DRUG THERAPY PROBLEMS AMONG PATIENTS ON PROTON PUMP INHIBITORS IN THE MEDICAL WARDS OF KENYATTA NATIONAL HOSPITAL

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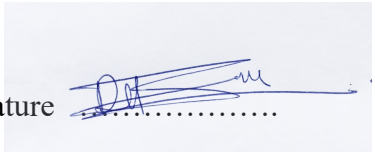
Signature  Date 3/12/2020

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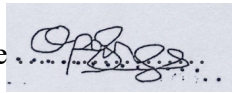
1. Signature  Date 24/11/2020

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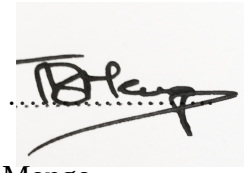
2. Signature  Date 28/11/2020

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Dedication

I dedicate this work to my parents Mr. and Mrs. Paul Kosgey, my wife Dr Viola Chemogos and my children; Migelle and Michelle for encouraging me during my studies. I salute them all.

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ABBREVIATIONS

BE- Barrett's esophagus

BMI-Body mass index

CDI-Clostridium difficile infection

DTPs –Drug therapy problems

DDIs-Drug –drug interactions

EE-Erosive esophagitis

FDA-Food Drug administration

GERD-Gastro-esophageal reflux disease

ICU-Intensive care unit

KNH-Kenya National hospital

MTRH-Moi Teaching and Referral Hospital

PPIs-Proton pump inhibitors

OPERATIONAL DEFINITIONS

Adherence: The extent to which the patient is able to follow instructions regarding the therapeutic agent given by a health care practitioner.

Adverse drug event: Any untoward occurrence that may present during treatment with a pharmaceutical product. It does not necessarily have a causal relation to the treatment.

Adverse drug reaction: An undesirable effect of a medication that occurs during usual clinical use.

Dosage: The total amount of active medication that a patient takes over a specified time and it entails the dose, duration, frequency and route of administration.

Dose: The amount of drug given to a patient as a single event.

Dosing interval:The period of time that elapses between administered doses.

Drug: A product or substance used for treatment, prophylaxis or diagnostic tests.

Drug therapy: Drug product or regimen taken by a patient for a therapeutic indication.

Drug therapy problems: Anything involving drug therapy that interferes with (or has the potential to interfere with) the desired outcome for a patient.

Effectiveness: the ability of a drug to produce the desired patient outcome.

Indication: A sign or a symptom a patient experiences that necessitates a therapeutic agent to be initiated.

ABSTRACT

Background: Drug therapy problems (DTPs) are major causes of morbidity, increased cost of health care, increased hospital stay and mortality. Proton Pump Inhibitor (PPI) use in hospitals has been increasing over time despite the myriad of side effects which compromise patient safety.

Main Objective: The objective of the study was to identify and describe DTPs associated with PPI use by patients admitted at the medical wards of KNH.

Methodology: A cross sectional study design was used targeting adult patients admitted in medical wards of KNH.A sample size of one hundred and seventy-six was consecutively selected. This was where all participants who met inclusion criteria were included until the desired sample size was attained. Data was collected through participant interviews and review of medical files. Descriptive statistics was summarized as means with standard deviation for normally distributed continuous variables and for non-normally distributed variables as median with interquartile range. Categorical variables at 95% significance level were presented as frequencies and percent proportions. Inferential statistics was used to evaluate association of patient- associated risk factors with occurrence of various types of DTPs. Chi-square test was used.

Results: The overall prevalence of DTPs associated with PPI use among patients admitted in medical wards of KNH was 43.2%. The prevalence of various types DTPs present were; the dosage was too high (**21.6%**), adverse drug interaction (**16.5%**), unnecessary drugs (**15.9%**), low dosage (**1.1%**), non- adherence (**1.1%**), the need of a different drug (**1.1%**) and the need of additional drug therapy (**0.6%**).

The multivariate analysis to assess the association between the DTPs and patient risk factors (comorbidities) was statistically insignificant, p value (0.104 to 0.860), at 95% confidence interval.

Discussion: The mean age of the participants was 43.6 (SD 16.5) years, while the median age was 39.0 years. The majority of the participants were ma le (95, (54.0%) as compared to females (81, (46.0%), with the leading age bracket of 30 – 39 years (28.4%) and majority having a minimum level of secondary education (39.8%). Among the patient risk associated

factors, the top five leading were Anemia (52, 29.5%), followed by hypertension (50, 28.4%), cancer (35, 19.9%), HIV (29, 16.5%), and respiratory diseases (28, 15.9%).

