PREVALENCE OF DRUG THERAPY PROBLEMS AND DETERMINATION OF OUTCOMES AMONG PATIENTS ATTENDING MEDICAL OUTPATIENT CLINIC AT KENYATTA NATIONAL HOSPITAL

DR. ELIZABETH WAMBUI GATHUA (B. PHARM – NBI)
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DECLARATION OF ORIGINALITY

Name of Student: Elizabeth Wambui Gathua

Registration Number: U56/88024/2016

College: Health Sciences

Faculty/School/Institute: School of Pharmacy

Department: Pharmaceutics and Pharmacy Practice

Course Name: Master of Pharmacy in Clinical Pharmacy

Title of the work: Prevalence of Drug Therapy Problems and Determination of Outcomes among Patients Attending Medical Outpatient Clinic at Kenyatta National Hospital

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This dissertation has been submitted for review with our approval as University supervisors:

Signature _____   Date _____

Prof. Francis Ndemo (B.Pharm, PharmD, MRPharmS, FPSK)

Associate Professor

Department of Pharmaceutics and Pharmacy Practice

University of Nairobi

Signature_____   Date_____

Dr. Tom Menge (B.Pharm, MSc Pharmacology & Toxicology, MPSK)

Deputy Director

Pharmaceutical Services

Kenyatta National Hospital

DEDICATION

This work is dedicated to my husband Jethro Chege, and our daughters Isabelle Wanjiru and Elsie Nyawira.

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ABBREVIATIONS AND ACRONYMS

ACEIs	Angiotensin converting enzyme inhibitors
ADR	Adverse Drug Reaction
ARBs	Angiotensin receptor blockers
ASHP	American Society of Health Systems Pharmacists
CCBs	Calcium channel blockers
DRP	Drug Related Problem
DTP	Drug Therapy Problems
KNH	Kenyatta National Hospital
MOPC	Medical Outpatient Clinic
MRP	Medicine/Medication Related Problem
NHIF	National Hospital Insurance Fund
PCNE	Pharmaceutical Care Network Europe
PCP	Pharmaceutical Care Practice
PPIs	Proton Pump Inhibitors
USA	United States of America

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OPERATIONAL DEFINITION OF TERMS

Assessment A systematic review and appraisal of the patient's drug –related needs. It is one of the steps in the patient care process described by Cipolle et al.

Compliance The ability and willingness of a patient to use a pharmacotherapeutic regimen agreed upon between patient and practitioner. Used interchangeably with adherence.

Contraindication A condition or factor that renders the use of a drug product improper or undesirable in the care of a particular patient

Disease Specific illness or medical disorder characterized by a recognizable set of signs and symptoms

Dosage The total amount of active medication that a patient takes over a specified period of time, and includes the dose, duration, frequency and method of administration

Dose The amount of drug administered to the patient as a single event

Dosing interval The amount of time between administered doses

Drug Any substance or product used by a patient for therapeutic, preventive or diagnostic purposes. Also medication.

Drug-related morbidity	The incidence and prevalence of disease and illness associated with drug therapy
Drug-related mortality	The incidence and prevalence of death associated with drug therapy
Drug-related need	The healthcare needs of a patient related to drug therapy for which the pharmacist can offer professional assistance. They include; appropriateness of indication, effectiveness of drug therapy, safety of the drug therapy and ability of the patient to take the medication
Drug therapy	Includes the drug product and the dosage regimen being taken by a patient for a therapeutic indication. Also known as pharmacotherapy.
Drug therapy problem	Any undesirable event experienced by a patient that involves or is suspected to involve drug therapy and that interferes with achieving the desired goals of therapy and requires clinical judgement to resolve or prevent
Effectiveness of drug therapy	Ability of drug therapy to produce the desired or intended beneficial outcome in a specific patient.
Goals of therapy	The desired endpoint for pharmacotherapy. It is expressed as prevention of a disease, curing a disease, the reduction or elimination of signs and symptoms, slowing the progression of a disease, the

normalization of laboratory values.

Indication for drug therapy	A sign or symptom to suggest the necessity or advisability to initiate pharmacotherapy. It is the reason for the use of drug therapy in a specific patient.
Patient	An individual who receives or requires health care services
Practitioner	An individual who possesses a unique body of knowledge, skills and values and uses this to meet the health care needs of a patient
Prevalence	The number of al cases or occurrences during a particular period of time

ABSTRACT

Background: Drug therapy problems (DTPs) have been defined as undesirable patient experiences that involve drug therapy and that actually or potentially interfere with a desired patient outcome. These outcomes include a cure of the disease, resolution or reduction of symptoms, slowing of a disease process and prevention of disease or symptoms. The most common intervention given for medical problems is drug therapy, and it is given with an ultimate goal of improved outcomes for the patient. However, presence of any drug related problem leads to lack of achievement of these therapeutic goals.

Objective: The study aimed to determine the prevalence of drug therapy problems, associated medical conditions and medications, and the extent to which goals of drug therapy had been met among medical outpatients attending KNH MOPC.

Methodology: A descriptive cross sectional survey was carried out of ambulatory adult patients using drug therapy to treat any medical condition and being followed up at KNH medical outpatient clinic. A questionnaire, modified from the pharmacotherapy workup© notes was administered to these patients by the principal investigator, and was used to collect sociodemographic data, information on the patient's medical condition, the medications they were using, how they were using it and its impact on the patient's health outcomes. Laboratory parameters were extracted from the patient's file. The information collected was entered into a Microsoft 2010 Excel data sheet for cleaning, and then the data underwent descriptive data analysis using STATA 13 statistical software package.

Results: Females were more at 71.7 %, and the median age was 58.5 [IQR 48, 66] years. Participants had an average of 7.0 (SD ±3.2) medical conditions and an average of 4.0 (SD ± 2.1) prescribed medications. Participants with at least one DTP were 44 (95.7 %), and 'additional drug therapy needed' was the most frequently occurring DTP identified in the participants, with a prevalence of 72.9 % of total DTPs. Participants had an average of 5.0 (SD ± 2.6) DTPs each. Goals of therapy had been achieved in 52.0 % of conditions for which drug therapy was already being taken, but in only 20.2 % of total indications.

Conclusion: Patients were using medications for 44 % of the total indications requiring drug therapy and of this, 52 % had achieved their goals of therapy. However, additional drug therapy was needed in 72.9 % of the total indications/conditions in order to achieve optimal health outcomes.

Recommendations: Provision of pharmaceutical care services by pharmacists can increase the number of actual or potential DTPs that are identified and resolved or prevented, and would reduce drug-related morbidities and mortalities, and reduce health care costs.

CHAPTER ONE: INTRODUCTION

1.1   Background to the study

The practice of Pharmacy has existed since time immemorial and as one writer puts it, "Pharmacy is as ancient as man on the earth", and "Pharmacy's history parallels that of the history of civilization"(1). Like all civilisations therefore, this practice has evolved over the years both in the terms used to refer to the practitioners of this profession and in the practice itself. Pharmacy has moved from a history of 'Apothecaries' compounding medicines from plants, animals and mineral extracts, to dispensing medicines, and on to a more patient-centred approach of clinical pharmacy. It has not been an easy transition, and as Hepler and Strand note, the profession is still struggling with a uniform description of its functions and role (2). They postulate that what is missing, even as the profession struggles with this issue, is an understanding of our responsibility to the patient. They state that pharmaceutical practice must place a clear emphasis on the patient's welfare with an ethical mandate to protect patients from harmful effects of drugs (2).

Since the 1970s, researchers have worked on developing a new patient-centred practice and this practice, termed 'pharmaceutical care practice', has been defined as one where the practitioner assumes responsibility for all drug related needs of the patient and is held accountable for this commitment (2). Meeting a patient's drug related needs involves an assurance that all the drugs the patient is taking are indicated, effective, safe and that the patient is able and willing to take the medication. In the event that one of these needs is not met, then the patient is said to be experiencing a drug therapy problem. A drug therapy problem that is not identified and resolved may lead to drug-related morbidities, which can eventually lead to drug-related mortalities (3). Drug therapy problems (DTPs) have been defined as, 'an undesirable patient experience that involves drug therapy and that actually or potentially interferes with a desired patient outcome'(3), where these outcomes include a cure of the disease, resolution or

reduction of symptoms, slowing of a disease process and prevention of disease or symptoms (2). In a study designed to develop a conceptual model for drug-related morbidity and mortality in the US, Johnson and Bootman estimated that the cost of drug-related morbidity and mortality in the ambulatory setting cost $76.6 billion(3). Five years later, Ernst and Grizzle sought to update the work of Johnson and Bootman, and found that the estimated costs of drug related morbidity and mortality had more than doubled to $177.4 billion (4). Recently, DTPs have been estimated to cost the health system around $200 billion in the United States. They are also the third leading cause of emergency hospital admissions in that country. This increase in DTPs and their increasing toll on the health system could be as a result of increased use of medications and the rising number of available medications now in the market. Studies done in other countries have also found that drug-related morbidity and mortality are associated with alarmingly high costs to patients and the health care system. These costs arise from hospitalizations, Doctor's visits, emergency room visits, as well as indirect costs such as missed work days.

In Kenya, there is no available research known to this author that has tried to estimate the costs associated with DTPs. However, studies have been carried out that characterize and estimate the prevalence of drug therapy problems. A study conducted by Birichi et al. identified medication related problems in 230 out of 236 patients in a medical ward in KNH, estimating the prevalence of MRPs to be 97.5% before introduction of an individualized dispensing system and 95.7% (198 out of 207) after introduction of the system (5), while Njeri et al found that each of her study participants in a medical ward had at least one MRP resulting in an overall prevalence of 100% (6). A recent study carried out among cervical cancer patients, both inpatients and outpatients, receiving care at KNH identified 215 DTPs in 76 of the 81 patients being studied, translating to a prevalence of 93.8% and a mean of 2.65 ± 1.22 DTPs per patient (7). These figures clearly illustrate that DTPs are an issue that should concern the health sector in the country.

1.2   Problem Statement

The most common intervention given for medical problems is drug therapy. Drug therapy is given with an ultimate goal of improved outcomes for the patient. This could include; cure of a disease, resolution or reduction of symptoms, slowing of a disease process and prevention of disease or symptoms (2). However, presence of any drug related problem leads to lack of achievement of these therapeutic goals.

Despite the earlier mentioned studies conducted in Kenya that have tried to identify and characterize drug related problems, the classification systems used have all been different. There is a need to streamline and utilize a common classification system for DTPs so that comparisons can be made and solutions for problems identified. Further to that, pharmaceutical care practitioners in Kenya have not identified a standard and validated patient care process that can be used to identify, treat and/or prevent drug therapy problems.

This research used the Pharmaceutical Care Process as developed by Cipolle et al. (8), as it can be used to help identify actual and potential DTPs and their causes, thereby enabling their treatment and or prevention. In this classification system, 7 categories of DTPs have been identified and their probable causes. The 7 include; 'Unnecessary drug therapy', 'Needs additional drug therapy', 'Ineffective drug', 'Dosage too low', 'Adverse drug reaction', 'Dosage too high', and 'Non-adherence'.

In addition, the study served as a pilot to establish a patient care process that can guide clinical pharmacists in providing the best pharmaceutical care for their patients to enable them achieve good therapeutic outcomes.

1.3   Purpose of the study

This study utilized the Pharmaceutical Care Process to identify DTPs and their probable causes. A survey was carried out on patients attending the Kenyatta National Hospital medical outpatient clinic (MOPC) to determine the percentage of patients who had achieved their goals of drug therapy, identify the prescribed medications commonly associated with DTPs, identify the most frequent medical

conditions associated with DTPs, determine the most frequent medical conditions requiring drug therapy, and to determine the common causes of DTPs occurring in patients attending KNH MOPC. The findings were also compared to those of the Minnesota study.

1.4   Objectives

1.1.1   Broad Objective

The objective of this study was to determine the prevalence of drug therapy problems, the associated factors and the extent to which goals of drug therapy had been met among medical outpatients attending KNH MOPC.

1.1.2   Specific Objectives

The specific objectives were;

1. To determine the proportion of medical outpatients attending KNH MOPC who were experiencing any of the 7 categories of drug therapy problems.
2. To identify the prescribed medications most frequently associated with each of the 7 categories of DTPs among patients who were attending KNH MOPC.
3. To identify the medical conditions most frequently associated with each of the 7 categories of DTPs among patients who were attending KNH MOPC.
4. To determine the proportion of medical outpatients attending KNH MOPC who had achieved their goals of drug therapy at the first pharmacotherapy evaluation

1.5   Research Questions

The research questions for this study were;

1. What is the percentage of medical outpatients attending KNH MOPC who are experiencing any of the 7 DTPs?
2. Which medications are most frequently associated with the 7 categories of DTPs among outpatients attending KNH MOPC?

3. Which medical conditions are most frequently associated with the 7 categories of DTPs among outpatients attending KNH MOPC?
4. What is the percentage of medical outpatients attending KNH MOPC and using medications who have achieved their goals of drug therapy compared to those who have not?

