this stage.
Glucose control remains unsatisfactory or deteriorates, or one of existing drugs not tolerated	Consider double therapy plus basal insulin. Consider triple therapy (sulphonylurea+glitazone+metformin or sulphonylurea+metformin+insulin-glargine)
Glucose control remains unsatisfactory	Further intensify insulin, or add basal insulin to metformin+glitazone

A new guideline representing the latest approach by NICE (National Institute for Health and Clinical Excellence) is available (Appendix 3). The remit of this guideline is to offer best clinical advice and management of type 2 diabetes based on evidence-based medicine, economic evaluation and taking into account patient choice (NICE 2008).

2.11 Gestational Diabetes Management

The goal of treatment is to reduce the risks of gestational diabetes for the mother and child. Scientific evidence is beginning to show that controlling glucose levels can result

in less serious fetal complications (such as macro somnia) and increased maternal quality of life. Counseling before pregnancy for example about preventive folic acid supplements and multidisciplinary management are important for good pregnancy outcomes (Kapoor *et al*., 2007). Most pregnant women can be managed with dietary changes and exercise. Self monitoring of blood glucose levels can guide therapy. Some women will need antidiabetic drugs, most commonly insulin therapy. Any diet needs to provide sufficient calories for pregnancy. The main goal of dietary modifications is to avoid peaks in blood sugar levels. There is some evidence that certain oral glycaemic agents might be safe in pregnancy, or at least, are significantly less dangerous to the developing fetus than poorly controlled diabetes. Glyburide, a second generation sulfonylurea, has been shown to be an effective alternative to insulin therapy (ADA, 2004 a). Metformin has shown promising results. Treatment of polycystic ovarian syndrome with metformin during pregnancy has been noted to decrease gestational diabetes levels (Simmons *et al*., 2004). A recent randomized controlled trial of metformin versus insulin showed that women preferred metformin tablets to insulin, and that metformin is safe and equally effective as insulin (Rowan *et al*., 2008).

CHAPTER THREE

MATERIALS AND METHODS

3.1 Study Area

This study was conducted at Machakos District and Embu Provincial hospitals between July 1st and 5th of August 2008. The two study areas were selected for several reasons:

- Embu Provincial general Hospital recorded a marked increase in the number of diabetes cases between the years 2001 and 2005 (from 265 in 2003 to 316 in 2004 – a 19% increment). A similar survey at Machakos District Hospital for the same period showed an increase from 245 in 2003 to 278 cases in 2004 (DNCD, 2007).
- They have well established diabetic clinic compared to other hospitals in Eastern province.
- Limited research funds and restricted time frame since the researcher has to complete the degree as per the period stipulated by the university.

3.1.1 Machakos District

Machakos District is one of the twelve districts that comprise Eastern Province. The district has an estimated population of 1,102,934 by 2006 (Kenya Central Bureau of Statistics, 2006). From North to South, the district stretches from latitude 0^0 45^{II} to latitude 1^0 31^{II} south. From East to West it is located 36^0 45^{II} and 37^0 45^{II} east. It is 65 kilometers South East of Nairobi (See figure 3.1).

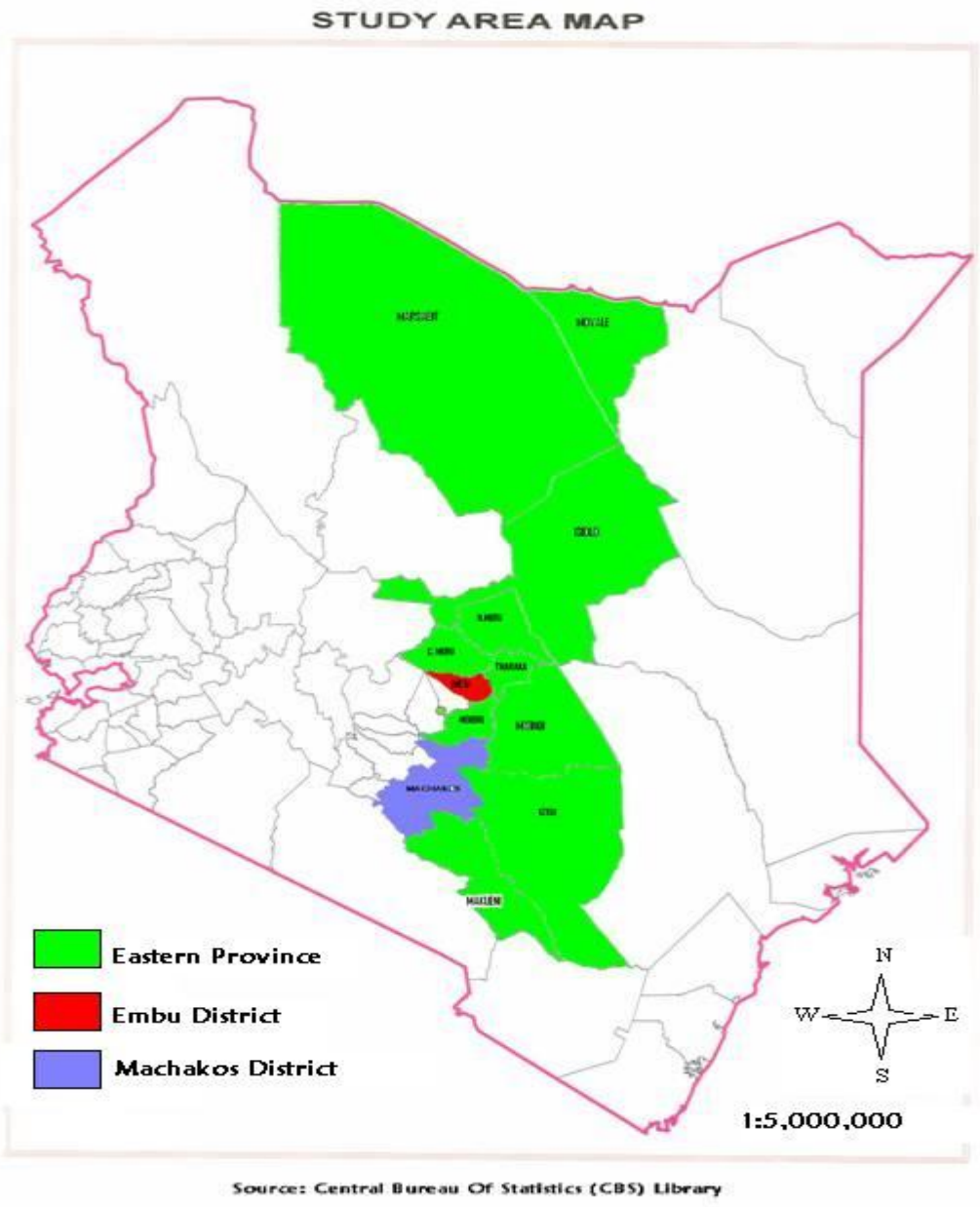

Figure 3.1 Study Area Map

3.1.1.1 Topography and Climate

The district has variety of topographical features. The landscape is largely a plateau that rises from 700m to 1,700m above sea level and is interrupted by an escarpment and a series of hill masses. The district is generally hot and dry. It has two rainy seasons, the long season which falls between October and February and the short rain season which falls between April and June. The average temperature ranges between 20 -25 degree Celsius.