The high prevalence of the DTPs presence could be as a result of physicians' prescribing patterns, lack of strict adherence to prescription guidelines, and failure to involve the clinical pharmacists in reviewing treatment sheets and monitoring PPI use.

Conclusion: From the study findings, it is evident that the presence of DTPs associated with PPI use is very high, and this warrant extra caution in prescription of PPIs. This will improve patient therapeutic outcomes and safety.

Recommendations: There is need for strict adherence to the guidelines during prescription, sensitization of healthcare workers on PPI use, and involvement of clinical pharmacists in reviewing treatments sheets and monitoring PPI use with view the of preventing occurrence of DTPs.

CHAPTER ONE: INTRODUCTION

1.1 Background

Optimal drug therapy for patients is very essential in provision of quality health care in patients through achievement of desired patient's outcomes (1). Drug therapy problems (DTPs) are defined as unacceptable patient occurrences involving drug therapy that lead to or potentially lead to undesired treatment outcomes (2). They are also termed as medication related problems, MRPs. Drug therapy problems have been classified by Hepler and Strand into eight categories; Untreated indication (UI), Improper drug selection (IDS), Failure to receive drug (FRD), Overdose (OD), Adverse drug reaction (ADR), Sub therapeutic dosage (STD), Drug-drug interactions (DDI) Drug without indication (DWI) (3). This classification of DTPs has been modified based on patient's needs which includes; appropriateness of indication, effectiveness, safety and patient compliance to therapy (4). Patients can experience DTPs to any prescribed drug/drug classes.

Clinical pharmacists play a critical role in identifying, resolving and preventing the occurrence of DTPS during the pharmaceutical care process where the patient needs come first and the provider of the service undertakes the individual responsibility for the decisions made. When all the four patient drug therapy needs are met, drug therapy problems will not occur. However follow-up/monitoring is still necessary in case of development of new DTPs

Proton pump inhibitors, PPIs, are a class of drugs that suppress gastric secretion through the H+-K+ ATPase pump blockade and are essential in management of several conditions that result from increased acid secretion. The drugs in this class are omeprazole, esomeprazole, lansoprazole, rabeprazole and pantoprazole (5). Food and Drug Administration, FDA, USA and National Institute of Clinical Excellence, NICE,UK has approved thirteen uses of this class of drugs and they include management of dyspepsia, gastro-esophageal reflux diseases (GERD) and its complications, Barrett's esophagus (BE), hyper secretory acid disorders like Zollinger-Ellison syndrome, Non-steroidal anti-inflammatory drugs (NSAID) induced ulcers, *H .pylori* related ulcers, stress ulcer prophylaxis in critically ill patients among others (6).

Proton pump inhibitors have been traditionally considered safe and effective compared to other acid suppressant therapies. There is lack of tolerance to PPIs as opposed to H2-receptor antagonists. However, there are emerging safety concerns regarding the use of these drugs which involve; electrolyte disturbances, especially hypomagnesaemia, hyponatremia and hypocalcaemia ,hypochlorhydria; acute kidney injury; drug-drug interaction; megaloblastic anemia; increased potential for clostridium difficile infections (CDI),community acquired pneumonia (CAP), and osteoporosis (7).

The reason for this research is to identify the prevalence of these DTPs among patients using PPIs. This will therefore be essential in ensuring their appropriate/rational use of PPIs and limit the occurrence of DTPs. Therefore, desired patient outcomes will be achieved and the cost of provision of healthcare will be reduced. Harm caused by occurrence of DTPs as well as mortality rate due these DTPs will also be reduced among patients on PPIs

1.2 Problem statement

Drug therapy problems are a major cause of morbidity, increased cost of healthcare and increased hospital stay. Several studies have found a correlation between PPIs use and DTPs as seen in Singapore where more than 54.1% of patients admitted were using PPIs for conditions not indicated and this resulted in the unnecessary costs to the patients (8) .Mortality associated with over-use of PPIs has been documented with kidney and cardiovascular causes (9). Prevalence of PPIs use in patients admitted in the hospital range from 40-70%((10).