1.6 Significance and anticipated output

Correct identification of actual or potential drug therapy problems and their causes enables pharmaceutical care practitioners to properly treat and prevent them, leading to optimal outcomes in goals of therapy of patients. This is not only beneficial to the patient, but to the health system as a whole. The patient's quality of life would be improved and their healthcare costs kept minimal. Their contribution to the well-being of their families would also be improved as there would be less sick days.

The burden on the health system would be reduced as there would be a reduction in patients seeking health care due to avoidable drug related problems. This would free up bed space in hospitals, reduce the queues in the emergency department and free up health workers time to enable more quality time spent on unavoidable medical and drug-related problems.

The government would also be able to allocate more resources to other neglected health problems.

1.7 Delimitations

The research focused on adult patients for comparison purposes. While the paediatric population would have benefitted a lot from such a study, not much information has been obtained on this population in other similar studies that have been conducted, and therefore the study would not have been able to compare findings.

The researcher also conducted the study in an ambulatory patient population in order to investigate all aspects of drug therapy problems. Problem no. 7 of compliance cannot be well investigated in an in-patient setting as medicine taking

is almost wholly reliant on the nurses responsible for administering medication in the wards.

According to the pharmaceutical care plan, the patient process consists of 3 parts i.e. the assessment, the care plan and the evaluation. Due to the time allocated for this study, the researcher limited herself to the assessment part only for purposes of this research report.

1.8   Limitation

Most of the participants were interviewed after their appointment with the doctor and before refilling their prescriptions. As such, there were patients who were in a hurry to collect their drugs and go home and therefore the interview was rushed.

Another major limitation was the lack of a proper functioning weighing scale. The one available at the clinic needed a lot of manoeuvring before getting a correct reading which led to the interview taking a longer time.

The amount of data that was collected was quite large and processing it manually proved to be a daunting task.

The study population of KNH might not represent the Kenyan population as a whole especially for those who seek health services from private hospitals, as they are likely to have better health insurance and therefore an availability of better treatment options.

1.9   Conceptual Framework
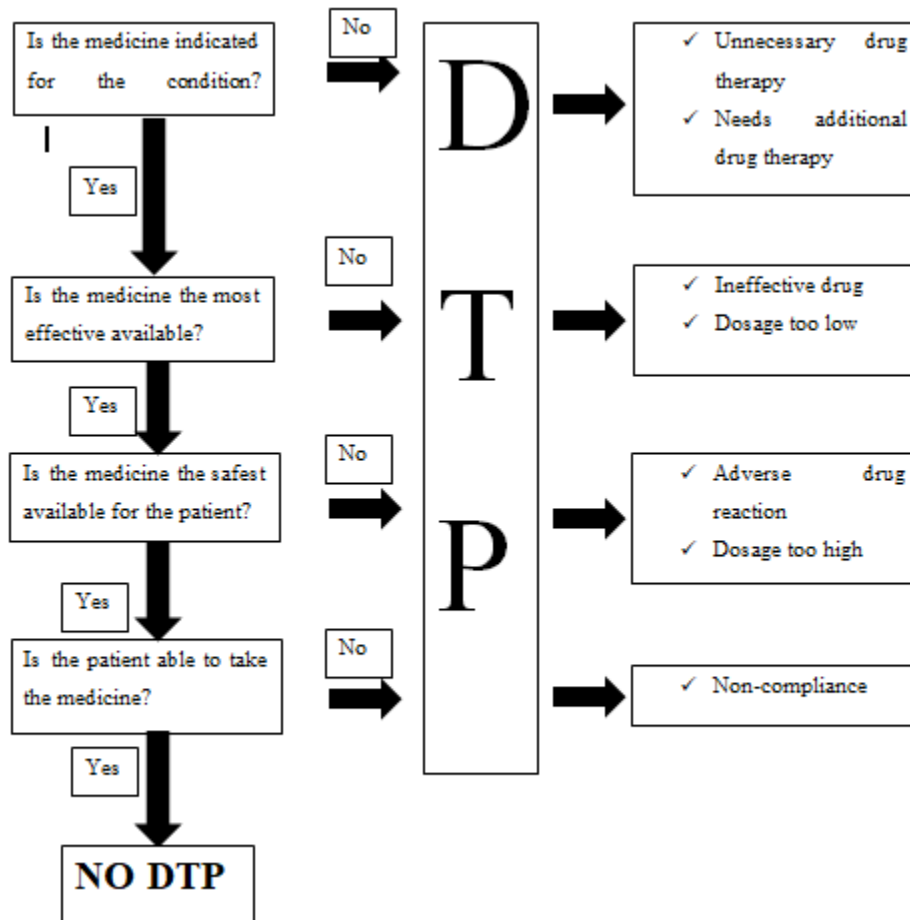
Figure 1: Conceptual Framework

CHAPTER TWO: LITERATURE REVIEW

2.1   Introduction

The core processes involved in the provision of pharmaceutical care is the identification, resolution and prevention of actual or potential drug therapy problems (9). It is therefore necessary to define and classify drug therapy problems in a way that all practitioners of pharmaceutical care and indeed other health professionals will understand in a uniform manner. However, this has not been the case and the definitions of a drug therapy problem have been as diverse as the many different classification systems. Van Mil et al. identified 14 classification systems, each with a different focus. Of these, they found 9 systems which were based on a clear definition of drug therapy problems, though the terms used ranged from 'drug therapy problems', 'drug-related problems', 'medication-related problems', 'medication therapy problems', 'pharmaceutical care issue', to 'clinical drug-related problem'

The earliest definition of a DTP from these 14 systems was from the Hepler-Strand classification, where they defined a drug-related problem (DRP) as "an event or circumstance involving a patient's drug treatment that actually or potentially interferes with the achievement of an optimal outcome"(2).

The American Society of Hospital Pharmacists (ASHP) adapted this definition from Hepler and Strand, and later used the term 'medication related problem', defining it as "an event or circumstance involving medication therapy that actually or potentially interferes with an optimum outcome for a specific patient" (10).

The Pharmaceutical Care Network Europe (PCNE), an official association established in 1994 by a number of European pharmaceutical care researchers (pcne.org) constructed a classification scheme for drug related problems in 1999. This system is validated and adapted regularly, and according to van Mil et al.(9), version 4.0, which was the most current version of the system at the time of their comparison study, came closest to meeting all the criteria for the most optimal classification of drug-related problems. PCNE defines a DRP as "an event or

circumstance involving drug therapy that actually or potentially interferes with desired health outcomes". Though the system came closest to meeting the criteria, it still had some shortcomings, especially in its usability in practice.

Bjorkman et al. in 2008 also undertook an exercise examining and comparing 4 classification systems for DRPs (11). The systems included the Strand classification (2,12), Granada 2, PCNE version 5.0 (13) and Apoteket. They also found that the characteristics of each system were different and therefore each had a different function. After their analysis, they determined that the function of the Strand classification system was "to help patients achieve their drug-related outcome", while the function of Granada 2 system was "to identify clinical outcomes of patient's drug therapy". PCNE's function was "to identify drug-related events known to lead to harm or jeopardize outcome in patients". Apoteket's function was "to help patients use their drugs properly and safely". Of these 4 systems, only the Strand classification system gives provision for documenting intended changes that have been agreed on, to better patient outcomes. The Cipolle et al. classification (14), which is an improvement of the initial Strand classification of 1990 (2) , defines a drug therapy problem as "any undesirable event experienced by the patient that involves or is suspected to involve drug therapy and that actually or potentially interferes with a desired patient outcome".

The Strand classification initially listed 8 DTPs (2) and later reviewed this to 7 categories of DTPs (14). In this new classification, they included 'causes' of DTPs, which had been one of the shortcomings that van Mil e al. had identified as a missing criteria to achieve optimal DTP classification. These 7 categories address the 4 drug-related needs of patients which include appropriate indication for medication, effectiveness of medication, safety of medication and ability of patient to take the medication. When these 4 needs are not met, a patient is said to be experiencing a DTP. The DTPs addressing indication are; 'unnecessary drug therapy' and 'needs additional drug therapy'. DTPs addressing effectiveness include; 'ineffective drug' and 'dosage too low'. DTPs addressing safety include; 'adverse drug reaction' and 'dosage too high'. The final DTP involves the ability

of the patient to take the prescribed medication and according to Strand et al., this DTP can only be determined after first establishing that the medication the patient is taking is indicated and all medical problems that a patient has are being addressed, the medication is the most effective for the condition and the safest for the patient.

2.2 Burden of DTPs

An actual or potential drug therapy problem that is not identified and resolved or prevented may manifest as drug-related morbidity, which has been defined as the failure of a therapeutic agent to produce the intended therapeutic outcome (2). When drug-related morbidity is not detected and resolved, it may lead to drug-related mortality (2)

In a systematic review of literature on DTPs that resulted in emergency department visits, Patel & Zed observed that one prospective study reported 28% of emergency visits being drug-related, while the retrospective studies reported a range of 0.86% to 10.6% of emergency department visits being drug-related. The reviewed studies estimated that 8.6% to 24.2% of patients who visited the emergency department with a drug-related problem were admitted. Patel & Zed postulated that the varying figures reported could be due to differences in study designs, objectives and definitions of drug-related visits in the literature reviewed (15). The different definitions and classifications of drug-related problems or drug therapy problems (9,11,15) are likely to cause variances in reported figures of drug-related emergency department visits considering that some researchers consider adverse drug reactions and non-compliance as the only categories of DTPs. Such studies are likely to underestimate the true burden of DTPs. In another systematic review of studies conducted between 1983 and 2002, the median percentage of drug-related admissions that were preventable was found to be 3.73% (1.36-15.42) (16), while in a national surveillance of emergency department visits in the US, it was found that adverse drug events accounted for 0.6% of estimated emergency room visits for all causes (17).

In three studies that Johnson and Bootman reviewed (3), they found that personal expenditures for prescription medications in 1994 in the US exceeded $73 billion, and that costs associated with inappropriate drug use behaviour could exceed these initial drug therapy expenditures (3). In their study, they estimated that drug-related morbidity and mortality cost $76.6 billion in the ambulatory setting (3). Five years later, Ernst and Grizzle found that the estimated costs of drug related morbidity and mortality had more than doubled to $177.4 billion (4). In 2010, the US national expenditure on prescription drugs totalled $260 billion (18). If the trend is the same as in 1994, then it would imply that inappropriate drug use behaviour could cost the US in excess of $260 billion.

This increase in DTPs and their increasing toll on the health system could be as a result of increased use in medications and the rising number of available medications now in the market. Also, the number of people living with chronic conditions requiring several medications in the US has increased as people live to an older age. Estimates indicate that 50% of US citizens are living with a chronic medical condition.

Studies done in other countries have also found that drug-related morbidity and mortality are associated with alarmingly high costs to patients and the health care system. These costs arise from hospitalizations, Doctor's visits, emergency room visits, as well as indirect costs such as missed work days.

In Kenya, there is no available research known to this author that has tried to estimate the costs associated with DTPs, or to determine the percentage of emergency department visits that are drug-related. However, studies have been carried out that characterize and estimate the prevalence of DTPs in specific populations, mostly hospitalized patients. A study conducted by Birichi et al estimated the presence of medication related problems in 97.5% of patients before, and in 95.7% of patients after introduction of an individualized dispensing system in the medial wards of KNH (5), while Njeri et al found that each of her study participants had at least one MRP resulting in an overall prevalence of 100% (6). A recent study carried out among cervical cancer patients estimated that 93.8% of the study population had a drug-related problem (7). While these

Kenyan studies all used different definitions and classifications of drug therapy problems, it is worthwhile to note that they all had DTP estimates of above 90%. These figures clearly illustrate that DTPs are an issue that should concern the health sector in the country.

2.3   Categories of Drug Therapy Problems

While Cipolle et al have described 7 categories of drug therapy problems, many other classification systems of DTPs are being used globally, all with different categories of problems. Van Mil et al were able to identify 14 different classification systems (9). This current study proposes to use the Cipolle et al. classification that was first developed by Strand et al. (12) with 8 categories of drug therapy problems, and later reviewed and modified to the 7 categories of DTPs. As such, this review will concentrate on those 7 DTPs.

2.3.1 DTPs arising from the unmet need of 'appropriate drug therapy'

These DTPs arise when the prescribed medication does not have a medical indication and so is considered unnecessary, or when a patient has a medical condition that has not been treated or addressed.

