ASSESSMENT OF DRUG THERAPY PROBLEMS IN ADULT PATIENTS WITH BOTH CARDIOVASCULAR DISEASES AND TYPE 2 DIABETES MELLITUS AT KENYATTA NATIONAL HOSPITAL

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A Dissertation submitted in partial fulfillment of the Requirements for the Award of the Degree of Master of Pharmacy in Clinical Pharmacy in the School of Pharmacy of the University of Nairobi.

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DECLARATION OF ORIGINALITY

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This is to certify that this dissertation has been submitted for review with our approval as the University supervisors.

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DEDICATION

To my loving wife Joyce Florence Wanjiku Njuguna who has tirelessly stood by my side with constant support and prayers during this study period and always.

APPRECIATION

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ABBREVIATIONS AND ACRONYMS

ACEIs	Angiotensin Converting Enzyme Inhibitors
ADE	Adverse Drug Events
ADR	Adverse Drug Reactions
BB	β-Blockers
BP	Blood Pressure
CHD	Coronary Heart Disease
CKD	Chronic Kidney Disease
COPD	Chronic Obstructive Pulmonary Disease
CVD	Cardiovascular Disease
DI	Drug Interaction
DTP	Drug Therapy Problem
ERC	Ethical and Research Committee
GDP	Gross Domestic Product
ICD	International Classification of Diseases
IDF	International Diabetes Federation
IHD	Ischemic Heart Disease
KNDS	Kenya National Diabetes Survey
KNH	Kenyatta National Hospital
MRP	Medication Related Problem

NCD	Non-Communicable Disease
NHSSP	National Health Sector Strategic Plan II
OPDMEC	Outpatient Diabetes Mellitus and Endocrinology Clinic
PCNE	Pharmaceutical Care Network Europe
PI	Principal Investigator
PVD	Pulmonary Vascular Disease
SA	Saudi Arabia
T2DM	Type 2 Diabetes Mellitus
UK	United Kingdom
WHO	World Health Organization

OPERATIONAL DEFINITION OF TERMS

Adherence: Is the ability and willingness of the patient to take medication that the prescriber has clinically judged to be appropriately indicated, adequately efficacious, and based on all available evidence, can produce the desired outcome.

Cardiovascular diseases: Refers to the presence of heart or blood vessel-related disorders.

Co-morbidities: This is the presence of an extra medical condition(s) concurrently with a primary disease and which require long-term treatment.

Diabetes mellitus: A set of related diseases in which the body is unable to regulate blood Glucose.

Drug therapy problem: A drug therapy problem is any undesirable event in a patient that involves, or suspected to involve drug therapy and interferes with the health outcomes and requires a professional judgment to resolve.

Long-term treatment: This is a length of time more than 90 days, and can even be as long as one year in a few situations.

Medication experience: Is the patient's personal approach to the use of medicines-why he believes or feels a certain way about a drug therapy.

Pharmaceutical care: Is a practice in which a practitioner (clinical pharmacist) takes responsibility and accountability for a patient's drug-related needs.

Pharmacotherapy workup plan: A rational thought process used to identify, resolve, and prevent drug therapy problems.

Polypharmacy: Is the use of five or more medications.

Single: Is unmarried person or person not involved in a stable sexual relationship including separated, window, widowers, divorced

ABSTRACT

Background information: Patients with both cardiovascular disease and type 2 diabetes mellitus conditions take multiple medications prescribed to them thus are more predisposed to drug therapy problems. Drug Therapy problems arise at any stage of the treatment process, which can lead to unplanned and costlier hospital admissions. There is limited published literature on drug therapy problems among these patients in Sub-Saharan Africa.

Study objective: The aim of this study was to characterize the types of drug therapy problems and their predictor factors in patients with both T2DM and CVD followed up at Kenyatta National Hospital (KNH).

Methodology: A cross-sectional study was conducted at outpatient diabetes clinic of KNH. One hundred and eighty adult patients aged 18 years and above, with both CVD and T2DM, were recruited using simple random sampling. Patient information such as social demographics, laboratory results, and treatment were collected from the patient files using a predesigned data collection tool. Prescribed related drug therapy problems were assessed through comprehensive review of systems and patients interviews. The appropriateness of medical therapy such as indication, dosage and needs additional drugs were assessed using World Journal of Non-communicable. The data was entered into Microsoft Excel 2010 and analyzed using STATA version 13.0. Descriptive, binary and multi-variable logistic analyses were employed to describe the population and determine the strength of association between the predictor and outcome variables. The p-value of less than 0.05 was considered statistically significant to study the association between predictive variables and drug therapy problem.

Results: There were 66.1% female patients and the mean age was 61.6±11.3 years. A total of 164 DTPs were identified. Among these patients, 91.1% had at least one DTP. Commonest problems were non-adherence, needs additional drug and low dosage. Nonadherence was associated with coercion to take medicines (AOR 0.28; 95% CI: 0.12, 0.67; P=<0.001), perception that one could stop taking medications when the condition was under control (AOR 6.99; 95% CI: 2.64, 18.51; P=<0.001) and expectations for a

cure (AOR 0.24; 95% CI 0.11, 0.56; p=<0.001). In addition, Needs additional drug was associated with use of furosemide (4.71; 95% CI: 1.72, 12.89; P=0.003) and duration of T2DM of >72 months (AOR 0.39; 95% CI 0.19, 0.78; p=0.007). Furthermore, under-dosing was associated with 2-hour postprandial blood glucose test (AOR 4.57; 95% CI: 2.19, 9.52; P=<0.001) and poor blood pressure control (AOR 2.76; 95% CI: 1.26, 6.09; p=0.012) and lower income (AOR 0.64; 95% CI: 0.47, 0.89; p=0.007).

Conclusion: Needs for an additional drug, dosage too low, and non-adherence were the most common types of Drug Therapy Problems identified among patients with both T2DM and CVD.

Recommendation: We recommend establishment of medication therapy management services in hospitals where pharmacist would routinely identify, resolve, and prevent DTPs among patients with both T2DM and CVD.

CHAPTER ONE: INTRODUCTION

1.1 Background to the study

A Drug Therapy Problem (DTP) is defined as an undesirable event in a patient that involves, or suspected to involve drug therapy and interferes with the health outcomes and requires a professional judgment to resolve (1). In 1999, Cipolle, Linda Strand, and Peter Morley defined a finite set of seven categories of DTP with a strong influence on the pharmaceutical care plan.

Studies have reported that DTPs present a challenge to the healthcare professionals, highly affecting patients clinical outcomes which have resulted in morbidity or mortality, long hospital stays, and increased health care expenditure burden to the patient or the government (2–4). Furthermore, the elaborated use of medicines in both institutionalized and ambulatory care settings present a favorable environment for the occurrence of medication use-related problems. Moreover, patients with comorbidities such as CVD and T2DM are more likely to be prescribed multiple drugs thereby increasing the chances of DTPs.

1.2 Burden of DTPs

According to Gurwitz et al study, drug therapy problems contribute more than $200 billion of United States health care costs (1). Another study reported that preventable admissions due to inappropriate prescribing, safety and compliance had a prevalence of 30.6%, 22.2%, and 33.3% respectively (5). In 1969, the first reporting of the drug therapy problem resulted in a hospital admission due to Adverse Drug Reactions (ADRs) (6).

According to World Health Organization (WHO) criteria, studies performed in European hospital revealed that ADRs-admissions encountered in France and Germany were 3.2% and 6.2% respectively. In south India, the accounted ADRs was 1.8% (7) while in Saudi Arabia (SA) DTPs seriously affected health care costs (3). In addition, a prospective study on DTPs conducted among 133 stroke patients in India showed a prevalence of 35% in ADRs, 32% prevalence in dosage too low, 27% prevalence in lack of preventive therapy, and finally, duplicate therapy (inappropriate drug combination) caused 16.6% of

DTPs (4). Another study conducted in 1494 patients with chronic diseases in Jordan identified 81.2% of patients with DTPs. Most prevalent DTPs among 26% patients had medication indication related problem followed by 19.6% patients with a problem of no valid indication requiring a drug (8).

A study conducted in an acute-care hospital in Singapore about DTPs in admitted geriatric patients showed that 32 cases of DTPs among 347 patients were reported. The most prevalent form of DTP reported was needs additional therapy at 31.3%, followed by non-compliance at 28.1% (6). There were 149 new cases of DTPs identified among patients hospitalized due to inappropriate treatment. The prevalence of untreated conditions was 64.4% among 118 patients hospitalized. Out of 118 patients, nine patients required additional medications as a synergistic therapy. Another five patients had unnecessary drug therapy that had the undocumented medical condition. Furthermore, 87 patients had duplicate therapy and 17 patients had unnecessary drug therapy.

Researchers have found that if pharmacists were available to provide pharmaceutical care there would be a decrease in drug therapy problems and an increase in optimal therapeutic outcomes (1). Additionally, studies have revealed that the patient care outcomes have improved because of assessment of their drug-related needs and the identification of DTPs. The present study, therefore, is geared towards characterization of DTPs among patients with both CVD and T2DM with the aim of their optimal management. This study achieves the initial step in enhancing the ideal pharmaceutical care process by analyzing the impact of current DTPs among CVD and T2DM adult patients at Kenyatta National Hospital (KNH). This would assist the Ministry of Health (MOH) and relevant stakeholders in optimizing intervention strategies according to needs and available resources. In contrast, little is known about pharmaceutical care services that would address drug therapy issues in developing countries more so in Kenya and sub-Saharan Africa (9).

1.3 Problem statement

Generally, drug therapy problems in patients with both Cardiovascular Disease (CVD) and Type 2 Diabetes Mellitus (T2DM), has contributed to a serious challenge for healthcare professionals. It has been associated with morbidity, mortality, long hospital stays, and increased health care expenditure burden to the patient or the government (10, 11). Several studies have identified DTPs in patients with CVD and or DM in the United Kingdom (UK), Saudi Arabia (SA), Australia and India (1,3,11,15).

In a retrospective study conducted, 300 patients reported to have DTPs in the UK and SA majority of patients had both CVD and DM (12). A couple of different studies of such nature have been conducted in Kenya, Ethiopia, and Nigeria whose (17–19).

Johnson and Bootman presented a red flag report by accounting the high cost of drug-related morbidity and mortality (1). These two researchers argued that in 1997 health costs reached $138 billion. Similar studies conducted by Howard and colleagues revealed that there were 30.6% preventable medication-related admissions, there were 33.3% adherence problems and 22.2% monitoring problems (1).

In Sub-Saharan Africa, the study conducted in CVD patients in Ethiopian referrals hospital identified 164 DTPs. In this study, DTPs associated with chronic diseases showed a prevalence of 95.83%, 91.67%, 81.48% among patients with functional heart failure and cor pulmonalae, rheumatic heart disease and hypertensive heart disease respectively (20).

In Kenya, for example, the high prevalence of undocumented DTPs was revealed in both CVD and DM patients (21). Nobody knows what types, the extent, and the predictor factors of DTPs that this particular group of patients faced. The study revealed that 55% of Kenyans had their BP measured and only 9% reported had information of their elevated BP. However, among them, only 22% were compliant with the treatment at that given period of time (21). In addition to that, 20% of Diabetes patients reported that they had been measured blood glucose and only <2% were informed they had raised blood

sugar. However, only 40% of the ones informed were compliant with their medications (21).

Currently, no small-scale interventions are in place to address this problem among CVD and DM patients in public health facilities. Furthermore, there seems to be scanty information regarding drug therapy problems in DM patients at Kenyatta National Hospital (22). Although baseline studies on DTPs have been performed in chronic kidney disease (CKD) patients and cervical cancer (17, 23), it is equally important to establish the current DTPs problems in CVD and DM patients before interventional campaign programmes are designed (19).

1.4 Justification of the Study

The burden of T2DM and CVD is rising in Kenya at an alarming rate. The cardiovascular disease is considered the leading cause of non-communicable related deaths ranging from 6.1% to 8% (21).

Drug therapy is key in the management of these conditions. In order to optimize the drug therapies, efforts must be made to identify, resolve and prevent any drug-related undesirable events that lead to poor outcomes, in this low resource settings.

To my best knowledge, DTPs have not been locally characterized in this population of patients. This study is therefore, going to bridge the gap and help identify DTPs with their respective causes. Additionally, the relative risks associated with these DTPs will be determined.

The study findings, therefore, will assist in addressing the modifiable risk factors that healthcare providers will address to reduce drug-related morbidity and mortality amongst CVD and T2DM patients.

1.5 Purpose of the study

The purpose of this study is to understand the predictors, types, and extent of DTPs among adult patients suffering from CVD and DM in Kenya. The aim is to inform the approach to DTPs identification and prevention in Kenya referral hospitals and Sub-Saharan Africa by answering the research question.

1.6 Objectives

1.6.1 Broad Objective

This study aims to characterize the drug therapy problems as well as their predictor factors in patients with both T2DM and CVD followed up at KNH.

1.6.2 Specific Objective

1. To describe the prescriber-related patterns of DTPs in patients with both T2DM and CVD
2. To characterize the DTPs in patients with both T2DM and CVD
3. To identify the predictors of DTPs in patients with both T2DM and CVD

1.7 Research Questions

The questions for this study will be:

1. What are the prescriber-related patterns of DTPs in patients with both T2DM and CVD?
2. What are the characteristics of DTPs in patients with both T2DM and CVD?
3. What are the predictor factors of DTPS in patients with both T2DM and CVD?

1.8 Conceptual framework

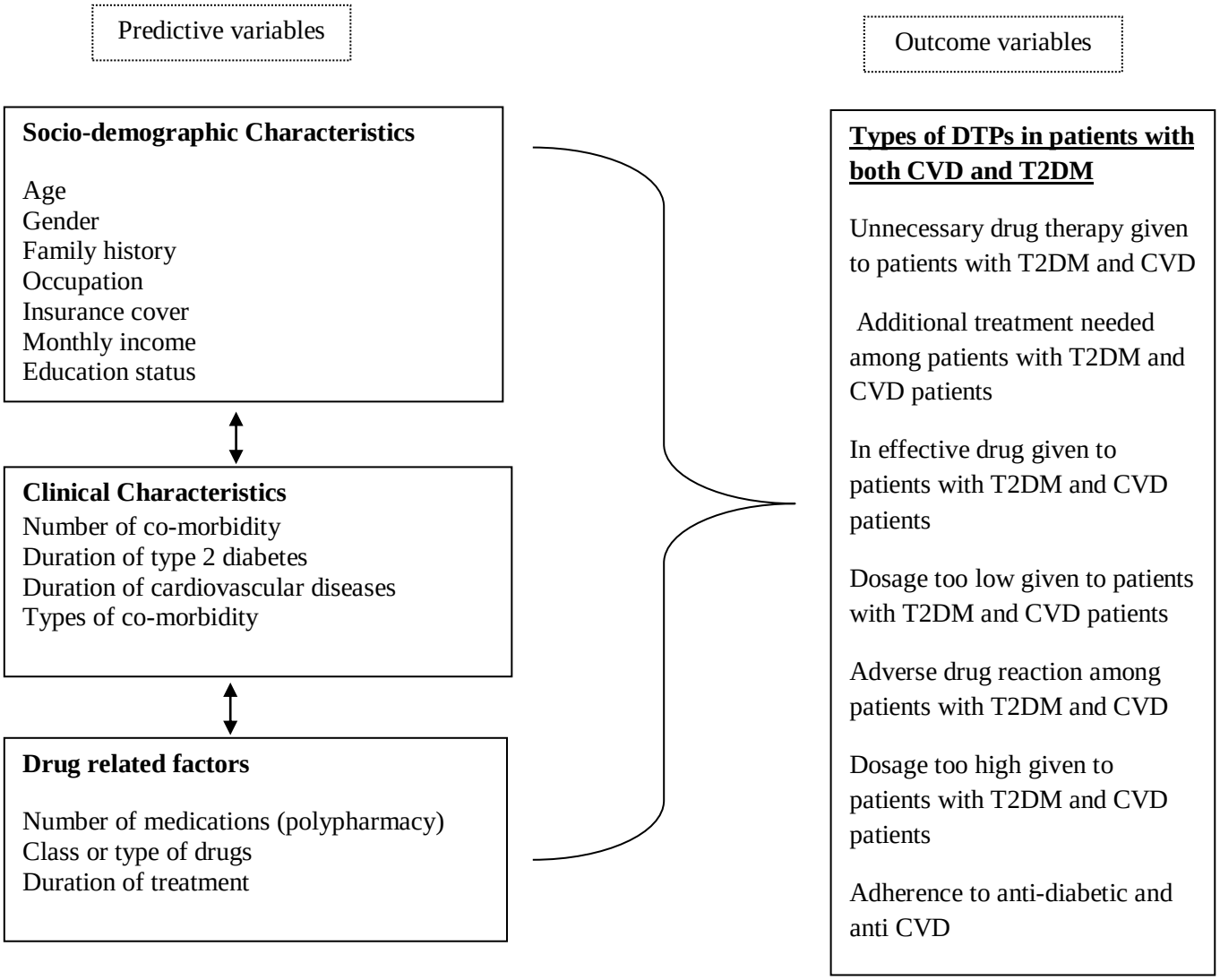

Figure 1: Conceptual framework (Source: Author)

CHAPTER TWO: LITERATURE REVIEW

2.1 Cardiovascular and DM burden

A number of studies have revealed that CVD and T2DM conditions correlate closely and that T2DM could lead to CVDs. It is evident that a T2DM patient is three times to four times more likely to have a CVD. Furthermore, the rate of mortality is reported to be high in diabetic patients because of cardiovascular disease, CHD, cerebrovascular disease, and PVD (24). In the USA, studies revealed that CVD contributed to 75% of all mortality in T2DM. In the UK, the Study showed that deaths due to CVD were 70 times of microvascular complications.

In Sub-Saharan Africa, the burden of CVD and T2DM has increased. A study in Nigeria reported a prevalence of stroke, Peripheral Arterial Disease (PAD), ischemic heart disease (IHD) as 4.95%, 3.3%, and 1.7% respectively. In Sudan, the prevalence was much higher IHD having 28% followed by PAD at 10% and then 5% stroke (17).In Kenya, studies maintain that NCD (Non-Communicable Disease) admissions were 50% and deaths were over 55%. Consequently, CVD, diabetes, and cancer are the major NCD. KNH data, for mortality attributed to a diabetic complication, showed that the year 2009 the mortality rate was 24.75% and in the year 2010 it was 31.46%. Essentially, it is evident that deaths due to diabetic complication are increasing (25).

IDF (International Diabetes Federation) estimated that the prevalence of diabetes in adults is 4.56% amounting to almost 750,000 persons and 20,000 annual deaths. In fact, globalization, urbanization, aging population, and adoption of unhealthy lifestyles have contributed to increased problems. It is estimated that 14% of the Kenya population have blood sugar raised beyond normal (21) due to sub-optimal medication (25). Kenya National Diabetes Strategy (KNDS) [2010-2015] statistics reveal that 1.5 million people in Kenya today are living with diabetes which is projected to rise to 2 million by 2030 if no preventive measures are put in place (25).

2.2 Drug therapy problem

Pharmacotherapy, when used appropriately in patients, can effectively improve quality of life, cure diseases, or control the prognosis of diseases. However, when they are prescribed inappropriately or failure of correct medication intake by patient leads to drug therapy problems (13, 28, 29). Increased morbidity and mortality has been shown to occur due to medicine misuse (1, 7, 13, 29). Additionally, medicine use can also cause the increased cost of care and quality of life (30, 31) and a high cost of health for patient and society (30).

A systematic thought process shown below guides the pharmacist to determine the patient's drug-related needs and identify drug therapy problem among patients (1). This has lead to reduced drug therapy problems and improved health outcomes to patients.