Proton pump inhibitors from studies done have been associated with a myriad of side effects which include drug-drug interactions, osteoporosis, vitamin B12 deficiency, infections especially *Clostridium difficile* infection (11). Mal absorption of some drugs that require acidic environment for absorption electrolyte imbalances such as hypomagnesaemia, hypocalcaemia, and hyponatremia. Proton pump inhibitors have also been found to cause gynaecomastia in some patients in Spain. However, this condition is reversible upon withdrawal of the drugs (12).

In developed countries efforts to de-prescribe PPIs are being made because of the above reasons (13). So far, no conclusive study has been done in Kenya concerning DTPs associated with PPIs. The study seeks to assess the prevalence of DTPs associated with PPIs use among patients admitted in medical wards at Kenyatta National Hospital. This will promote rational use of PPIs, decrease cost of treatment, minimize the occurrence of DTPs as well as improved patient safety.

1.3 Purpose of the study

This study seeks to inform the prescribers on the need to be cautious when prescribing PPIs so as to improve the patient desired therapeutic outcomes. The findings of this study will inform on the practice and treatments guidelines in Kenya regarding PPIs use. The study results may also contribute to policy change on PPIs use in medical wards for patients admitted in the hospitals across the country. The findings will justify the internationally recommended de-prescribing of PPIs in Kenya.

1.4 Objectives

1.4.1 Broad objectives

To identify and describe DTPs associated with PPI drug use by patients admitted in medical wards at KNH.

1.4.2 Specific objectives

1. To determine the overall prevalence of DTPs among patients using PPIs admitted in medical wards of KNH.

2. To determine the prevalence of various types of DTPs among patients on PPIs therapy in medical wards.

3. To investigate the patient associated risk factors associated with the various DTPs among patients using PPIs in medical wards of KNH.

1.5 Research questions

1. What is the overall prevalence of DTPs among patients using PPIs in medical wards of KNH?

2. What is the prevalence of the different types of DTPs among patients using PPIs in medical wards of KNH?

3. What patient risk factors are associated with the different types of DTPs among patients admitted in medical wards of KNH?

1.6 Significance/ Justification

This research will be of interest to Kenyatta National Hospital, specifically the medical wards. The results will potentially be used in the clinical setting by health care providers to better address the DTPs associated with the use of PPIs among admitted patients in the medical wards. The findings will also help KNH to come up with treatment protocols on PPI use and how to monitor DTPs occurrence. This will in turn be beneficial to the patient and improve quality of life. Health care cost will be reduced since hospital stay will be reduced when these DTPs are prevented.

The academic institutions concerned with training health-care personnel will use the study findings in training their students and staff to better manage patients on the use of PPIs. These findings will also be used as resource materials for future reference in research undertakings and form a basis for further research in this area.

The government will benefit by being informed on other areas needing the allocation of resources. The study findings will inform the policy makers on any policy changes required on the use of PPIs in in-patient settings. Since no studies have been done concerning DTPs associated with PPIs use in Kenya, the findings of this study will inform the development of guidelines on PPIs use in non-ICU patients.

1.7 Study delimitation

The study was carried out in medical wards of KNH. The DTP on patient adherence may not have been well investigated in an in-patient setting since medicine taking was reliant on the nurses responsible for drug administration in the medical wards.

1.8 Study Limitation

This was a cross-sectional study that included participants above 18 years old admitted in the medical wards at KNH with a prescription of PPI. Thus, the findings of the study will only be limited to this population group