2.3.1.1 Unnecessary Drug Therapy

The drug therapy is not needed because the patient does not have an indication at this time. Cipolle et al identified 5 possible causes of this problem and listed them as; duplicate therapy (patient using more than one drug where only one is indicated), no medical indication at this time, non-drug therapy is more appropriate at this time, drug is being used recreationally or being abused, and drug is being used to treat an avoidable drug reaction. When they pulled data from the databases of patients of pharmaceutical care practitioners in Minnesota, they discovered after analysis that 7.2% of patients <65 years old were experiencing this category of DTPs, and 6.7% of patients >65 years had the problem. It was the 6th most common problem of 7 in <65yrs and the 5th most common problem of 7 in the >65yrs groups of patients. The sample data was for patients cared for

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between January 1996 and December 2002 (19). In a comparative study carried out for patients cared for between March 1999 and February 2000 in Minnesota and South Australia, the Minnesota sample showed that this problem was experienced by 6% of patients on drug therapy, while the South Australian sample showed that the problem occurred in 7% of the patients on drug therapy. It was the least common problem in both studies (20). The analysis of the database in Minnesota stated the causes of this DTP, with almost 50% of the cases being 'no medical indication at this time'. Some reasons for this were postulated to be the fact that patients often don't know the reason for taking a certain drug and without proper instructions may not know when to discontinue a drug or if it is safe to do so. The comparative study of Minnesota and South Australia however did not report on the causes for this category of DTP. However, the prevalence of the problem appeared to be similar.

Doucette et al. who also used the Cipolle classification of 7 DTPs, however determined a slightly higher figure of prevalence of this DTP with 12.9% of 150 patients experiencing it (21).

2.3.1.2 Needs Additional Drug Therapy

Additional drug therapy is needed to prevent or to treat a medical condition. The causes for such a problem developing were identified by Cipolle et al as; 'preventive therapy needed', 'untreated condition' and/or 'synergistic therapy needed'. In the analysis of practitioner data that is reported in chapter 2 of *Pharmaceutical Care Practice: A Clinician's Guide* (19), this was the most common problem experienced by patients on drug therapy. 'Untreated condition' was the most common cause of the DTP in patients <65yrs, while preventive therapy needed was the most common cause of the DTP in patients > 65yrs (19). Many other studies carried out in the US place this DTP as the most common among the 7 categories. In the South Australian comparative study, this DTP was the 2nd most common, and the category of drugs most associated with it were salicylates, calcium supplements and tetanus vaccines (20).

Table 1: Drug therapy problems arising from unmet need of appropriate indication

Drug Therapy Problem	Cause
1.Unnecessary drug therapy	Duplicate therapy
	No medical indication at this time
	Non-drug therapy more appropriate
	Addiction/recreational drug use
	Treating avoidable adverse reaction
2.Needs additional drug therapy	Preventive therapy
	Untreated condition
	Synergistic therapy

2.3.2 DTPs arising from the unmet need of 'medication effectiveness'

2.3.2.1 Ineffective Drug

This is when the drug product prescribed is not producing the desired outcome. The reasons for classifying this problem could be that; 'a more effective drug is available', the condition could be 'refractory to the disease', patient is using drug in an 'inappropriate dosage form', 'a contraindication is present', or 'the drug is not indicated for that condition' (14). This was the 3rd most frequently identified DTP in the South Australian sample of the comparison study with Minnesota, occurring in 15.7% of total DTPs identified. The most common cause for the problem was wrong or inappropriate drug being prescribed (20). In the Minnesota pharmaceutical projects, this particular DTP accounted for 8.6% (22), 6% (20) and 7.6% (19) of the total DTPs identified. Doucette et al. collected data on 150 patients and identified a total of 886 drug related issues. Out of this, 13.2% was attributed to 'wrong drug' (21).

2.3.2.2 Dosage Too low

In this category of DTP, the drug prescribed is the right drug for the indication; however, the dosage is too low to produce the desired response. The dosage is

looked at in terms of the dose, frequency and duration, therefore could be either of or a combination of 'too low a dose',' too long of a dosing interval' or 'too short a duration' to produce the desired effect. Other causes for a low dosage could be 'incorrect administration of the drug', 'incorrect storage of the drug', and 'drug interactions'. The drug could also need 'additional monitoring to determine if dosage is too low' (14). Rao et al. found that this DTP accounted for 23% of a total of 3631 DTPs identified in 1225 patients in a Minnesota sample and 11% of 1997 DTPs identified in 885 patients in a South Australian sample (20). Cipolle et al. identified the DTP in 21% of 1853 total DTPs identified in patients <65 years old and in 23.2% of 2142 total DTPs identified in patients >65 years old (19). The most common reason for 'dosage too low' in the Cipolle study was that the dose was too low to produce the desired response. This was the 2nd most commonly occurring DTP they identified. Gitau reported that out of 156 interventions made by a clinical pharmacist to correct drug therapy problems in the medical wards of KNH, 22% were a correction of dose, frequency or duration of treatment in order to increase effectiveness of medication (23).

Table 2: Drug therapy problems arising from unmet need of effectiveness

Drug Therapy Problem	Cause
3.Ineffective drug	More effective drug available
	Condition refractory to drug
	Dosage form inappropriate
	Contraindication present
	Drug not indicated for condition
4.Dosage too low	Ineffective dose
	Needs additional monitoring
	Frequency inappropriate
	Incorrect administration
	Drug interaction
	Incorrect storage
	Duration inappropriate

2.3.3 DTPs arising from the unmet need of 'Safety'

2.3.3.1 Adverse Drug Reaction

This is the most commonly studied problem of the 7 categories of DTPs. This DTP is said to occur when the drug product causes an undesirable reaction that is not dose related, a safer drug is needed due to risk factors, when a drug interaction causes an undesirable reaction that is not dose related, when drug product is incorrectly administered, when the drug product causes an allergic reaction, when the dosage regimen is administered or changed too rapidly and when the drug product is contraindicated due to risk factors (14). Cipolle et al. reported this DTP as accounting for 14.3% of 1853 total DTPs identified in patients <65 years and 12.6% of 2142 total DTPs identified in patients >65 years. The most common cause was a drug product causing an undesirable reaction that was not dose related (19). Rao reported this DTP as accounting for 11% of the total DTPs identified in 1225 patients from the Minnesota sample and 12% of the total DTPs identified in 885 patients from the South Australian sample (20). Kongkaew et al. conducted a systematic review of prospective observational studies and from 25 studies they determined that prevalence rates of adverse drug reactions (ADRs) ranged from 0.16% to 15.7% with an overall median of 5.3% (24).

2.3.3.2 Dosage Too High

The dosage is too high, resulting in undesirable toxic effects. The common causes of this drug therapy problem as described by Cipolle et al. are, 'the dose is too high', 'the drug needs additional monitoring to determine if the dosage is too high', 'the dosing frequency is too short', 'the duration of the drug therapy is too long', or 'a drug interaction has occurred thereby resulting in a toxic reaction to the drug product' (14). They found that this DTP accounted for 4% and 4.8% of the total DTPs identified in patients <65 years and patients >65years, respectively. (19). The most common cause of this problem was the dose being too high, with the second most common cause being that the dosing frequency was too short.

Table 3: Drug therapy problems arising from unmet need of Safety

Drug Therapy Problem	Cause
5.Adverse drug reaction	Undesirable effect, not dose-related
	Unsafe for patient due to patient risk factors
	Drug interaction
	Incorrect administration
	Allergic reaction
	Dosage increase/decrease too fast
6.Dosage too high	Dose too high
	Needs additional monitoring
	Frequency too short
	Duration too long
	Drug interaction resulting in toxic reaction

2.3.4   DTPs arising from the unmet need of 'Patient compliance'

2.3.4.1 Non-compliance

After ADRs this is the 2nd most commonly studied problem of the 7 categories of DTPs. In the care process described by Cipolle et al., this DTP can only be identified once the patient's drug related needs of indication, effectiveness and safety have been met (8). This means that if for example a patient is not taking their medication due to adverse drug reactions, the problem cannot be classified as a compliance issue, but as a safety issue. The practitioner must therefore first meet the patient's drug related need of safety. Cipolle et al., went on to identify this DTP in 14.3% and 17.9% the total DTPs identified in patients <65 years and patients >65years, respectively (19).

Table 4: Drug therapy problems arising from the unmet need of compliance

Drug Therapy Problem	Cause
7.Inappropriate compliance	Patient does not understand instructions
	Patient cannot afford drug product
	Patient prefers not to take the medication
	Patient forgets to take medication
	The medication is not available
	Patient cannot take the medication

2.4 Outcome status

The practitioner of pharmaceutical care assumes responsibility for all outcomes of drug therapy and therefore there is a need to determine what a patient's therapy outcomes are.

At the time of initiating drug therapy, the status of the patient's medical condition should be determined and this can be labelled as the 'initial' status. After drug therapy is initiated, subsequent evaluations compare current status to initial status in order to determine the outcome of therapy. Cipolle et al. have proposed standard terminology that can be used to describe clinical outcome status as shown in the table below (8).

Table 5: Categories of clinical outcome status and their descriptions

Outcome Status	Description
Resolved	This outcome is associated with acute conditions and represents the goals of therapy being achieved. Drug therapy should be discontinued on attainment of this status.
Stable	This outcome is associated with chronic conditions and represents the goals of therapy being achieved. Drug therapy is continued with no change on attainment of this status.
Improved	There is adequate progress being made towards attaining goals of therapy and same drug therapy should be maintained without any changes.
Partially improved	Some progress has been made towards attaining the goals of therapy but a change in dosage or addition of synergistic or additive therapy is required in order to better meet the desired goals of therapy.
Unimproved	Slight or no progress in attaining goals of therapy. The same drug therapy should be continued to give more time to evaluate full response of the drug regimen.
Worsened	The patient has declined in health status while they have been on the drug therapy.an adjustment in the drug regimen is required.
Failure	Goals of therapy have not been attained despite adequate dosage and duration of therapy. Current drug therapy should be discontinued and new drug therapy initiated.
Expired	The patient died while receiving drug therapy

2.5 Pharmaceutical Care

Pharmaceutical care is defined as the direct, responsible provision of medication-related care for the purpose of achieving definite outcomes that improve a patient's quality of life (2,10). It is therefore a patient-centred approach that allows practitioners to help their patients identify and meet their medication related needs, and it was first developed and studied at the University of Minnesota (20). Drug related needs include indication, effectiveness and safety of a drug and finally the patient's ability to comply with the therapeutic regimen. However, the steps must be followed sequentially and therefore a practitioner must first establish that each drug being taken by the patient is the most appropriate for the indication, and then determine that it is the most effective for the indication. Once the two needs have been met, the practitioner may then go on to establish whether the drug is the safest for the patient, and finally, determine the ability of the patient to take the medication.

If any of the needs are unmet, then the patient is said to be experiencing a drug therapy problem. Drug therapy problems affect the outcomes of therapy in individual patients.

Pharmaceutical care practice allows for better patient outcomes and potential healthcare savings, as its core function is to identify, treat and prevent actual or potential drug therapy problems. DTPs negatively impact attainment of patient's desired goals of therapy and can lead to high medical expenditures (3,4)

According to Strand et al, in order to correctly identify drug therapy problems, an assessment of a patient's drug related needs must be conducted, and this entails the carrying out of a detailed and systematic patient care process. This systematic process, which is the pharmaceutical care process, is the result of decades of research aimed at the development of a new practice for pharmacists (12). Project ImPACT: Hyperlipidemia, a community pharmacy based demonstration project, was initiated in March 1996 and completed in October 1999, and involved offering pharmaceutical care to patients who had either been newly diagnosed with dyslipidemia or who had been on therapy with lipid lowering medication but were not achieving their desired goals of therapy. The results of the project

revealed that pharmaceutical care services, carried out in a collaborative practice environment can lead to significant improvement in attainment of patients' goals of therapy (25). Similarly, Bunting & Cranor (26) and Bunting et al. (27) in the Asheville projects, found that pharmaceutical care positively impacted on patients' outcomes, with significant improvements in the percentage of patients achieving their goals of therapy

2.6 Minnesota pharmaceutical care project

Several papers have reported different aspects of the pharmaceutical care project in Minnesota (19,20,22,28,29), with most of the findings being common. The distribution of drug therapy problems identified was as follows

Table 6: Types of drug therapy problems identified in Minnesota pharmaceutical projects

Type of drug therapy problem	Percentage of Drug Therapy Problems Identified (%)				
	Cipolle(19)		Rao(20)	Isetts(28)	Strand (22)
	<65yrs	>65yrs	All pts	All pts	All pts
Additional drug therapy needed	31.6	30.1	32	33.9	30.6
Unnecessary drug therapy	7.2	6.7	6.0	6.0	5.5
Ineffective drug	7.6	4.9	6.0	11.6	8.6
Dosage too low	21.0	23.2	23.0	19.9	21.2
Adverse drug reaction	14.3	12.6	11.0	14.1	10.1
Dosage too high	4.0	4.8	6.0	4.9	5.6
Non-adherence	14.3	17.9	16.0	9.6	18.4

CHAPTER THREE: METHODOLOGY

3.1 Introduction

This chapter describes the components of methods that were used to carry out the study. These components include: research design, location of the study, target population, sampling technique, data collection instruments, quality assurance, data management and analysis techniques. It also includes logistical and ethical considerations.

3.2 Research Design

A hospital-based cross sectional survey of adult medical outpatients using drug therapy and being followed up at KNH was conducted. The principal investigator (PI) administered to these patients a questionnaire based on the patient care process described by Cipolle et al. The information obtained during the assessment process was utilized to generate data for this study. Additional data such as lab parameters and additional drug information was extracted from the patients' files.