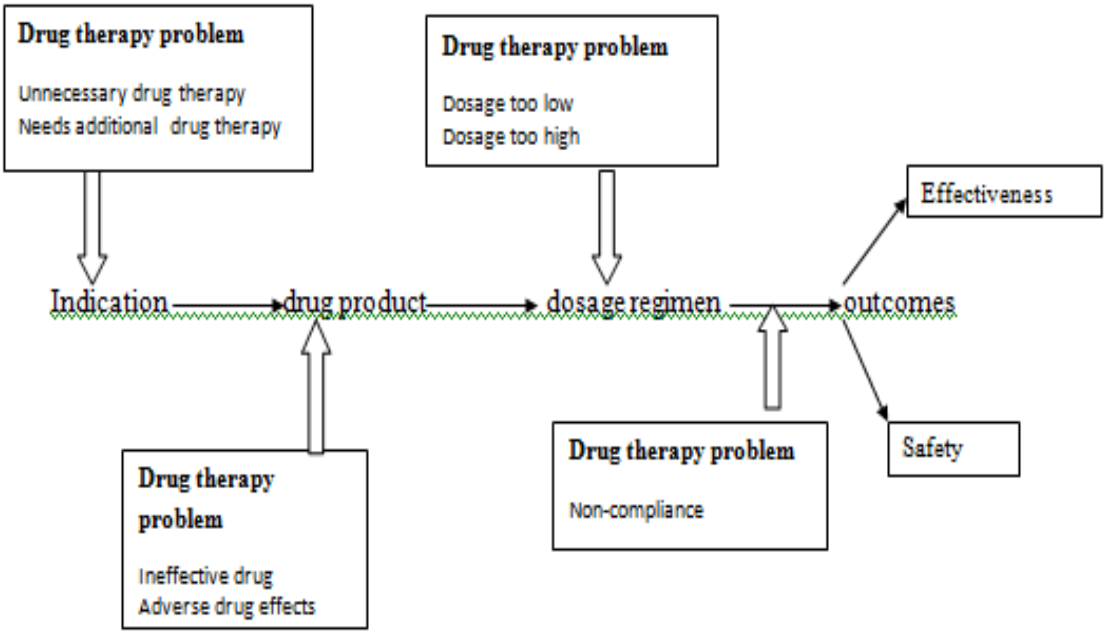

Figure 2: Clinician guide in identification of DTPs
(Source: Cipolle et al., 2004)

2.3 Terminologies, definitions, and Classification of medication-related problems

In 1998, Granada consensus arrived at defining and classifying a negative clinical outcome. They defined what drug therapy problem is and classified six items grouped and grouped them into three categories, which complied with the basic characteristics for an ideal classification. That same time the classification was criticized because it did not consider a hierarchical classification, classification of causes and neither acquire potential DTP into considerations (31). In 2014, Adusumilli et al made a systematic review of MRPs classification and gave a general idea about definition and classifications of DRPs. All were for use in pharmaceutical care and research. Generally, After reviewing kinds of literature he identified 14 classifications systems employed for identifying and categorizing all medication-related problems (MRPs) occurring in a patient which became useful to various researchers. The classifications include Hepler and Strand classification, National Coordinating Council for Medication Error Reporting and Prevention (NCC-MERP) taxonomy of medication errors, Pharmaceutical Care Network Europe (PCNE) system (Version 6.2), Granada consensus, Westerlund System, ABC of Drug related Problems, Problem Assessment and Solutions (PAS) system, American Society of Health Systems Pharmacists (ASHP) classification, Cipolle *et al* classification, Health Base Foundation Subjective Evaluation Plan (SHB-SEP) classification, Krska et al system, Problem Intervention Documentation (PI-Doc), Mackie classification and Hanlon approach (32).

Out of these fourteen published classifications, few have a hierarchical organization that classifies problems from causes and interventions.

Apparently, a number of studies have widely used the term DRPs (1,6,10,32,34). Nevertheless, different researchers have used different terminologies for problems encountered in medical therapy such as treatment-related problems (36), medication-related problems (4,12,13,19,37,38), drug therapy problem (41, 42), medication errors (41) and finally medication therapy problem (42).

Existing evidence in the literature shows that some definitions recognized the patient perspective as the focus for identifying, resolving and preventing MRPs (4, 44), and some

on healthcare professionals' perspectives for identifying, resolving and preventing MRPs (36,40,41).

Consequently, DRP, DTP, MRP, or MTP are terms that depict drug results in problems other than what is intended. In contrast, they can describe a problem that does not result in an unintended problem. A medication error (ME) is any preventable event that may lead to inappropriate medication use or patient harm attributed to iatrogenic harm or patient (43). This was a prescription-focused approach focusing on drug prescribing and delivery and not the clinical condition of the patient (1). Two studies argued that the term drug therapy problem should replace the other terms that describe DRPs because it includes problems from the patient perspective as the scope of pharmaceutical care (34, 38). Therefore, this study will use the term DTP rather than DRP.

According to Cipolle/Morley/Strand classification, these authors used the term "drug-therapy problem" rather than "DRP" to refer to a system approach. Essentially, it included problems from the patient perspective in the entire drug therapy sequence. Since 1999, the classification is used in the USA community pharmacies to assess pharmacists' activities in providing pharmaceutical care (32).

Cipolle/Morley/Strand classification is significant because it has a rational, systematic, and comprehensive decision-making process for identifying, resolving, and preventing seven set of medication-related problems. For instance, when Eichenberger et al and Roosendaal et al used PCNE classification to identify DTPs they found it to be clinically significant when Angiotensin Converting Enzyme Inhibitors (ACEIs) and Sulfonylureas interact. However, this was inconsistent with Cipolle/Morley/Strand classification (39). It is evident that Cipolle/Strand/Moley classification has a hierarchical structure and validated instrument currently lacking in most of the classifications (1). It has seven classifications of DTPs as follows: Unnecessary therapy, Need for additional therapy, Ineffective drug, Dosage is too low, Adverse drug reaction; Dose is too high, Adherence problem. The conceptual framework in figure 1 exemplifies this.

The definition of DTP is any undesirable event that a patient experiences bound on suspicion or involving a drug treatment, and that interferes with the desired therapy outcomes and requires professional to resolve (44).

Therefore, this study will use Cipolle/Morley/Strand classification to classify all DTPs found among CVD and T2DM patients because it is able to diagnose a drug therapy problem and address four drug-related needs a patient may have such as indication, effectiveness, safety, and adherence. It is also a validated tool for use in pharmaceutical care research.

2.4 The prevalence of DTPs in adult patients with both T2DM and CVD

In a number of studies, diabetic patients with multi-morbidity are much predisposed to DTPs because of multi-medication therapy. In the last ten years, studies published to manage and prevent CVD in older adults with DM have taken a treatment paradigm shift away from condition-focus treatment goals to patient-centered approach treatment recommendations where DTPs certainly need to be addressed.

A study revealed that 89.6% T2DM patients have many types of DTPs such as unnecessary drug therapy, needs additional therapy, overdosage, and under-dosage, an ineffective drug for the treatment of renal and liver dysfunction and adherence (37). In a prospective study of DTPs in T2DM with hypertension, 261 DTPs were identified with an average of three problems per patient (35). The other study reported quite high DTPs in patients with angina pectoris and T2DM. Relatively, there were 329 DTPs in 118 angina pectoris patients and 635 DTPs in 155 T2DM patients (45). It is evident that each study had a different pattern of DTPs in CVD and T2DM. Nearly all studies have incorporated the number of DTPs identified and the frequent DTPs in the study population. Furthermore, some studies have identified predictor factors associated with different types of DTP among CVD and T2DM patients (12, 13).

2.4.1 Unnecessary Drug Therapy

This DTP results when the patient does not have a clinical indication at the time drug therapy is initiated (1). A study reported 13.2% prevalence of “drug use without indication” among patients with CVD (2) which slightly varied with three studies having

a prevalence of 15-18% (2). Another study reported that five T2DM patients had unnecessary drug therapy that had an undocumented medical condition. In addition, 87 patients had duplicate therapy for a condition that required only a single therapy. Furthermore, a study conducted in 1494 patients with chronic diseases in Jordan identified 81.2% of patients with DTPs. Most prevalent DTPs among 26% patients had medication indication related problem followed by 19.6% patients with a problem of no valid indication requiring a drug (8).

2.4.2 Needs additional drug therapy

This DTP results when a medication is required to treat or prevent a medical condition or illness from developing (1).

The DTP needed additional therapy at 31.3% was also documented in a study conducted in Singapore (6).

In a cross-sectional observational study conducted in five hospitals in Jordan, they identified 32,348 DTPs in 2,898 patients. The most common DTPs reported included need for additional therapy followed by non- adherence. An Indian study and Koy et al study reported untreated condition as 3.77% and 64.4% respectively (2). The untreated condition reported among the patients with chronic diseases included anemia, dyslipidemia, urinary tract infection, and a cough (1, 20). Similarly, another study reported a higher untreated condition and lack of preventive therapy cases as 25.3% to 22.3% respectively (35).

Another study identified a needs additional drug therapy with a prevalence of 56.37% was in contrast with two studies (39). A prospective analytical study identified 66 DTPs, in which indication without drug therapy had a prevalence of 47%. This was evident when hypertensive patient's stage 2 received only a single captopril medication. However, the prevalence of 21.2% was reported in another study where the hypertensive patients received amlodipine and captopril combination (46).

2.4.3 Adherence

The DTP results when the patient is not willing to take the drug therapy as intended (1). Consequently, non-adherence to therapy was reported higher in the UK than SA studies as 14% and 6% respectively (12). This DTP occurred because of wrong beliefs that drug are toxins and unsafe. This was supported by four studies (12).

Patients identified with non-adherence had a prevalence of 60% and 70% angina pectoris in T2DM respectively. The study documented a high prevalence because there was knowledge gap about drugs and fear to take medications (45).

Essentially, two studies documented a prevalence of 13.45% and 14% in non-adherence among patients with heart failure (47) which agreed with studies done in Australia. Malaysian and Jordan study documented similar results of non-adherence. They showed that non-adherence was purely due to lack understanding practitioner's instructions (47).

Another study reported that patients with higher values of Hemoglobin A1c test failed to take the prescribed drugs hence the non-adherence. This evidence was supported by two studies (48).

2.4.4 Ineffective drug

A prospective study conducted in an Indonesia hospital on T2DM and hypertensive patients identified DTPs using PCNE classification. It reported two types of DTPs with a prevalence of 55.2% in inappropriate drug choice for a condition. In addition, another study documented similar results, which was due to lack of prescribing an antihypertensive to a hypertensive patient (35).

Some other uncommon causes of DTPs revealed in Jordan study included availability of medication that is more effective for a given indication but not in use, the presence of contraindication, an inappropriate dosage form of the drug product, and drug not indicated (47,48).

2.4.5 Adverse Drug Reactions

Another study conducted at cardiology department in India, the researcher used Hepler and Strand classification to document his DTP results (2). He reported a prevalence of 49.05% in drug interactions as the most common DTP followed by a prevalence of

18.86% in ADRs. In contrast, another study documented a high prevalence of 43.42% in ADR (2). Moreover, two studies showed a prevalence of 34.8% in DI. The high prevalence reported among these two studies was attributed to medications used commonly by CVD and DM patients such as antiplatelets, antihypertensive, and Gastro-intestinal drugs (2). In addition, the ADRs reported in a Danish study had a prevalence of 14.3% and 8.7% in angina pectoris and T2DM respectively. However, the study findings were inconsistent with two studies. These latter findings showed high prevalence of ADRs due to prescribing agents with low therapeutic index. In contrast, another study argued that the high prevalence of ADRs documented before was purely due to use of a different tool for DTP classification and a different DTP data collection tool (45).

2.4.6 Dosage too low

The prevalence of dosage too low reported by in a study was 13.20%. In contrast, three studies reported low prevalence in dosage too low (2). In addition, another study reported a prevalence of 32% in dosage too low. In contrast, three studies documented different findings (4). The too low dose of captopril was reported in 1.5% of the DTPs (46). Another study showed that 97 patients reported 22% of DTPs with inadequate dose, wrong regimen and wrong dosage duration (49).

2.4.7 Dosage too high

The dosage too high was reported at a prevalence of 3.9% by a study conducted in Singapore (6). In addition, another study documented that Hypotension was caused by the high dose of frusemide and enalapril while the nasal bleeding was caused by high dose un-fractionated heparin and warfarin (20). Another study reported that 15% of T2DM patients with dyslipidemia had dosage too low or dosage too high types of DTPs caused by ineffective dose. In contrast, another study showed that only 5.9% had ineffective doses (48).

2.5 Predictors of DTPs

Age and gender have been cited as some of the major predictors of DTPs found in patients with both T2DM and CVD patients (12).

In another study conducted among 112 patients with CVD, 53 out 44 patients reported having DTPs. Out of this 44 patients, 72.72% males and 27.28% females reported having DTPs (2). The high prevalence of DTPs reported in males was because they were smokers, alcoholics and suffered multimorbidity (2). Moreover, three studies documented similar results (2).

Consequently, it was reported in another study that 55.53% of patients aged 41-60 years had increased incidences of DTPs. Similarly, another study also reported that adults over 65 years old had increased rate of DTPs occurrence when receiving more than 6 medications (2). Furthermore, another study reported 36% of new cases of DTPs among ages 51 to 60 (4).

In a study conducted in Jordan, out of 2,898 patients with chronic diseases, 40.1% were males and 59.5% were females (8). Their mean ±SD age was 56.59±13.5 of which 90% of these patients also reported to have health insurance. Single Patients with more than 57 years, gone or not through high school and without health insurance had significantly more DTPs (8).

In a Malaysian study, females were 82.8% and males 17.2%. In this study, 57.8% patients aged <56 years were found to have T2DM and Hypertension (11). In Malaysian study, carried out among 200 T2DM patients, showed that there was a high prevalence of DTPs in elderly patients more than non-elderly patients. This was in contrast to Mafauzy et al and global data (11).

Other predictor factors of DTPs documented in a study included obesity, renal dysfunction, hepatic dysfunction, and smoking (12). Additionally, seven predictors reported in the UK study included patients living dependently, patients with cognitive dysfunction, hypertensive patients, caffeine addicts, stress, anemia, and history of CVDs in a family. Furthermore, four predictors also reported in SA included depressive disorders, epilepsy, smoking, and anorexia (12).

In addition to that, a retrospective study identified 85.7% patients aged 18 to 50 years who were at a high risk of DTPs (37). In contrast, another study documented that T2DM

patients aged <65 years were at a greater risk of DTPs than >65 years. Essentially, patients <65 years had the inability to understand the importance of adhering to a drug (37).

A study showed a prevalence of 96.4% and 86.5% in male and female respectively. These study findings showed consistency with another study findings that the low prevalence in women was contributed by adhering to medication and attending clinic appointment (48). In addition, the high prevalence of DTPs reported in male was purely due to drinking alcohol and smoking (48).

In a study conducted in southern Ethiopia, DTPs were 5 times more likely to develop in patients aged 45-54 years than <44 years old. However, DTPs were 9 times more likely to develop in >65years old than in <44years old because of multiple diseases and multiple drugs. These study findings were supported by other three studies (39). However, these findings were inconsistent with a study done in Malaysia (48).

A study performed among admitted patients with heart disease reported that female gender was associated with increased risk of DTPs. This was supported by another study that revealed that female patients were not taking the prescribed drugs such as angiotensin-converting enzyme inhibitor (ACEI) and low doses of beta-blockers (BB) (49).

2.6 Clinical Characteristics that affect DTPs

In another study carried out among 2,898 patients, hypertensive, diabetic, and dyslipidemia patients had a prevalence of 74%, 52.2%, and 38.0% respectively. Essentially, studies documented that patients with T2DM, Hypertension, dyslipidemia, heart failure, ischemic heart disease, cardiac catheterization, and gout had significantly higher numbers of DTPs. Similarly, six studies reported that co-morbidity was related with DTPs (8,39)

In addition, another study associated CVD drugs and DM with hypertensive patients. Similarly, two studies documented that most CVD drugs were highly associated with

DTPs. These findings implicated antihypertensive, antiplatelet and anticoagulants drugs (11).

Another retrospective study showed that 82% of T2DM got macrovascular complications purely due to coronary heart disease (CHD) with a prevalence of 79.7%. Moreover, it was reported that retinopathy was the cause of microvascular complications with a prevalence of 25.8% (37). This study also reported that comorbidities due to hypertension and dyslipidemia was associated with DTPs (37).

Additionally, two studies documented that patients with comorbidities were six times more likely to have DTPs than those without comorbidities. These findings were consistent with three studies (50).

2.7 Inappropriate Prescribing patterns in patients with CVD and T2DM

The prescriber-related patterns can address the undesirable effects caused by medications and hence improve the patient health outcomes. The four types of drug-related needs are divided into prescriber-related-patterns and patient-related patterns. Prescriber-related patterns and patient-related patterns are the indications, effectiveness, safety, and adherence respectively. If all the four types of drug-related needs were met, then, the high prevalence of DTPs reported in literature would significantly reduce (1).

Essentially, cardiovascular drugs prescribed were potentially implicated to DI (Drug Interaction). A study reported a high potency of an interaction among cardiovascular drugs when co-administered with proton pump inhibitors, pantoprazole and calcium channel blocker (2).

Another study documented that 52.30% patients, using 6 to 10 drugs, had more DTPs. Similarly, two studies reported the same outcome. This high prevalence implicated antiplatelets, antihypertensive, and gastrointestinal drugs due to their potential to cause drug toxicity (2).

A study conducted in SA and UK reported a high prevalence of DTPs due to prescriber-related patterns. In a study conducted in the UK showed that CVD and diabetes

medicines contributed to 83 and 21 types of DTPs respectively (12). Additionally, 11 and 21 types of DTPs were implicated in insulin and oral hypoglycemic agents respectively (12). Consequently, these DTPs were because of ADRs, type of regimen and doses used.

Studies carried out in SA, showed a different trend in DTPs due to prescribing. Diabetic medications prescribed had the most DTPs compared to CVD medications. Five and 44 DTPs were implicated in oral hypoglycemic agents and insulin respectively. Those associated with CVD medications were hypertensive medications (calcium channel brokers and ACEIs), arrhythmic medications (digoxin and beta-blockers), aspirin, and statins. In SA, The higher prevalence was reported in patients using insulin in which doses were poorly adjusted for insulin-dependent diet patients, especially during Ramadan and Hajj events (12).

Penicillin medication was associated with most 150-drug allergies for 114 T2DM patients. In addition to that, 37.8% of anti-diabetic, 36.9% cardiovascular medications, and 10% narrow therapeutic index (warfarin) were prescribed frequently resulting in DTPs (37).

In addition, another study documented that anti-diabetic drugs caused a third of ADRs in T2DM patients. Moreover, the most ADR-causing agents were metoprolol causing bradycardia, nitrates causing hypotension and headache, dopamine causing tachycardia (39).

2.8 Polypharmacy and DTPs

A study documented polypharmacy as a predictor factor for ADRs (6). In addition, polypharmacy was associated with increased DTPs among admitted patients with heart disease. A Jordan study documented similar results with other 12 studies that DTPs are associated with polypharmacy, multi-comorbidity and increasing age (8,12).

Another study conducted in KNH oncology ward showed that patients taking more than five drugs were three times more like to have DTPs (23).

A cross-section study of elderly patients enrolled in Florida Long-Term Care Diversion (Florida LTCD Program) reported that 87% of admitted patients were taking more than

five drugs. In addition, a study conducted among 97.8% of the patients documented DTPs purely due to multi-medications (39).

Moreover, another study conducted among T2DM patients with dyslipidemia revealed that there was a positive association between patients receiving multiple medications and DTPs (48).

2.9 Adherence pattern and comorbidity that affects DTPs

Promoting medication adherence is a major clinical obstacle in reducing the untimely morbidity and mortality related to these comorbid conditions. According to WHO 2003, medication adherence is a person's behavior in taking medication or making healthy lifestyle changes that match up with an established recommendation from a health care worker (52).

A cross-sectional study conducted in Nigeria revealed that less than half (43.3%) of the patients were highly adherent to their prescribed medication. Those participants with medium and low adherence were 30.3% and 26.7% respectively. This study also reported that the patients with the comorbidity of NCDs had 49.2%, 26.3% and 24.6% for high, medium and low adherence respectively (52). Consequently, the clinical and disease factors that affected adherence-DTP pattern included; combined drug regimens, drug side effect, and complication of diseases. He concluded that diseases and the drug regimen are important descriptive factors for patient’s medication adherence (52).

Studies conducted on adherence to initial drug therapy for antihypertensive have shown that many patients non-adhere to their treatment over time. For example, a study among British patients showed that less than 50% of the study participants continued therapy after six months of initiation (53).

2.10 Literature Gap

As established by the literature review, it is evident that patients with both T2DM and CVD are at a higher risk of DTPs compared to the general population. This has been attributed to non-modifiable and modifiable factors such as age, gender, and comorbidities, polypharmacy respectively.

Although studies on DTPs have been done in CKD patients and cervical cancer patients, they never studied both T2DM and CVD (19,23).

There is a dearth of data from African countries including Kenya regarding extent and type of DTPs in patients with both T2DM and CVD. Furthermore, predictor factors associated with DTPs in patients with both T2DM and CVD in Kenya have not been established.

The study will aim to establish the extent of DTPs among patients with both T2DM and CVD as well as exploring associations of different variables with each category of DTP identified. In addition, it will inform the approach to DTPs identification and prevention in Kenya referral hospitals and Sub-Saharan Africa by answering the research question.

CHAPTER THREE: METHODOLOGY

This section of the research was describing the methodology to be used in order to meet the objectives of the study. It was describing the research design, study area, and site, target population, eligibility criteria, sample size, sampling technique, participant recruitment, research instruments, pilot study, validity, reliability, methods for data collection, data management, and ethical considerations.

3.2. Research Design

This was a hospital-based cross-sectional study of adult patients with both T2DM and diagnosed with CVD attending their follow-up care in the diabetic and cardiovascular clinic during the study period. This design of the study was used because it was analyzing whether the adult patients of ≥18 years of age have both CVD and T2DM and whether they have the DTPs as the outcome of interest. Furthermore, it was feasible to use this type of design because everything was done at the same time. The only limitation is that time was not enough to follow up the outcome of the collected data.

The advantage of this design was that adult patients were neither deliberately exposed, treated, or not treated and therefore rare difficulties in ethics. Relatively, it was a cost-effective and efficient exploratory tool for the study that determined prevalence in a population at a given point in time (54).