1.9 Conceptual Framework

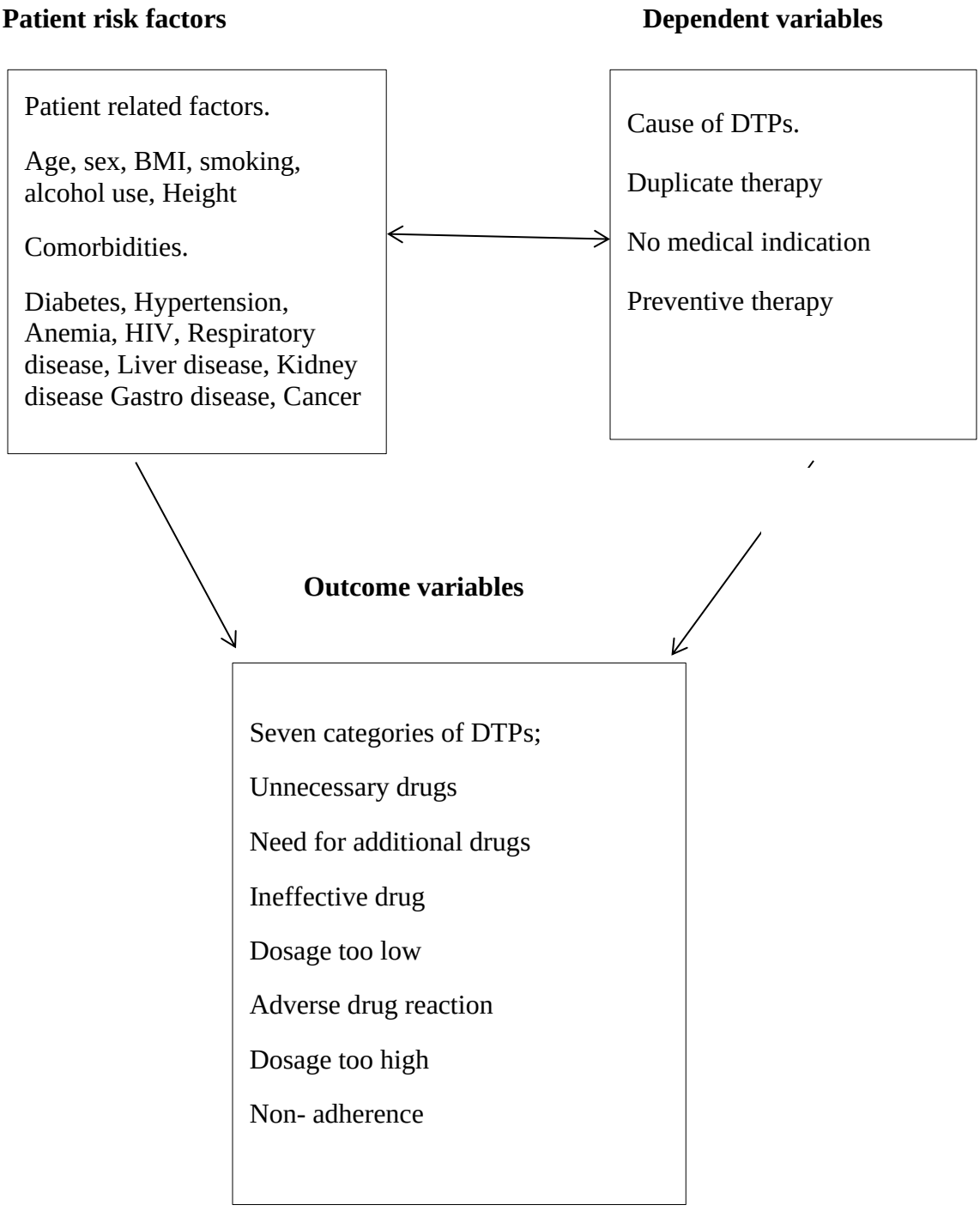

Figure 1: Conceptual Framework partially [Adapted from Linda *et al*,(14)

The conceptual framework tries to establish the relationship between patient risk factors and the dependent variables in the development of the seven categories of the DTPs. The patient risk factors include age, sex, weight, height, BMI, smoking and alcoholism. The other one was the existence of comorbidities. The dependent variables are the causes of the various categories of the DTPs. The outcome variables were the seven categories of DTPs namely: unnecessary drugs, needs additional therapy, dosage too low, ineffective drugs, adverse reaction, dosage too high and non-adherence.

CHAPTER TWO: LITERATURE REVIEW

2.1 Introduction

Drug Therapy Problems (DTPs) are undesirable events usually associated with drug therapy that may potentially harm the patient and result in negative clinical outcomes. Drug therapy problems are also called Medication-Related Problems (MRPs) and are usually identified during the assessment stage of the Pharmaceutical Care Process. Pharmaceutical care providers have the responsibility of identifying, resolving, and preventing occurrence of DTPs. Medication Management Service play a critical role in tackling of the DTPs. All patients experience DTPs as long as they are on medication. A systematic approach is used to address the DTPs which include assessment, care plan and follow-up/monitoring. Prioritization of the DTPs is very important, with the most severe being first addressed (14).

2.2 Categories of DTPS

Drug therapy problems are categorized into seven according to the patient's drug related needs which are: indication, effectiveness, safety and compliance. These DTPs are: an unnecessary drug, patient needs an additional drug for medical condition which is not at the time being treated, an ineffective drug given to the patient, drug dosage being too low, drug causing an adverse drug reaction, drug dosage being too high, and non- compliance (14).