3.3 Location of the Study

The study area was the Kenyatta National Hospital, a referral hospital in Nairobi, Kenya. It is also the largest referral hospital in East and Central Africa, and also serves as the teaching hospital for the University of Nairobi, College of Health Sciences and the Kenya Medical Training College. It has a bed capacity of 1800 located in 50 wards and 22 outpatient clinics. The study site was the KNH medical outpatient clinic which is on ground floor, clinic number 17. However, some of the clinics e.g. Diabetes are held in other areas of the hospital and therefore to capture the diabetic patients, participants were sampled from the diabetes centre. Clinic 17 serves general medicine patients, special cardiac patients, neurology, and rheumatology patients on specified days of the week. The study site was chosen because of; the high number of patients it receives, the

different conditions seen here and the high number of medications utilized by the patients attending this clinic.

3.4 Target Population

The study targeted all adults, 18 years and above, who were on drug therapy.

3.5 Eligibility Criteria

3.5.1   Inclusion criteria:

All ambulatory medical outpatients aged 18 years and above who were on drug therapy for non-communicable diseases.

3.5.2   Exclusion criteria:

Patients who did not give informed consent and those who had psychiatric problems were not included in the study.

3.6 Sample size determination

There has been no study conducted in the KNH outpatient setting in a general population to determine the prevalence of DTPs. There have however been studies conducted in the inpatient setting in the medical wards. A study conducted by Birichi et al estimated the presence of medication related problems in 97.5% of patients before, and in 95.7% of patients after introduction of an individualized dispensing system in the medial wards of KNH (5), while Njeri et al found that each of her study participants had at least one MRP resulting in an overall prevalence of 100%. The sample size for this study was based on these estimates from the KNH medical wards and we utilized the lowest prevalence of 95.7% and rounded it off to 96%.

The Cochran formula was applied to determine the sample size as follows (30);

$$n = Z^2 * \frac{p(1-p)}{d^2}$$

Where:

Z- Level of significance (1.96%)

p- Prevalence of DTPs

d- Precision Estimate around DTPs (5% or 0.05).

n- Sample size.

Working on the assumption of 96% as the frequency of DTPs, the sample size (n) was;

$$n = 1.96^2 * \frac{0.96(1-0.96)}{0.05^2} = 59$$

However, only 46 patients were included in the study due to incomplete data from the other interviews.

3.7 Sampling method

Convenience sampling was carried out to select participants to include in the study.

Participants were approached at the clinic's health records office as they came to rebook appointments after being seen by the physician. Participants were asked a few questions using the eligibility criteria form, to determine their eligibility for inclusion into the study.

3.8 Participant Recruitment

The PI built a rapport with the participants after they saw the physician and explained verbally what the objectives of the study entailed i.e. procedure, confidentiality, benefit, or harm (Appendix 2A). The PI made the participants aware that they could voluntarily withdraw and leave the study at any time.

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). Any patient who disagreed to participate in the study was asked to explain the reason for their decline.

Those who consented to the study were taken through the questionnaire outlined in Appendix 4 by the PI.

3.9 Research Instruments

3.9.1 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

The data collection form was modified from the Pharmacotherapy workup© notes developed by Cipolle et al. (8). The Pharmacotherapy workup© notes are a validated tool used to offer systematic and structured pharmaceutical care to patients. This structured and modified questionnaire method 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 had signed the consent form (Appendix 3B).

3.10   Data Collection

Data was collected using the modified Pharmacotherapy workup© notes and this was done through a face to face interview with the patient. Other data that was also collected from the patient's medical files and medication charts was used to carry out patient assessment.

The data was collected over a period of 6 weeks from August 2018 to mid-September 2018.

Appropriateness of drug therapy was determined using the relevant National Guidelines for the different conditions that the patients had, and where these were not available, American and European guidelines were used. Effectiveness of the drug therapy was determined through comparison of the patient's goals of therapy and their lab parameters as well as absence, presence or reduction of signs and symptoms. Safety of medication was determined from the patient's signs and symptoms, which were determined by the review of systems, and laboratory parameters for safety monitoring. Adherence to medication was determined through the Morisky Medication Adherence Scale (MMAS), as well as through several questions that were cleverly put to the patient.

3.11   Pre-testing of data collection form

A pilot study was carried out with 7 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 medical outpatient clinic during clinic days. Amendments were made for the ambiguities that were identified, to make the data collection tool easy to use.

3.12   Validity

Internal validity of the data collection tool was established by carrying out a pilot study, while external validity was established by carrying out appropriate sampling. The pilot study ensured that the modified 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.

Moreover, the study site chosen was chosen to give a good representation of the general population since KNH receives referrals and attends to patients from all parts of the country.

3.13 Reliability

The Pharmacotherapy workup© notes that was modified to generate the data collection tool is a validated tool that is in use in many pharmacies in the US. Before the study was carried out, a pre-testing of the tool was carried out to establish reproducibility of the results. Amendments were done on the instrument where necessary, in order to improve its efficiency and effectiveness.

3.14 Data Collection Techniques

The study participants were interviewed by the principal investigator and the data entered into the data collection form. Further to that, treatment charts and medical records belonging to every study participant were also reviewed by the principal investigator. Data collection was conducted in two phases. The initial step was the patient interview, while the second phase involved perusal and abstraction of data from the patient's medical records and medication charts. The modified Pharmacotherapy workup© notes was used to collect the data.

3.15 Variables and Definitions

3.15.1 Case definitions

Drug Therapy Problems: This is defined as an undesirable event in a patient that involves, or is suspected to involve drug therapy and interferes with the health outcomes of a patient. A DTP occurs when a patient's drug-related needs of indication, effectiveness, safety and adherence are not met and requires professional judgment to resolve. The seven drug therapy problems identified by Cipolle et al. are;

a. Unnecessary drug therapy - where drug therapy is unnecessary because the patient does not have a clinical indication for the drug.

b. Needs additional drug therapy – where additional drug therapy is needed to treat or prevent a medical condition in the patient.

c. Ineffective drug – where the drug product is not being effective at producing the desired response in the patient.

d. Dosage too low – where the dosage given is too low to produce the desired pharmacotherapeutic response in the patient.

e. Adverse drug reaction – where the drug therapy causes an adverse reaction to the patient.

f. Dosage too high – where the dosage is too high leading to undesirable effects in the patient.

g. Non-adherence – where the patient is not able or willing to take the drug therapy as agreed upon with the prescriber.

3.15.2 Variables

The outcome variable was any of the 7 drug therapy problems.

The exposure variables included;

Duplicate therapy	No medical indication at this time
Non-drug therapy more appropriate	Addiction/recreational drug use
Treating avoidable adverse reaction	Preventive therapy needed
Untreated condition	Synergistic therapy needed
More effective drug available	Condition refractory to drug
Dosage form inappropriate	Contraindication present
Drug not indicated for condition	Ineffective dose
Needs additional monitoring	Frequency inappropriate
Incorrect administration	Drug interaction
Incorrect storage	Duration inappropriate
Undesirable effect, not dose-related	Unsafe for patient due to patient risk factors
Drug interaction	Incorrect administration
Allergic reaction	Dosage increase/decrease too fast
Dose too high	Patient does not understand instructions
Patient cannot afford drug product	Patient prefers not to take the medication
Patient forgets to take medication	The medication is not available
Patient cannot take the medication	

3.16   Data management

Confirmation of completion of the questionnaire took place after each interview. Data was entered and stored into a Microsoft excel 2010 workbook, which the researcher could access. After data collection, participant's 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.

3.17   Data analysis

The data was entered into Microsoft Excel 2010 and was analysed using STATA version 13.0. Descriptive summary statistics were presented as means with standard deviation for normally distributed continuous variables, and medians with interquartile range for non-normally distributed continuous variables. Categorical variables were summarized using frequencies and percent proportions.

3.18   Ethical and logistical considerations

3.18.1 Ethical approval

Clearances from the University of Nairobi and Kenyatta National Hospital-Ethics and research Committee were obtained and after this, authorisation from Kenyatta National Hospital administration was also obtained before carrying out the study. Participation in the study was voluntary and only after the participants consented to participate through signing of a consent declaration form (appendices 2B).

3.18.2 Informed Consent

All Participants were taken through the nature of the study using an explanation form (appendices 2A) and upon understanding, the participants were presented with a consent declaration form to sign (appendix 2B).

3.18.3 Risks and benefits

The participants participated without exposure to any harm. The study did not involve any invasive procedures.

3.18.4 Confidentiality

The collected information was treated confidentially and access to it was restricted. Signed copies of the consent participation forms were kept under lock and key. Only the principal investigator and assistant researcher had access to the documents.

CHAPTER FOUR: RESULTS

4.1 Patient demographic characteristics

Forty six patients were included in the study and were interviewed at the medical outpatient clinic in Kenyatta National Hospital.

Of these forty-six, 33 (71.7%) were female while the male participants were 13 (28.3%). The age ranged between 21 and 79 years with a median of 58.5 [IQR 48, 66] years. The median age of the female participants was 58[IQR 49, 63] years, while that of the males was 59[IQR 36, 70] years. Only 19.6% of the participants were of normal weight, with a majority of the participants falling within the BMI category of 'Overweight (37.0 %)' and 'Class I Obesity (32.6%)'. Women comprised of 82.9 % of the people who were above normal weight. All participants had had some form of official schooling.

Table 7: Descriptive demographic data

Variable	N	%
Sex		
Female	33	71.7
Male	13	28.3
Age in years		
20 – 29	3	6.5
30 – 39	7	15.2
40 – 49	4	8.7
50 – 59	11	23.9
60 – 69	10	21.7
70 – 79	11	23.9
Marital status		
Single	13	28.3
Married	33	71.7
Highest education		
Informal		
Incomplete primary	10	21.7
Complete primary	8	17.4
Incomplete secondary	9	19.6
Complete secondary	13	28.3
Tertiary	6	13.0
BMI Category		
Normal weight	9	19.6
Overweight	17	37.0
Class I obesity	15	32.6
Class II obesity	2	4.3
Class III obesity	1	2.2

Thirty-three patients (71.7%) claimed to have medical insurance cover, with 31 (93.9%) of those patients stating that they had taken that cover with National Hospital Insurance Fund (NHIF). However, only 4 patients had their medications purchased and clinic visits paid for, by their insurance provider, with the remaining 42 patients having to pay out-of-pocket, for the same. More patients (21.7%) claimed to have missed medications due to the cost, than those who missed to undergo diagnostic/investigative procedures (10.9%) due to the cost, implying that patients would rather go without medications than miss medical tests.

Table 8: Medical insurance information

Variable	N	%
Patients with insurance cover	33	71.7
Patients covered by NHIF	31	67.4
Clinic visits covered	4	8.7
Medications purchase covered	4	8.7
Medications occasionally missed due to cost	10	21.7
Diagnostic procedures/Investigations occasionally missed due to cost	5	10.9

Indications for drugs included treatment as well as prophylaxis. The indications identified were twenty, with the total number of indications identified in the participants, being 286. The mean number of indications per patient was 7.0 (SD ± 3.2). The most common indication for treatment was hypertension, with 39 (84.8%) patients being hypertensive, while prevention of pneumococcal disease (84.8%) and prevention of seasonal influenza (82.6%) were the most common indications for preventive/prophylactic therapy.

Table 9: Indications for medications among patients assessed at the MOPC

	Medical condition/Indication	No. of patients (%)	Percentage of conditions
1	Hypertension	39 (84.8%)	13.6
2	Prevention of pneumococcal diseases	39 (84.8%)	13.6
3	Prevention of seasonal influenza	38 (82.6%)	13.3
4	Prevention of Hepatitis B	23 (50.0 %)	8.0
5	Prevention of meningococcal diseases	20 (43.5%)	7.0
6	Dyspepsia/GERD	19 (41.3 %)	6.6
7	Back pain	17 (37.0 %)	5.9
8	Osteoarthritis	16 (34.8 %)	5.6
9	Primary prevention of cardiovascular events	14 (30.4 %)	4.9
10	Diabetes mellitus type 2	12 (26.1 %)	4.2
11	Heart failure	11 (23.9 %)	3.8
12	Secondary prevention of cardiovascular events	8 (17.4 %)	2.8
13	Neuropathic pain	7 (15.2 %)	2.4
14	DVT	5 (10.9 %)	1.7
15	Hyperthyroidism	5 (10.9 %)	1.7
16	Asthma	4 (8.7 %)	1.4
17	Hyperlipidaemia	2 (4.3 %)	0.7
18	Rheumatoid arthritis	2 (4.3 %)	0.7
19	Seizures	2 (4.3 %)	0.7
20	Rheumatic heart disease	2 (4.3 %)	0.7
21	Prevention of human papilloma viral infection	1 (2.2%)	0.3
	Total	**286**	**100 %**

The drug products that had been prescribed for the patients were 56 and the total medications for the patients were 186. The mean number of prescribed medications per patient was 4.0 (SD ± 2.1). The top ten products prescribed accounted for 50% of medications prescribed for the patients.