3.3. Study Area and Site

The study area was Kenyatta National Hospital because it is the referral hospital in Kenya where most of the conditions are attended. The hospital was located 3.5 kilometers away from the Nairobi city's central business district along the Hospital Road (off Ngong Road). According to the Kenyatta National Hospital website, the hospital was established in 1901 and is serving patients from all over the country and East Africa hence a large catchment area. It is one of the largest teaching referral hospitals in the region with 2000-inpatient beds, 22 outpatient clinics, 24 theaters, 50 wards. This teaching hospital hosts the University of Nairobi, College of health sciences, and the Kenya Medical Training College that produces skilled health professionals. In this good referral hospital is a site study, KHN Outpatient Diabetes, and Endocrinology clinic (KNH OPDMEC), where

most of the participants with both T2DM and CVD conditions are referred to, seen, and offered quality care. Currently, there are about 200 type 2 diabetic patients diagnosed with CVD referred and treated here. All are served at the OPDMEC, in monthly review clinics, as from Monday to Thursday and annual review clinics happening on Friday.
Normally the KNH OPDMEC serves around 80 patients daily approximately 30 of whom have both T2DM and CVD. The team of healthcare workers involved in referring, treating, and managing these patients is Physicians, Endocrinologists, and nurses among others.

3.4. Study Population

The study participants were T2DM adult patients aged ≥18 years diagnosed with any group of diseases of heart and blood such as stroke, ischemic heart disease, cerebrovascular disease, hypertensive heart disease, cardiomyopathy, valvular heart disease, rheumatic heart disease, aortic aneurysm, arrthymias, hypertension, endocarditis and pericarditis, and other cardiovascular and circulatory disease. Furthermore, must be undergoing a long-term treatment and follow-up care in Kenyatta National Hospital OPDMEC during the study period.

3.5. Eligibility Criteria

3.5.1 Inclusion criteria

Male and female adult T2DM patients diagnosed with CVD and aged ≥18 years. In addition, they should be receiving at least one anti-diabetic and a CVD medication. They should have had at least one follow-up evaluation in the last 3 months prior to the study.

3.5.2 Exclusion criteria

Psychosocially challenged patients like the mentally ill, patients with dementia and Parkinson's disease, among others. These conditions may limit activity and communication.

3.6 Sample size determination

In a systematic review of medicine related issues in hospitalized CVD and DM adult patients showed that the overall frequency of Drug Therapy problem is 4.6-12.1% (12). The Cochran formula (55) was used to assess the sample size as follows

$$n = Z^2 \frac{p\,(1-p)}{e^2}$$

Where:

Z- Level of significance is (1.96%)

p- Prevalence of DTPs in T2DM with CVD is 12.1%(55)s

e- Precision Estimate around DTPs in T2DM with CVD is (5% or 0.05).

n- a Sample size of DTPs in T2DM with CVD is

Assuming 12.1% of the prevalence of drug therapy problems among these patients, the sample size (n) will be:

$$n = \frac{1.96^2 * 0.121 * (1-0.121)}{0.05^2} = 163.4$$

The sample size was adjusted for 10 % non-response. Therefore, the number of participants that was recruited in the study was 180.

3.7 Sampling method

Simple random sampling method was used to achieve a representative sample of the target population. The research assistant generated a table of random numbers using a computer program. Essentially, all patients with T2DM and CVD had an equal chance of participating in the research study.

Patients' files were normally collected from the Central health records office of KNH well in advance before any clinic day. In the morning of a particular clinic day, the Principal Investigator (PI) went through the patient file, screening the file using eligibility criteria (Appendix 1). A list of the eligible patients' outpatient file numbers was made. For ease of identification, the research assistant immediately tagged the files meeting the inclusion criteria using random unique numbers. The tag remained in the file until the completion of the study.

To avoid duplicate sampling, the PI assigned a random unique number to every patient. This unique number was different from the outpatient file number. In addition, retaining the tags in the files was a challenge due to improper filing. Therefore, it was compulsory to assign the random unique number to each patient to avoid picking the files again. Additionally, the random unique numbers was recorded in a list for ease of identification.

On average, 30 patients out of 80 attending the clinic daily had both T2DM and CVD. Of the 30 files tagged daily, every other file was sampled in order to achieve a daily target of 6 patients. To achieve a daily target of 6 patients, the PI listed the outpatient numbers of the 30 files tagged and entered them into the computer program, Microsoft excel sheet. Then the PI gave a command to the program to randomly list 6 outpatient numbers. This represented 6 patients per day recruited in the study. The 6 patients was called by the PI for recruitment. In case the PI found out that the number of patients was less, he used the computer program to generate another random outpatient numbers to correct the deficit. This process continued until the daily target of 6 patients was achieved.

In case the patients selected by the computer are called in the room randomly to see the clinician, the attending clinician was requested to send the patient with a tagged file to the PI for recruitment in the study.

This represented 30 patients per week recruited in the study. In fact, in six weeks of data collection, the desired sample size had been achieved. Those willing to participate in the study were taken through the consent process using the patient information and consent form (Appendices 2A and 2B). The procedure was repeated on following clinic days until the desired sample size was achieved.

3.8 Participant Recruitment

In the morning after seeing the clinician at the clinic, the Principal Investigator (PI) built a rapport with the patients. Afterward, with the help of eligibility screening forms the PI went to screen the patients (Appendix 1).

The PI explained orally to the patient what the objectives of the study entailed (procedure, confidentiality, benefit, or harm) and administered the English version of the patient information form to the patient (Appendix 2A). The PI made the patient aware that they can voluntarily withdraw and leave the study anytime. Thereafter, the PI provided them with a verbal and written consent form (Appendix 2B) and the Kiswahili version (Appendix 3A). After obtaining patient consent to participate, the PI proceeded to give the participants the consent declaration form to sign (appendices 2B/3B). The PI requested the patient disagreeing to participate in the study to explain the reason for their decline. Furthermore, the PI documented all the recruited patients undertaking the study. Finally, the PI took them through the questionnaire (Appendix 4) at the OPDMEC.

3.9. Research Instruments

3.9.1 A screening eligibility form:

This inclusion criterion guided and assisted the PI to select eligible patients for the study (Appendix 1).

3.9.2 Informed consent form:

This form was used to obtain approval from those who meet the eligibility criteria. Kiswahili version (Appendix 2B) was administered when eligible participants were unable to understand English version (Appendix 2A). Proxy consent was obtained from the caregiver because of inability to understand English version.

3.9.3 Data Collection Form:

A structured modified questionnaire derived from pharmacotherapy workup© notes (1) was used to put together all information from the patient (Appendix 4). All laboratory information and treatment used by the patient was abstracted from the patient medical files and treatment sheets using the questionnaire (Appendix 4) after the patient has signed the consent form (Appendix 3B).

3.10 Data collection

Patients who met inclusion criteria and attending routine check-up at OPDMEC KNH were approached and explained the purpose of the study. A consent form was then completed prior to collecting information from the patient. A face-to-face interview was commenced as soon as consent was given.

Once the consent had been obtained, a face-to-face interview was commenced using a structured modified questionnaire (appendix 4). Data was collected in order to assess whether all drug-related needs were met; all the drug therapies were most appropriate, were most effective available, were the safest available and that the patient was adhering to the instructions for their proper use.

The appropriateness of medical therapy was assessed and compared using World Journal of T2DM, Global Status on Non-Communicable Disease, Kenya National Strategy for Prevention and Control guidelines of NCD. Drug Interaction will be assessed using Epocrates, Medscape, and Micromedex.

3.11 Pre-testing of data collection form

A pilot study was carried out with 18 patients (10% of the study sample) to test the relevance, completeness, and ease of data collection form. The pre-testing of the collection tool was conducted at the KNH OPDMEC on Monday to Friday, clinic days. This was the precise setting where the actual study was conducted.

In the morning of the clinic day, before the clinic started, the PI went through the patient files, screening the file using eligibility criteria (Appendix 1). A list of the participant's outpatient numbers was drafted in accordance with those meeting the inclusion criteria. For ease of identification, the assistant researcher immediately tagged the files meeting the inclusion criteria using random unique numbers.

Essentially, patients were called in the room randomly and the attending clinician was requested to guide every other patient with a tagged file to the PI for recruitment in the study. The patients were included until a target of 18 patients was realized. Necessary corrections were done on the document to remove ambiguities made and improve its ease of use.

3.12 Validity

The validity of the study was maintained by ensuring that the questionnaire was well laid out and relevant with regard to objectives of the study. The questions were arranged sequentially using simple, clear, concise, and acceptable language. All the research assistants were chosen from among the trained nursing staff of the KNH OPDMEC. Moreover, the study site chosen gave a good representation of the general population since KNH, and by extension OPDMEC, received referrals, saw and attended to patients from all parts of the country.

3.13 Reliability

Data collection tools were pre-tested as described in the pilot study for reproducibility before the actual study to ensure there were no ambiguities in responses.

Amendments were done on the instrument where necessary in order to improve their precision.

3.14 Data Collection Techniques

The study participants had each completed an interviewer-administered questionnaire (see appendix 4). Furthermore, all participants prescription, treatment charts, and medical records were reviewed by the Principal Investigator after each routine encounter using the questionnaire (see appendix 4). Data collection was conducted in two phases. The initial phase (Part A) was interviewing the patient and second phase (Part B) was abstraction of data from medical records and medication charts. A structured modified questionnaire was used for data collection and was administered by the study investigator. It was a modified questionnaire because certain parts of the pharmacotherapy workup© notes questionnaire (1) were not applicable in our local setting. Furthermore, the time given to interviewing patients using the pharmacotherapy workup© notes questionnaire was not possible in a cross-sectional study. Hence, certain parts of the pharmacotherapy workup© notes questionnaire were deliberately omitted during modification because of the period of the study design of this proposal. The questionnaire had two main sections (see appendix 4).

3.14.1 Patient interview

After the patients had signed and given their informed consent, the PI invited the eligible patient in a room, after seeing the clinician and immediately interview the patient using a guided structured modified questionnaire. Part A of the questionnaire obtained the participant baseline social demographic data details such as age, sex, marital status, level of education, occupation, level of income, smoking, alcohol, comorbidities, medication experiences among others. In addition to that, this section also obtained comprehensive medication history and general review of systems as well as DTPs reported by the patient and other aspects of patient related risk factors associated with DTPs.

3.15 Medical Record and Medication Chart Review

The PI perused medical records and medication chart and abstracted the information of each patient such as physical examination notes and results of laboratory and diagnostic tests, diagnosis and treatment. This was done using the Part B of the questionnaire (see Appendix 4). The results of vital signs and diagnosed medical condition (T2DM, CVD and among others) was obtained. Additionally, drug therapy information was also abstracted from the medical records such as name (s) of the drug (s), dose, frequency and duration as well as the pharmacological class of the drugs.

3.16 Variables and Definitions

3.16.1 Case definitions

Drug Therapy Problems: was defined as an undesirable event in a patient that involved, or suspected to involve drug therapy that interfered with the health outcomes and required a professional judgment to resolve. This occurred when drug-related needs were not met. The following were seven drug therapy problems.

1. Unnecessary drug therapy. This could occur when the patient has no clinical condition of the drug. The patient has too many medications for their condition and the drug is not needed.
2. Needs additional drug therapy. The occurrence of this DTP in a patient is when he or she needs more medication to treat their condition.

3. A drug that is ineffective. This occurrence is detected when a patient is using a drug that does not treat the patient's condition. Example, a heart medication to treat an infection.
4. Dose too low. This occurrence is determined when a medication is administered to a patient that hardly can give therapeutic effects.
5. Dose too high. The occurrence of this is observed when a too strong medication is administered upon which detrimental effects are felt.
6. Adverse drug reaction. This could occur when a patient is given a medication in right doses but still produce an allergic response.
7. Inappropriate adherence. This could occur when a patient chooses not to take or forgetting to take a treatment.

Outcome status terminology

The outcome status terminology used to describe clinical outcome status resulting from drug therapies was precise and represented both the decisions and actions on the part of the practitioner and patient. These outcome terms described the progress, or lack of progress, in achieving the desired goals of therapy and action, if any, taken to adjust the patient's drug therapies (Appendix 5).

3.16.2 Variables

The outcome variables was drug therapy problems. The predictor variables included age, gender, disease condition, number of medication per prescription, type of medication, dose, and diagnosis.

3.17 Data management

Confirmation of completion of the questionnaires took place after each interview and any missing information required seeking particular participants for clarification.

Data collected was entered and stored in a customized Microsoft access 2010 and Microsoft excel 2010 where the researcher can access. After data collection, participants data was entered daily and backed-up after three days. The information collected was backed-up using hard disk and flash disk. For the sake of confidentiality of the

participant's information, all files and directories were protected by a password. At the data entry phase, all categorical variables were stored as coded data and each code attached to a label. After data entry, data cleaning was carried out and exported into STATA version 13.0.

3.18 Data analysis

The data was entered into Microsoft Excel 2010 and was analyzed using STATA version 13.0. Descriptive statistics like frequency, mean, and percentage were generated for continuous and categorical variables. Graphs and frequency tables represented categorical variables such as the number of adult patients showing DTPs. Both binary and multi-variable logistic analyses were adapted to control for confounders and predictors of DTPs that may be age, gender, comorbidities, and polypharmacy. Chi-square (X^2) tested the association between DTPs and patient's characteristics. Consequently, a p-value of less than 0.05 was considered statistically significant to study the association between predictor factors and drug therapy problem.

3.19 Ethical and logistical considerations

3.19.1 Ethical approval

Clearances from the University of Nairobi and Kenyatta National Hospital-Ethics and research Committee (KNH UON-ERC) was obtained before carrying out the study. Authorization to conduct the study was obtained from KNH administration. Participation in the study was voluntary and only after the participants consented to participate through signing a consent declaration form (Appendix 2B).

3.19.2 Informed Consent

All eligible patients were taken through the nature of the study and an explanation on filling the form (Appendix 2A). The patients were presented with a consent declaration form to sign (Appendix 2B). Patients were informed up front that the study was voluntary and they were free to withdraw from the study at any point without any problems. Adequate information on the nature of the study were provided. No incentives or coercion was provided in order to participate in the study. Patients were free to ask any

questions about the study in the course of the encounter and were informed that if they had any concerns about their rights as patients they would contact KNH UoN-ERC.

3.19.3 Risks and benefits

The participants participated without harm imposed to them. During patient guided interviews, the Principal Investigator addressed any concerns regarding their CVD and T2DM conditions and management. The findings of this study were placed in the respective patient files and were shared with the various concerned parties. This benefitted the participant and improved their health outcomes. Furthermore, this study was descriptive and did not involve any invasive procedures or involve taking additional medications.

3.19.4 Confidentiality

During the data collection and analysis process, the study serial numbers were generated and were used instead of patient names and contact details. The collected information was treated confidential and restricted for access using password protected electronic medical record. Signed copies of the consent participation forms were kept in a locked office file cabinet. Only the principal investigator and assistant researcher accessed the documents.

CHAPTER FOUR: RESULTS

4.1 Introduction

Data analysis was performed using STATA software version 13. This chapter contains analyzed data, which is presented according to objectives. Descriptive analysis was done to organize the data into frequencies, proportions and figures. Bivariate analysis was done to show relationship between predictor variables (sociodemographic and clinical characteristics of patients) versus outcome variables as measured by the presence of drug therapy problem.

4.2 Socio-demographic characteristics of the study

A total of 180 patients with both T2DM and CVD participated in the study, and out of these, 119 (66.1%) were females. Most of the patients, (107, 59.4%) were aged between 36 to 65 years. The mean age of the patients was 61.6 (+/-11.3years) with a range of 27 to 95 years old. In addition, majority of the patients, (76, 42.2%) were overweight followed those who were obese at (70, 38.9%). About three quarters (141, 78.3%) of the patients were married. Seventy-four (41.1%) had attained primary level of education and a similar proportion was self-employed. Majority (176, 97.8%) of the patients were Christians. Six (3.3%) and 10 (5.6%) were current smokers and alcohol consumers, respectively (**Table 1**).

Table 1: Sociodemographic of the study participants (N=180)

Variables	Frequency (n)	Percentage (%)
Sex		
Male	61	33.9
Female	119	66.1
Age Years		
<35	2	1.1
36-65	107	59.4
>65	71	39.4
BMI		
0-18.5	1	0.6
18.6-24.9	33	18.3
25-29.9	76	42.2
>30	70	38.9
Marital Status		
Single	39	21.7
Married	141	78.3
Religion		
Christian	176	97.8
Muslim	4	2.2
Smoking status		
Never smoked	138	76.7
Previous smoker	36	20
Current smoker	6	3.3
Alcohol intake status		
Never drunk	108	60
Previously drinking	62	34.4
Currently drinking	10	5.6
Level of education		
Primary	74	41.1
Secondary	70	38.9
College/university	27	15
Informal	9	5
Employment status		
Self employed	74	41.1
Not employed	54	30
Formally employed	52	28.9
Monthly Income, KES		
None	57	32
0-5000	53	29.8
5000-10000	29	16.3
10000-30000	24	13.5
>30000	15	8.4
More than two comorbidities of DM and CVD	62	34.4

Age (mean ±SD) Years	61.6(±11.3) range 19-95

KEY-BMI-Body Mass Index, SD-Standard Index, KES-Kenyan shillings

4.3 Clinical characteristics of the study patients

4.3.1 Duration of diabetes and cardiovascular disease

The mean duration of T2DM was 12 years (SD ± 9 years) ranging from 3 months to 45 years. The mean duration of CVD was 11 years (SD ± 8) and the range was 3 to 40 years. Over 70% of the patients had had both T2DM and CVD for more than 6 years.

4.3.2 Glycaemic and Blood Pressure measurements

With at least, two hours postprandial blood sugar levels recorded at two different times, it was noted that 59 (32.8%) patients had inadequate glycemic control at the time of study (**Figure 3**). Additionally, there was poor long-term glycemic control in 21(11.7%) patients for whom HbA_1C results were available. More than half of the patients, (114, 63.3%) had inadequate blood pressure control.

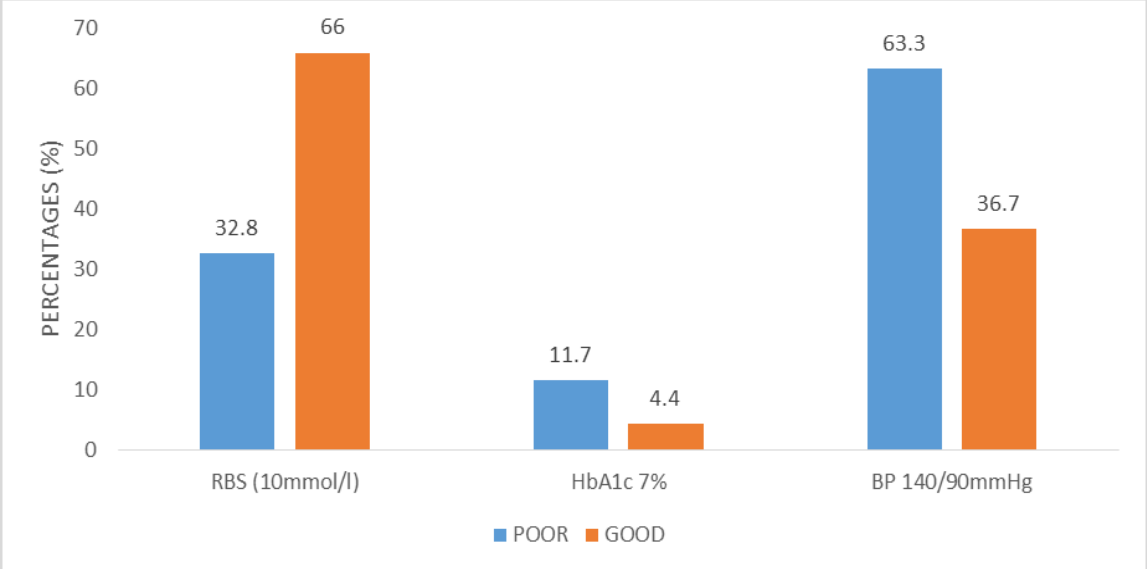

Figure 3: **Adequacy of Blood Sugar and Pressure control in patients with CVD and type 2 DM.**

Key: HbA1c-glycated hemoglobin, BP-Blood Pressure
**Poor controlled 2 Hour post prandial: >10mmol/l, Poor controlled HbA1c: >7%, Poor controlled BP :> 140/90mmHg*

4.3.3 Comorbidities among the study patients

A total of (62, 34.4%) patients had more than two comorbidities where (31, 17.2%) patients had arthritis while (16, 8.9%) had CKD and (4, 2.2%) experienced PUD in that order (**Figure 4**)

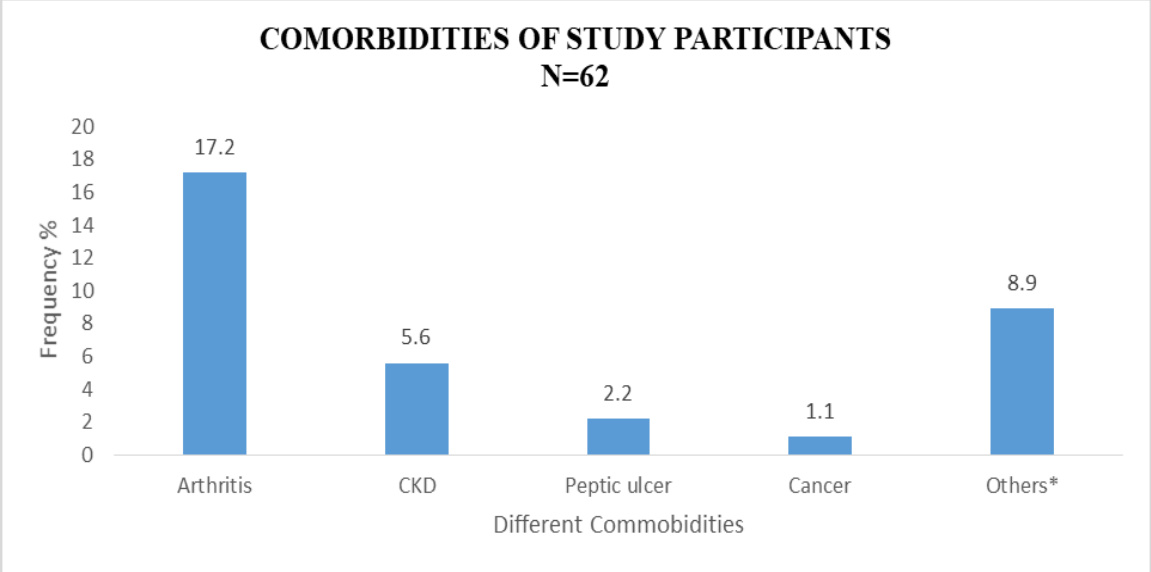

Figure 4: **Comorbidities among study patients.**

Key: CKD-Chronic Kidney Disease

**TB-Tuberculosis, HIV-Human Immunodeficiency Virus, fibroids, primary hypothyroidism, asthma, bronchitis, BMD-Bipolar Mood Disorder, anaemia, allergic rhinitis, parkinsonism, Alzheimer, diarrhea, vitiligo*

4.4 Prescription Patterns of Medications for the DM and CVD

4.4.1 Antidiabetic Drugs Prescribed

A total of 322 antidiabetic drugs were prescribed to the study population. In **Table 2**, the classes of drugs frequently prescribed to patients for T2DM were biguanides (155, 86.1%), insulin (105, 58.3%), sulfonylureas (46, 25.6%), Thiazolidinedione (9, 5%) and gliptins (5, 2.8%), in that order.