Table 1: Drug Therapy Problems due to unmet drug-related needs

Patient needs	**Categories of drug related problems**
INDICATION	Need additional drug therapy Unnecessary drug therapy
EFFECTIVENESS	Dosage too low Ineffective drug
SAFETY	Dosage too high Adverse drug reaction
ADHERENCE	Non-compliance/ non-adherence

Adapted from **Linda *et al,***(14)

2.2.1 Drug therapy problems arising from unmet needs of Indication

This occurs when the patient is receiving a drug that is not necessary because they do not have any clinical condition at that time or the patient is not receiving a drug therapy yet they need it for prevention or treating a particular medical condition (14). A cross sectional study conducted in Singapore in 2016 found that 45.9% of inpatients using PPIs had appropriate indication (8). Another cross sectional study in Ireland in 2011 found only 30% of PPIs users was in line with the Irish guidelines (15).

2.2.1.1 Unnecessary drug therapy

This occurs when the patient does not have an indication at that time so the drug therapy is not needed. Some of the probable causes for unnecessary drug therapy are; no medical indication is present at that time, an adverse drug reaction that is avoidable is being treated, multiple drugs used to treat a condition that requires a single drug therapy, treating a condition caused by recreational or addictive agents, and treating a condition where non-drug therapy would be more appropriate (14).

A prospective study was done in United Kingdom in 2015 to determine whether over-prescription of PPIs was related to multi-morbidities in older patients aged 75 years old. The study concluded that 73.9% of the older patients were using PPIs inappropriately (16). In another nationwide drug utilization survey carried out in France in 2015, PPI drug users were identified in the French database. The study found out that 29.8% of the population was using PPIs. This was considered as an overuse of the PPIs and it was not in line with the French guidelines. The study also revealed that 53.5% of the new users indicated for PPI therapy was due to a co-prescription with NSAIDs of whom 79.7% had no measurable risk factor supporting the prophylactic co-prescription (17). A cross-sectional study in France was done in 2015 to determine off-label drug prescriptions in general practice. Omeprazole and esomeprazole were among the top ten most prescribed off-label drugs (18).

A cross-sectional study in Ireland in 2013 was carried out to determine the inappropriate use of PPIs among medical in-patients. Two hundred and five medical inpatients were assessed of whom 79% were using PPIs. 45% of the PPI drug users did not have any documentation of a valid indication for using the PPIs (19). An observational study was

carried out in Italy to assess the appropriateness of PPI use among oncology and non-ICU patients. 62.9% of the 343 patients assessed were on PPIs and only 29.1% were considered to be appropriate. The study also showed that the reasons for inappropriate use were unwarranted gastro-protection in drug treated patients and stress ulcer prophylaxis in low risk patients (20).

A cross-sectional survey carried out in Switzerland in 2019 assessed PPIs prescriptions in a tertiary care hospital. 180 patients were included in the study and 54% of these patients were using PPIs of whom 29% had their treatment started in the hospital. In conclusion, 72% of the patients on PPIs did not have a justified indication and only 28% had a justified indication (21).

2.2.1.2 Additional drug therapy needed

The patient is not receiving a required medication for either treating or preventing a particular disease. Three possible causes for need of additional therapy are; the medical condition is not being treated, drug therapy needed for prophylaxis, and a drug therapy needed for synergistic effects (14). A review done on the impact of pharmaceutical care practice on the practitioner, patients requiring additional drug therapy were among the most common categories of DTPs. Need for preventive therapy was a common type of DTP identified to prevent health problems such as esophagitis (22).

Table 2: Drug therapy problems arising from unmet needs of Indication

Drug therapy problem	**Cause**
Unnecessary drug therapy	Medical condition absent Treating avoidable adverse drug reaction Duplicate therapy Recreational/addictive drug use Non-drug therapy more appropriate
Additional drug therapy	Untreated condition Prophylactic therapy Synergistic therapy

Adapted from **Linda *et al*,**(14)

2.2.2 Drug therapy problems arising from unmet needs of effectiveness

This is when the drug therapy is not effective, or the dosage is too low hence the desired patient outcomes are not being met.