3.1.1.2 Economic Activities

Agricultural and livestock production are the main economic activities. The main food crops grown are maize, beans, sorghum, millet and pulses. Coffee is grown in some parts of the district as the main cash crop.

3.1.1.3 Health Facilities

There were a total of 76 health facilities by the year 2004. Out of these seven were hospitals, eleven were health centers and fifty eight were sub-health centers.

3.1.1.4 Machakos District hospital

This is the main hospital in Machakos district. The hospital serves as referral institution for other sub-district hospitals and health centers in the district. The diabetic clinic mainly serves patients from both rural and urban areas. Approximately forty patients attend the clinic weekly which operates on Fridays and is usually run by consultants, medical officers, nurses and interns. On average four new cases of diabetes were

registered every diabetic clinic day. Patients were served at the filter clinic/casualty during other days (Monday to Thursday).Medical files for the diabetic patients are usually kept in the records department. The hospital pharmacy serves and maintains a record of prescriptions for all drugs dispensed for both inpatients and outpatients. However, patients who fail to get the prescribed drugs in the hospital pharmacy can choose to purchase them in the private market.

3.1.2 Embu District

Embu District is one of the twelve districts which make up the Eastern province. The district has an estimated population of 304,802 according to 2007 projections from the analytical report on population (Kenya Central Bureau of Statistics, 2006). It lies approximately between latitudes $0^0\ 8^{II}$ and $0^0\ 35^{II}$ south and longitudes $37^0\ 19^{II}$ and $37^0\ 42^{II}$ East. It is approximately 130 kilometers from Nairobi, the capital city of Kenya (see figure 3.1 above).

3.1.2.1 Topography and Climate

Being one of the districts that form part of Kenya's Eastern Highlands, the landscape of Embu District is characterized by typical highlands and midlands and other topographical features which include hills and valleys. Rainfall pattern is bimodal with two distinct rainy seasons, March to July and October to February.

3.1.2.2 Economic Activities

The above physical features, along with climatic conditions, create a very favorable environment for growing high value crops like tea, coffee and macadamia. Other crops are cereals such as maize and beans and horticultural crops such as French beans, tomatoes and avocados. Commercial activities also contribute to the economy of the district.

3.1.2.3 Health Facilities

There were a total of 31 health facilities by the year 2004. Out of these, hospitals were five, three health centers and twenty three dispensaries which are evenly distributed. The health services in the district are provided by the government, the missions and by private medical practitioners.

3.1.2.4 Embu Provincial General hospital

The hospital serves as a referral institution for surrounding areas such as Kirinyaga and Runyenjes. It has adequate specialized doctors and nurses. Diabetic clinic mainly serves patients from both rural and urban areas. Approximately fifty two patients attend the clinic weekly which operates on Mondays. Five new cases were registered on average per every diabetic clinic day. The clinic is run by Medical specialists, medical officers, nurses and interns. Patients are served at the filter clinic/casualty during other days (Tuesday to Friday). Medical files for the diabetic patients are usually kept in the records department. The hospital pharmacy serves and maintains a record of prescriptions for all drugs dispensed for inpatients and outpatients. However, the hospital also operates an

amenity pharmacy within the main pharmacy where drugs are sold at market rates. Drugs are usually procured direct from the pharmaceutical firms and distributors. Patients who fail to get the prescribed drugs at subsidized costs can buy the drugs at the amenity pharmacy. Majority of the drugs are brands which are usually costly.

3.2 Study Design

This was a cross-sectional study in which data was collected retrospectively using diabetic patients' medical records and prescriptions for drugs purchased at the hospital pharmacy from January 2006 to December 2007.

3.3 Study Population

All diabetic patients who attended the diabetic clinic in Machakos and Embu hospitals during the study period January 2006 to December 2007.

3.3.1 Inclusion Criteria

- All diabetic patients who bought drugs from the hospital pharmacy during the study period

3.3.2 Exclusion Criteria

- All diabetic patients who never bought drugs from the hospital pharmacy during the study period.

3.4 Sampling Methods

The Ministry of Health supplies drugs to all government hospitals through the Kenya Medical Supplies Agency (KEMSA) based on essential drug list (EDL) or hospital formulary. Patients buy these drugs at a subsidized price which is cheaper compared to the private establishments. However, the availability of these drugs in the hospitals is not consistent due to procurement delays. This shortage limits the patient choices to purchase drugs from the private market where the prices are unaffordable to the majority.

Diabetic patients were identified if they had one or more prescription for either insulin or any of the oral hypoglycemic drugs. As in previous studies (Roper *et al*., 2001) ,patients were classified as having type 1 diabetes if they had been diagnosed under the age of 35 years and were receiving insulin and those above 35 years were classified as type 2.

All prescriptions for insulin and oral antidiabetic drugs at the pharmacy during the period January 2006 to December 2007 were identified. To ensure confidentiality, the prescription data files were extracted without personal identifiers like names which were replaced with Hospital outpatient/inpatient numbers. Since prescriptions were incomplete, without demographic and diagnosis details, the outpatient and inpatient numbers from the prescription forms were used to link to the patient file. The link was to enable the principal researcher obtain demographic and diagnosis characteristics of the study population. The prescriptions which had no corresponding medical files were not considered. Some medical files had clinical summary sheets missing and hence were

also not considered. After sorting out the medical files in each hospital, the principal researcher came up with a list which served as a sampling frame.

3.5 Sample Size Calculation

According to the Ministry of Health, prevalence of diabetes in Kenya was estimated to be 10 % by 2007 (Division of Non Communicable Diseases, DNCD, 2007). Sample size was calculated using the formulae (Fishers *et al,* 1998) as follows:

$n= (Z^2_{1-\alpha/2} pq)/d^2$

Where:

n=desired minimum sample size

Z=standard normal deviate (1.96) at 95% confidence interval

P=proportion of the target population with diabetes

q=1-p

d=degree of accuracy desired (0.05)

Z=1.96 p=0.1 q=1-0.1=0.9 d=0.05x0.05

Therefore:

$n= \{(1.96^2*0.1*0.9)/0.0025\}$

n=139.