Table 2: Prescribing pattern of anti-diabetic drugs among Study Participants

Antidiabetic drugs		Frequency (n)	Percentage (%)
Biguanides		155	86.1
	Metformin	155	86.1
Insulin		106	58.9
	Insulin mixtard	105	58.3
Sulphonyl ureas		46	25.6
	Gliclazide	16	8.9
	Glimepiride	19	10.6
	Glibenclamide	11	6.1
Thiazolidinedione		9	5.0
	Pioglitazone	9	5.0
Gliptins		5	2.8
	Sitagliptin	5	2.8

4.4.2 Antihypertensive and other associated Drugs Prescribed

The most prescribed antihypertensive class was ARBs (102, 56.7%) followed by CCBs (90, 50.1%). The least frequently prescribed was vasodilators (4, 2.2%). The most frequently prescribed individual medications were losartan (102, 56.7%) followed by hydrochlorothiazide (76, 42.2%) and amlodipine (52, 28.9%). More than a half (105, 58.3%) of the patients were prescribed atorvastatin, while more than a quarter (49, 27.2%) of the patients were prescribed aspirin as shown below (**Table 3)**.

Table 3: Types of Cardiovascular drugs Prescribed among the study participants

Cardiovascular drugs		Frequency (n)	Percentage (%)
CCB		90	50.1
	Amlodipine	52	28.9
	Nifedipine	37	20.6
	Nicardipine	1	0.6
Beta-blockers		58	32.3
	Carvedilol	29	16.1
	Atenolol	21	11.7
	Nebivolol	6	3.3
	Propanolol	1	0.6
	Metoprolol	1	0.6
ACEI		46	25.6
	Enalapril	46	25.6
ARBs		104	57.8
	Losartan	102	56.7
Loop diuretics		24	13.3
	Furosemide	24	13.3
Potassium sparing diuretics		8	4.4
	Spironolactone	8	4.4

Thiazides		76	42.2
	Hydroclorthiazide	76	42.2
Vasodilators			
	Hydralazine	4	2.2
Antiplatelet			
	Aspirin	49	27.2
	Clopidogrel	4	2.2
Statins			
	Atorvastatin	105	58.3
	Rosuvastatin	5	2.8
Others*		16	10

***CCB**-Calcium Channel Broker, **ACEI**-angiotensin Converting Enzyme Inhibitor, **ARBs**- Angiotensin II Receptor Broker.*

4.4.3 Concomitant Medication Prescribed for other Comorbidities

The other medications prescribed along with cardiovascular and antidiabetic drugs were antibiotics, (6, 3.3%), anti-arthritis and anticancer drugs as shown below (**Table 4)**.

Table 4: Other drugs concurrently used with Anti-diabetic and anti-CVD

Concurrently used medications	Frequency N=123	Percentage (%)
Antibiotics	6	3.3
Anti-cancer	2	1.1
Arthritis drugs		
Glucosamine	14	7.8
NSAIDS	9	5
Others*	92	51.2

**Neurobion-forte, Benzhexol, Cereboprotein, Erythropoietin, Ferrous-sulphate, Levodopa/Carbidopa, Allopurinol, Cachinerve, Albendazole, carbimazole, Risperidone, olanzapine, Carbamazepine, Mannix, Esomeprazole, Resonium Cartil-forte, Neurocare Anticancer: Letrozole, Bicalutamide.Methotrexate. Antibiotics: Septrin, Ciprofloxacin, Cefuroxime, azithromycin, NSAIDs: Ibuprofen, Naproxen,Diclofenac*

4.5 Patterns of Prescriber related DTPs

The summary of prescriber related DTPs is presented. There were five prescriber related patterns of DTPs noted in this study. These was as shown in **table 5.** Eighty-seven (48.3%) patients had untreated conditions in this study. Additionally, among the treated patients, 59 (32.8%) were prescribed too low doses. The least frequent prescriber related DTP was prescribing unnecessary drug therapy found in only one (0.6%) patient**.** No patient was found to have too high doses (**Table 5**).

Table 5: Summary of prescriber related DTPs

DTP	Frequency (N=226)	Percentages (%)
Needs additional drug*	87	48.3
Giving too low doses	59	32.8
Prescribing a drug causing ADR	7	3.9
Prescribing Unnecessary drug	1	0.6
Prescribing Ineffective Drug	1	0.6

*U*ntreated condition*

4.6. Review of Systems

A comprehensive review of systems and complete physical examination was conducted in patients and untreated indications were identified as one of the prescriber related DTPs. In general physical examination, ninety-two (51%) patients presented with unmanaged malaise while 35 (19.4) had untreated fever as shown below (**Table 6)**.

Table 6: General Physical Examination

Variables	Frequency (N=279)	Percentages (%)
General system		
Malaise	92	51.1
Weight change	80	44.4
Pain	72	40.2
Fever	35	19.4

In ENT system examination, majority, (34, 18.9%), of the patients presented with untreated ringing ears followed by hearing loss (24, 13.3%), nasal congestion (14, 7.8%) and throat problem, (5, 5.6%). The study also recorded a significant percentage of patients with untreated visual impairment, (19, 10.6%) (**Table 7**).

Table 7: Ear/Eye/Nose and Throat (EENT)

Variables	Frequency (N=197)	Percentages (%)
Eyes		
Vision impaired	19	10.6
Itching	33	18.3
Painful eyes	24	13.3

	Swelling	7	3.9
Ear			
	Ringing ears	34	18.9
	Loss of balance	26	14.4
	Hearing loss	24	13.3
Nose			
	Congestion	14	7.8
	Sneezing	8	4.4
Throat			
	Pain while swallowing	5	2.8
	Haemoptysis	3	1.7

In respiratory system examination, 32 (17.8%) complained of chest pain, 30 (16.7%) presented with cough while, 29 (16.1%) complained of shortness of breath. In genito-urinary system, 65 (36.1%) patients complained of frequent urination while in digestive system, most patients, (63, 35.0%) complained of epigastric pain (**Table 8)**.

Table 8: Respiratory, digestive and genito-urinary system

Variables	**Frequency (N=418)**	**Percentages (%)**
Respiratory system		
Chest pain	32	17.8
Coughing	30	16.7
Shortness of breath	29	16.1
Wheezing	22	12.2
Digestive system and associated systems		
Heartburn	63	35
Anorexia	34	18.9
Abdominal pain	31	17.2
Constipation	25	13.9
Nausea	23	12.8
Diarrhoea	9	5.0
Dysphagia	6	3.3
Genito-urinary system		
Frequency urination	65	36.1
Reduced sexual drive	40	22.2
Pain urinating	9	5.0

Further examination on the other systems including neurological system revealed that more than 50% of the study population had tingling sensation in their lower extremities

while 81 (45%) patients presented with memory loss. In musculoskeletal system, more than 38.3% of patients had joint pains. Untreated backache and difficult in walking were encountered at (65, 36.3%) and (61, 33.9%) among the patients, respectively. Few patients had anaemia (12, 6.7%), itchiness of the body, (28, 15.6%) and skin rashes (14, 7.8%). (**Table 9)**.

Table 9: Neurological, Musculoskeletal, Haematological and Integumentary System Examination

Variables	Frequency (n)	Percentages (%)
Neurological system		
Tingling in extremities	104	57.8
Memory loss	81	45
Dizziness	62	34.4
Drowsiness	58	32.2
Insomnia	48	26.7
Headache	40	22.2
Musculoskeletal system		
Joint pain	69	38.3
Backache	65	36.3
Difficult in walking	61	33.9
Muscle pain	38	21.2
Joint stiffness	35	19.4
Swelling of joints	24	13.3
Haematological system		
Anaemia	12	6.7
Integumentary system		
Itchiness	28	15.6
Rashes	14	7.8

4.7 Characterization of Drug Therapy Problems among the Participants

The seven drug category problems, as described by Cipolle et al 2012 (1) were reported and characterized among the study patients.

4.7.1 Unnecessary drug therapy

The five sub-categories that characterize unnecessary drug therapy, as DTP, included duplicate therapy provided, no medical indication for the prescribed drug, only non-drug

therapy indicated, addiction to drug and presence of avoidable adverse reactions. Out of five sub-categories of unnecessary drug therapy identified, only one (0.6%) had a non-drug therapy indicated rather than pharmacologic therapy**.**

4.7.2 Patient Requiring Additional Drug Therapy/Unmet Medical Needs

The three sub-categories that characterize this DTP included preventive therapy required, identified untreated condition and synergistic therapy required. For the purposes of this study, any patient with both CVD and T2DM, and not on antiplatelet and hypolipidemic drugs, was considered a need for an additional drug. The list of unmet medical needs are presented **(Table 10)**.

Table 10: Participants' unmet medical needs

Causes	Frequency (N=87)	Percentages (%)
Anti-platelet needed	127	70.6
Failure to control blood pressure	114	63.3
Failure to control blood sugar	59	32.8
Pneumococcal vaccine needed	71	39.4
Hypolipidemic drug needed	70	38.9
Need for alcohol cessation program	10	5.6
Need for smoking cessation therapy	6	3.3

4.7.3 Ineffective drug

There were five sub-categories that characterizes ineffective drug as a DTP. These comprised of more effective drug available, condition refractory to drug, inappropriate dosage form, contraindication present, and drug not effective for condition. Only one cause among five causes was observed in one (0.6%) patient whereby a drug product given was assessed to be ineffective.

4.7.4 Dosage too low

There were seven sub-categories of this DTP. These included ineffective doses, needs additional monitoring, inappropriate frequency, inappropriate duration, incorrect administration, drug interaction, and incorrect storage. Out of the seven causes that characterize dosage too low, the most frequent cause of dosage too low was among (43, 23.9%) patients taking ineffective dose. Twelve (6.7%) patients did not require altering

doses but to further monitor their glycemic and blood pressure levels. The lowest dosage too low was among 4 (2.2%) patients who required dose frequency adjustment in their antihypertensive medications **(Table 11)**.

Table 11: Characteristics of Dosage too low

DTPs	Causes	Frequency (N=59)	Percentages (%)
Dosage too low	Ineffective dose	43	23.9%
	Needs additional monitoring	12	6.7%
	Dose frequency inappropriate	4	2.2%

4.7.5 Adverse drug reaction

There were seven sub-categories of this DTP. These included undesirable effect, unsafe drug for the patient, drug interaction, incorrect administration, allergic reaction and dosage increases and decreases too fast. Out of seven causes of adverse drug reactions, two causes were identified. These were undesirable effects and unsafe drug (7, 3.9%) and (1, 0.6%), respectively.

4.7.6 Adherence to Medications among the study participants

The rate of non-adherence, as a DTP, to the prescribed drugs among the study participants was at 71(39.1%). Patient was considered noncompliant only when drug therapy is determined to be clinically indicated, effective, and safe, yet the patient is not taking medication as intended. There were several reasons for non-adherence. Thirty (16.7%) patients did not understand instructions given to them by the prescriber and therefore failed to take their medications. Additionally, 24 (13.3%) patients deliberately stopped the prescribed drug product. In addition, 13 (7.2%) patients failed to take their medications because of high cost of drug product (**Table 12)**.

Table 12: Reasons for non-Adherence to medications by T2DM patient at KNH

DTPs	Causes	Frequency N=71	Percentages (%)
Adherence	Patient does not understand instructions	30	16.7
	Patient prefers not to take drug	24	13.3
	Cannot afford drug product	13	7.2
	Patient forgets to take	2	1.1
	Drug product not available	2	1.1

4.7.7 Non-adherence secondary to medication experiences

As illustrated in **Figure 5**, 136 (75.6%) patients had general negative perceptions about medications, which might have interfered with medication-taking behavior. There were 96 (53.3%) patients complaining of not taking medications due to high cost of drugs while, 15 (8.3%) patients complained of unavailability of drugs in hospital pharmacy. Only three (1.7%) patients had a strong dislike for taking medications for unknown reasons (**Figure 5**).

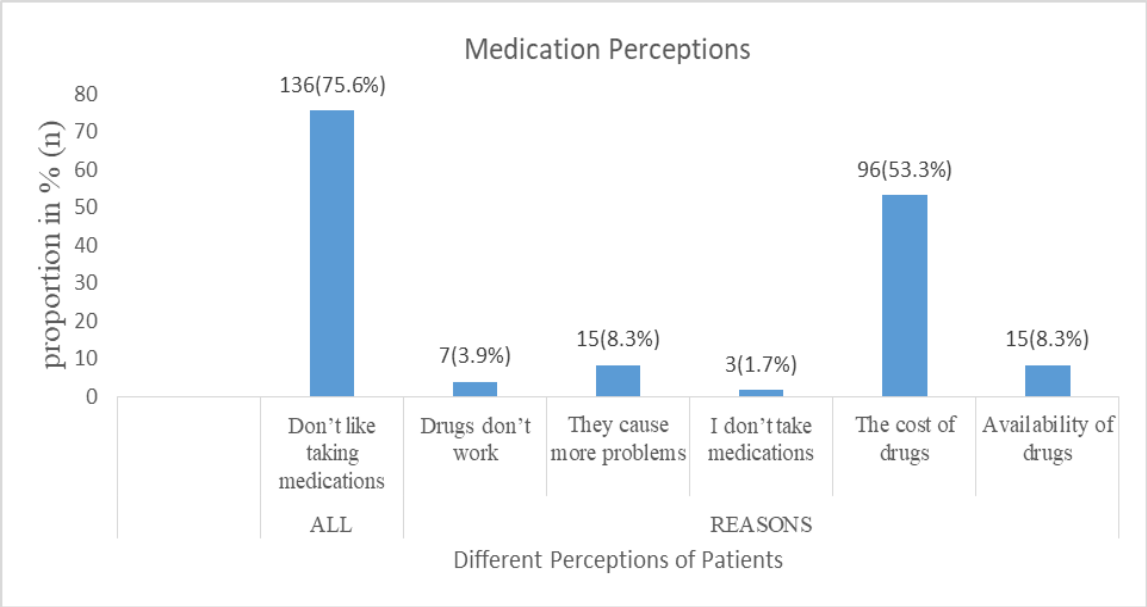

Figure 5: Medication taking behavior among the study patients.

4.8 Summary of the Prevalence of various DTPs among the patients

A total of 164 (91.1%) patients had at least one drug therapy problems. Patients requiring additional drug, noncompliance and with too low dosage were found to be the most frequent DTPs at 87 (48.3%), 71 (39.4%) and 59 (32.8%), respectively (**Figure 6)**.

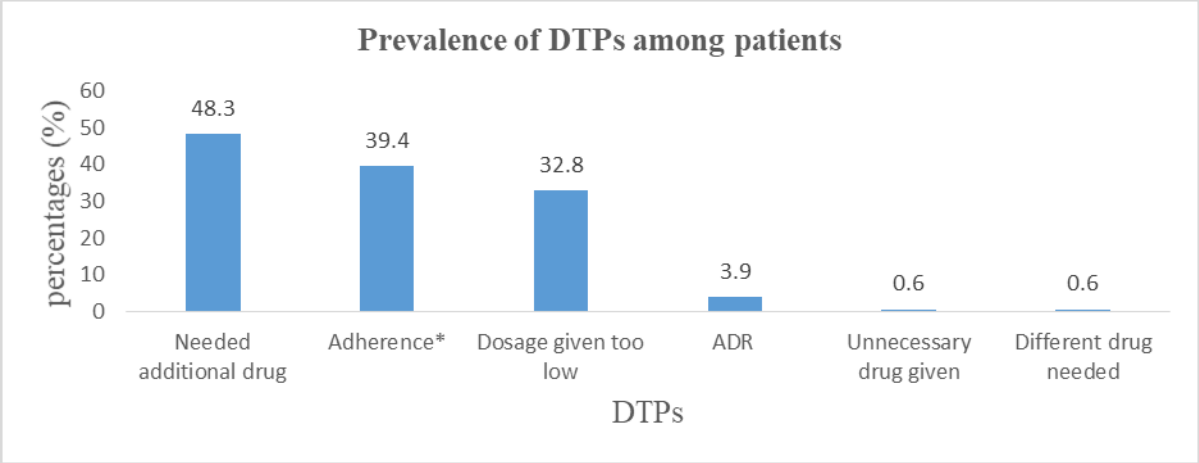

Figure 6: Prevalence of DTPs among patients.

Key: ADR-adverse drug reaction, DTPs-drug therapy problems

4.9 Concerns of patients regarding medications

A total of 149 (82.8%) patients had significant concerns regarding their medications. In general, (96, 53.3%), (82, 45.6%) and (58, 32.2%) patients were concerned about pill burden, high frequency of administration and side effects. Majority, (130, 72.2%) of patients expected a relief and not a cure from the medications they were using (**Table 13**).

Table 13: Concerns regarding medications among patients

Variables	Frequency (N=180)	Percentage (%)
Patients concerns about medication	149	82.8
Pill burden	96	53.3
Frequency of taking drugs	82	45.6
Side-effects	58	32.2

Additionally, 122 (67.8%) patients reported being compelled to take their medications by the persons they were living with. Furthermore, 35 (19.4%) patients also had reduced the doses or omitted taking some medications when feeling that their condition was under control or when feeling worse. Fifteen (8.3%) patients forgot to come for medications refill.

There were 40 (22.2%) patients complaining of various side effects that were caused by cytotoxic, nonsteroidal anti-inflammatory drugs (NSAIDS), and sulphur medications, they used (T**able 14**).