2.2.2.1 Ineffective drug therapy

There are some probable causes of the drug being ineffective during treatment. These causes include existence of a contraindication on the use of the drug, the condition is not responding to the drug and the drug product is not approved for the existing medical condition. Others include; inappropriate drug dosage form and the drug given is not the most effective for the existing medical condition (14). A cross-sectional study conducted in Saudi Arabia in 2013 on the prescribing pattern of PPIs in a tertiary hospital revealed that PPIs were irrationally used without following the approved guidelines. The study included 114 patients showed that the intravenous (IV) route was used in 65% of the patients out of whom 46 patients could take it orally. Therefore the study concluded that the IV route used was unjustified in the majority of the patients (23). A prospective observational study carried out in India in 2014 assessed the prescribing patterns of intravenous PPIs in a tertiary care hospital. The study included 611 patients aged 18 years and above admitted in the internal medicine, gastroenterology, and surgical wards receiving IV PPIs. The study revealed significant inappropriateness of PPI administration with reference to changeover therapy, indication, and duration of therapy (24).

2.2.2.2 Dosage too low

This DTP is the cause of ineffective drug therapy. Possible causes include inappropriate route of drug administration, improper storage of the drug product and the dose being too low to elicit a desired response. The other reasons are infrequent dosage interval and presence of drug interactions, additional monitoring required to determine if the dosage is too low, and drug therapy duration being too short (14). A prospective study was carried out in UK in 2010 on 276 hospitalized patients to assess the inappropriate utilization of intravenous PPIs. The study revealed that 75.4% of intravenous PPI prescriptions were inappropriate in terms of dose or duration of therapy (25). A cross-sectional study conducted in Switzerland in 2019 assessing PPIs prescription pattern by using 180 register-based electronic records of patients revealed that 63% of the justified indications did not

have an adequate dosage. The study concluded that only 11% of the patients on PPIs had a justified indication with an adequate dosage (21). In Denmark, a retrospective study in all hospitals was carried out from 1997-2006. The study assessed the risk of myocardial infarction, stroke, and cardiovascular death associated with the use of PPIs. 16.9% of aspirin treated patients had an increased risk of adverse cardiovascular events when treated with PPIs (26).

Table 3: Drug therapy problems arising from unmet needs of effectiveness

Drug therapy problem	**Cause**
Ineffective drug	Contraindication present Refractory condition Drug not approved for the condition Dosage form not appropriate More effective drug available
Dosage too low	Inappropriate route of administration Poor drug storage Ineffective dose Dosage interval too infrequent Drug interaction Addition monitoring required Shortened duration of therapy

Adapted from **Linda *et al*,**(14)

2.2.3 Drug therapy problems arising from unmet needs of safety

Safety needs not being met refers to the dosage of the drug being too high or an adverse drug reaction occurring from use of a drug (14).

2.2.3.1 Dosage too high

Dosage of a drug being too high may be caused by the following: a drug interaction resulting in increase of the amount of active drug available, additional monitoring required to assess if the dosage is too high, the drug dose being too high causing toxicity, duration of drug therapy being prolonged than is necessary, and the dosing frequency of the drug

being too short for the patient (14). A pharmacosurveillance study was carried out in Italy in 2007 to investigate the relationship between PPI use and risk of death. Four hundred and ninety-one patients in eleven acute care medical wards were included in the study. The study concluded that in discharged older patients from acute care hospitals, there was an increased 1-year mortality rate associated with the use of high-dose PPIs.

2.2.3.2 Adverse drug reaction (ADR)

This DTP affects the safety needs of the patient. The probable causes of ADRs are undesirable drug reaction which is not dose-related, allergic reaction and drug interaction. The other causes are unsafe drug product, incorrect administration of the drug product and rapidly increasing the dosage too fast during administration causing an increase in drug concentration (14). A 10-year longitudinal observational cohort study in USA from the year 2002 estimated all cause and specific mortality causes associated with PPIs among US veterans. The study found out that there were 45.20 excess deaths per 1000 patients taking PPIs. The causes of deaths were due to cardiovascular disease, chronic kidney disease and upper gastrointestinal cancer (9). A 15-month prospective study was carried out in six Canadian hospitals to assess host and pathogen factors for Clostridium difficile infection and colonization. The study involved 4143 patients and it revealed that 117 (2.8%) patients had Clostridium difficile infection while 123 (3.0%) patients had Clostridium difficile colonization. The study concluded that PPI use, antibiotic use, and older age were significantly associated with Clostridium difficile infection in the health-care setting (27). Taiwan conducted a prospective study in medical wards from 2011-2013. The study assessed the risk factors of Clostridium difficile associated diarrhea (CDAD) among 451 patients. The study concluded that PPI use, prior cephalosporin use, and malignancy were independently related to CDAD (28). A meta-analysis conducted in China in 2016 is in agreement with other studies on a significant association between Clostridium difficile infection and PPI use especially in general ward patients (29).