The minimum sample required for this study was **139** diabetic patients. For Machakos district hospital a sampling frame of 392 diabetic patients was listed while for Embu provincial hospital, it was 601. The total cases for both study sites was; 392+601= 993.

To cater for data incompleteness from the records, the minimum sample size, 139, was increased by 57%. This resulted to a sample size of **218**. The calculations were as follows;

{139+ (57/100 ×139)}=218

Proportionate sampling was done to achieve the desired sample size for each hospital as follows; Total cases for the two study sites=993

For Embu hospital 601/993 x 218 =132 cases.

For Machakos hospital 392/993 x 218 =86 cases.

The first file in each site was picked at random. Systematic random sampling was done using the sampling frame list for each hospital and the n^{th} file was selected as follows;

For Embu Provincial hospital 601/132 =5^{th} file

For Machakos hospital 392/86 =5^{th} file

3.6 Data Collection Tools and Procedures

A Structured data abstraction form was used to enter variables like age, sex, duration of diabetes, Co morbidity, prescribing pattern for anti-diabetic drugs and other drugs. To capture the patterns, variables like: drug name, strength, duration of prescription, dosage, Brand/Generic, Class, cost, Monotherapy/combination was highlighted. The cost of drugs in the prescription was calculated by using a list of the prices of individual drugs obtained from the hospital pharmacy. The drug costs were converted to US dollar

(72 ksh) which was the average rate of exchange during the study period. In this study polypharmacy was classified as the multiple use of >4 drugs simultaneously. Data abstraction forms were initially pre-tested in a private hospital for ease of use, ease of analysis and proper collection of desired information. Trained research assistants who were qualified pharmaceutical technologists were hired in order to enter the prescription details.

3.7 Data Management

After data entry, hard copies of forms were stored in locked long-term storage units, which was restricted to relevant project staff. Data backup was enabled by use of flash disks and CD-R. Every effort was made to ensure data confidentiality. Access to these files was limited to relevant persons (Investigator/ supervisors).

3.8 Data Analysis

Analysis involved descriptive statistics like mean, mode, median, range, standard deviations, and frequency distributions. Statistical Package for Social Sciences (SPSS) version 12.0, software for data processing and statistical analysis was used. Chi square test was used for test of significance.

3.9 Data Presentation

The results were presented in text and use of tables, graphs and pie charts.

3.10 Quality Assurance

Research assistants were trained prior to the study. Pre-testing of the data abstraction forms was done at Equator Hospital which is a private hospital. The principal researcher supervised data collection, data entry, and checked completed forms for completeness. Data collected was coded and double entry done to ensure consistency and accuracy.

3.11 Ethical Considerations

This study was approved by the KEMRI/National Ethical Review Board. The implementation of all the aspects of the project was in agreement with the international ethical guidelines for research involving patients' records. Consent to collect data from the medical records was approved by the respective medical officers of health in charge of the hospitals.

3.12 Research Variables

Data on the following variables was collected:

Socio-demographic Factors:

- Age
- Sex

Duration of Diabetes since diagnosis

Co morbidity

Prescribing patterns:

- Ant diabetic drugs
- Other drugs

Cost of drugs

3.13 Expected Outputs

- Prescribing patterns.
- **C**ost of the various types of drugs prescribed.

CHAPTER FOUR

RESULTS

4.1 Demographic characteristics

Figure 4.1 illustrates the age and sex distribution of the study population. A total of 218 study subjects fulfilled the inclusion criteria of which 40.4% (n=88) were males, 59.6% (n=130) were females giving a male to female ratio of 1:2. The mean (±SD) age of the study population was 55.18(16.6) years. The mean (±SD) age of the male respondents was 54.57(18.58) years while that of females was 55.6(15.19) years. The minimum age for males was 19 years and maximum was 98 years while that of females was 25 years and maximum was 88. There was no statistically significant difference between the means of ages for males and females.

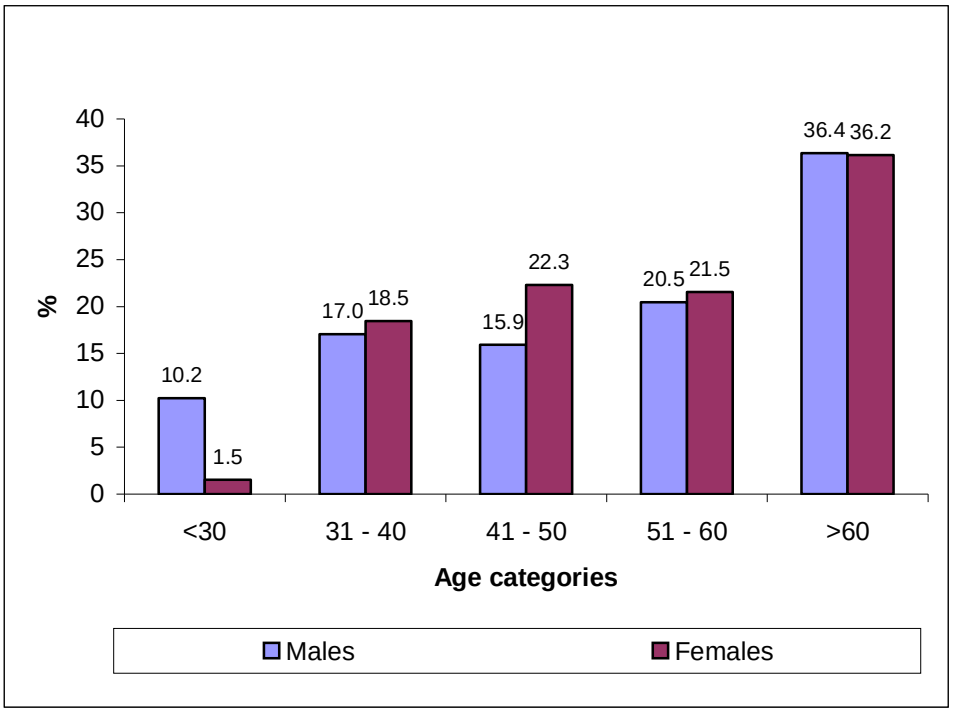

Figure 4.1 Age and Sex distribution of study participants.

4.2 Duration of diabetes in years.

Majority of the diabetic patients had a duration of <6 years (28%) with the disease. (See Table 4.1). Majority of patients presented with type 2 diabetes (90%) compared to type 1 (10%) resulting to a ratio of 9:1. There were more men presenting with type 1 diabetes (59.1%) compared to females (40.9%) while for type 2 females were more (61.7%) compared to men 38.3%.