Table 14: Patient Attitudes towards medications

Variables	Frequency (N=212)	Percentages %
Compelled to take their medications	122	67.8%
Complained of side effects caused by medications	40	22%
Stopped taking medications when there condition stabilised	35	19.4%
Chose not to refill their prescriptions	15	8.3%

4.10 Patients' Knowledge and Understanding of Drug Therapy

Better understanding of the dose and frequency of the medications use was found among 72 (40%) and 52 (28.9%) patients. Regarding to medication use in relation to meals, only 57 (31.7%) patients had knowledge of the optimal time to take their medications **(Figure 7).**

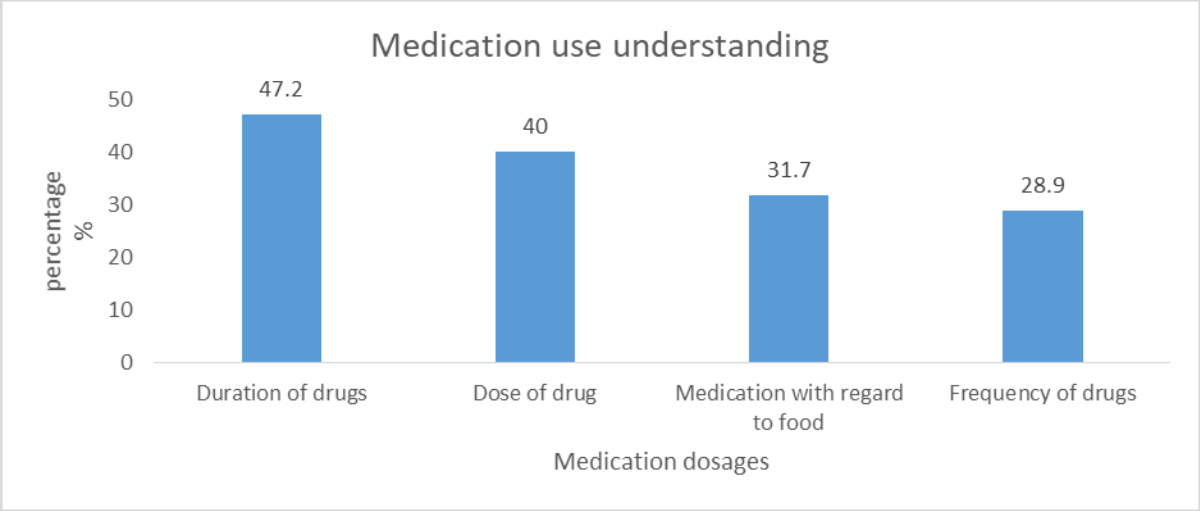

Figure 7: Patient better understanding about medications use.

4.11 Categorization of the therapeutic outcomes Status in the Management of T2DM

The outcome status of patients was categorised using the criteria described by Cipolle et al (1). This system had eight different categories. One hundred and five (58.3%) patients were categorised as stable T2DM. Only one patient (0.6%) was categorised as having an 'improved therapeutic status'. Cumulatively, 41.2% of the participants required some form of medication change. The prevalence of 'worsened' outcome status was very high at 20.6%. The remaining 20.6% had shown no or minimal clinical improvement (**Table 15**).

4.12 Categorization of the therapeutic outcomes in the Management of CVD

Only 34.4% of the participant were categorized as stable. A much higher proportion of patient whose condition worsened was observed for CVD disorders (27.2%). Cumulatively, majority of the patients (65.5%) had experienced little or no improvement or worsening CVD condition. The two extreme categories labelled as failure and expired 'were not observed'. Similarly, the most optimal outcome 'resolved' was not observed (**Table 15**).

Table 15: Categorization of patient status using the Cipolle et al criteria (N=180)

STATUS	T2DM n (%)	CVD n (%)
Stable	105 (58.3%)	62 (34.4%)
Improved	1 (100%)	0
Partially improved	18 (10%)	33 (18.3%)
Unimproved	19 (10.6%)	36 (20%)
Worsened	37 (20.6%)	49 (27.2%)

4.13 Bivariate Analysis on Factors Associated with Drug Therapy Problems

4.13.1 Association between social demographics characteristics with non-adherence

Bi-variable analysis was carried out to compare non-adherence as a drug therapy problem with the various predictor variables such as social demographic characteristics and medication perceptions among the study patients as seen below (**Table 16**). Half of the unmarried study participants were adherent to treatment. However, this difference was not statistically significant (p=0.098). In addition, all the (4, 100%) Muslim patients adhered to medications compared to Christian patients and this was found to be statistically significant (p= 0.023). Thirty-seven (50%) self-employed patients reported adherence as opposed to 32.7% formally employed and 31.5% not employed patients. However, this difference was not statistically significant (p= 0.056). The monthly income of the patient did not have any significant influence on occurrence of non-adherence (p= 0.213). BMI, smoking status, alcohol intake, level of education did not have statistical significant effect on non-adherence as seen below (**Table 16**).

Table 16: Association between social demographics characteristics with non-adherence

Variables	Drug Therapy Problem Adherence		
	Adherent n (%)	**Non-Adherent** n (%)	**P-Value**
Age :			
Young adult	1(50%)	1(50%)	
Middle age	62(57.9%)	45(42.1%)	0.597
Old age	46(64.8%)	25(35.2%)	
Sex:			
Male	33(54.1%)	28(45.9%)	0.259
Female	76(63.9%)	43(36.1%)	
BMI:			
Underweight	1(100%)	0	
Healthy weight	22(66.7%)	11(33.3%)	0.846
Overweight	45(59.2%)	31(40.8%)	
Obesity	41(58.6%)	29(41.4%)	
Marital status:			
Single	19(48.7%)	20(51.3%)	0.098
Married	90(63.8%)	51(36.2%)	
Smoking status:			
Current smoker	2(33.3%)	4(66.7%)	
Previous smoker	20(55.6%)	16(44.4%)	0.279
Never smoked	87(63%)	51(337%)	
Religion:			
Christians	109(61.9%)	67(38.1%)	**0.023***
Muslim	0	4(100%)	
Alcohol intake:			
Currently drinking	7(70%)	3(30%)	
Previously drinking	34(54.8%)	28(45.2%)	0.651
Never drunk	67(62.6%)	40(37.4%)	
Abstained drinking	1(100%)	0	
Level of education:			
Primary	46(62.2%)	28(37.8%)	
Secondary	39(55.7%)	31(44.3%)	0.612
College/university	17(63%)	10(37%)	
Informal	7(77.8%)	2(22.2%)	
Employment status:			
Formally employed	35(67.3%)	17(32.7%)	
Not employed	37(68.5%)	17(31.5%)	0.056
Self employed	37(50%)	37(50%)	
Monthly income(KES)			
None	38(66.7%)	19(33.3%)	
1-<5000	35(66%)	18(34%)	
5000-10000	13(44.8%)	16(55.2%)	0.213
10000-30000	12(50%)	12(50%)	
>30000	10()66.7%	5(33.3%)	

**statistically significant; BMI=Body Mass Index*

4.13.2 Association between medication experiences and adherence

Thirty one (32.3%) patients complained of high cost of drug compared to those who complained of low cost of drugs and that observed difference was statistically significant (p=0.047). In addition, 38 (29.2%) patients who had expectations of a relief and not a cure were compared to those who had expectation of a cure and was statistically significant (p<0.001).

Fifty six (45.1%) patients received more than five medications compared to those who received less than five medications had no difference observed and thus not statistically significant (p= 0.093). Additionally, twelve (30%) patients who suffered from side effects, were compared to those who had not suffered from side effects and was not statistically significant (p=0.201).

Thirty-seven (30.3%) patients compelled to take their medications were non-adherent to medication and this was statistically significant (p= 0.001). Additionally, majority of patients stopping medications when their condition was under control were compared to those who did not stop their medications when their condition was under control. This observed difference was statistical significance (p= <0.001). Complains of drugs not working, unavailability of drugs, and concerns about side effects of medications, did not have significant effect on non-adherence (**Table 17).**

Table 17: Association between medication experiences with non-adherence

Medication experiences	Drug Therapy Problems Adherence		
	Adherent n (%)	**Non-adherent n (%)**	**P-Value**
Not like taking medications:			
No	83(61%)	53(39%)	0.860
Yes	26(59.1%)	18(40.9%)	
Dislike drugs because they do not work:			
No	105(60.7%)	68(39.3%)	1.000
Yes	4(57.1%)	3(42.9%)	

Patient generally don't take medications			
No	109(61.6%)	68(38.4%)	0.06
Yes	0	3(100%)	
The cost of drugs			
No	44(52.4%)	40(47.6%)	**0.047***
Yes	65(67.7%)	31(32.3%)	
Availability of drugs			0.588
No	101(61.2%)	64(38.8%)	
Yes	8(53.3%)	7(46.7%)	
Patient expectations			
Expects a Cure	17(34%)	33(66%)	**<0.001***
Relief and no cure	92(70.8%)	38(29.2%)	
Concerned about number of drugs			0.224
No	55(65.5%)	29(34.5%)	
Yes	54(56.3%)	42(43.7%)	
Concerned about frequency of therapy			
No	64(65.3%)	34(34.7%)	0.170
Yes	45(54.9%)	37(45.1%)	
Polypharmacy			0.093
<5	36(70.6%)	15(29.4%)	
>5	73(56.6%)	56(43.4%)	
Concerned about side effects of medications:			
No	74(60.7%)	48(39.3%)	1.000
Yes	35(60.3%)	23(39.4%)	
Currently suffering from any side-effects:			0.201
No	81(57.9%)	59(42.1%)	
Yes	28(70%)	12(30%)	
Compelled to take medications			**0.001***
No	24(41.4%)	34(58.6%)	
Yes	85(69.7%)	37(30.3%)	
Choosing to refill prescription			0.103
No	6(40%)	9(60%)	
Yes	103(62.4%)	62(37.6%)	
Stopping when Condition is under control			
No	101(69.7%)	44(30.3%)	**<0.001***
Yes	8(22.9%)	27(77.1%)	

**statistically significant*

4.13.3 Independent Predictors of non-adherence

A binary logistic regression was run using a forward stepwise model building approach. This was carried out by regressing non-adherence against each of the covariates as shown below (**table 18)**.

The most important predictors for non-adherence were social demographic characteristics and six patient medication experiences; disliking drug because they don't work, concerns about number of pills, concerns about frequency of therapy, experiencing side-effects, compelling to take medications, stopping when condition is under control. For instance,

patients who had expectations of relief and not a cure had 0.24 times the odds (AOR=0.11-0.56; 95% CI: p=<0.001) of being non-adherent compared to those with expectations of cure.

Moreover, patients compelled to take medications had 0.28 times the odds (AOR=0.12-0.67; 95% CI: p=<0.001) of being non-adherent compared to those not compelled.

Also the odds (AOR=2.64-18.51; 95% CI: p=<0.001) of non-adherence amongst those who believed that they could stop taking medications when the disease was under control was 6.99 times the odds of non-adherence amongst patients who believed that they needed to take their medicines in the absence of any symptoms.

Table 18: Independent predictors of non-adherence

Variable	Bivariate analysis COR (95%CI)	P-Value	Multivariate analysis AOR (95%CI)	P-Value
Cost of drugs	0.52(0.29-0.96)	**0.037**	0.52 (0.25-1.08)	0.081
Patient expectations	0.21(0.11-0.43)	**<0.001**	0.24 (0.11-0.56)	**0.001***
Compelled to take medications	0.31(0.16-0.59)	**<0.001**	0.28 (0.12-0.67)	**<0.001***
Stopping when condition is under control	7.74(3.26-18.39)	**<0.001**	6.99 (2.64-18.51)	**<0.001***

*COR=Crude Odds Ration; AOR=Adjusted Odds Ratio: CI=Confidence Interval; *statistically significant result.*

4.14 Bivariate and multivariate results of Needs additional drug and dosage too low as prescriber related patterns

Bi-variable analysis was carried out to need for an additional drug as a drug therapy problem with the various predictor variables such as social demographic characteristics and clinical characteristics among the study patients. There were no correlation between the socio-demographic characteristics and the requirement for an additional drug (**Table 19**).

Table 19: Association between social demographic characteristics with Needs Additional drug

Variables	Drug Therapy Problem		
Social demographics characteristics	Needs additional drug		
	No n %	Yes n %	P-Value
AGE :			0.823
Young adults	1(50%)	1(50%)	
Middle age	57(53.3%)	50(46.7%)	
Old age	35(49.3%)	36(50.7%)	
Sex:			0.876
Male	31(50.8%)	30(49.2%)	
Female	62(52.1%)	57(47.9%	
BMI:			0.826
Underweight	1(100%)	0	
Healthy weight	17(51.5%)	16(48.5%)	
Overweight	41(54%)	35(46%)	
Obesity	34(48.6%)	36(51.4%)	
Marital status:			0.588
Single	22(56.4%)	17(43.6%)	
Married	71(50.4%)	70(49.7%)	
Smoking status:			0.205
Current smoker	3(50%)	3(50%)	
Previous smoker	14(38.9%)	22(61.1%)	
Never smoked	76(55.1%)	62(44.9%)	
Religion:			1.000
Christians	91(51.7%)	85(48.3%)	
Muslim	2(50%)	2(50%)	
Alcohol intake:			0.937
Currently drinking	5(50%)	5(50%)	
Previously drinking	33(53.2%)	29(46.8%)	
Never drunk	55(51.4%)	52(48.6%)	
Abstained drinking	0	1(100%)	
Level of education:			0.645
Primary	34(46%)	40(54.1%)	
Secondary	39(55.7%)	31(44.3%)	
College/university	15(55.6%)	12(44.4%)	
Informal	5(55.6%)	4(44.4%)	
Employment status:			0.929
Formally employed	28(53.9%)	24(46.2%)	
Not employed	27(50%)	27(50%)	
Self employed	38(51.3%)	36(48.7%)	
Monthly income:			0.540
None	34(59.6%)	23(40.4%)	
<5000	23(43.4%)	30(56.6%)	
5000-10000	15(51.7%)	14(48.3%)	
10000-30000	13(54.2%)	11(45.8%)	
>30000	7(51.7%)	8(48.3%)	

BMI=Body Mass Index

4.14.1 Association between Participants' Clinical Characteristics with Needs Additional Drug

There was statistically significant association between the duration of T2DM and the requirement for an additional drug (p=0.034). The proportion of patients who had diabetes for less than 72 months who were requiring an additional drug were more than patients who had more than 72 months of T2DM. In addition, 34 (57.6%) patients with poorly controlled blood sugar were compared to those who had normal blood sugar. However, no statistical difference was observed in the requirements for an additional therapy (p=0.068). However, eighteen (75%) patients prescribed furosemide had statistical difference observed (p=0.008) on the requirements for an additional treatment.

The association between the rest of the clinical characteristics and the need for additional drug revealed no statistical difference **(Table 20).**

4.14.2 Independent Predictors of Needs Additional Drug

A binary logistic regression was run using a forward stepwise model building approach. This was carried out by regressing need for additional drug against each of the covariates as shown in (**Table 21)**. As seen in the table below, the proportion of patients with more than 72 months of T2DM had 0.39 times the odds (COR=0.18-0.79; 95% CI: P=<0.010) of getting an additional drug compared to those who lived with it for less than 72 months. Patients with poorly controlled blood sugars using 2 hours post prandial test had two times the odds (AOR= 1.80; CI: 0.94-3.44; P= 0.075) of getting an additional drug compared to those who had normal 2 hours post-prandial test. Patients taking furosemide had 4.71 times the odds (AOR=1.72-12.89; CI: P=< 0.003) of being prescribed an additional drug compared to those who had none.

Table 20: Association between Participants' Clinical Characteristics with Needs Additional Drug

Clinical characteristics	Drug Therapy Problem Needs additional drug No n (%)	Yes n (%)	P-Value
Duration of T2DM			**0.034***
<72months	21(38.9%)	33(61.1%)	
>72months	72(57.1%)	54(42.9%)	
Duration CVD			0.425
<72months	27(46.6%)	31(53.5%)	
>72months	66(54.1%)	56(45.9%)	
Comorbidities			0.348
No	65(54.2%)	55(45.8%))	
Yes	28(46.7%)	32(53.3%)	
Blood Pressure test			0.164
Normal range	39(59.1%)	27(40.9%)	
Poor controlled	54(47.4%)	60(52.6%)	
2 Hours post prandial test			0.068
Normal range	68(56.7%)	52(43.3%)	
Poorly controlled	25(42.4%)	34(57.6%)	
HbA1c test			0.814
Normal range	5(62.5%)	3(37.5%)	
Poorly controlled	10(47.6%)	11(52.4%)	
Metformin			0.130
No	9(36%)	16(64%)	
Yes	84(54.2%)	71(45.8%)	
Gliclazide			0.066
No	81(49.4%)	83(50.6%)	
Yes	12(75%)	4(25%)	
Beta-blockers			0.110
No	59(47.6%)	65(52.4%)	
Yes	34(60.7%)	22(39.3%)	
Furosemide			**0.008***
No	87(55.8%)	69(44.2%)	
Yes	6(25%)	18(75%)	

*T2DM= Type 2 Diabetes Mellitus; CVD= Cardiovascular diseases;*statistically significant result;* HbA1c= Haemoglobin A1c

Table 21: Independent variables of Needs Additional Drug

Variable	Bivariate analysis		Multivariate analysis	
	COR (95%CI)	P-Value	AOR (95%CI)	P-Value
Duration of T2DM	0.48(0.25-0.92)	**0.026***	0.39 (0.19-0.78)	**0.007***
2 hours post prandial test	1.62(0.88-3.00)	0.123	1.80 (0.94-3.44)	0.075
Furosemide	3.78(1.42-10.04)	**0.008***	4.71 (1.72-12.89)	**0.003***

*COR=Crude Odds Ration; AOR=Adjusted Odds Ratio: CI=Confidence Interval; *statistically significant result; T2DM=Type 2 Diabetes Mellitus;* HbA1c= Haemoglobin A1c

4.15 Bivariate analysis between Dosage too low and other variables

4.15.1 Association between Dosage too low and the Participants' sociodemographic and clinical characteristics

Bi-variable analysis was carried out on dosage too low as a drug therapy problem with the various predictor variables such as social demographic characteristics and clinical characteristics among the study patients as seen below **(Tables 22 and 23).** At least a third (45, 37.8%) of the female patients had dosage too low to treatment, which showed statistical significant difference in getting a low dose (p=0.046). Cumulatively, patients with no income showed a statistically significant difference in getting a low dose (p=0.045). Body Mass Index, marital status, religion, alcohol intake, level of education and employment status showed no statistically significant effect on the occurrence of dosage too low as shown below (**Table 22 and 23).**

Table 22: Association between Dosage too low and socio-demographic characteristics of the study participants

Social Demographic characteristics	Drug Therapy Problem		
	Dosage too low		
	No n (%)	Yes n (%)	P-Value
Age:			1.000
Young adults	2(100%)	0	
Middle age	71(66.4%)	36(33.6%)	
Old age	48(67.6%)	23(32.4%)	
Sex:			**0.046***
Male	47(77.1%)	14(22.9%)	
Female	74(62.2%)	45(37.8%)	
BMI:			0.212
Underweight	0	1(100%)	
Healthy weight	19(57.6%)	14(42.4%)	
Overweight	55(72.4%)	21(27.6%)	
Obesity	47(67.1%)	23(32.9%)	
Marital status:			0.338
Single	29(74.4%)	10(25.6%)	
Married	92(65.3%)	49(34.7%)	
Smoking status:			0.059
Current smoker	6(100%)	0	
Previous smoker	28(77.8%)	8(22.2%)	
Never smoked	87(63%)	51(37%)	
Religion:			0.305
Christians	117(66.5%)	59(33.5%)	
Muslim	4(100%)	0	
Alcohol intake:			0.931

Currently drinking	7(70%)	3(30%)	
Previously drinking	43(69.4%)	19(30.6%)	
Never drunk	70(65.4%)	37(34.6%)	
Abstained drinking	1(100%)	0	
Level of education:			0.630
Primary	51(68.9%)	23(31.1%)	
Secondary	49(70%)	21(30%)	
College/university	16(59.3%)	11(40.7%)	
Informal	5(55.6%)	4(44.4%)	
Employment status:			0.700
Formally employed	35(67.3%)	17(32.7%)	
Not employed	34(63%)	20(37%)	
Self employed	52(70.3%)	22(29.7%)	
Monthly income:			**0.045***
None	30(52.6%)	27(47.4%)	
<5000	37(69.8%)	16(30.2%)	
5000-10000	21(72.4%)	8(27.6%)	
10000-30000	19(79.2%)	5(20.8%)	
>30000	13(86.7%)	2(13.3%)	

**statistically significant; BMI=Body Mass Index*

Forty-five (39.5%) patients had poor controlled blood pressures and this was found to be statistically significant with low doses of medication (p=0.014). More than a half (35, 59.3%) patients had poor controlled blood sugar and this was found to be statistically significant in getting low doses of medication (p= 0.0001). Almost a half (10, 47.6%) of the patients screened with HbA1c reported to have dosage too low to treatment. This difference was statistically significant (p= 0.050). Patients taking metformin did not have any significant changes in their dosages (p= 0.172). T2DM and CVD durations, gliptins use, gliclazide use, beta blockers and furosemide did not have statistical significant effect on dosages as seen below **(Table 23)**.