A review on complications of prolonged PPI use was conducting by searching Medline, Scholar, and Scopus databases in India, 2018. The studies reported short-term adverse events as clostridium associated diarrhea, cholecystitis, bacterial peritonitis, pneumonia, liver cirrhosis, pyogenic liver, interstitial nephritis, esophageal inflammations, nocturnal

breakthrough acid reflux, drug interaction and nutritional deficiencies mainly of Vitamin B 12 and iron. The long-term adverse events due to PPI use were barrettes esophagus, concomitant dyspepsia, dementia, osteoporosis, cancers at GE junction, and hypomagnesia (30). Another review was done by conducting a PubMed search in 2016 to identify studies evaluating the potential long-term effects of PPI therapy in older adults was published from 1990-2016. The review concluded that PPI use is associated with the risk of vitamin B12 deficiency, dementia, kidney disease, osteoporotic-related fractures, community-acquired pneumonia and Clostridium difficile infection (11).

A systematic review and meta-analysis were carried out in Canada in 2018 to assess the association between PPI use and the risk of adverse kidney outcomes. Two thousand and thirty-seven studies were identified by searching Embase, MEDLINE, SCOPUS, Cochrane Library, CINAHL, Web of Science, and grey literature. The study concluded that adverse kidney outcomes were associated with PPI usage (31). A retrospective cohort study carried out in France during 2015 to 2016 winter season investigated the association between acute gastroenteritis (AGE) occurrence and PPI use. The adjusted relative risk of AGE for those receiving PPI therapy was 1.81 (95%CI, 1.72-1.90) for all ages considered, 1.66 (95%CI, 1.54-1.80) among those aged 45 to 64 years, 2.19 (95%CI, 1.98-2.42) among those aged 65 to 74 years, and 1.98 (95%CI, 1.82-2.15) among those aged 75 years and older. In conclusion, increased risk of developing AGE during periods of highest circulation of enteric viruses was associated with continuous PPI use (32).

Table 4 : Drug therapy problems arising from unmet needs of safety

Drug therapy problems	Cause
Dosage too high	Drug interaction Additional monitoring required Drug dose too high Prolonged duration of therapy Dosing frequency to short
Adverse drug reaction	Undesirable reaction not due to dose Allergic reaction Drug interaction Drug unsafe for the patient Incorrect administration Dosage administered increasing too rapidly

Adapted from **Linda *et al*,**(14)

2.2.4 Drug therapy problems arising from unmet need of patient adherence

Non-adherence will occur when there are problems with the willingness and ability of the patient to use the drug as advised by the health care practitioner (14).

2.2.4.1 Non-adherence

Non-adherence occurs when the patient is not taking medication as instructed. Possible causes include the patient forgets to take the drug, prefers not to take the drug and when the patient does not understand the instructions. Other reasons are the patient is unable to administer or swallow the drug, the drug product is not available and the patient cannot afford the drug product. A total of 88,556 DTPs were identified and resolved in 22,694 patients receiving treatment from 2006-2010. Among these DTPs identified, 14% was due to patients' ability and willingness to adhere to the medication regimens (14).

Table 5: Drug therapy problems arising from unmet need of patient adherence

Drug therapy problem	Cause
Non-compliance	Forgetfulness of patient to take the drug Patients prefers not to take the drug Patient does not understand the instructions Patient unable to administer/swallow the drug Drug product not available Drug product not affordable to the patient

Adapted from **Linda *et al*,**(14)

2.3 Summary and Literature gap

Drug therapy problems associated with PPIs are common as seen from the previous studies conducted in various parts of the world. There is a notable gap in the literature about DTPs due to PPI use in Africa especially locally in Kenya.

None of such studies have been done in Kenya so far, so the information will be useful filling an existing gap and improving therapeutic outcomes through guidelines among this patient population. Prevalence of PPI use particularly in hospitalized patients is high.

This research aimed to fill this existing gap. As a result, the study findings will be contributing to the existing literature and reveal the prevalence and types of DTPs associated with PPI use in Kenya. This will help identify, resolve, and prevent these DTPs associated with PPI use hence improving patient treatment outcomes and their quality of life.