Table 10: Commonly prescribed drug products

	Drug Product	No. of patients (n)	Percentage %	Cumulative percentage %
1	Amlodipine	15	8.1	8.1
2	Junior aspirin	14	7.5	15.6
3	Atorvastatin	14	7.5	23.2
4	Losartan/HCTZ	11	5.9	29.1
5	Metformin	9	4.8	33.9
6	Carvedilol	7	3.8	37.7
7	HCTZ	6	3.2	40.9
8	Losartan	6	3.2	44.1
9	Enalapril	6	3.2	47.3
10	Atenolol	6	3.2	50.6
11	Mixtard Insulin	5	2.7	53.3
12	Nifedipine	5	2.7	55.9
13	Furosemide	5	2.7	58.6
14	Warfarin	5	2.7	61.3
15	Nebivolol	4	2.2	63.5
16	Omeprazole	4	2.2	65.6
17	Carbimazole	4	2.2	67.8

The most common medications prescribed by drug class were the calcium channel blockers (50% of patients), followed by the thiazide diuretics (47.8%). These frequencies included drugs in combination product e.g. for hydrochlorthiazide (HCTZ), the count included both the HCTZ that was prescribed as a single product and that which was prescribed as a combination product.

Table 11: Commonly prescribed medications by drug class

	Drug product	No. of patients (%)
1.	**Calcium channel blockers**	**23 (50%)**
	Amlodipine	18
	Nifedipine	5
2.	**Thiazides**	**22 (47.8%)**
	Hydrochlorthiazide	18
	Indapamide	3
	Chlorthalidone	1
3.	**Angiotensin receptor blockers (ARBs)**	**21 (45.7%)**
	Losartan	17
	Telmisartan	4
4.	**Beta – blockers**	**20 (43.5%)**
	Carvedilol	7
	Atenolol	7
	Nebivolol	5
	Propranolol	1
5.	**HMG –CoA reductase inhibitors**	**15 (32.6%)**
	Atorvastatin	14
	Rosuvastatin	1
6.	**Salicylates (JASA)**	**14 (30.4%)**
7.	**Oral antidiabetics**	**13 (28.3%)**
	Metformin	10
	Sitagliptin	1
	Pioglitazone	1
	Gliclazide	1
8.	**Proton pump inhibitors**	**7 (15.2)**
	Omeprazole	5
	Esomeprazole	2
9.	**ACE inhibitors (Enalapril)**	**6 (13.0%)**

4.2 Prevalence of drug therapy problems

The prevalence of drug therapy problems (DTP) was approached in two different ways. First, it was described as the proportion of patients experiencing any drug therapy problem. It was found that 44 (95.7 %) of the patients were experiencing at least one DTP. The DTPs were then categorised and their prevalence calculated. The total number of DTPs identified was 229, with the mean number of DTPs per patient being 5 (SD ±2.6). 'Additional drug therapy needed' was the DTP with the highest prevalence (72.9 %), while 'dosage too low' followed, at 8.7 % prevalence of the total DTPs. 'Unnecessary drug therapy' was the least identified DTP (1.7 %).

Table 12: Distribution of drug therapy problems by category

	Drug therapy problem category	No. of drug therapy problems	Percentage of total (%)
1	Unnecessary drug therapy	4	1.7
2	Additional drug therapy needed	167	72.9
3	Different drug product needed	5	2.2
4	Dosage too low	20	8.7
5	Adverse drug reaction	9	3.9
6	Dosage too high	7	3.1
7	Non-compliance	17	7.4
	Totals	**229**	**100**

For each drug therapy problem that was identified, the causes of the same were also identified. The most common cause for 'unnecessary drug therapy' was duplicate therapy (50.0%), while the most common cause for 'additional drug therapy needed' was preventive/prophylactic therapy.

Table 13: Drug therapy problems and their most common causes

DTP	DTP cause	N	%
Unnecessary drug therapy		**4**	**100.0**
	Duplicate therapy	2	50.0
	No medical indication	1	25.0
	Treating avoidable ADR	1	25.0
Additional drug needed		**167**	**100.0**
	Preventive/prophylactic therapy	129	77.2
	Untreated condition	30	18.0
	Synergistic/potentiating therapy	8	4.8
Different drug needed		**5**	**100.0**
	More effective drug available	3	60.0
	Drug not indicated for condition	2	40.0
Dosage too low		**21**	**100.0**
	Ineffective dose	18	85.7
	Frequency inappropriate	2	9.5
	Incorrect administration	1	4.8
Adverse drug reaction		**9**	**100.0**
	Undesirable effect	9	100.0
Dosage too high		**6**	**100.0**
	Dose too high	4	66.7
	Needs additional monitoring	2	33.3
Non compliance		**17**	**100.0**
	Patient cannot afford drug product	10	58.8
	Directions not understood	5	29.4
	Patient prefers not to take	2	11.8

4.3 Medications most frequently associated with each category of DTPs

Medications that were most likely to be needed as additional therapy were the vaccines (pneumococcal, seasonal influenza, hepatitis B, meningococcal – 69.6 %), analgesics (9.0 %), proton pump inhibitors (6.0 %) and the statins (3.6 %).

Table 14: DTPs arising from unmet need of appropriate indication

Drug therapy problem	Drug class	N	%
Unnecessary drug therapy		**4**	**100%**
	Thiazides	1	25.0
	Beta blocker/Thiazide	1	25.0
	Proton pump inhibitor (PPI)	1	25.0
	Anti-asthmatics	1	25.0
Needs additional drug therapy		**167**	**100%**
	Pneumococcal vaccine	39	23.4
	Seasonal influenza vaccine	36	21.6
	Hepatitis B vaccine	21	12.6
	Meningococcal vaccine	20	12.0
	NSAIDs	15	9.0
	PPI	10	6.0
	Statins	6	3.6
	Anti-platelets	5	3.0
	Loop diuretic	4	2.4
	Anticonvulsants (pain)	3	1.8
	Thiazides	2	1.2
	Beta blockers	2	1.2
	HPV vaccine	1	0.6
	folic acid	1	0.6
	Oral antidiabetic	1	0.6

Medications that most frequently needed to be changed to more effective drugs were the beta blockers (60.0 %), while those that were more frequently prescribed at a dosage that was too low were the statins (26.3 %), loop diuretics (15.8 %) thiazides (10.5 %) and combination products containing an angiotensin receptor blocker and a thiazide (10.5 %).

Table 15: DTPs arising from the unmet need of medication effectiveness

Drug therapy problem	Drug class	N	%
Needs different drug product		**5**	**100**
	Beta blockers	3	60.0
	Thiazides	1	20.0
	Vasodilators	1	20.0
Dosage too low		**19**	**100**
	Statin	5	26.3
	Loop diuretic	3	15.8
	ARB/Thiazide	2	10.5
	Thiazide	2	10.5
	Antibiotic	1	5.3
	Beta blocker	1	5.3
	Insulins	1	5.3
	ACEI	1	5.3
	Calcium channel blocker	1	5.3
	Anticoagulant	1	5.3
	Anticonvulsant (seizures)	1	5.3

Adverse drug reactions most frequently occurred with the use of antiplatelet therapy (33.3 %) and calcium channel blockers (33.3 %), while drugs that tended to be prescribed at a dosage that was too high were most frequently the anticoagulants (28.6 %) and the anti-thyroid (28.6 %) medications.

Table 16: DTPs arising from unmet need of medication safety

Drug therapy problem	Drug class	N	%
Adverse drug reaction		**9**	**100**
	Antiplatelet	3	33.3
	Calcium channel blocker	3	33.3
	Statin	2	22.2
	Beta blocker	1	11.1
Dosage too high		**7**	
	Anticoagulant	2	28.6
	Anti-thyroid	2	28.6
	Beta blocker	1	14.3
	CCB	1	14.3
	Thiazide	1	14.3

Medication therapy that was not adhered to by patients most frequently was the calcium channel blockers (17.6 %) and aldosterone antagonists (11.8 %).

Table 17: DTPs arising from unmet need of compliance to medication

Drug therapy problem	Drug class	N	%
Non-compliance		**17**	**100**
	CCB	3	17.6
	Aldosterone antagonist	2	11.8
	Antiplatelet	1	5.9
	Thiazide	1	5.9
	Statin	1	5.9
	Oral antidiabetic	1	5.9
	Insulins	1	5.9
	ARB	1	5.9
	Methyldopa	1	5.9
	Beta blocker	1	5.9
	Antibiotic	1	5.9
	ARB/Thiazide	1	5.9
	Vasodilator	1	5.9
	Antiseizure	1	5.9

4.4 Conditions/ indications frequently associated with DTPs

Indications that most frequently required additional drug therapy were the vaccine preventable diseases such as pneumococcal diseases (22.5 %), seasonal influenza (20.8 %), Hepatitis B viral disease (12.1 %) and meningococcal diseases (11.6 %). Back pain (6.9 %) and dyspepsia (5.8%) were commonly occurring untreated conditions.

Table 18: Conditions/indications associated with unmet need of appropriate drug therapy

Drug therapy problem	Medical indication	N	%
Unnecessary drug therapy		4	100.0
	Hypertension	2	50
	Heart failure	1	25
	Dyspepsia	1	25
Needs additional drug therapy		173	100.0
	Prevention of pneumococcal disease	39	22.5
	Prevention of Seasonal influenza	36	20.8
	Prevention of Hepatitis B	21	12.1
	Prevention of meningococcal disease	20	11.6
	Back pain	12	6.9
	Dyspepsia	10	5.8
	Primary prevention of CVD	9	5.2
	Osteoarthritis	8	4.6
	Hypertension	4	2.3
	Secondary prevention of CVD	3	1.7
	Neuropathic pain	3	1.7
	Heart failure	2	1.2
	Rheumatoid arthritis	2	1.2
	Prevention of HPV infection	1	0.6
	Type 2 diabetes mellitus	1	0.6
	Hyperlipidaemia	1	0.6
	Hyperthyroidism	1	0.6

Indications that were most frequently associated with the need for a different drug product were hypertension (60.0 %), and heart failure (40 %), while those that were more frequently associated with medication that had been prescribed at a dosage that was too low included hypertension (42.1 %), secondary prevention of a cardiovascular event (26.3 %) and heart failure (10.5 %), among others.

Table 19: Conditions/ indications frequently associated with unmet need of medication effectiveness

Drug therapy problem	Medical indication	N	%
Needs different drug product		**5**	**100**
	Hypertension	3	60
	Heart failure	2	40
Dosage too low		**19**	**100**
	Hypertension	8	42.1
	Secondary prevention of CVD	5	26.3
	Heart failure	2	10.5
	Rheumatic heart disease	1	5.3
	Type 2 diabetes mellitus	1	5.3
	DVT	1	5.3
	Seizures	1	5.3

Medical conditions that were frequently associated with the occurrence of an adverse drug reaction or the potential for one to occur were hypertension (44.4 %), primary (22.2 %) and secondary (22.2 %) prevention of a cardiovascular event. Medical conditions most frequently associated with medications that were prescribed at a dosage that was too high included; hypertension (42.9 %) and hyperthyroidism (28.6 %) among others.

Table 20: Conditions /indications frequently associated with unmet need of Safety of medications

Drug therapy problem	Medical indication	N	%
Adverse drug reaction		**9**	**100**
	Hypertension	4	44.4
	Primary prevention of CVD	2	22.2
	Secondary prevention of CVD	2	22.2
	Hyperlipidaemia	1	11.1
Dosage too high			
	Hypertension	3	42.9
	Hyperthyroidism	2	28.6
	DVT	1	14.3
	Rheumatic heart disease	1	14.3

Non-compliance was frequently associated to indications such as hypertension (58.8 %), type 2 diabetes mellitus (11.8 %) and primary prevention of cardiovascular events (11.8 %).

Table 21: Conditions/indications frequently associated with unmet need of compliance to medications

Drug therapy problem	Medical indication	N	%
Non-compliance		**17**	**100**
	Hypertension	10	58.8
	Type 2 diabetes mellitus	2	11.8
	Primary prevention of CVD	2	11.8
	Heart failure	1	5.9
	Seizures	1	5.9
	Eye condition	1	5.9

4.5 Goals of therapy achieved at the initial pharmacotherapy assessment

The total indications for which patients were already taking medications were 125, and of these, those whose goals of therapy had been achieved at the time of the assessment were 65, while those whose goals of therapy had not been met were 49. There were 11 conditions for which patients were taking medications but

whose outcomes of drug therapy could not be ascertained as they needed additional laboratory monitoring. These included seven type 2 diabetes mellitus patients who did not have blood sugar results, and two patients on warfarin who did not have INR results. The indications whose outcome of therapy was termed as 'initial' were those that required medication(s) but had not been prescribed any, e.g. patients who had an indication for immunization but had not received the needed vaccine, or those who had an untreated condition such as back pain, that could benefit from medication(s).