Table 23: Association between Clinical characteristics with Dosage Too Low

Clinical characteristcs	DRUG THERAPY PROBLEMS		
	Dosage too low		
	No (n %)	Yes n (%)	P-Value
Duration of T2DM			0.606
<72months	38(70.4%)	16(29.6%)	
>72months	83(65.9%)	43(34.1%)	
Duration CVD			0.314
<72months	36(62.1%)	22(37.9%)	
>72months	85(69.7%)	37(30.3%)	
Comorbidities			1.000
No	81(67.5%)	39(32.5%)	
Yes	40(66.7%)	20(33.3%)	
Blood Pressure test			**0.014***
Normal range	52(78.8%)	14(21.1%)	
Poor controlled	69(60.5%)	45(39.5%)	
2 Hours post prandial test			**<0.0001***
Normal range	97(80.8%)	23(19.2%)	
Poorly controlled	24(40.7%)	35(59.3%)	
HbA1c test			0.050*
Normal range	8(100%)	0	
Poorly controlled	52(52.4%)	10(47.6%)	
Gliclazide			1.000
No	110(67.1%)	54(32.9%)	
Yes	11(68.8%)	5(31.3%)	
Metformin			0.172
No	20(80%)	5(20%)	
Yes	101(65.2%)	54(34.8%)	
Beta-blockers			1.000
No	83(66.9%)	41(33.1%)	
Yes	38(67.9%)	18(32.1%)	
Furosemide			1.000
No	105(67.3%)	51(32.7%)	
Yes	16(66.7%)	8(33.3%)	

*T2DM= Type 2 Diabetes Mellitus; CVD= Cardiovascular diseases;*statistically significant result;* HbA1c= Haemoglobin A1c

4.15.2 Independent Predictors of dosage too low

A binary logistic regression was run using a forward stepwise model building approach. This was carried out by regressing dosage to low against each of the covariates as shown below (**Table 24)**.Female patients had 2.04 times the odds (COR=1.01-4.12; 95% CI: P=<0.046) of being prescribed low doses of drugs compared to their male counterparts.

Cumulatively, patients with no income had 0.64 times the odds (AOR=0.47-0.89; 95% CI: P=<0.007) of receiving dosage too low as compared to those who were earning.

Patients with poorly controlled blood pressure had 2.76 times the odds (AOR= 1.26-6.09; 95% CI: p= 0.012) of getting dosage too low as compared to those who had normal blood pressure. Patients with poorly controlled blood sugars using 2 hours post prandial test had 4.57 times the odds (AOR= 2.19-9.52; CI: p=< 0.001) of getting dosage too low compared to those who had normal 2 hours post prandial test.

Table 24: Independent predictors of Dosage too low

Variable	Bivariate analysis		Multivariate analysis	
	COR (95%CI)	**P-Value**	**AOR (95%CI)**	**P-Value**
Sex	2.04(1.01-4.12)	**0.046**	1.76 (0.81-3.86)	0.155
Monthly income	0.66(0.49-0.87)	**0.003***	0.64 (0.47-0.89)	**0.007***
Poor Blood pressure control	2.42(1.20-4.88)	**0.013***	2.76 (1.26-6.09)	**0.012***
2 hours post prandial test	5.21(2.65-10.24)	**<0.0001***	4.57 (2.19-9.52)	**<0.0001***
HbA1c	1.22(0.78-1.93)	0.386	1.14 (0.65-2.01)	0.630
Metformin	2.14(0.76-6.02)	0.150	1.80 (0.58-5.61)	0.311

*COR=Crude Odds Ration; AOR=Adjusted Odds Ratio: CI=Confidence Interval; *statistically significant result;* HbA1c= Haemoglobin A1c

CHAPTER FIVE: DISCUSSION, CONCLUSIONS AND RECOMMENDATIONS

5.1 Introduction

This section discusses the results obtained after data collection and analysis. The initial part of this section describes the study participants and comparison of these characteristics with other similar studies. This is followed by a comparison or contrast of the results with other similar studies.

5.2 Characteristics of the study population

Majority of participants suffering from both T2DM and CVD were aged between 36 to 65 years. The mean age of the patients was 61.6 (±11.3years) with only 1.1% of those affected below 35 years. Studies have shown that both type 2 DM and CVD are more experienced as the age advances (30). There was higher proportion of females with both T2DM and CVD compared to males. Probably the rates of attendance of males to outpatient clinics was lower than that of female counterparts as has been revealed in many settings (2). Additionally, majority of the participants were married which tallies with a closely related study done in the same setting (19,56). Most (95%) had attained some formal education, ranging from primary school to the university. Having education predisposes the recipient to better health. In comparison, a study conducted in USA showed a similar findings that those patients with lower education level of primary school had a risk of poor health outcomes (4, 5).

5.3 Prevalence of cardiovascular and diabetic complications

A comprehensive review of systems and complete physical examination was conducted to identify any drug-related adverse events, untreated and poorly managed cardiovascular and diabetic complications, which were classified as a prescriber-related DTPs.

In this study, ninety two (51%) participants had severe daytime malaise which is a sign of many illnesses. Furthermore, chronic malaise is one of the signs of chronic uncontrolled DM especially in patients with obesity (59). In Kenya, chronic malaise is not usually recognized as a key problem amongst patients with CVD and DM. Given that slightly

over 50% of participants complained of severe daytime malaise, this is an issue that needed to be addressed.

Eighty (44.4%) patients complained of weight gain, which could have been an adverse drug reaction of sulphonyl-ureas, thiazolidinediones and insulin (60). Nearly a third of the participants complained of frequent urination (65, 36.1%) which was probably suggesting poor glycemic control. Chronic hyperglycemia may cause diabetic neuropathy resulting in bladder dysfunction leading to urinary retention. This leads to decreased bacterial clearance by micturition, thus facilitating bacterial growth and urinary tract infection (60, 61).

The comprehensive review of systems also revealed there were several other prescriber related DTPs. The most prevalent were hearing impairment with nearly 34 (18.9%) complaining of tinnitus and 24 (13.3%) had hearing loss. In India it has also been observed that there is a very high prevalence of auditory and visual impairments amongst diabetes patients (8, 9). Nineteen (10.6%) patients had poor vision with whom 44.5% had poor glycemic control.

In addition, the study revealed that HbA1c were not routinely done. Furthermore, one study conducted in KNH showed that levels of glycated hemoglobin (HbA1c) are rarely monitored (65) and yet the relationship between HbA1c and microvascular complications are well established. Glycemic levels of >8% HbA1c have been linked to alteration in the host defense in the pulmonary system increasing the risk of pneumonia, or recurrent or chronic bacterial pneumonia and therefore, frequent monitoring in T2DM is critical (12, 13).

Under-dosing of antidiabetic medications, which was encountered in our study, may contribute to poorly controlled diabetes (1). It was noted in the study that the clinicians in Kenyatta national Hospital did not have a pocket reference guidelines and as such probably under-dosed the patients. A study by Professor English found that in many settings in Kenya, clinicians do not have access to treatment guidelines (68). Therefore, they could have been forced to make uninformed decisions with regard to patient

management. This problem could be addressed by making guidelines readily available within the clinic.

A key finding was that there was a very high prevalence of obesity with nearly four out of ten patients being classified as obese. In the USA and other countries a high prevalence of obesity has also been observed amongst T2DM patients (60, 69). Obesity exacerbates diabetes in patients with both T2DM and cardiovascular disease (70). It is notable that patients who were on insulin had gained weight (69).

An unexpected findings was a high prevalence and symptoms of upper respiratory tract complains such as nasal congestion, throat problems and chest pain, coughing and shortness of breath. A possible explanation was the cold climate over the month of June and July under which the study was conducted. The high prevalence of higher respiratory complains highlights the need for prophylaxis with influenza and pneumococcal vaccines (66,71,72). Unfortunately, these vaccines are not routinely administered to adults in Kenya.

5.4 Drug therapy problems in out-patients with diabetes and cardiovascular disease

All the seven different types of DTPs were adequately studied. The findings showed four types of drug therapy problems. Needs additional drug therapy, dosage too low, adverse drug reactions and nonadherence had significant prevalence. Each of these four problems are discussed separately.

5.4.1 Needs for additional drug therapy

Firstly, most patients needed pneumococcal vaccine against pneumonia. Pneumococcal pneumonia is a common disease among patients with chronic illness such as T2DM. The American Diabetes Association (ADA) recommends that adults aged ≥65 years, should receive a 23-valent pneumococcal polysaccharide vaccine (PPSV23), regardless of prior pneumococcal vaccination history (17, 18). Most participants required a vaccine but none had received one.

Another unmet medication need was poorly controlled diabetes. As described by Moses et al (2014), most glucose-lowering therapies have limitations, including insulin-

dependent mechanisms of action, losing efficacy over time (73). In addition, they are associated with side effects such as hypoglycemia and weight gain. However, there are new glucose-lowering drugs that act independently of insulin, and provide improved tolerability compared with traditional medications for T2DM. These include SGLT2 inhibitors which have a novel insulin-independent mechanism and are preferred to lower elevated plasma glucose levels in patients with T2DM. Most of the patients in this study may have required this class of agents especially in combination with metformin for the optimal glycemic control.

Poorly controlled hypertension was another unmet need. Based on JNC 8 guidelines, with a target level of ≤140/90 mm Hg (74), a hundred and fourteen (63.3%) patients were not at goal, which put patients at risk for both micro- and macrovascular diseases. Though most patients were on a calcium channel blockers, it seemed to be inadequate alone or in combination with other drugs for the attainment of adequate blood pressure control. A significant number of patients on antihypertensive medications required the combination of losartan and hydrochlorothiazide for better control of blood pressure (21, 23). Limitation of existing guidelines is that they are based on Caucasian populations who tend to respond better to existing antihypertensive drugs such as ACEI (76). Local guidelines need to be developed to identify combinations that are effective in African populations (75). The JNC 8 guidelines attempt to address problems of poorly controlled hypertension in black populations. Self-monitoring of blood pressure needs to be promoted to improve blood pressure control (77).

The third unmet medication therapy need was prophylactic use of hypolipidemic, and antiplatelet therapy agents. This was in line with findings in other studies that showed need for such preventive therapy (4). Hypolipidemic therapy is required in diabetic patients aged 40-75 years and LDL-C of 70 to 189mg/dl according to 2013 America College of Cardiology and America Heart Association guidelines and many other supporting studies (11,38,78,79). This is important in order to reduce the risk of atherosclerotic cardiovascular diseases (79). However, in our study, seventy (70, 38.9%) patients who were eligible for hypolipidemic therapy were not on these drugs. These

findings concur with a study from Australia where 42% of patients were not receiving statins (80).

American Diabetes Association guideline (2013) recommends use of low dose Aspirin (75-162mg/day) in patients aged >40years with Diabetes and CVD for prevention of thrombotic attacks. One twenty seven (70.6%) patients were not on this preventive medication subjecting them to a high risk of developing stroke (78).

It is imperative that non-pharmacological interventions including changes in lifestyle must be addressed in order to fully manage the two conditions. In this study, seventy (38.9%) obese patients, (6, 3.3%) and (10, 5.6%) smokers, required an intensive counselling program behavior change, with ongoing support and frequent follow-up. These were needed for management of weight, cardiovascular risk factors, and glycaemia in diabetes. These results were almost similar to a study performed in France which recommended diet, physical activity and weight control as cornerstones of DM treatment (70,81).

Upon review of systems, there were other untreated medical conditions noted which were constipation and diarrhea. Possible reasons are that patients with uncontrolled diabetes may suffer from small intestinal and colorectal dysfunctions characterized by constipation and diarrhea. Constipation alternating with diarrhea is one of the most common symptoms of diabetic enteropathy (82).

Thirty-eight (21.1%) patients complained of neuropathic pain due to poor controlled glucose. These results were similar to a study conducted in UK which showed painful neuropathic pain among T2DM patients. This study highlighted the need for early identification and treatment (83)

5.4.2 Low doses of prescribed medications

The prevalence of under-dosage was, 59 (32.8%). Dosages were considered low if glycemic or cardiovascular goals were not attained. The prevalence of under-dosage was similar to that reported in a study conducted by Kanagala et al at 32.28% (4). Two other studies, conducted in high income countries where there are well established systems for

electronic prescribing and drug monitoring, found a lower prevalence of under-dosage (34, 35). The high prevalence of under-dosage in the study site could be due to lack of published dosing guidelines and inter-patient variation in drug response which was beyond the scope of the present study.

5.4.3 Adverse drug reactions

Only eight patients (4.5%) responded that they had experienced any adverse drug event. However, there were significant number of symptoms that could be related to drug adverse events such as tinnitus, rash, headache, and abdominal pains. A study done by strand et al in USA and Lisper et al in KNH, reported that the prevalence of suspected ADRs amongst patients with CKD and DM reported a higher prevalence of 8% (3, 20). However, the data collection tool of this study was also not well designed to collect data on all possible types of ADRs. Better designed studies have reported much higher prevalence of ADRs ranging from 8.7 to 32.28% (2,4,6,45).

The overall prevalence of any cough was 16.7% making it the most commonly suspected ADR. This could be attributed to ACEIs which constituted more than 25% of all prescribed antihypertensive. This is a manageable adverse drug event as ARBs can be used as alternatives. This findings were found to be similar by CHEST evidence-based clinical guideline 2006 (86). All patients on insulin seemed to gain weight (87). Metformin and insulin were the most common causes of ADR amongst diabetic patients (13–15, 29, 38, 39).

5.4.4 Prevalence of non-adherence and its risk factors

Non-adherence is a patient-related DTP. The adherence to prescribed medications was assessed using questionnaire that addressed patient perception on medication use. This was adopted from pharmacotherapy work-up ® notes on medication experience (1). This elucidated the patient experience with multiple aspects of medication use including adherence. This approach differs substantially from established quantitative methods for measuring adherence such as Morisky scale (90) and pill-counts (91) and refills

reference. The approach delineates causes of nonadherence. Often the patients admitted non-adherence before being asked directly on their adherence status.

The prevalence of non-adherence in this study was high at 39.4%. However, other study findings showed extremely high prevalence of non-adherence (22, 46). The key reasons for nonadherence provided by the patient was failure to understand the instructions (30, 16.7%). This showed that patients never received adequate counselling on the use of their medication. A study done in Malaysia also reported that one of the key reasons for failure to understand the instructions led to non-adherence (48).

The second most common cause of non-adherence was patients preferring not to take medications because they simply disliked them. In many settings all-over the world, patients view medication taking as 'interruptive, discouraging, frustrating, confusing, and tiring' (1). These findings highlight the need for medication management as a solution to non-adherence. The pharmacist role is critical to understanding the preferences, beliefs, expectations and concerns of the patient about medications and in order to meet their drug-related needs (1). These patients admitted to have received inappropriate advice from their families and friends while some admitted inability to understand prescriber instructions. This led to 24 (13.3%) patients deliberately stopping the prescribed drug product.

Additionally, 13 (7.2%) patients failed to take their medications because of high cost of drug product. Most of these patient's socio-economic status was wanting as most antihypertensive, anticancer, and anti-arthritis drugs purchased from private chemist were expensive. This finding was similar to other findings conducted in USA (92).

On interviewing the patients, many complained that they were required to pick medications from the main pharmacy which is almost half a kilometer from the T2DM clinic. They often find long queues in the pharmacy, and therefore they failed to pick medicines and went to pick medications in private pharmacies. To improve patient management and adherence, the hospital needs to look into ways, to start a pharmacy within T2DM clinic.

In our study, (164, 91.1%) patients had at least one drug therapy problems in each category. This high prevalence was found similar to other studies done in Kenya (100%), Indonesia (62.2%), and Malaysian (90.5%) (19, 33, 42, 46, 47). However, no participants reported to have dosage too high, although there was dosage too high that was reported in a study done in Malaysia (3).

5.4.5 Predictors of non-adherence

Logistic regression was done to identify the key predictors of nonadherence. The only variables that had significant were perceptions of cost, expectations of a cure, coercion to take medicines and wrong believes about drug holidays. Unexpectedly a greater proportion of those who claimed found drugs affordable were adherent compared to those who claimed that medication were costly (47.6% verse 32.3%; p=0.047).

The crude measure of association between non-adherence and perceived cost of medications was negatively associated (COR 0.52; 95% CI 0.29, 0.96; p=0.037).

Therefore, the association between perceived cost of medications and non-adherence lost significance on adjusting for confounding by patients expectations and being forced to take medications and stopping to take when condition is under control. This meant that perceived cost of drug is not a major predictor of nonadherence, though it has an influence. This might be attributed by the fact that most patients obtained medications from the KNH pharmacy where the cost is subsidized at a cost of shillings 200. This means that patient expectation and beliefs are more important predictors of non-adherence.

The most important predictor was the belief that it was acceptable to stop taking medications when diabetes was under control. The impact of this belief was very powerful because 77.1% of those who believed that they could take drugs holiday were non-adherent. To address this issue the pharmacist should train patients that taking holiday is unacceptable. A guideline on good practice in managing drugs noted that pharmacist can provide reassurance and information to patients and improve adherence (1,93).

The second key predictor of nonadherence was willingness to take medicines. One twenty two patients admitted that they had to be forced to take medicines by a relative. Of this number, 30% were non-adherent as opposed to 58.6% of those who claimed that they took their medic without any coercion from relative. On logistic regression we found a negative association between coercion to take medicines and nonadherence (AOR 0.28; 95% CI: 0.12, 0.67; p=<0.001). This means that patients who did not have a relative to force them to take medications, were less likely to be adherent. This observation adds support to the concept of DOT (Directly Observed Therapy) and medication buddies which is employed in the TB-program. The studies conducted in USA (94) and New Zealand (95) noted the same findings. As an intervention, there should be a greater involvement of a significant others and close relatives in outpatients management.

The strongest risk factor was perception that one could stop taking medications when the condition is under control. The adjusted odds ratio for association between this wrong perception and non-adherence was 6.99 (95% CI: 2.64, 18.51; p=<0.001). One study has shown that patients stopping medications when their condition was under control were non-compliant. The same study reported that perceived long term side effects can be the reason for stopping medications (96).

Similarly, a negative association was noted between patient expectations for a cure and nonadherence. The adjusted odds ratio was 0.24 (95% CI 0.11, 0.56; p=<0.001). This means that patients who had expected a cure were more likely to be non-adherent compared to patients who expected a relief and not a cure. The main reason for non-adherence among the patients who wrongly expected a cure were a reflection of their understanding of the disease. Patients who wrongly expected a cure are less likely to understand an illness and they tend to be less educated. Lower levels of education are generally associated with poor adherence (53, 54).

5.4.6 Predictors of needs additional drug

A logistic regression analysis was conducted to establish key predictors of needs addition drug.

The strongest risk factor was an antihypertensive, furosemide. The adjusted odds ratio for association between furosemide and need for an additional drug was 4.71 (95% CI: 1.72, 12.89; p=0.003). The reason for this association is unclear. However, we would postulate that perhaps furosemide was being used for the management of hypertension and we know that furosemide duration of action is very short and thus not working to control blood pressure. Therefore, this patient required an additional drug to control blood pressure (99, 100).

There was a negative association between the duration of illness (more than 72 months) and need for an additional drug (AOR 0.39; 95% CI 0.19, 0.78; p=0.007). This meant that patients who had had T2DM of more than 72 months were less likely to need an additional drug. A possible explanation was that patients developed self-care skills for their long-term condition over a long period of time. This makes them adhere to prescribed medications and practice self-monitoring of BP and blood sugar. This reduces the need for an additional drug. This finding was similar to another study finding conducted in UK (101) which showed patients better equipped to coordinate their care, leading to fewer missed general practice and outpatient appointments.

5.4.7 Predictors of patients receiving low dose medications

We found that patients who had elevated sugar levels on conducting the two-hour postprandial test were more likely to be on a low dosage. This was the strongest predictor that the patient was on a low dosage. This shows that the test could be a reliable indicator of poor patient management. The adjusted odds ratio for association between this test and under-dosing was 4.57 (95% CI: 2.19, 9.52; p=<0.001). Under-dosing can be caused by a drug interaction which reduces the amount of active drug prescribed. A possible reason was that patients on insulin therapy were prescribed high doses of (25mg) hydrochlorothiazide which reduced sensitivity of insulin (102).

With respect to hypertension, most patients had poor blood pressure control. This variable was positively associated with low medication dosages. The adjusted odds ratio for association between poor blood pressure control and under-dosing was 2.76 (95% CI: 1.26, 6.09; p=0.012). The possible explanation was that all patients who received

inadequate dosages of antihypertensive had elevated blood pressure. Heavy workload on a busy clinic days could have contributed to poor quality of prescribing (103) leading to poor patient management. A study done in Brazil noted a high prevalence of under-dosing leading to poor management (104)

There was a negative association between lack of income and under-dosing (AOR 0.64; 95% CI: 0.47, 0.89; p=0.007). This negative association indicates that as income increased the chances of being under-dosed decreased. Lack of income among patients do not promote under-dosing. This therefore could not be evaluated and therefore the reason was beyond the scope of this study. However a study conducted in USA showed that paying for medications contributed to non-adherence (105).

5. 5 Strengths and weakness of the Study

This was our first study conducted in sub-Saharan Africa that attempted to assess drug therapy problem among adult patients with T2DM and CVD in KNH. The study identified social demographic characteristics, clinical characteristics and medication experiences of patients associated with other types of DTPs. It identified statistically significant association of patient expectations and non-adherence, coercion to take medications and behavior of stopping medications when the condition is under control. Additionally, there was a statistically significant association of needs for additional drug therapy and duration of T2DM, needs for additional drug and furosemide medication. Statistically significant association of dosage too low and monthly income, poor blood pressure control, and 2 hours postprandial test. However, the study was not able to identify other diagnosed CVD other than hypertension. Furthermore, documentation of other CVD in the site of study was found wanting. In addition, the data collection tool of this study was not well designed to collect data on all possible types of ADRs. The study was only limited to T2DM and CVD patients and therefore, its finding could not be generalized to patients with other chronic conditions. Finally, this study selection and information was highly biased due to carrying out cross-sectional design. Possible reasons were patients could not be able to recall important information regarding their illnesses and medications particularly the elderly.