Table 4.1 Duration of diabetes among study participants.

Duration of diabetes in years	Frequency	Percentage
<6	42	28.0
6-10	34	22.7
11-15	7	4.7
16-20	32	21.3
>20	35	23.3
Total	**150**	**100.0**

Eleven of those with duration of diabetes < 6 years were aged below thirty years while those >20 years were aged over 60 years. Duration for diabetes was not indicated in sixty eight cases.

4.3 Co morbidity

Hypertension was reported in 50.2% of the study population, Upper respiratory tract infection (3.7%), Arthritis (3.7%), peptic ulcer disease (3.3%), Diarrhea (3.3%), Urinary

tract infection (1.2%), Asthma (2.5%). Hypertension was highest among age group >60 years (64.8%) compared to (9.1%) among age group <30 years. More cases of arthritis were reported among the elderly than the young age group. Asthma and Urinary tract infections were common among younger people. The elderly population was associated with multiple illnesses compared to the young. Diagnosis was not indicated among (22.8%) of the study population. Table 4.2 shows co morbidity profile among study subjects.

Table 4.2 Co morbidity profile among diabetic patients.

Disease/Illness	**Number**	**Percentage**
Hypertension	121	50.2
Rheumatoid Arthritis	9	3.7
Malaria	4	1.7
Peptic Ulcer Disease	8	3.3
Asthma	6	2.5
Foot Ulcer	2	0.8
Allergic Rhinitis	3	1.3
Vaginal candidiasis	2	0.8
Diarrhea	8	3.3
Upper Respiratory Tract Infections	9	33.7
Urinary Tract Infections	3	1.2
*Others	7	2.8
Total	**184**	**100**

*****Others: Cataract, Pneumonia, Epilepsy, Tuberculosis, HIV/AIDS, Hyperthyroidism, Erectile Dysfunction, Depression.

One case for HIV/Aids was reported among the study subjects. Hypertension cases increased with age; <30 years (1 case), 31-40 years (11 cases), 41-50 years (21 cases), 51-60 years (29 cases) and >60 years (59 cases). Other illness which increased with age were; Rheumatoid arthritis < 30 years (1 case) and >60 years (3 cases), Peptic ulcer disease < 30 years (1 case) and > 60 years (3 cases). Erectile dysfunction was reported among the elderly (50-60) years. Urinary tract infections were common among the age between thirty and fifty years.

4.4 Prescribing Patterns

4.4.1 Antidiabetic drug use patterns

Use of major antidiabetic drugs from January 2006 to December 2007 is shown in Figure 4.2. Sulfonylurea was the most popular class (38.6%) followed by Biguanides (34.2%), Insulin (25.4%) and Thiazolidinediones (1.9%).

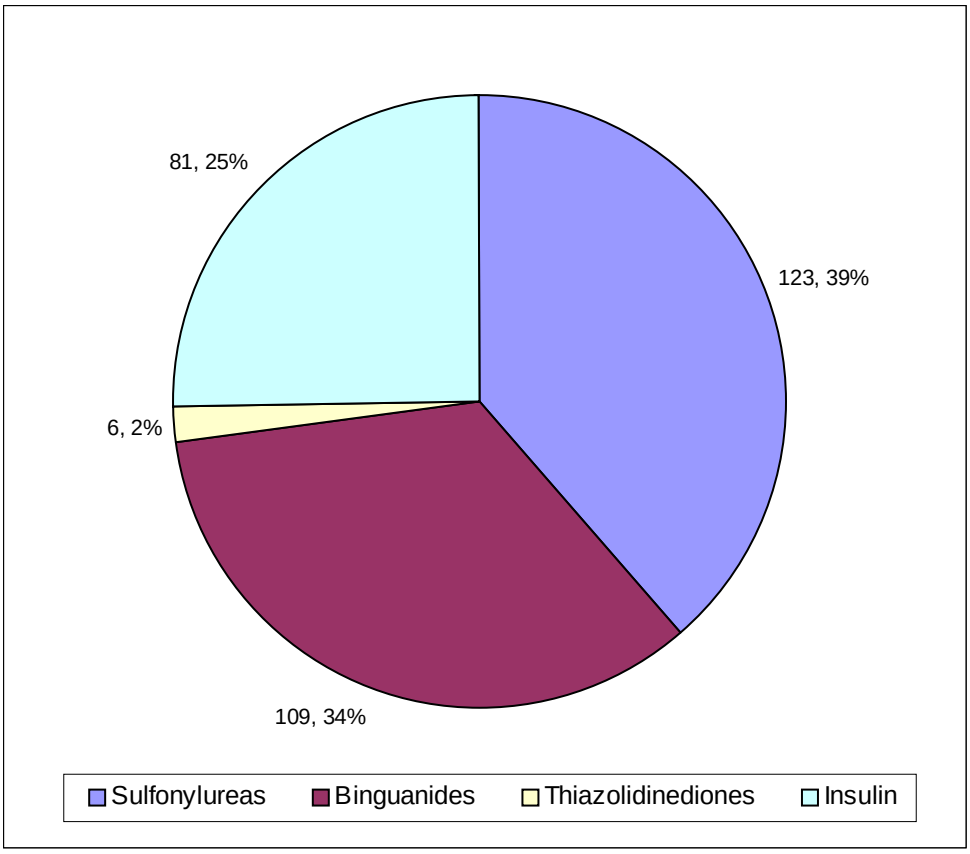

Figure 4.2 Distribution of Antidiabetic drug classes

The use for the individual antidiabetic drugs is shown in Table 4.3. Most (56.1%) drugs were prescribed by brand name while 43.9% were prescribed by generic name.

Table 4.3 Individual antidiabetic drug utilization.

Drug Name	**Number**	**Percentage (%)**
Diabenese	52	16.3
Glibenclamide	48	15
Glucophage	35	11
Metformin	72	22.6
Mixtard	75	23.5
*Others	10	11.6
Total	319	100

*****Others**:** Glucomet, Glyformin, Nogluc, Glicon, Dibonis, Insulin, Chropropamide, Euglucon, Pioglitazone.

Diabenese, Mixtard, Dibonis, Glicon, Nogluc, Glyformin, Glucophage and Glucomet were the major Brand names while Chropropamide, Insulin, Pioglitazone, Euglucon, and Metformin were the most commonly used generic names.

Treatments with the major antidiabetic drug groups were evaluated according to patient age and sex. Odds ratio (OR) and Confidence Interval (CI) were compared for different categories.