Table 22: The goals of therapy achieved at the initial pharmacotherapy assessment

Outcome of therapy	N	%
Goals met	65	20.2
Goals not met	49	15.2
Initial	159	61.2
No results	11	3.4
Totals	**284**	**100.0**

CHAPTER FIVE: DISCUSSION, SUMMARY, CONCLUSION AND RECOMMENDATIONS

5.1 Introduction

This chapter discusses the results obtained and summarizes the findings of the study.

5.2 Discussion

5.2.1 Socio-demographic characteristics

This study showed that the number of female patients (71.7%) at the medical outpatient clinic is more than the males (28.3%). Similar studies conducted at the same hospital in the inpatient setting also found that the females were more (5,6). This could either mean that women fall ill more often than men, or their health seeking behaviours are better than for males. Females were also found to be more in the outpatient setting in the work reported by Strand et al. (22). The median age of the participants was 58.5 [IQR 48, 66] years, also similar to what Njeri et al. found (6). More than 80.0 % of patients were above normal weight, with 90.6 % of women found to be above normal weight as compared to 50.0 % of men. This finding could also serve to explain why there were more female patients than males in the MOPC, as obesity is closely associated with several non-communicable or lifestyle diseases. A noteworthy fact was that anthropometric measurements were not carried out routinely at the clinic yet it has been reported that an average weight loss of 10 kg can reduce SBP by 5 to 20 mm Hg (31). Routine weight-taking was only done for the patients attending the diabetes clinic. Seventy-one point four percent of patients had health insurance cover, with 93.9% of those using NHIF as their insurance provider. It is noteworthy that 21.7% of patients claimed that they had missed their medications occasionally due to cost, while 10.9% of patients had occasionally missed to have a diagnostic investigation carried out due to cost, suggesting that patients would rather go without medications than miss a medical procedure.

5.2.2 Prevalence of drug therapy problems

Participants found to be experiencing at least one DTP were 44 (95.7 %) and this was quite high when compared to the Minnesota pharmaceutical projects and other similar studies carried out in the west (14,20,28), while similar studies carried out in the same setting, showed a prevalence that was above 90% in all of them (5–7). This difference is likely to arise from policy differences in the different countries, especially as pertains to vaccine use in adults.

The most common DTP identified was 'additional drug therapy needed' (72.9%). This was consistent with the findings of Rao et al., (20) Isetts et al. (28) and Strand (22) , who also found this DTP to be the most frequently occurring, though its percentage of occurrence was on average 30% in those populations. This was in contrast to Njeri et al. who found the most common medication related problem (MRP) to be 'drug interactions' accounting for 21.8% of the identified MRPs. It is worthy to note however that she used the initial Strand classification which listed 8 categories of MRPs (12), and which included drug interactions as an MRP, whereas this study used the updated Strand classification of 7 categories (14) , which lists drug interactions as a cause of several DTPs including 'dose too low', adverse drug reactions', and 'dosage too high'. The commonest cause for 'additional drug therapy needed' in this study was a need for preventive/prophylactic therapy (77.2%) and this was because more than 80% of the participants had an indication for vaccine use according to the *Kenya Immunization Policy Guidelines of 2013* (32), but had never received those vaccinations. On further questioning, all patients responded that they had never been recommended to get vaccinated by their health care providers. This highlights the fact that while there may be an immunization policy in place in the country, it is not being utilized, either due to the fact that there is a lack of awareness on its existence, or there is prescriber/health care giver apathy or unavailability of the vaccines. It is likely a combination of all these factors leading to a lack of immunization of the adult cohort of patients in Kenya. Pharmacists can play a key role by offering immunization services especially in the community setup.

A number of patients also had untreated conditions (18%), with the most common being osteoarthritis, back pain and heartburn. Conversely, in the South Australian/Minnesota comparative study (20), salicylates, calcium supplements and tetanus vaccines were the most needed additional drugs for preventive/prophylactic therapy. Untreated conditions were identified through carrying out of a thorough review of systems, where many patients expressed regret that they had forgotten to mention the condition to the doctor during their appointment. This highlights the fact that review of systems is not always carried out thoroughly by the medical practitioner and the reason is most likely due to the high workload in the medical outpatient clinic. The queues were overwhelming, and sometimes patients were turned away due to the high number of patients Vis a Vis the available doctors. 'Untreated condition' was the second most common medication related problem that Njeri et al. found at 18.1% (6), using the initial Strand classification.

The second most frequently identified DTP in our study was 'dosage too low' at 8.7%. It was comparable to other studies in that it was second most frequent DTP (8,20,22,28), however those studies found this DTP to average 20% prevalence. It appears that medical practitioners are very cautious in prescribing medications and pharmacists would be of immense help, no doubt, in advising prescribers on maximum effective dosage that is also safe to the patient.

Non-compliance was the third most frequently occurring DTP in this study, with a prevalence of 7.4%. In the inpatient population of the same hospital, Birichi et al. found this DTP to occur at a prevalence greater than 80% (5), while Njeri et al. found it to occur at 70% prevalence (6). However, this DTP cannot be appropriately compared between in and out patient populations, as a patient who is admitted will be reliant on another person to give them the medication. However, it shows that patients take medicine better on their own at home than when they are admitted. Non-compliance was also found to be the third most frequently occurring DTP in the Minnesota pharmaceutical projects (19,20,22,28) Surprisingly, adverse drug reactions were not the commonest drug related problem as many studies seem to suggest (33,34). In this study, it had a

prevalence of 3.9% of total DTPs identified, and was the fourth most frequently identified DTP. This shows that while many have concentrated on adverse drug reactions being the major drug related problem, they have been missing out on many DTPs and therefore have underestimated the extent and impact of drug related problems. Degu et al. however found this DTP to be the most frequently occurring in a population of cervical cancer patients at the same hospital (7), showing that in certain special populations, this DTP can be quite frequent due to the nature of the unavoidable medications used for therapy.

The least identified DTP was 'unnecessary drug therapy'. Duplicate therapy was the most common reason given for this DTP.

5.2.3 Medications most frequently associated with drug therapy problems

The calcium channel blockers (50%) and the thiazides (47.8%) were the most commonly prescribed drugs while the top ten drug products prescribed accounted for 50% of total prescribed medications. Other studies have found oral diabetics, diuretics, salicylates, ACEIs to be among some of the most frequent drug classes prescribed (19). In the local setting in the inpatient population, it was reported that anti hypertensives, anti-infectives, anticoagulant and lipid lowering agents were among some of the most frequently used drugs (6) in one study, while another reported that anti-infectives, cardiovascular and alimentary drugs were the most common drugs in use (5). Common drugs that appear in the top 5 of all these studies include; diuretics, salicylates/anti-platelets, anticoagulants and analgesics. It would therefore make sense for pharmaceutical care practitioners to be well-versed with the commonly prescribed drugs (possibly top 10 prescribed drugs) as it would give them the capability to solve 50 % of patients DTPs.

Due to the large number of prescribed drug products and the relatively small sample size, meaningful statistical associations between drug therapy problems and medications could not be drawn conclusively. However, medications that were most frequently needed as additional therapy were the vaccines

(pneumococcal, seasonal influenza, hepatitis B, meningococcal – 69.6 %), analgesics (9.0 %), proton pump inhibitors (6.0 %) and the statins (3.6 %).

Medications that frequently needed to be changed to more effective drugs were the beta blockers (60.0 %), while those that were more frequently prescribed at a dosage that was too low were the statins (26.3 %), loop diuretics (15.8 %) thiazides (10.5 %) and combination products containing an angiotensin receptor blocker and a thiazide (10.5 %). In their study, Strand et al found that beta blockers were used in ineffective dosages. In addition they found that statins, calcium supplements, ACEIs, warfarin and insulins were being given at sub-therapeutic dosages (22). These findings give another opportunity to pharmaceutical care practitioners to strive for more in-depth understanding of these classes of medications that commonly cause drug therapy problems, thereby placing them in a position of authority to give advice concerning their use.

Antiplatelet therapy (33.3 %) and calcium channel blockers (33.3 %) were the medications that most frequently led to development of adverse drug reactions, while drugs that tended to be prescribed at a dosage that was too high were most frequently the anticoagulants (28.6 %) and the anti-thyroid (28.6 %) medications.

Medication therapy that was not adhered to by patients most frequently was the calcium channel blockers (17.6 %) and aldosterone antagonists (11.8 %). Differences between studies is most likely due to the fact that commonly prescribed drugs are varied in different settings, and it is expected that the commonly used drugs are the ones that cause most DTPs (22).

Howard et al. found four groups of drugs to account for more than 50% of drugs associated with preventable hospital admissions. These included; anti-platelets, diuretics, NSAIDs and anticoagulants (16). They further classified the drug-related admissions as those caused by adverse drug reactions, overtreatment, under treatment and patient adherence problems. Medication that was most commonly associated with ADRs and overtreatment included anti-platelets, diuretics and NSAIDs. In our study, medications most associated with ADRs included anti-platelets and CCBs, while medication most associated with a dosage that was too high included anticoagulants and anti-thyroid medications.

Howard et al. reported that drug related admissions due to under treatment, were associated with the use of anti-epileptics and adherence related admissions were associated with use of diuretics, anti-diabetic drugs and anti-epileptic drugs.

5.2.4 Medical conditions/indications most frequently associated with DTPs

The most common medical condition was hypertension (84.9% of patients), and it was therefore expected that it would be the most common medical condition associated with drug therapy problems. The small sample size did not enable meaningful statistical associations to be drawn between medical conditions and drug therapy problems. Other similar studies also found that hypertension was the most commonly occurring medical condition (6,19,20).

Indications that most frequently required additional drug therapy were those requiring vaccines for prevention of diseases such as pneumococcal diseases (22.5 %), seasonal influenza (20.8 %), hepatitis B viral disease (12.1 %) and meningococcal diseases (11.6 %). As discussed earlier, this problem is not comparable to the Minnesota pharmaceutical projects as there is a more defined policy in the setup of those studies regarding vaccine use in adults (35). Back pain (6.9 %) and dyspepsia (5.8%) were commonly occurring untreated conditions that require medical practitioners to actively probe for, as most patients seemed to have accepted these conditions as 'normal', and mostly reported them only when probed.

5.2.5 Outcomes of drug therapy

Outcomes of drug therapy were also evaluated and this study found that from a total of 284 indications, patients were taking medications for only 125 of them, and had achieved their goals of drug therapy in 65 (20.2%) conditions, while they had yet to meet their goals in 49 (15.2%) of their conditions. The indications which had not been prescribed for therapy were termed as 'initial' and accounted for 61.2% of the total indications. Overall, for the patients who were already using drug therapy, 52% of conditions had achieved their goals of therapy, while 39.2%

of conditions had not achieved their goals of drug therapy. In one study, they found that goals had been met in 67.2 % of patients' goals of therapy (<65 years) and in 77.6 % of patients' goals of therapy (>65 years) during the initial pharmacotherapy assessment. These figures significantly improved after the provision of pharmaceutical care services (PCS) to 90.5 % and 90.6 %, respectively. They also found that goals at initial therapy were 23.1 % (<65 years) and 11.9 % (> 65 years) (19). Another study found that 76 % of patient's goals of therapy were being met at the initial pharmacotherapy assessment and improved to 90 % after provision of PCS (28). Our study found that goals of therapy that were at 'initial' status were high at 61.2 % and this contributed to 'goals met' being lower than what other studies found.

5.3 Summary

This study was able to identify drug therapy problems occurring in patients attending medical outpatient clinic at Kenyatta National Hospital, and further to that, identify the causes of those DTPs. The most common intervention given for medical problems is drug therapy, and it is given with an ultimate goal of improved outcomes for the patient. The presence of any drug related problem leads to lack of achievement of these therapeutic goals. Similar studies that have been conducted in Kenya have used different classification systems to identify drug related problems. This study utilized the updated Strand classification system and found it to be a very resourceful tool that enabled us to not only identify drug therapy problems but their causes as well. This means that a pharmaceutical care practitioner can design interventions since they already know the source of the problems.

Implications of the findings

Patel & Zed found that 28% of all emergency department visits were drug-related and of this, 70% were preventable (15). Howard et al. found four groups of drugs to account for more than 50% of drugs associated with preventable hospital admissions. These included; anti-platelets, diuretics, NSAIDs and anticoagulants (16). We do not know of any study in Kenya that has tried to determine what

percentage of emergency department visits and admissions is related to drug therapy problems, but we now have studies that have determined the prevalence of DTPs, which on average is quite high. This study has also shown the medications and conditions that are most frequently associated with DTPs. It is therefore possible to prevent drug-related morbidity and mortality, which several studies in the US have shown to cost upwards of $100 billion (3,4), by paying special attention to these identified drugs and conditions. By correctly identifying actual or potential DTPs in patients, pharmacists can design interventions that resolve or prevent DTPs and therefore reduce the number of drug-related emergency department visits and the associated costs.