In spite of above mentioned weaknesses, this study qualifies as a benchmark for further research among patients with T2DM and CVD.

Conclusion

Needs for an additional drug, dosage too low, and adherence were the most common types of DTPs identified among patients with both T2DM and CVD. The multivariate logistic regression identified statistically significant association of patient expectations and non-adherence, coercion to take medications and behavior of stopping medications when the condition is under control. Additionally, it identified a statistically significant association of needs for additional drug therapy and duration of T2DM and furosemide medication. Statistically significant association of dosage too low and monthly income, poor blood pressure control, and 2 hours postprandial test.

Recommendations for practice

1. The fact that the study uncovered a number of DTPs using a validated pharmacist's patient care process, training pharmacists on this approach will greatly enhance diagnosis of DTPs in other types of conditions.
2. Since non-adherence was significant in this study, the KNH should be encouraged to have educational counselling program to improve adherence in these patients.
3. Lack of immunization was a problem identified among all elderly patients in this study. Therefore, public health programs should address this gap including provision of influenza and pneumococcal vaccines use in all elderly patients.
4. Obesity was the most significant among the patients secondary to sulphonyl-ureas and insulin. Therefore, inclusion of Dipeptidyl peptidase-4 (4 DPPT) inhibitors and Sodium-glucose co-transporter-2 (SGLT) inhibitors in KNH Formulary is advised.
5. More frequent monitoring of drug therapy outcome is necessary to address two DTPs 'needs additional drug and dosage too low' as prescriber-related DTPs in KNH.

Recommendations for future research

1. Further prospective studies should be done in Kenya to establish the impact of patient's beliefs, perceptions, experiences and concerns on the medications prescribed to them as an effort to address poor compliance.
2. This was a cross-sectional study and therefore, interventional studies are important to establish the impact of Pharmacists involvement in the medication therapy management of patients with T2DM and CVD.

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APPENDICES

Appendix 1: Eligibility screening form

Kenyatta National Hospital Diabetes and Endocrinology clinics **OPC number_____** **Study unique number_____**	
Criteria	**Remark as YES or NO**
Adult aged more than 18 years	
On insulin/ oral anti T2DM and an ANTI-CVD	
On psychiatric problem	
Not pregnant	
No any organ dysfunction	
Given consent	

If all **YES** please proceed to the study Questionnaire

Appendix 2A: Participant information form

ASSESSMENT OF DRUG THERAPY PROBLEMS IN ADULT PATIENTS WITH BOTH CARDIOVASCULAR DISEASES AND TYPE 2 DIABETES IN KNH

Principal Investigator

Dr. George Njuguna Mugane- Master of Pharmacy (Clinical Pharmacy) Second-year student at the University of Nairobi

Supervisors: Prof Ndemo-Lecturer, UoN; Dr. Nyamu – Lecturer, UoN

Introduction

I, George Njuguna Mugane, a postgraduate student at the University of Nairobi, school of pharmacy, would like to tell you about a study being conducted by the above-listed researchers. The purpose of this consent form is to give you the information you will need to help you decide whether or not to be a participant in the study. Feel free to ask any questions about the purpose of the research, what happens if you participate in the study, the possible risks and benefits, your rights as a volunteer, and anything else about the research or this form that is not clear. When we have answered all your questions to your satisfaction, you may decide to be in the study or not. This process is called 'informed consent'. Once you understand and agree to be in the study, I will request you to sign your name on this form. You should understand the general principles which apply to all participants in a medical research: i) Your decision to participate is entirely voluntary ii) You may withdraw from the study at any time without necessarily giving a reason for your withdrawal iii) Refusal to participate in the research will not affect the services you are entitled to in this health facility or other facilities. We will give you a copy of this form for your records.

May I continue? **YES** **NO**

This study has approval by The Kenyatta National Hospital-University of Nairobi Ethics and Research Committee protocol No.: _____

WHAT IS THIS STUDY ABOUT?

Most adult patients with multi-morbidity are known to be disadvantaged when it comes to health care access, management, and treatment. They have drug therapy problems simply due to the severity of their conditions and multi-medications. In this study, we will ask you to state your experiences with medications and the issues you get with taking medications. Our purpose is to find out whether the medications you are prescribed are working for you or have any trouble, to find out whether they are safe and effective, to find out which drugs the patient is using and identify things the patient is doing or not doing that may be significantly increasing occurrences of Drug Therapy Problems. There will be approximately 80 participants in this study randomly selected. We are asking for your consent to consider participating in this study.

WHAT WILL HAPPEN IF YOU DECIDE TO BE IN THIS RESEARCH STUDY?

If you agree to participate in this study, you will be interviewed by a trained interviewer in a private area where you feel comfortable answering questions. Administration of the questionnaires will be at your own convenience and you are free to skip questions that you do not wish to answer. The interview will last approximately twenty minutes. The interview will cover topics such as your medication history, biodata, comorbidities, medication experiences, and general review of the systems.

ARE THERE ANY RISKS, HARMS DISCOMFORTS ASSOCIATED WITH THIS STUDY?

Psychological, emotional, social and physical factors are risks introduced by a medical research. However, a concerted effort must be put in place to mitigate the risk. One of the risk that you may encounter is lack of privacy. Your information will be treated confidential and will use a code number to identify you in a password protected computer database restricted for access using password protected electronically. Signed copies of your consent participation forms will be kept in a locked office file cabinet. Only the principal investigator and assistant researcher will access the documents. Additionally, during the administration of the questionnaires, this study will consume your personal

time. However, we promise to observe time to avoid inconveniencing you as the study participant. Furthermore, this study does not involve any invasive procedures or taking additional medications and therefore no harm to the participants.

ARE THERE ANY BENEFITS?

The study findings will help us improve health outcomes especially prioritizing each drug therapy problem identified among adult patients with cardiovascular disease and Type 2 Diabetes Mellitus. By so doing, it will help develop guidelines and protocols that will prevent drug therapy issues from occurring.

WILL BEING IN THIS STUDY COST YOU ANYTHING?

This study will cost you about twenty minutes of your time.

ARE THERE ANY REIMBURSEMENTS?

There will be no payments inform of fiscal, gifts or incentives as a result of participation in the study.

WHAT IF YOU HAVE QUESTIONS IN FUTURE?

If you have further questions or concerns about participating in this study, you are free to call or send a text message to the Principal Investigator before, during, and after the study. For more information about your rights as a research participant you may contact the Principal Investigator on Email: njumorgan1980@gmail.com, and Telephone Number 0711903447. In addition, you may contact the Secretary/Chairperson, Kenyatta National Hospital-University of Nairobi Ethics and Research Committee Telephone No.: **2726300** Ext: **44102** Email:*uonknh_erc@uonbi.ac.ke.*

WHAT ARE YOUR OTHER CHOICES?

Your decision to participate in research is voluntary. You are free to decline participation in the study and you can withdraw from the study at any time without injustice or loss of any benefits.

Appendix 2B: Consent declaration form

Participant's Statement

I have read this consent form or had the information read to me. I have had the chance to discuss this research study with a study counselor. I have had my questions answered in a language that I understand. The risks and benefits have been explained to me. I understand that my participation in this study is voluntary and that I may choose to withdraw anytime. I freely agree to participate in this research study. I understand that all efforts will be made to keep information regarding my personal identity confidential. By signing this consent form, I have not given up any of the legal rights that I have as a participant in a research study.

I agree to participate in this research study: **YES** **NO**

I agree to provide contact information for follow-up: **YES** **NO**

Participant printed name:

_____

Participant signature / Thumb stamp _____

Date _____

Witness_____Date_____

Researcher's statement

I, the undersigned, have fully explained the relevant details of this research study to the

participant named above. The participant has understood and has freely given his/her consent.

Researcher‘s Name: _____ **Signature** _____

Date: _____

Role in the study: _____

For more information contact _____ at _____from _____ to _____

Appendix 3A: Maelezo kuhusu kushiriki katika utafiti
Kichwa cha Uchunguzi

KUCHUGUZA MATATIZO YA DAWA ZA TIBA KWA WAGONJWA AMBAO NI WATU WAZIMA WENYE MATATIZO YA MAGONJWA YA MOYO NA MISHIPA YA DAMU NA UGONJWA WA KISUKARI AINA YA 2.

Mchunguzi mkuu

Dkt Njuguna Mugane-mwanafunzi wa mwaka wa pili akiwa ni mwanafunzi wa chuo kikuu cha Nairobi.

Wasimamizi: profesa Ndemo, Mhadhiri, Chuo Kikuu cha Nairobi, Dkt. Nyamu, Mhadhiri, Chuo Kikuu cha Nairobi

Utangulizi

Mimi ni George njuguna mugane, mwanachuo katika chuo kikuu cha Nairobi, kitongo cha shule ya pharmacia.

Nafanya uchunguzi wa matatizo ya dawa za tiba kwa wagonjwa ambao ni watu wazima waliozaidi ya miaka 18 wenye kusumbuliwa na magonjwa ya moyo na mishipa ya damu pamoja na kisukari, wanaopata tiba ya kisukari na mfumo ya homoni kwenye hospitali ya kitaifa ya Kenyatta

UMUHIMU WA MAFUNZO

Wagonjwa wengi wanajulikana kama wameathirika na magonjwa endapo wanamatatizo ya kiafya na matibabu ya magonjwa mbalimbali, pamoja na matatizo ya dawa ya tiba kutokana na hali zao mbaya. Katika mafunzo haya tutazungumzia utumiaji dawa na mambo unayopata unapotumia dawa.

Lengo letu ni kujua na kuelewa kivipi au nini wagonjwa watu wazima wanaoumwa kutokana na magojwa ya roho na mishipa ya damu na kisukari, wanatatizwa na aina ya DTPs na kuchunguza yanayo sababisha matatizo na aina ya DTPs.

Haya yatachunguzwa kwa kutumia sehemu tatu ya maswali nitakayo kuuliza.

Tutafwata utaratibu ambapo unaweza ukakubali kushiriki kwenye mafunzo. Utatakiwa kujibu dodoso mbili ambalo litachukua makadirio ya dakika 20 na usimamizi wa dodoso utakuwa wako na utakuwa huru kuruka maswali ambayo hutaki kujibu. Taarifa zote zitakusanywa na mchunguzi mkuu na mtafiti msaindizi na zitakuwa ni za siri.

USHIRIKI WA KUJITOLEA

Katika mafunzo haya, kuchagua kushiriki ni kujitolea na unaonesha uhuru wako baada ya kukubali kushiriki. Unaweza ukawa nje ya mafunzo kwa muda wote, kwa kufanya hivyo hutakosa faida ambazo utapewa.

HATARI NA MADHARA

Kisaikolojia, kihisia, kijamii na kimwili hizi ni hatari zilizo ndani ya utafiti. Vilevile juhudi halisi ziwepo kupelekea kupunguza hatari, moja wapo unayoweza kukutana nayo ni ukosefu wa usiri. Taarifa inayokusanywa itakuwa ni ya siri na italindwa kwa kutumia nywila inayolindwa na umeme wa mfumo wa taarifa ya madawa. Nakala zako zilizosahiniwa zenye mawazo yako za ushiriki wako zitafungiwa kwenye karatasi la kuhifadhi nyalaka ya kiofisi. Mchunguzi mkuu na mtafiti msaidizi pekee hao ndio watakao fanyia kazi taarifa yako. Kwa kuongezea, wakati wa ufanyaji wa dodoso, mafunzo yatachukua muda wako binafsi, tunaahidi kuangalia muda kuondoa mwingiliano ukiwa kama mshiriki wa mafunzo, zaidi mafunzo haya hayatahusisha au kutumia madawa

TAREJESHEWA PESA ZAKO?

Utafiti huu hautakugharimu pesa.

NA KAMA UTAKUWA NA MASWALI BAADAYE?

Kama una maswali zaidi au lolote ambalo hulielewi kuhusu utafiti huu, tafadhali usisite kuwasiliana nasi kupitia nambari ambazo zimeandikwa hapa chini.

Kwa maelezo zaidi kuhusu haki za mshiriki katika utafiti, wasiliana na Mtafiti Mkuu Tovuti:njumorgan1980@gmail.com Simu: 0711903447

au Kabitu/Mwenyekiti Simu.: **2726300** ongezo: **44102** Tovuti: *uonknh_erc@uonbi.ac.ke.* Utarudishiwa ada ya mazungumzo kupitia laini hizi kama mazungumzo yenyewe yanahusu utafiti huu.

Appendix 3B: Ridhaa (kukubali kushiriki)

Taarifa ya Mshiriki

Nimesoma au nimesomewa nakala hili. Nimepata kuzungumza kuhusu utafiti huu na mtafiti mwenyewe. Maswali yangu yamejibiwa kwa lugha ninayoielewa vizuri. Madhara na manufaa yameelezwa wazi. Ninaelewa kushiriki kwangu ni kwa hiari na kwamba ninao uhuru wa kutoshiriki wakati wowote. Ninakubali bila kushurutishwa kushiriki katika utafiti huu. Ninaelewa kwamba bidii itatiwa kuhakikisha habari zangu zimewekwa siri. Kwa kutia sahihi kwa daftari hili, sijapeana haki zangu za kisheria ambazo ninazo kama mshiriki katika utafiti huu.

Nimekubali kushiriki katika utafiti huu: NDIO ☐ **LA** ☐

Nimekubali kupeana nambari ya mawasilianao baadaye: **NDIO** ☐ **LA** ☐

Jina la Mshiriki: _____

Sahihi / Kidole _____

Tarehe _____

Taarifa ya Mtafiti

Mimi, ninayetia sahihi hapo chini, nimeelezea maswala muhimu ya utafiti huu kwa mshiriki aliyetaja hapo juu na ninaamini ya kwamba ameyaelewa vilivyo na kwamba ameamua bila kushurutishwa kukubali kushiriki.

Jina la Mtafiti: _____ **Sahihi** _____

Tarehe: _____

Kazi yangu kwa utafiti huu: _____

Kwa maelezo zaidi wasiliana na_____kwa_____

Saa_____ hadi _____

Appendix 4: Participants questionnaire

UNIVERSITY OF NAIROBI

RESEARCH TOPIC: ASSESSMENT OF DRUG THERAPY PROBLEMS IN ADULT PATIENTS WITH BOTH CARDIOVASCULAR DISEASES AND TYPE 2 DIABETES IN KNH

STUDY ASSISTANT:.....

DATE: .....

OPC number_____

Study unique number_____:

INSTRUCTIONS

a. Please answer the following questions and fill in these details in the spaces provided. My research assistant will assist you in case of any need.
b. Feel at liberty to ask for clarifications whenever in need.

PART A (TO BE ANSWERED BY THE PARTICIPANTS)

i. Demographic information

1) Age: _____years
2) Sex: .Male (0) Female (1)
3) Weight……kg…height……Meters…BMI……
4) Category for BMI

Category	Code
18.5 and below (underweight)	0
18.5 to 24.9 (healthy weight)	1
25 to 29.9 (over weight)	2
30 and above (obesity)	3

5) Marital Status: Single (0) Married (1)
6) Pregnancy status: Yes (1) No (0)

7) Religion: Christians (0) Muslim (1) Others (2)
8) Smoking status: current smoker (0) previous smoker (1) never smoked (2)
9) What is your preferred beverage? Tea (0) coffee (1) cocoa (2) drinking chocolate (3) others…….
10) How many cups do you take per day? (1) one (2) two-three (3) four -five
11) Alcohol intake status: currently drinking (0) previously drinking (1) never drunk (2)
12) How many glasses of alcohol do you take per week? (1) one (2) two-three (3) >four
13) Level of Education: Primary (1) Secondary (2) College/University (3) none (4)

ii. **Occupation**

14) What is your employment status? Formally employed (0) not employed (1) self employed (2)

15) On average, how much do you make in a month……..shillings?

16) Categories of monthly income: <5000 (1) 5000-10000 (2)

10000-30000 (3) >30000 (4)

iii. Living situation

17) Who lives and cares for you at home? Kindly tick

Parents	(1)
Extended Relatives	(2)
Siblings	(3)
Spouse	(4)
Children	(5)
Grandchildren	(6)
Friends	(7)
None	(8)

18) Where do you get your medications?

Hospital (0)

Private clinics (1)

Private pharmacy (2)

Others…… (3)

iv. Comorbidities

19) Do you suffer from any other disease or medical problem apart from what I am seeing the doctor has told you. No (0) Yes (1)

If yes to question (19) above, which one(s) _____

	Yes	**No**
20) **Arthritis**	**1**	**0**
21) **Heart failure**	**1**	**0**
22) **Anemia**	**1**	**0**
23) **CKD**	**1**	**0**
24) **CANCER**	**1**	**0**
25) **Others**	**1**	**0**

26) What is the duration of the CVD_____months

27) What is the duration of T2DM?_____months

v. **Medication experiences**

28) Do you like taking medications? No (0) Yes (1)

If No to question (28) above, what is the reason?

29) Drugs don't work? No (0) Yes (1)

30) They cause more problems? No (0) Yes (1)

31) I don't take medications? No (0) Yes (1)

32) The cost of drugs? No (0) Yes (1)

33) Availability of drugs? No (0) Yes (1)

34) What do you expect from the medications you use?
Cure (0) Relief but no cure (1)

35) Do you have any concerns regarding your medications? No (0) Yes (1)

If yes to question (35) above, what are the concerns?

36) Is the number of pills a concern? No (0) Yes (1)

37) Is the number of times you take drugs a concern? No (0) Yes (1)

38) Do you have any concern about side-effects of medications?
No (0) Yes (1)

39) Do you currently suffer from any side effects No (0) Yes (1)

40) Do you choose taking your medications without being compelled?
No (0) Yes (1)

41) Do you choose to refill your prescription? No (0) Yes (1)

42) When you feel like your condition is under control, do you sometimes stop taking your medication? No (0) Yes (1)

vi. Patients understanding of drug therapy

Ask the patient the following questions 42-44, and fill in the table below.

43) Do you know the dose (s) of the medication (s) you are taking_____?

Correct (1) Incorrect (0)

44) How many times do you take the in a day_____?

Correct (1) Incorrect (0)

45) Do you know the duration for which you should be on your medication (s)____?

Correct (1) Incorrect (0)

46) How should you take this medication with regard to food? with food (1)

before food (2) after food (3) without regard to food (4) I don't know (5)

Condition	Drug name	Dose	Frequency	Duration	Taking drug with regard to food

vii. Review of systems

i. General system

47) Fever? No (0) Yes (1)

48) Malaise? No (0) Yes (1)

49) Are you experiencing pain anywhere? No (0) Yes (1)

50) Do you have weight change? No (0) Yes (1)

ii. Special senses:

Eyes

51) Do you have any problem with your eyes? No (0) Yes(1)

If yes above, which problem?

52) Impaired vision occasionally? No (0) Yes (1)

53) Pain in your eyes? No (0) Yes (1)

54) Itching ? No (0) Yes (1)

55) Swelling? No (0) Yes (1)

Ears

56) Do you have any problem with your ears?	No (0)	Yes (1)
If yes above, which problem?		
57) Loss of hearing?	No (0)	Yes (1)
58) Ringing in the ears?	No (0)	Yes (1)
59) Loss of balance?	No (0)	Yes (1)

Nose

60) Do you have any problem with your nose?	No (0)	Yes (1)
If yes above, which problem?		
61) Congested nose?	No (0)	Yes (1)
62) Sneezing?	No (0)	Yes (1)

Throat

63) Do you have any problem with your throat?	No (0)	Yes (1)
If yes above, which problem?		
64) Coughing bloody mucus?	No (0)	Yes (1)
65) Pain while swallowing?	No (0)	Yes (1)

iii. Respiratory system

66) Do you have any problem with your respiratory system?	No (0)	Yes (1)
If yes above, which problem?		
67) Chest Pain?	No (0)	Yes (1)
68) Shortness of breath?	No (0)	Yes (1)
69) Wheezing?	No (0)	Yes (1)
70) Coughing	No (0)	Yes (1)

iv. Digestive system and associated systems

71) Do you have any problem with your digestive system?	No (0)	Yes (1)
If yes above, which problem?		
72) Pain in the abdomen?	No (0)	Yes (1)
73) Poor appetite?	No (0)	Yes (1)
74) Heartburn?	No (0)	Yes (1)
75) Difficult in swallowing?	No (0)	Yes (1)
76) Diarrhea?	No (0)	Yes (1)
77) Hard stool ?	No (0)	Yes (1)
78) Nausea?	No (0)	Yes (1)

v. Genito-urinary system

79) Do you have any problem with your Genitourinary system?	No (0)	Yes(1)
If yes above, which problem?		
80) Pain when urinating?	No (0)	Yes(1)
81) Decreased sexual drive?	No (0)	Yes(1)
82) Increased frequency of urination?	No (0)	Yes (1)

vi. Neurological system

83) Do you have any problem with your Neurological system?	No (0)	Yes (1)
If yes above, which problem?		
84) Feeling dizziness?	No (0)	Yes (1)
85) Feeling drowsiness?	No (0)	Yes (1)
86) Experiencing memory loss?	No (0)	Yes (1)
87) Experiencing numbness or tingling in extremities?	No (0)	Yes (1)
88) Lack of sleep?	No (0)	Yes (1)

89)	Headache?	No (0)	Yes (1)

vii. Hematological system

90)	Do you have any problem with bleeding?	No (0)	Yes (1)
	If yes above, which problem?		
91)	Do you bruise easily?	No (0)	Yes (1)
92)	Have you ever been told you have anemia?	No (0)	Yes (1)

viii. Musculoskeletal system

93)	Do you have any problem with musculoskeletal system?	No (0)	Yes (1)
	If yes above, which problem?		
94)	Backache?	No (0)	Yes (1)
95)	Muscle pain?	No (0)	Yes (1)
96)	Joint pain?	No (0)	Yes (1)
97)	Joint stiffness?	No (0)	Yes (1)
98)	Difficult in walking?	No (0)	Yes (1)
99)	Swelling of joints?	No (0)	Yes (1)

ix. Integumentary system

100)	Are you having any problems with your skin?	No (0)	Yes (1)
	If yes above, which problem?		
101)	Itchiness ?	No (0)	Yes (1)
102)	Rashes?	No (0)	Yes (1)

PART B (TO ABSTRACT PATIENT INFORMATION FROM THE MEDICAL RECORDS)

Vital signs and laboratory tests

What are the laboratory test done in this patient?