Overall males were less likely to be treated with sulfonylurea than females P=0.09, (OR=0.61; CI: 0.35-1.08). Men were also more likely to be treated with insulin compared to females with a marginal significance *P*=0.069, (OR=1.71, CI=0.96-3.04).Young patients were on insulin treatment than old patients (OR=2.74). For the biguanide treatment, the odds ratio (OR) follows a trend suggesting that older people were associated with their use. However use of biguanides among age group 31-40 was statistically significant, *P*=0.023, (OR=0.40; CI: 0.18-0.88).

Table 4.4 below illustrates the OR and CI of selected categories for age and sex.

Table 4.4 Odds ratio and CI of selected categories for age and sex.

	2006 – 2007		
`	O.R	95% C.I	*P* - value
Sulphonylureas treatment			
Sex			
Women	1.00		
Men	0.61	0.35 - 1.08	0.090*
Age groups			
>60	1.00		
<30	0.81	0.22 - 2.95	0.747
31 - 40	0.83	0.38 - 1.79	0.630
41 - 50	0.60	0.28 - 1.28	0.187
51 - 60	1.64	0.77 - 3.53	0.203
Insulin treatment			
Sex			
Women	1.00		
Men	1.71	0.96 - 3.04	0.069*
Age groups			
>60	1.00		
<30	2.74	0.72 - 10.44	0.139
31 - 40	1.51	0.69 - 3.35	0.304
41 - 50	1.32	0.61 - 2.87	0.483
51 - 60	0.76	0.34 - 1.69	0.503
Biguanides treatment			
Sex			
Women	1.00		
Men	0.78	0.45 - 1.38	0.396
Age groups			
>60	1.00		
<30	0.30	0.07 - 1.23	0.093*
31 - 40	0.40	0.18 - 0.88	0.023**
41 - 50	0.81	0.38 - 1.71	0.579
51 - 60	0.71	0.34 - 1.49	0.367

CI: Confidence Interval *P = marginal significance **P = statistically significant OR= Odds ratio

4.4.2 Prescribing Patterns for other Medications

Over the study period, the major therapeutic categories for non-diabetic drugs were analyzed. Table 4.5 highlights the frequency of prescribing. Antihypertensive drugs were commonly prescribed, 57.8% followed by Multivitamins 10.3%, NSAIDs 9.6%, Antibiotic 8.3%, Antacids 3.7%. Generic prescribing contributed to 53.4% while brand contributed to 46.6%. Monotherapy contributed to 84.5% while combination therapy was 15.5%.

Table 4.5 Non-diabetic drug use among study participants.

Therapeutic category	Frequency	Percentage
Antihypertensives	252	57.8
Multivitamins	45	10.3
NSAIDs	42	9.6
Antibiotics	36	8.2
Antacids	16	3.7
*Others	45	10.4
Total	436	100

*Others: Diuretics, Statins, Corticosteroids,

Among the antihypertensive drugs Enalapril was widely prescribed (46%) followed by Nifedipine (21%) and Atenolol (10%). Lasix was the most prescribed loop diuretic drug (90%) followed closely by methyldopa (5%). Among statins, artovastatin and stevostatin were equally prescribed (40% each). Aspirin (JASA) was the only anticoagulant prescribed.

4.4.3 Polypharmacy

Analysis of the individual consistency of drug use showed that the number of drugs per prescription varied among study population. An estimate of the prevalence of drug use is shown in Table 4.6. It shows the distribution of patients exposed to various types of drugs.

Table 4.6 Polypharmacy among study participants.

No.of drugs per prescription	Number	Percetage
1	21	9.6
2	50	22.9
3	40	18.3
4	48	22
>4	59	27.1
Total	**218**	**100**

The average number of drugs per prescription was 3.47. Polypharmacy was more prevalent in the female strata 3.63 compared to the male strata 3.23. Males were prescribed drugs in the range one to six while females utilized drugs in the range one to eight per prescription.

4.5 Drug Costs

Table 4.7 summarizes the cost of antidiabetic drugs per day for the four classes encountered during the study period. Insulin was the most expensive 11 ksh (0.15 **US$**), Biguanides 4 ksh (0.056 **US$**), Thiazolidinediones 3 ksh (0.04 **US$**) and Sulfonylurea 2ksh (0.03 **US$**) respectively.

Table 4.7 Average Cost of antidiabetic drugs by class per day.

Class	Cost per day KSH (US $)
Insulin	11 (0.15)
Biguanides	4 (0.056)
Thiazolidinediones	3 (0.04)
Sulfonylureas	2 (0.03)

Mixtard was the most prescribed brand of insulin costing 300 ksh (4.11US$) per dose of one month. Among the binguanides, Glucophage was sold at 100 ksh (1.38US$) per dose of one month whereas metformin, the generic form was dispensed at a cost of 60 ksh (0.83US$) per dose. Pioglitazones, a generic version of thiazolidinediones was sold at 100 ksh (1.38US$) per dose. Diabenese, Nogluc and Dibonis were the main brands prescribed among the sulfonylurea class and sold at a cost of 100 ksh (1.38US$) per dose.

Cost for the non-diabetic drugs is highlighted in the Table 4.8. Multivitamins, Antacids and antibiotics accounted for large proportion of the total cost. The average cost per day for major therapeutic class is shown below.

Table 4.8 Average cost per day for non-diabetic drugs commonly prescribed.

Therapeutic Class	Cost per day KSH (US $)
Multivitamins	13 (0.18)
Antacids	12 (0.17)
Antibiotics	12 (0.17)
NSAIDS	6 (0.08)
Antihypertensive	3 (0.04)

Among the multivitamins prescribed by brand names, Neurobion forte was the most expensive dispensing at 200 ksh (2.78 US$) per dose of two weeks followed by vitaplus costing 180 ksh (2.5 US$). The generic form which is supplied by the government through KEMSA was dispensed at 30 ksh (0.42 US$) per dose. Relcer gel and flatameal antacids were the most expensive brands prescribed each dispensing at 240 ksh (3.3 US$) per dose of one week compared to the generic version which costed 30 ksh (0.42 US$) per dose. The most expensive antibiotic was Augmentin and Ciproxin each dispensing at a cost of 300 ksh (4.2 US$) per dose of one week. Similar antibiotics in generic form costed 30 ksh (0.42 US $) per dose. Adalat and Norvasc were the most expensive antihypertensive drugs each costing 300 ksh (4.2 US$) per dose of one month while the generics costed 60 ksh (0.83 US$) per dose. Lasix was highly prescribed among the loop diuretics followed closely by methyldopa. Both were dispensed at a cost of 60 ksh (0.83 US$) per dose of one month.