5.4 Conclusions

Women made up for majority of the MOPC patients and they also made up for majority of the overweight and obese patients.

Slightly over half of indications for which patients are taking drug therapy achieve their goals of therapy, while a majority of patients (72.9 %) require additional drug therapy. These additional medications are needed, either for preventive therapy or an untreated condition, in order to achieve optimal health outcomes.

The second most frequently occurring DTP is 'dosage too low', highlighting the fact that pharmacists are needed to give advice on optimal dosages of medications that are both effective and safe for the patient.

The top 10 prescribed drugs account for 50% of the total prescribed drugs, therefore pharmaceutical care practitioners should ensure that they have in-depth knowledge of these few medications in order to solve majority of the DTPs.

5.5 Recommendations

5.5.1 Recommendations for policy and practice

The most common drug therapy problem that was identified in the study involved a need for additional drug therapy either due to a need for adult immunizations or presence of an untreated condition. Vaccines have been found to be one of the

most cost effective and successful interventions in safeguarding public health, after hand washing, and while there is a national vaccine policy published (32), it is not adhered to, leaving many high risk individuals unvaccinated. It is therefore prudent that health workers are trained on the use of adult vaccines, and the health system strives to make these available to the patient.

The pharmacotherapy assessment tool together with the DTP classification system of Cipolle et al. offer pharmaceutical care practitioners a well-organized, practical step by step methodology of assessing patients, evaluating them and offering interventions and solutions to help patients achieve their goals of therapy. It is a method which can be adopted by all practitioners so that we standardize the practice of pharmacy in the country.

The workforce in the outpatient clinics in Kenyatta National Hospital, and indeed all public hospitals in the country should be increased to allow for quality patient assessment that will lead to better patient health outcomes.

Standards of care should be adopted at the hospital and throughout the country that ensure all patients get uniform and quality service. For example, up to date clinical guidelines should be published that are relevant to the country and all medical practitioners should use them as a reference point. A review of systems should also be carried out comprehensively on patients to avoid missing indications and untreated conditions. These measures would ensure patients receive the same quality of care no matter which health provider they visit.

Monitoring for medication safety and effectiveness requires to be done more rigorously and pharmaceutical care practitioners should be at the forefront in offering and advocating for these services.

Anthropometric measurements were not routinely carried out at the MOPC yet the study found only 19 % of patients to be of normal weight. This practice should be taken more seriously and made mandatory to ensure better health outcomes for patients.

The third most common DTP identified was non- compliance, with 58.8 % of this DTP being caused by patient's inability to purchase medications due to cost. This can potentially be resolved by availing outpatient insurance cover for patients

attending the MOPC at KNH, several of whom complained that despite their having NHIF cover, it did not help them most of the time and only came in handy in the event of a hospital admission.

5.5.2 Recommendations for further research

This study should be carried out on a wider scale to allow for more meaningful associations of variables to outcomes to be determined. However it would require team work of a bigger team of investigators.

The economic and clinical impact of pharmaceutical care (as described by Cipolle et al.) should be assessed, and would serve as a good reference point to determine the needs for pharmaceutical care practitioners.

A study to determine the percentage of emergency room visits and hospital admissions that are related to drug therapy problems and associated costs should be carried out.

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APPENDICES

APPENDIX 1: ELIGIBILITY SCREENING FORM

Kenyatta National Hospital Medical Outpatient Clinic **OP number**_____ **Study number**_____	
Criteria	**Remark as YES or NO**
Adult aged 18 years and above	
Patient on drug therapy for non-communicable disease	
No psychiatric problem	
Consent Given	

If all answers are **YES,** please proceed to the study Questionnaire

Title of the Study: Determination of the Extent of Drug Therapy Problems at a Kenyan Referral Hospital

Institution: Department of Pharmaceutics and Pharmacy Practice, School of Pharmacy, University of Nairobi, P.O BOX 30197-00400, Nairobi

Principal Investigator: Dr. Gathua Elizabeth Wambui - Master of Pharmacy (Clinical Pharmacy) Second-year student at the University of Nairobi, P.O BOX 30197-00400, Nairobi

Supervisors: Prof Ndemo- Associate Professor, UoN; Dr. Menge – Deputy Director, KNH

Introduction: I am Elizabeth Wambui Gathua, a postgraduate student at the University of Nairobi, school of pharmacy. I am conducting a study to determine the extent of drug therapy problems at Kenyatta National Hospital in patients 18 years and above who are receiving drug therapy and are being followed up at the medical outpatient clinic of KNH.

The purpose of the study: Majority of patients receive drug therapy for the management of their medical conditions. Drug therapy problems can prevent the patient from achieving their drug therapy goals. 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 know if your drug related needs are being met and to know if any drug therapy problems exist. We will determine this using a two parts modified pharmacotherapy questionnaire.

Procedures to be followed: Should you agree to participate in the study, you will be required to answer questions in an interview that will take approximately 20 minutes. The process will be at your own convenience and you are free to skip questions that you do not wish to answer. All information the principal investigator and the assistant researcher collect from you will be treated with confidentiality and restricted for access.

Voluntary participation: In this study, choosing to participate is entirely voluntary and you are justified to drop out by your own free will even after agreeing to participate. You may decline to enroll or drop out of the study at any time. By doing so, you will not lose any benefits that you may be entitled.

Risks and harms: Psychological, emotional, social and physical factors are risks found in a medical research. However, a concerted effort must be generated to mitigate the risk. One of the risks that you may encounter is lack of privacy. The collected information will be treated confidentially and restricted for access using password protected electronic medical record. 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.

Benefits: The study findings will help us to improve health outcomes in patients by identifying common drug therapy problem experienced by patients and their causes. By so doing, it will help develop guidelines and protocols that will prevent drug therapy problem occurrences among patients.

Reimbursements: There will no payments in form of fiscal, gifts or incentives as a result of the participation of adults in the study.

Contacts: You are free to contact the Principal investigator before, during, and after the study for any queries you might have regarding the study. Please feel free to use the contacts below.

Dr. Elizabeth Wambui Gathua. P.O. Box 72055-00200, Nairobi. Telephone Number – **0720244562**. Email: gathualiz@yahoo.com or the Secretary/Chairperson, Kenyatta National Hospital-University of Nairobi Ethics 44 and Research Committee Telephone No.: **2726300** Ext: **44102** Email: *uonknh_erc@uonbi.ac.ke.*

Supervisors:

Prof. Francis Ndemo: Department of Pharmaceutics and Pharmacy practice, University of Nairobi.

Dr. Tom Menge: Deputy Director, Pharmaceutical Services, Kenyatta National Hospital. P.O. Box 19676-00202, Nairobi. Tel: +254 2726771, +254771946687

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 counsellor. 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 at any time. 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: _____

APPENDIX 3A: MAELEZO KUHUSU KUSHIRIKI KATIKA UTAFITI

Kuhusu utafiti huu: Tathmini ya matatizo yanayoweza tokea kwa wagonjwa wanapotumia dawa za matibabu

Taasisi: Idara ya Pharmaceutics and Pharmacy Practice, Shule ya Pharmacy, Chuo Kikuu Cha Nairobi,

Mtafiti Mkuu: Dkt Elizabeth W. Gathua, Mwanafunzi uzamili (utabibu dawa), Chuo kikuu cha Nairobi, SLP 30197-00400, Nairobi.

Wasimamizi: Profesa Ndemo, Mhadhiri, Chuo Kikuu cha Nairobi, Dkt. Menge, Idara ya Pharmacy, Hospitali Kuu ya Kenyatta.

Utangulizi: Mimi ni Elizabeth Wambui Gathua, mwanafunzi katika Chuo Kikuu cha Nairobi, kitongo cha shule ya pharmacia.

Ninafanya uchunguzi wa matatizo ya madawa ya tiba kwa wagonjwa ambao ni watu wazima waliozaidi ya miaka 18 na ambao wanahudhuria kliniki katika hospitali Kuu ya Kitaifa ya Kenyatta.

Madhumuni ya Utafiti: Wagonjwa wengi hutibiwa kwa njia ya utumizi wa madawa ya tiba. Matatizo yanayotokana na utumizi wa haya madawa yanaweza yakasababisha wagonjwa wasipate nafuu waliyotarajia kupata, au kufikia malengo yao ya matibabu. Katika utafiti huu, utaulizwa ueleze jinsi ambavyo unavyotumia madawa, tajiriba na changamoto unazozipata kwa kutumia haya madawa. Utaulizwa pia ueleze maoni yako ya kibinafsi kuhusu utumizi wa madawa ya tiba. Lengo letu ni kujua kama mahitaji yako yanayohusiana na madawa ya tiba yamekidhiwa na kujua kama unayo matatizo yoyote ya tiba ya dawa.

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

Utarejeshewa pesa zako?: Utafiti huu hautakugharimu pesa.

Na ukiwa na maswali baadaye?: Kama una maswali zaidi au lolote ambalo hulielewi kuhusu utafiti huu, tafadhali usisite.

Wasiliana nasi kupitia nambari ambazo zimeandikwa hapa chini.

Mtafiti Mkuu Tovuti: gathualiz@yahoo.com Simu: 0720244562 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 _____

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APPENDIX 4: QUESTIONNAIRE

RESEARCH TOPIC: Prevalence of Drug Therapy Problems among Ambulatory Patients Attending the Kenyatta National Referral Hospital's Medical Outpatient Clinic

Date: ....

Questionnaire Code: ……………..

SECTION A: PATIENT INTERVIEW

Part 1: Patient's Socio-Demographic Data

1. Age: _____years.

2. Age category: (0) 18-34 (1) 35-49 (2) 50-64 (3) 65-79 (4) ≥80 years.

3. Weight: _____Kilograms (Kg).

4. Height: _____Meters (M).

5. Crude BMI_____ Kg/M^2.

6. BMI Category (0) <18.5 Underweight (1) 18.5-24.9 Normal (2) 25.0-29.9 Overweight (3) 30.0-34.9 Class I obesity (4) 35.0-39.9 Class II obesity.

7. Sex: (0) Female (1) Male

8. Marital status: (0) Single (1) Married (2) Widowed (3) Separated (4) Divorced.

9. Highest education qualification:

    (0) Informal (1) Incomplete Primary (2) Complete Primary

    (3) Incomplete Secondary (4) Complete Secondary (5) Tertiary.

10. Occupation: (0) Self-employed (1) Employed (2) Unemployed (3) Retired.

11. On average how much do you earn per month? _____

12. Do you have health insurance? (0) No (1) Yes

Question 12-14 for female participants only

13. Are you pregnant? (0) No (1) Yes

14. Trimester (0) 1st (1) 2nd (2) 3rd

15. Are you breastfeeding? (0) No (1) Yes

16. Do any of your family members have a chronic illness? (0) No (1) Yes (2) I don't know

17. If yes, which condition(s)? (0) Hypertension (1) Diabetes mellitus (2) Osteoarthritis (3) Tuberculosis (4) Others

Part 2: Patient's Medication Experience

Condition	Drug Product	Dose	Freq	Duration	Storage	Food	Side effects	Expect	Source of drug

Ask the patient questions 23 – 29 and fill in the table above for each drug they are taking

18. Can you match your medical condition(s) to the medication(s) you are taking? (0) No (1) Yes *(ask patient to list all drugs they have used in the past 6 month, including non-prescription and herbals)*

19. Do you know the dose(s) of the medication(s) you are taking? (0) No (1) Yes

20. Do you know the frequency at which you should take your medications? (0) No (1) Yes

21. Do you know the duration for which you should be on your medication? (0) No (1) Yes

Part 3: Patient's Medication Taking Behaviour (MMAS-8)

Question	No	Yes
Do you sometimes forget to take your medicine?		
In the last two (2) weeks, was there any day that you did not take your medicine?		
Have you ever stopped taking your medicines or reduced the dose without telling your doctor because you felt worse when you took it?		
When you travel or leave the house, do you sometimes forget to carry/take your medicine?		
Did you take your medicine yesterday?		
When you feel like your condition is under control, do you sometimes stop taking your medication?		
Taking medicine every day is a real inconvenience for some people. Do you ever feel hassled about sticking to your treatment plan?		
How often do you have difficulty remembering to take all your medicines?		
a. Never/Rarely b. Once in a while c. Sometimes d. Usually e. All the time		
TOTAL Yes Score		

22. The patient's adherence to medications is (total 'yes' score of) (0) >2, Low (1) 1-2

Medium (2) 0 High

Part 4: Patient's immunization status

Which of the following vaccinations have you received?