Vital signs and labs	**Previous readings**	**Current readings**	
103) **BP**			**1. Normal range <140/90mmHg** **2. High** **3. Low** **4. Not available**
104) **2 hours postprandial test**			**1. Normal range(< 10mmol/l)** **2. High** **3. Low** **4. Not available**
105) **HbA1c**			**1. Normal <7%** **2. Poorly controlled > 7%** **3. Low** **4. Not available**

What are the Prescription patterns and characteristics of drug therapy problems in patients?

Serial number	Condition	Drug name	Class of drug	Dosage	Lab results/signs/ symptoms	Pharmacotherapy Outcome Status	DTPs and causes
0							
1							
2							
3							
4							
5							
6							
7							

Key to above table

DTP	**CODE**	**CAUSES**	**CODE**	**REMARKS**
106) Unnecessary drug therapy	A	Not available	0	
		No valid medical indication	1	
		Duplicate therapy	2	
		Nondrug therapy indicated	3	
		Treating avoidable ADR	4	

		Addictive /recreational	5	
107) Needs additional drug therapy	B	Not available	0	
		Untreated condition	1	
		Preventive	2	
		Synergistic/potentiating	3	
108) Different drug needed	C	Not available	0	
		More effective drug available	1	
		Dosage form inappropriate	2	
		Condition refractory to the drug	3	
		Contraindication present	4	
		Drug not effective for the condition	5	
109) Dosage too low	D	Not available	0	
		Ineffective dose	1	
		Needs additional monitoring	2	
		Frequency inappropriate	3	
		Drug interaction reduces amount of active drug	4	

		Duration inappropriate	5	
110) ADR	E	Not available	0	
		Undesirable effect	1	
		Unsafe drug for patient	2	
		Dosage administered or changed too rapidly	3	
		Drug interaction causes undesirable reaction that is not dose-related	4	
		Allergic reaction	5	
		Contraindications present	6	
111) Dosage too high	F	Not available	0	
		Dose too high	1	
		Needs additional monitoring	2	
		Frequency too short	3	
		Duration too long	4	
		Drug interaction results in a toxic reaction to the drug	5	
112) Noncompliance	G	Not available	0	
		Patient does not understand instructions	1	
		Patient prefers not to take	2	

		Cannot afford drug product	3	
		Patient forgets to take	4	
		Drug product not available	5	
		Cannot swallow/administer	6	

DTPs		**Yes**	**No**
113)	Unnecessary drug therapy	1	0
114)	Needs additional drug	1	0
115)	Different drug needed	1	0
116)	Dosage too low	1	0
117)	ADR	1	0
118)	Dosage too high	1	0
119)	Noncompliance	1	0

120) **Current status of Diabetes condition**

Pharmacotherapy outcome status	**Code**	**Definition**
Stable	2	Goals of therapy have been achieved. The same drug therapy will be continued with no changes. Usually associated with therapy for chronic disorders
Improved	3	Adequate progress is being made toward achieving the goals of therapy at this point in time. The same drug

		will be continued with no changes.
Partially improved	4	Some measurable progress is being made toward achieving the desired goals of therapy, but adjustments in drug therapy are required to better achieve the goals. Usually, dosage changes or the addition of addictive or synergistic therapies is required.
Unimproved	5	No or only minimal progress in achieving goals of therapy can be demonstrated at this time. it is judged that more time is needed to evaluate the full response of this drug regimen. Therefore, the same drug therapy will be continued at this time.
Worsened	6	There has been a decline in the health status while receiving the current drug therapy. Some adjustments in drug regimen (product and/or dosage) are required.
Failure	7	The goals of therapy have not been achieved despite adequate dosages and adequate duration of therapy. Discontinuation of the present medication and initiation of new drug therapy are required

121) **Current status of cardiovascular condition**

Pharmacotherapy outcome status	**Code**	**Definition**
Stable	2	Goals of therapy have been achieved. The same drug therapy will be continued with no changes. Usually associated with therapy for chronic disorders
Improved	3	Adequate progress is being made toward achieving the goals of therapy at this point in time. The same drug will be continued with no changes.
Partially improved	4	Some measurable progress is being made toward achieving the desired goals of therapy, but adjustments in drug therapy are required to better achieve the goals. Usually, dosage changes or the addition of addictive or synergistic therapies are required.
Unimproved	5	No or only minimal progress in achieving goals of therapy can be demonstrated at this time. it is judged that more time is needed to evaluate the full response of this drug regimen. Therefore, the same drug therapy will be continued at this time.
Worsened	6	There has been a decline in the health status while receiving the current drug therapy. Some adjustments in drug regimen (product and/or dosage) are required.
Failure	7	The goals of therapy have not been achieved despite adequate dosages and adequate duration of therapy. Discontinuation of the present

		medication and initiation of new drug therapy are required

Classification of Antidiabetics drugs

Class		**Yes**	**No**
122)	**Biguanides**	**1**	**0**
123)	**Insulin**	**1**	**0**
124)	**Sulphonyl ureas**	**1**	**0**
125)	**Gliptins**	**1**	**0**
126)	**Glutazones**	**1**	**0**
127)	**Acarbose**	**1**	**0**
128)	**Others**	**1**	**0**

Antidiabetic drugs

Drugs		**Yes**	**No**
129)	**Metformin**	**1**	**0**
130)	**Insulin**	**1**	**0**
131)	**Gliclazide**	**1**	**0**
132)	**Glimepiride**	**1**	**0**
133)	**Glibenclamide**		
134)	**Pioglitazone**	**1**	**0**
135)	**Sitagliptin**	**1**	**0**
136)	**Vildagliptin**	**1**	**0**
137)	**Others**	**1**	**0**

Classification of CVS drugs

Class		Yes	No
138)	**Beta-blockers**	**1**	**0**
139)	**Calcium Channel blockers**	**1**	**0**
140)	**Angiotensin Converting enzyme inhibitors**	**1**	**0**
141)	**Angiotensin II Receptor Blockers**	**1**	**0**
142)	**Loop Diuretics**	**1**	**0**
143)	**Potassium Sparing diuretics**	**1**	**0**
144)	**Thiazides**	**1**	**0**
145)	**Others**	**1**	**0**

Cardiovascular drugs

Drugs		Yes	No
146)	**Nifedipine**	**1**	**0**
147)	**Amlodipine**	**1**	**0**
148)	**Nicardipine**	**1**	**0**
149)	**Carvedilol**	**1**	**0**
150)	**Nebivolol**	**1**	**0**
151)	**Atenolol**	**1**	**0**
152)	**Enalapril**	**1**	**0**
153)	**Losartan**	**1**	**0**
154)	**Furosemide**	**1**	**0**
155)	**Spironolactone**	**1**	**0**

156)	**Hydrochlorthiazide**	**1**	**0**
157)	**Hydralazine**	**1**	**0**
158)	**Others**	**1**	**0**

Anti-platelets drugs

Drugs		**Yes**	**No**
159)	**Aspirin**	**1**	**0**
160)	**Others**	**1**	**0**

Lipid lowering drugs

Class		**Yes**	**No**
161)	**Atorvastatin**	**1**	**0**
162)	**Others**	**1**	**0**

Arthritis drugs

Class		**Yes**	**No**
163)	**NSAIDS**	**1**	**0**
164)	**Glucosamine**	**1**	**0**
165)	**Others**	**1**	**0**

Other drugs

Class		**Yes**	**No**
166)	**Anti-cancer**	**1**	**0**

167)	**Antibiotics**	**1**	**0**
168)	**Others**	**1**	**0**

Thanks for your participation

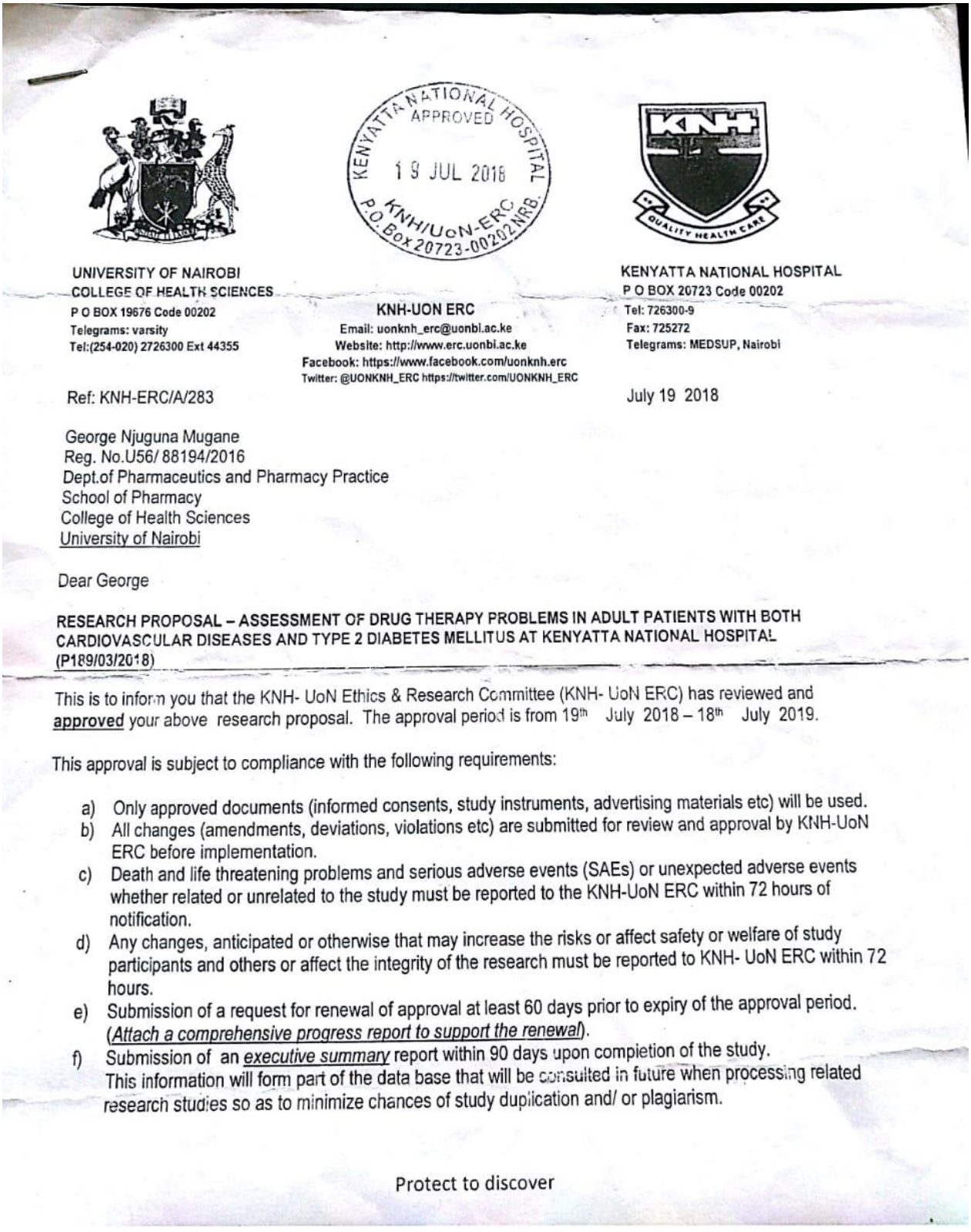
Appendix 5: Outcome status terminology

A summary of the outcome status terminology with standard definition is given in the table below

Pharmacotherapy outcome status	**Definition**
Resolved	Goals of therapy have been achieved, drug therapy has been completed and can now be discontinued. Usually associated with therapy for acute disorders
Stable	Goals of therapy have been achieved. The same drug therapy will be continued with no changes. Usually associated with therapy for chronic disorders
Improved	Adequate progress is being made toward achieving the goals of therapy at this point in time. The same drug will be continued with no changes.
Impartially improved	Some measurable progress is being made toward achieving the desired goals of therapy, but adjustments in drug therapy are required to better achieve the goals. Usually, dosage changes or the addition of addictive or synergistic therapies are required.
Unimproved	No or only minimal progress in achieving goals of therapy can be demonstrated at this time. it is judged that more time is needed to evaluate the full response of this drug regimen. Therefore, the same drug therapy will be continued at this time.
Worsened	There has been a decline in the health status while receiving the current drug therapy. Some adjustments in drug regimen (product and/or dosage) are required.

Failure	The goals of therapy have not been achieved despite adequate dosages and adequate duration of therapy. Discontinuation of the present medication and initiation of new drug therapy are required
Expired	The patient died while receiving drug therapy

Appendix 6: Ethical Approval



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Ref: KNH-ERC/A/283

July 19 2018

George Njuguna Mugane
Reg. No.U56/ 88194/2016
Dept.of Pharmaceutics and Pharmacy Practice
School of Pharmacy
College of Health Sciences
University of Nairobi

Dear George

RESEARCH PROPOSAL – ASSESSMENT OF DRUG THERAPY PROBLEMS IN ADULT PATIENTS WITH BOTH CARDIOVASCULAR DISEASES AND TYPE 2 DIABETES MELLITUS AT KENYATTA NATIONAL HOSPITAL (P189/03/2018)

This is to inform you that the KNH- UoN Ethics & Research Committee (KNH- UoN ERC) has reviewed and **approved** your above research proposal. The approval period is from 19th July 2018 – 18th July 2019.

This approval is subject to compliance with the following requirements:

a) Only approved documents (informed consents, study instruments, advertising materials etc) will be used.
b) All changes (amendments, deviations, violations etc) are submitted for review and approval by KNH-UoN ERC before implementation.
c) Death and life threatening problems and serious adverse events (SAEs) or unexpected adverse events whether related or unrelated to the study must be reported to the KNH-UoN ERC within 72 hours of notification.
d) Any changes, anticipated or otherwise that may increase the risks or affect safety or welfare of study participants and others or affect the integrity of the research must be reported to KNH- UoN ERC within 72 hours.
e) Submission of a request for renewal of approval at least 60 days prior to expiry of the approval period. (*Attach a comprehensive progress report to support the renewal*).
f) Submission of an *executive summary* report within 90 days upon compietion of the study. This information will form part of the data base that will be consulted in future when processing related research studies so as to minimize chances of study duplication and/ or plagiarism.

Protect to discover

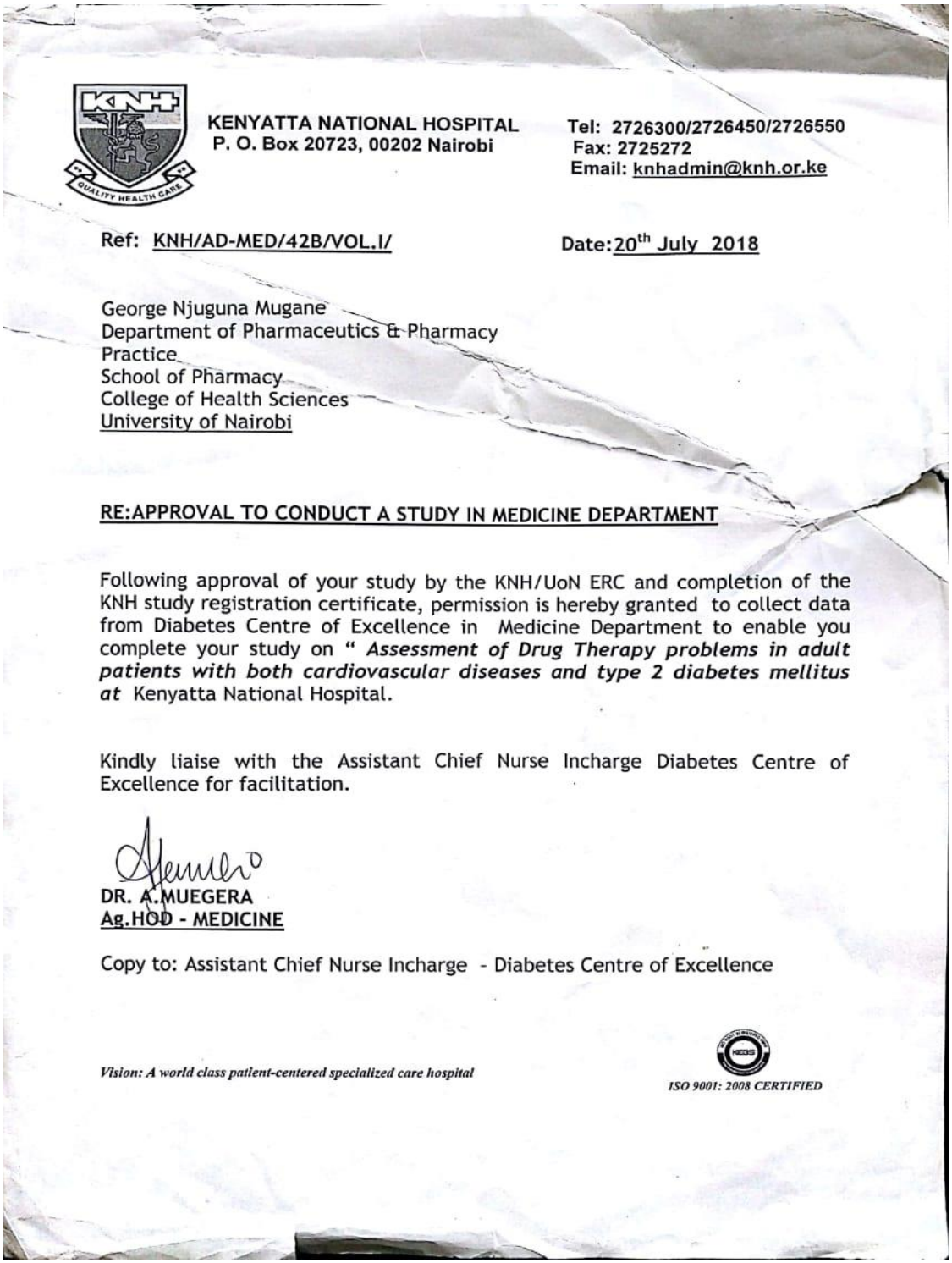
For more details consult the KNH- UoN ERC website **http://www.erc.uonbi.ac.ke**

Yours sincerely,

PROF. M. L. CHINDIA
SECRETARY, KNH-UoN ERC

c.c. The Principal, College of Health Sciences, UoN
The Director, CS, KNH
The Chairperson, KNH-UON ERC
The Assistant Director, Health Information, KNH
The Dean, School of Pharmacy, UON
The Chair, Dept. of Pharmaceutics and Pharmacy Practice, UON
Supervisors: Prof. Francis Ndemo, Dr. David Nyamu

Appendix 7: Institutional Approval



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Ref: KNH/AD-MED/42B/VOL.I/

Date: 20th July 2018

George Njuguna Mugane
Department of Pharmaceutics & Pharmacy Practice
School of Pharmacy
College of Health Sciences
University of Nairobi

RE:APPROVAL TO CONDUCT A STUDY IN MEDICINE DEPARTMENT

Following approval of your study by the KNH/UoN ERC and completion of the KNH study registration certificate, permission is hereby granted to collect data from Diabetes Centre of Excellence in Medicine Department to enable you complete your study on " ***Assessment of Drug Therapy problems in adult patients with both cardiovascular diseases and type 2 diabetes mellitus at*** Kenyatta National Hospital.

Kindly liaise with the Assistant Chief Nurse Incharge Diabetes Centre of Excellence for facilitation.

DR. A.MUEGERA
Ag.HOD - MEDICINE

Copy to: Assistant Chief Nurse Incharge - Diabetes Centre of Excellence

Vision: A world class patient-centered specialized care hospital

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