CHAPTER FIVE

DISCUSSION

Diabetes presents a significant public health burden on the basis of its increased morbidity, mortality and economic costs (ADA, 2003 (a). This progressive disease and the associated co morbidity calls for multiple therapies and in the process of providing evidence-based medical care to the patients polypharmacy comes in as a natural consequence (ADA,2003 (a).

Of the diabetic patients evaluated in this study there was a male to female ratio of 1:2 which may reflect a gender difference in health seeking behavior of the population under study, rather than true gender disparity. However, it is of note that some countries have recorded higher female prevalence of diabetes (King *et al*., 2005). This may be partially explained by the longer life expectancy in the female population.

The mean (±SD) age of patients studied was 55.18 (16.61) years which compares well with that found in other studies (Davis *et al.*,1997,Otieno *et al.*,2005). The range of prescribing areas being affected by Diabetes was striking, reflecting the frequent presence of multiple co morbidity.

The higher prevalence of Hypertension (50.2%) in the population is not unique to this study and has been noted elsewhere (Heffner *et al*., 1990). Both hypertension and diabetes are conditions that cluster, and more so with age (Heffner, 1996). This may suggest interplay between the polygenic factors and the environment that interact to cause both these conditions. This is consistent with a study done in Kenya (Mwendwa e*t al*., 2005). Hypertension, Arthritis, Upper respiratory tract infections, Diarrhea, Asthma

and Peptic ulcer disease were the most recorded co morbid conditions. These findings demonstrate the wide range of clinical conditions for which Diabetes is a contributory factor and for which there is an increased healthcare requirement.

The findings of high prevalence of Arthritis may be explained by the aging population which supports the high utilization of NSAIDs among the study population. The ageing patients could explain the tendency towards more intense pharmacotherapy.

Multi-morbidity increased with age and population-based studies have shown that approximately 80% of persons aged 65 or more have at least one chronic health problem (Lesagel, 1991). In a study from general practice in the Netherlands, more than half of individuals aged 65 years or more had two or more co-existing diseases (Van den *et al*., 1996), a feature that may be explained by the fact that the elderly are examined more and are therefore more likely to be diagnosed and treated for subsequent conditions.

5.1 Antidiabetic drug utilization patterns.

The three commonly prescribed oral hypoglycemic agents were: Metformin, Chlopropamide and glibenclamide. This is in conformity with a previous study in the same population (Turner *et al*., 2005, UKPDS,1998) Brand prescribing was common among the anti diabetic drugs despite the recommended generic prescribing by world health organization (WHO, 1995). Insulin was highly prescribed by brand name followed by chlopropamide and metformin. Most drugs were prescribed as monotherapy.

5.2 Other drugs.

Overall for all ages, the four most prescribed drugs in descending order were: Antihypertensive, Antibiotics, NSAIDs, and Multivitamins. Appropriate use of antihypertensive agents may improve blood pressure (BP) control and reduce complications in patients with diabetes. Evidence also supports the need for using multiple anti-hypertensive agents rather than monotherapy to achieve target BP control and greater renoprotection (UKPDS; 1995).The syst-Euro study (Tuomiletho *et al*., 1999), showed that only one half of the patients with hypertension achieved blood pressure control while receiving monotherapy, the other half did require combination of two or more agents to achieve treatment targets.

In our findings, the use of Enalapril, lorsatan, amlodipine, atenolol and Nifedipine supports the above evidence. The three commonly prescribed anti-hypertensive drugs in our study were: Nifedipine, Enalapril and atenolol. Frusemide was the most widely used diuretic followed by Methyldopa and Hydrochlorothiazide. This pattern is in conformity with those in recent reports and has been extensively reported elsewhere (Michael *et al*., 2005). The large consumption of antibiotics in our study concurs with evidence in other studies (Shankar *et al*., 2003). Amoxicillin was the major class of antibiotics used followed by Norfloxacin and Ciprofloxacin. Their uses are likely to be accounted for by more frequent skin infections e.g. foot ulcers, respiratory and urinary tract infections. Brands like Augmentin and Ciproxin also featured in the prescribing patterns. Diclofenac, Meloxicam, Nimesulide and Ibuprofen were the major NSAIDs used. These are also likely to be prescribed in relation to lower back pain, musculoskeletal pain and

in Arthritis. The uses of multivitamins are less easily explained and there is an urgent need to evaluate the use of individual drugs. The use of NSAIDs together with antacids, NSAIDs and antihypertensive also need further evaluation. This is because antacids tend to impair both NSAIDs and antihypertensive effect. Diabetes, therefore, affects prescribing volume both at population level and at individual level.

5.3 Polypharmacy among study population.

An important finding of the study is the number of drugs per prescription. It was comparable to a previous study (Upadhyay *et al.*, 2006). The advanced age of the study population may explain this finding, while different attitudes towards drug therapy, both among doctors and patients, may contribute to it. The high prevalence of prescribing for the elderly and particularly among females is in agreement with the findings of the other studies (Elliot *et al*., 2003).

The possible reason for such findings may well reside in the fact that the female population visits their clinics more frequently than male. The fact that the number of drugs per single prescription has increased proportionally with each age group corresponds well with the findings of previous report (Hemminki *et al*., 1975).

Polpharmacy may also be ascribed to multiple morbidity and the severity of disease, more than to irresponsible prescribing (Larsbjerrum, 1999). Individuals exposed to polypharmacy are of particular interest because of increased risk of drug-related complications and also cost. Many patient-related factors contribute to polypharmacy. Most studies showed that polypharmacy increased with age and that females were more exposed to polypharmacy than males (Helling *et al*., 1987, Heerdink *et al*., 1995). Drug

information in general is obtained from many sources (Haayer, 1982), and the pharmaceutical industry has a significant impact on the prescribing rate (Peay *et al*., 1988). In particular, the prescription rate of new drugs is dependent on the marketing pressure. In most studies of polypharmacy, female sex and advanced age have been predictors of polypharmacy, but a few studies have not found a higher prevalence of drug use among women than men, and a similar trend was observed for polypharmacy. Among the elderly, however, there was no difference between the sexes in the prevalence of polypharmacy. This is in accordance with Nolan and O'Malley's studies of age-related prescription patterns in general practice (Nolan *et al*., 1988, Nolan *et al*., 1987). They found a steady increase in the proportion of men taking prescription drugs, while prescribing rates for women decreased up to the age of 70 years and from this age there were no significant differences between the sexes.