Vaccine	No	Yes
Hepatitis B		
Typhoid		
Influenza		
Tetanus		
Rabies		
PCV 13		
23 valent pneumococcal		
Polyvalent meningococcal		
HPV		

23. Is patient current on all adult immunizations? (0) No (1) Yes

Social drug use

24. History of smoking (0) Never (1) Current smoker (2) Former smoker

25. If yes, how much do you smoke? (0) 0-1 packs per day (1) >1 packs per day

(2) Attempting to quit

26. Do you take alcohol? (1) Yes (0) No.

27. If yes, which is your preferred alcoholic drink? (0) Beer (1) Wine (2) Spirits (3) Local Brew (4) Other.

28. If yes, how much? (0) < 2 drinks per week (1) 2-6 drinks per week (3) > 6 drinks per week (4) History of alcohol dependence

29. If Yes to 46 above, for how long? _____Years.

30. Caffeine use? (0) No (1) Yes

31. If yes, how much?(0) < 2 cups per day (1) 2-6 cups per day (2) > 6 cups per day (3) History of caffeine dependence

32. Other recreational drug use? (0) No (1) Yes

33. If yes, which drug do you use? _____

34. Have you ever had any adverse reactions to drugs in the past? (0) No (1) Yes

35. Which medication was involved? _____

36. What reaction occurred when you took the medicine? (0) Rash (1) Shock (2) Asthma (3) Nausea (4) Anaemia (5) Other

37. How soon did the reaction occur after taking the medicine? _____min.

38. Other Alerts/Health Aids/Special Needs (0) Sight (1) Hearing (2) Mobility (3) Literacy (4) Disability

SECTION B: PATIENT PHYSICAL ASSESSMENT

Carry out a physical assessment of the patient and check the boxes appropriately, then answer questions 60 & 61 below

Vital signs: BP _____/_____   HR _____bpm   Resp Rate _____Temp _____

General Systems		Poor appetite	GU/Reproductive		Dysmenorrhea/menstrual bleeding
		Weight change			Incontinence
		Pain			Impotence
		Headache			Decreased sexual drive
		Dizziness (vertigo)			Vaginal discharge or itching
EENT		Change in vision			Hot flashes
		Loss of hearing	Kidney/Urinary		Urinary Frequency
		Ringing in the ears (tinnitus			Blood urine (hematuria)
		Bloody nose (epistaxis)			Renal dysfunction
		Allergic	Hematopoietic Symptoms		Excessive bruising
		Glaucoma			Bleeding
		Bloody sputum (hemoptysis			Anemia
Cardiovascular		Chest Pain	Musculoskeletal		Back pain
		Hyperlipidemia			Arthritis (osteo/rheumatoid)
		Hypertension			Tendonitis
		Myocardial Infraction			Painful muscles
		Orthostatic hypotension	Neuropsychiatric		Numb, tingling in extremities (parasthesia)
Pulmonary		Asthma			Tremor
		Shortness of breath			Loss of Balance
		Wheezing			Depression
Gastrointestinal		Heartburn			Suicidal
		Abdominal pain			Anxiety, nervousness
		Nausea			Inability to concentrate
		Vomiting			Seizure
		Diarrhea			Stroke/TIA
		Constipation			Memory loss
Skin		Eczema/Psoriasis	Infectious Disease		HIV/AIDS
		Itching (pruritis)			Malaria
		Rash			Syphilis
Endocrine Systems		Diabetes			Gonorrhea
		Hypothyroidism			Herpes
		Menopausal symptoms			Chlamydia
Hepatic		Cirrhosis			Tuberculosis
		Hepatitis			
Nutrition/Fluid/ Electrolytes		Dehydration			
		Edema			
		Potassium deficiency			

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SECTION B: PATIENT PHYSICAL ASSESSMENT

39. Based on the patient's physical assessment and data from the patient file, are there deviations from normal that could be due to drug therapy (side effects)? (0) No (1) Yes

40. Based on the patient's physical assessment and data from the patient file, are there any deviations from normal that require a treatment plan? (0) No (1) Yes

SECTION C: FILE DATA ABSTRACTION

Use data from the Patient's file to fill in the following table. Some information may be gotten from patient.

CONDITION (INDICATION)	DRUG PRODUCT (Include route, dose , frequency, duration, start date)	DESIRED OUTCOMES	RESULTS	OUTCOME STATUS	DTP	CAUSE

SECTION D: IDENTIFY DTP AND ASSOCIATED MEDICATION AND MEDICAL CONDITION

Evaluate data from sections A, B and C to identify any DTP, associated medications and medical conditions.

41. Is there unnecessary drug therapy? (0) No (1) Yes
If yes, answer question 75 - 77
42. What is the possible cause? (0) Duplicate therapy (1) No medical indication at this time (2) Non-drug therapy more appropriate (3) Addiction/recreational drug use (4) Treating avoidable adverse reaction
43. Which drug is involved? _____
44. Which disease/condition is involved? _____

45. Does the patient need additional drug therapy? (0) No (1) Yes
If yes, answer question 79 - 81
46. What is the possible reason? (0) Preventive therapy (1) Untreated condition (2) Synergistic therapy
47. Which drug is involved? _____
48. Which disease/condition is involved? _____

49. Is there any ineffective drug in the patient's regimen? (0) No (1) Yes
If yes, answer question 83 - 85
50. What is the possible cause? (0) More effective drug available (1) Condition refractory to drug (2) Dosage form inappropriate (3) Contraindication present (4) Drug not indicated for condition

51. Which drug is involved? _____
52. Which disease/condition is involved? _____

53. Is there any drug whose dosage is too low in the patient's regimen? (0) No (1) Yes
If yes, answer question 87 - 89
54. What is the possible cause? (0) Ineffective dose (1) Needs additional monitoring (2) Frequency inappropriate (3) Incorrect administration (4) Drug interaction (5) Incorrect storage (6) Duration inappropriate
55. Which drug is involved? _____
56. Which disease/condition is involved? _____

57. Is there any drug causing (or has potential to cause) an adverse drug reaction in the patient? (0) No (1) Yes
If yes, answer question 91 - 93
58. What is the possible cause? (0) Undesirable effect, not dose-related (1) Unsafe for patient due to patient risk factors (2) Drug interaction (3) Incorrect administration (4) Allergic reaction (5) Dosage increase/decrease too fast
59. Which drug is involved? _____
60. Which disease/condition is involved? _____

61. Is there any drug whose dosage is too high in the patient's regimen? (0) No (1) Yes

62. What is the possible cause? (0) Dose too high (1) Needs additional monitoring (2) Frequency too short (3) Duration too long (4) Drug interaction resulting in toxic reaction
63. Which drug is involved? _____
64. Which disease/condition is involved? _____

65. Is the patient non-compliant? (0) No (1) Yes
66. What are the possible causes? (0) Patient does not understand instructions (1) Patient cannot afford drug product (2) Patient prefers not to take the medication (3) Patient forgets to take medication (4) The medication is not available (5) Patient cannot take the medication
67. Which drug is involved? _____
68. Which disease/condition is involved? _____

PARAMETERS COMMONLY USED TO EVALUATE EFFECTIVENESS AND/OR SAFETY OF DRUG THERAPY		
PARAMETER	**GOALS OF THERAPY (NORMAL VALUES)**	**CLINICAL USE**
Blood pressure	Goals of therapy include: systolic blood pressure of 110-140 mmHg diastolic blood pressure of 75-85 mmHg <130/80 with diabetes or kidney disease	Used to evaluate effectiveness and safety of antihypertensive drug therapies such as diuretics, beta blockers, ACE inhibitors, angiotensin II receptors blockers, aldosterone antagonists, calcium blockers.
Total Cholesterol	Goal of therapy < 200 mg/dl (SI < 5.17 mmol/L)	Represents all of the different kinds of cholesterol in the blood and includes high-density lipids (HDL), low-density lipids (LDL), and triglycerides (TG).
LDL Low-density lipoprotein	Goal of therapy varies depending on other risk factors including cigarette smoking, hypertension, HDL<40mg/dl, family history of CHD and male>45 or female>55. • without other risk factors <160 mg/dl (SI <4.1 mmol/L) • with 2 risk factors <130 mg/dl (SI <3.4 mmol/L) • with CHD and >2 risk factors <100 mg/dl (SI <2.6 mmol/L) Optional high risk <70 mg/dl	Used to evaluate the effectiveness of lipid lowering drug therapies including atorvastatin (Lipitor®), fluvastatin (Lescol®), lovastatin (Mevacor®), pravastatin (Pravachol®), rosuvastatin (Crestor®), simvastatin (Zocor®) ezetimibe/simvastatin (Vytorin®) nicotinic acid (Niacin®) gemfibrozil (Lopid®), clofibrate (Atromid-S®) colestipol (Colestid®), cholestyramine (Questran®)
HDL High-density lipoprotein	Goals of therapy > 40 mg/dl (SI >1.04 mmol/L)	HDL removes excess cholesterol from peripheral tissues and is considered "good" cholesterol. Elevated HDL levels are associated with decreased risk for coronary heart disease.
Triglycerides	<160 mg/dl <1.8 mmol/L	Elevated triglycerides considered an independent risk factor for coronary heart disease.
Glucose	Goal of therapy includes: preprandial blood glucose of 80-120 mg/dL bedtime blood glucose of 100-140 mg/dL Fasting plasma glucose of > 126 mg/dL on two occasions is consistent with the diagnosis of diabetes mellitus	Used to evaluate drug therapy to manage hyperglycemia associated with diabetes mellitus including insulin (Humulin®) (Novolin®), glipizide (Glutcotrol®), glyburide (Diabeta®) (Mircronase®), pioglitazone (Actos®), rosiglitazone (Avandia®)
HbA_{1c} Hemoglobin A_{1c}	Goal of therapy < 7% Normal range 4-6%	Used to evaluate the effectiveness of glucose control in patients with diabetes. Reflects the blood glucose control over the past 2 to 3 months.
TSH Thyroid Stimulating Hormone	Goals of therapy include the reduction of TSH levels to the normal range of 0.3-5 µU/ml (SI 0.3-5 mU/L)	Used to evaluate the effectiveness of thyroid replacement therapy to manage hypothyroidism. levothyroxine (Synthroid®). Elevated TSH levels are indicative of hypothyroidism.
INR International Normalized Ratio	Goal of therapy varies with the indication. INR 2.0-3.0 for atrial fibrillation, deep vein thrombosis, pulmonary emboli INR 2.5-3.5 for mechanical prosthetic values	Used to evaluate the effectives and safety of anticoagulant therapy. Used to determine dosage adjustments for warfarin (Coumadin®) therapy.
K^+ Serum Potassium	Goal of therapy is to maintain serum potassium within the normal range of 3.5 – 5.0 mEq/L (SI 3.5 – 5.0 mmol/L)	Used to evaluate and prevent cardiac toxicity associated with hypokalemia caused by diuretics, diarrhea/vomiting. Can aggravate digoxin (Lanoxin®) toxicity. Hyperkalemia associated with renal dysfunction, ACE inhibitors including captopril (Capoten®), enalapril (Vasotec®), lisinopril (Prinivil®) (Zestril®), ramipril (Altace®)
Creatinine serum creatinine (SCr) creatinine clearance (CrCl)	Creatinine normal range 0.6-1.3 mg/dL (SI 53-115 µmol/L) Creatinine Clearance normal range 80-100 ml/min Drug dosage adjustments often required when CrCl is <30 ml/min	Used as a guideline to determine appropriate dosage of medications which are dependent on renal function for elimination. Used to determine if drug therapy is causing nephrotoxicity or if drugs are accumulating to unsafe levels due to decreasing renal function.
ALT Alanine aminotransferase AST Aspartate aminotrasnferase	Normal values Males 10-40 Units/ml Females 8-35 Units/ml Males 20-40 Units/ml Females15-30 Units/ml	Used to evaluate liver damage caused by medications such as simvastatin (Zocor®), pravastatin, lovastatin (Mevacor®), atorvastatin (Lipitor®) (Pravachol®), fluvastatin (Lescol®), rosuvastatin (Crestor®), simvastatin (Zocor®), carbamazepine, phenytoin, acetaminophen If elevated 2-3 times drug-induced hepatic damage suspected

APPENDIX 5: ERC APPOVAL

UNIVERSITY OF NAIROBI
COLLEGE OF HEALTH SCIENCES
P O BOX 19676 Code 00202
Telegrams: varsity
Tel:(254-020) 2726300 Ext 44355

KNH-UON ERC
Email: uonknh_erc@uonbi.ac.ke
Website: http://www.erc.uonbi.ac.ke
Facebook: https://www.facebook.com/uonknh.erc
Twitter: @UONKNH_ERC https://twitter.com/UONKNH_ERC

KENYATTA NATIONAL HOSPITAL
P O BOX 20723 Code 00202
Tel: 726300-9
Fax: 725272
Telegrams: MEDSUP, Nairobi

Ref: KNH-ERC/A/284

July 19 2018

Elizabeth Wambui Gathua
Reg.No.U56/88024/2016
Dept. of Pharmaceutics and Pharmacy Practice
School of Pharmacy
College of Health Sciences
University of Nairobi

Dear Elizabeth

RESEARCH PROPOSAL – PREVALENCE OF DRUG THERAPY PROBLEMS AND DETERMINATION OF OUTCOMES AMONG PATIENTS ATTENDING MEDICAL OUTPATIENT CLINIC AT KENYATTA NATIONAL HOSPITAL   (P261/04/2018)

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 completion 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.

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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. Tom Menge

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