5.4 Cost of Drugs.

The distribution of drug exposure has an important cost and quality care implications. A study by Anderson *et al* have shown that exposure to multiple drugs is among the most important factors when focusing on the high level of drug expenditures (Anderson *et al*, 1996). Multiple uses of drugs have been associated with increase in drug expenditure and the majority of drug users are elderly individuals (Hallas *et al*., 1994). A similar trend was confirmed in this study and this may be due to the increasing co morbid conditions with age among the elderly. Brand prescribing was common compared to generic. This trend contributes to high cost of medication incases where the hospital pharmacy runs out of stocks. The option available to the patient in such circumstances is

to buy drugs from the private market where drugs are relatively expensive (Humaigan *et al*, 2003). Attempts to reduce drug over utilization, polypharmacy and expenditures have been investigated elsewhere (muehlberger *et al*., 1997). However, the occurrence of multi-morbidity was found to contribute to high prescribing costs. A considerable part of healthcare expenditure is thus used to offset costs due to expensive multiple drug regimes and expenditures caused by drug-related morbidity attributable to polypharmacy (Larsbjerrum, 1999).

CHAPTER SIX

Conclusions and Recommendations

6.1 Conclusions

The study findings suggest that there may be a significant contribution of clinicians to the relatively high cost of diabetic treatment. The study findings also reveal a wider spread of drug costs attributable to diabetes. The presence of other conditions and in particular hypertension has an impact on prescribing independent of diabetes. Inappropriate prescribing still exists among the clinicians. This was observed in brand prescribing where affordable alternatives in generic forms were available. The use of multivitamins and more so their prescription by brand names was evident.

6.2 Recommendations

- There is an urgent need for review of current prescribing guidelines for diabetic patients and introduce a standard prescribing guideline for diabetes management.
- Other studies should be conducted in other primary health care settings in Kenya in order to learn more about prescribing patterns.
- The study can also be extended to cover the private hospitals for comparison and may be identify any gaps or discrepancies in prescribing.
- Regular trainings for clinicians on rational prescribing should be emphasized. Continuous Medical Education (CME) is ideal in primary health care setups.

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APPENDICES

APPENDIX 1

STRUCTURED DATA ABSTRACTION FORM
TITLE: PRESCRIBING PATTERNS AND DRUG COST IMPLICATIONS FOR DIABETIC PATIENTS IN EASTERN PROVINCE, KENYA

Instructions to the Research Assistant: Enter the correct details.

Date……../……./……

Health Facility…….

PATIENT NO…….

PART 1.

1. SOCIO-DEMOGRAPHIC DETAILS.

1.1 SEX: MALE ☐ FEMALE ☐

1.2 AGE (yrs) ☐

1.3 DURATION OF DIABETES (yrs) <6 ☐ 6-10 ☐ 11-15 ☐

16-20 ☐ **>20** ☐

2.1 DIAGNOSIS/PATIENT INFORMATION
Often, the diabetic patients present with multiple diseases. Please enter the co-existing illness in the table below as per the diagnosis indicated in the patient medical file.

S.no	Diagnosis
1	
2	
3	
4	

PART: 2

PRESCRIBING DETAILS FOR ANTIDIABETIC DRUGS.
Enter the prescribing details as per the prescription in the table provided below.

S.No	Drug Name	Strength	Duration of treatment	Dosage	Generic/ Brand	Class	Cost (Ksh)	Monotheraphy/ Combination
1								
2								
3								
4								
5								
6								
7								
8								

PART: 3

PRESCRIBING DETAILS FOR OTHER MEDICATIONS.
Enter the prescribing details as per the prescription in the table provided below.

S.No	Drug Name	Strength	Duration of treatment	Dosage	Generic/ Brand	Therapeutic category	Cost (Ksh)	Monotheraphy/ Combination
1								
2								
3								
4								
5								
6								
7								
8								

APPENDIX 2

Informed consent form

Study Title: PRESCRIBING PATTERNS AND DRUG COST IMPLICATIONS FOR DIABETIC PATIENTS IN EASTERN PROVINCE, KENYA

Investigators and institutions

	Name	Institution	Contact
Principal Researcher	Mwanza Patrick Mutunga	JKUAT-ITROMID	0733872497
Supervisors	Dr. Yeri Kombe	KEMRI	0734257864
	Professor S.M Bhatt	UON	0722771826
	Dr. Joseph K.Gikunju	JKUAT	0722808671

Introduction.

Diabetes mellitus (DM) accounts for a significant proportion of morbidity and mortality in all age groups and therefore emerging as an important global public health problem. An estimated 380 million people globally will have diabetes by 2025, with the largest increase occurring in developing countries. Recent projections by WHO 2004 suggest that at least 194 million people suffer from diabetes worldwide.

The epidemic of Diabetes is particularly serious in developing countries like Kenya where living conditions are changing dramatically and urbanization and demographic changes are the greatest. Diabetics are at a higher risk of numerous medications and are more vulnerable to irrational prescription.

An essential component of evaluating and improving diabetic care is the assessment of drug prescribing standards and quality of care. Given the limited resources within the health care sector in the country it is important to evaluate the prescribing patterns and cost of drugs among diabetic patients.

This study, which proposes to assess the prescribing patterns and drug cost implications for Diabetic patients in Kenya, is expected to contribute to the scientific basis towards achieving a better diabetic care outcome.

Purpose of the study

The purpose of this study was to determine the prescribing patterns and drug cost implications for diabetic patients. Two hospitals were chosen for this study, namely Machakos and Embu. The study involved:

- **Review of diabetic patient prescriptions and medical files from January 2006 to December 2007**.

Benefits

There were no direct benefits from the information obtained from the study. However the results can be used to assist in formulating policies that may lead to improving diabetic management.

Records Privacy and Confidentiality

Permission to access the patient's records was sought from the respective hospital administration. Every effort was made to keep the information obtained from the records private and confidential. However absolute confidentiality could not be guaranteed. Personal information may be disclosed if required by law. The information obtained may be may be reviewed by:

- Study investigators

- Ethics Committee at KEMRI

Problems and questions

If you ever have questions about this study, you should contact: The principal Investigator, Mwanza Patrick Mutunga (Mobile 0733872497 or email nzapat@yahoo.com.You can also mail by using the address given below

P.O Box 60148 00200 Nairobi.

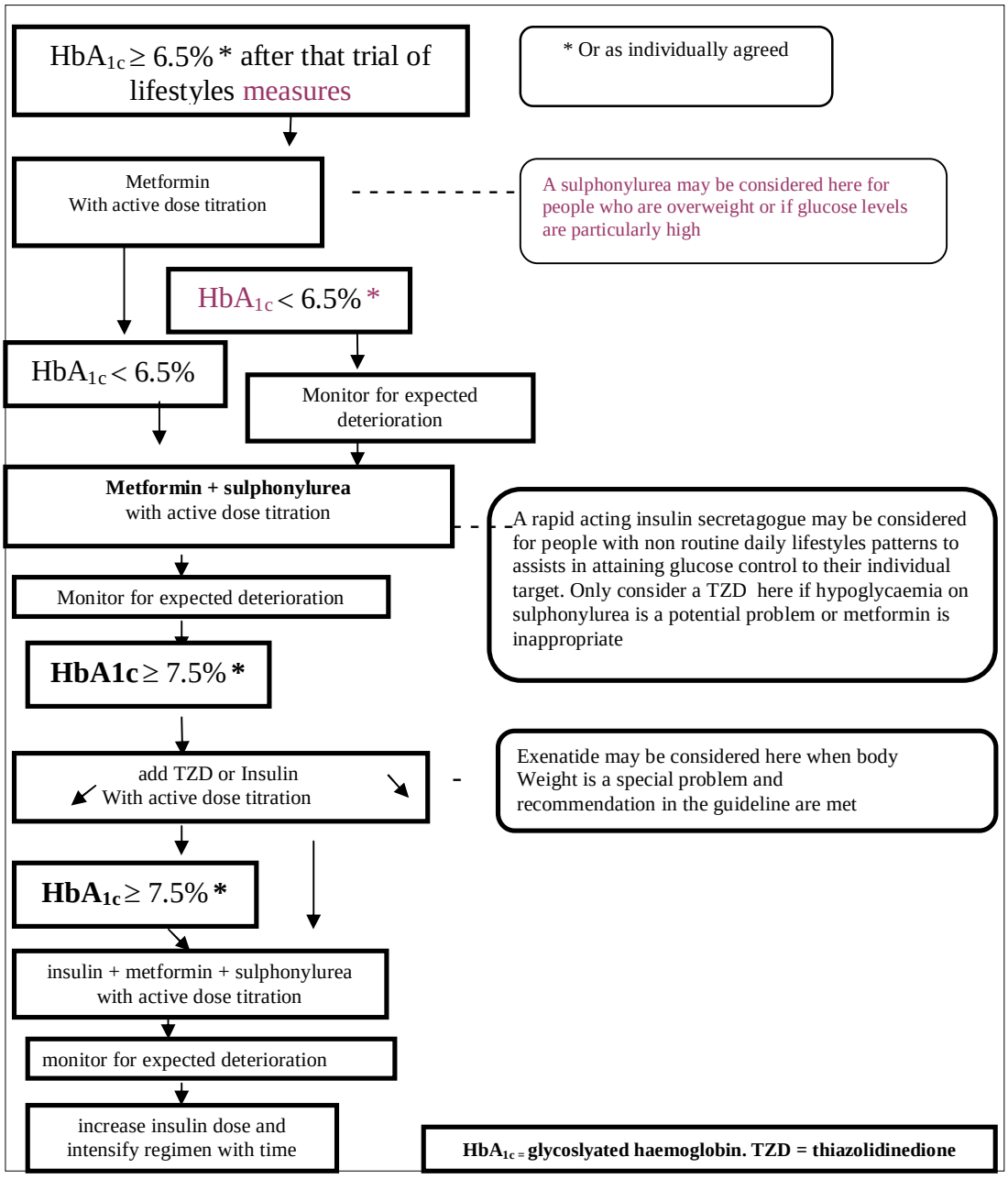
This research proposal has been reviewed and approved by the KEMRI's Scientific Steering Committee. The committee has reviewed this study in order to help protect patient's information privacy and confidentiality.

If you have any ethical questions you may contact: The secretary, KEMRI/National Ethical Review Committee, P.O Box 54840-00200 NAIROBI, Kenya

Tel: (254) (020) 2722541, 2713349, 0722-205901, 0733-400003; Fax☹254) (020) 2720030 E-mail: director@kemri.org Website: www.kemri.org

APPENDIX 3

Scheme for the pharmacotherapy of glucose lowering in type 2 diabetes



APPENDIX 4

Selected Drug Costs during the study period.

Brand name	Formulation	Generic name	Class	Hospital Pharmacy) cost (US$)	Private Market cost (US$)
Diabenese	Tab 250mg 28	Chlopropamide	Sulfonylurea	0.83	8.33
Mixtard 70/30	Inj 3ml 5	Insulin(human)	Insulin	4.17	43.3
Mixtard 70/30	Inj 10mkl 1	Insulin(human)	Insulin	0.83	22.9
Glucophage	Tab 850mg 28	Metformin	Biguanide	1.37	7.08
Glucophage	Tab 500mg 28	Metformin	Biguanide	1.37	3.89
Glitter	Tab 30mg 30	Pioglitazone	Thiazolidediones	1.37	8.33
Lasix	Tabs 20mg	Frusemide	Loop Diuretic	0.83	4.86
Adalat	caps 10mg 28	Nifedipine	Calcium channel blocker	0.83	12.5
Adalat Retard	Tabs 10mg 28	Nifedipine	Calcium channel blocker	0.83	20.83
Repace	Tabs 50mg 30	Lorsatan	Angiotensin II Receptor	1.37	8.33
Relcer gel	Susp 180ml 1	Antacid/Antiflatulent	Antacid	3.33	3.33
Flatameal	Susp 200ml 1	Antacid/Antiflatulent	Antacid	3.33	3.33
Ranferon	Syr 200ml	Iron/Haematinic	Haematinic/Minerals	2.08	4.37
Neurobion Forte	Tabs 30	Vitamin	Vitamins/Minerals	2.77	5.83
Orofer	Tabs 30	Iron/Haematinic	Haematinic	2.77	5.83
Neurobion	Tabs 30	Vitamin	Vitamins/Minerals	1.37	6.94
Astymin	syr 200ml 1	Vitamin/Mineral	Vitamins/Minerals	2.08	4.86
Duphalac	Susp 200ml 1	Lactulose	Laxatives	2.77	9.72
Lipitor	Tabs 20mg 28	Artovaststin	Statins	1.37	41.67
Lipitor	Tabs 10mg 28	Artovaststin	Statins	1.37	34.7
Ascard -75	Tabs 75mg 30	Aspirin	NSAID	0.28	1.37
Mobic	Tabs 7.5mg 30	Meloxicam	NSAID	1.39	29.16
Ciproxin	Tabs 500mg 10	Ciprofloxacin	Quinolone antibiotic	4.17	27.78
Augmentin	Tabs 625 mg 14	Amoxicilin/Clavulanate	Penicillin	4.17	22.9
Glevonix	Tabs 500mg 5	Levofloxacin	Quinolone antibiotic	2.77	9.72

Source:PharmaFinder.Current Drug Prices.Vol.2.1 January 2006