CHAPTER THREE: METHODOLOGY

3.1 Introduction

This chapter entails an overview of how the study was conducted. It describes the study design, location of the study, study population, duration of the study, sample size, sampling technique, and research instruments. Data collection and analysis will also be described in this chapter. Logical and ethical considerations, quality assurance and dissemination plan will also be included in this chapter.

3.2 Study design

A cross-sectional design was used to identify and describe DTPs associated with PPI drug use by patients admitted in medical wards at KNH. A cross-sectional study was chosen because its best suited for prevalence studies. It was also not time consuming, more affordable to the researcher, and a quick method to realize the study objectives. The prevalence and types of DTPs associated with PPI use in patients in the medical wards was determined as well as the risk factors associated with the DTPs. The study method allowed us to measure both the outcomes and exposures at the same time.

3.3 Location of the study

The study was conducted at Kenyatta National Hospital, one of the largest public referral hospitals in Kenya. It is located in Nairobi, the capital city of Kenya. It has a bed capacity of 1800 with 8 medical wards located at 7^{th} and 8^{th} floor. Medical patients referred to the hospital are admitted in wards 7A to 7D and wards 8A to 8D. A multidisciplinary team consisting of nurses, pharmacists, physicians, surgeons, nutritionists, laboratory technologists, among others are involved in providing health care services to patients admitted in the medical wards. It acts as a training center for the College of Health Sciences at the University of Nairobi. The site chosen is suitable because it receives a huge number of patients with unique medical conditions. This is likely to result in over-utilization of medicines.

3.3.1 Duration of the study

The study was conducted over a period five months after approval by Ethics Committee. The first one month was utilized in pre-testing of research tools while the last four months was used for data collection, data analysis and report presentation.

3.4 Target and study population

Target population was all adult patients above the age of 18 years on PPIs in Kenya. The study population was patients admitted at the medical wards 7A, 7B, 7C, 7D, 8A, 8B, 8C, and 8D. Only the patients who met the inclusion criteria were allowed to take part in the study.

3.4.1 Inclusion criteria

Patients included in the study were those having the following characteristics:

a) Aged eighteen years and above.
b) Admitted in the medical wards at KNH.
c) Patients on PPIs.
d) Patients who communicated effectively in either English or Kiswahili.
e) Patients who consented to participate in the study.

3.4.2Exclusion criteria

a) Patients who met eligibility criteria but declined to consent.

b) Medical patients in the common mini ICU (the patients were critically ill and were not in a position to communicate).

3.5 Sampling

3.5.1 Sample size calculation

3.5.2 Sampling method

The sample size for this study was based on two African studies that looked at inappropriate use of PPIs in critical care unit (33) and in secondary and tertiary health facilities (34). The estimated prevalence of inappropriate use of antacids and PPIs range from 18.2% to 36%. However, the context of these two studies did not exactly match our proposed study.

Therefore, we estimated that the prevalence of inappropriate use of PPIs was the mean of the findings of these two studies which was 27.1%. We therefore settled for these studies because they were both done in Africa and in resource limited settings.

Applying the sample size calculation formula for cross-sectional studies, the sample size was calculated as follows (35):

$$\mathbf{n} = \frac{\boldsymbol{Z^2\alpha/2}\ \boldsymbol{p(1-p)}}{\delta^2}$$

Where:

n= The desired sample size.

$\boldsymbol{Z^2\alpha/2}$ **=** The square of the standard normal deviate that cuts off an area α at the tails (2 sided). **Z**= 1.96 for 95% confidence level.

P= Estimated prevalence of inappropriate use of PPIs was the mean of the findings of two studies which was 27%.

δ = Margin of error/desired level of precision. Set at 5% (0.05).

$$\mathbf{n} = \frac{\mathbf{1.96^2 \times 0.27(1-0.27)}}{0.05^2}$$

n= 302

KNH has 8 medical wards with approximately 42 patients admitted in each ward. This makes a total of about 340 patients admitted in the medical wards. This constitutes a finite study hence the sample size was corrected for a finite population. The formula used for finite population sample size correction is as shown (36):

$$\textbf{Corrected sample size} = \frac{\mathbf{n \times N}}{\mathbf{n+N-1}} = \frac{\mathbf{340 \times 302}}{\mathbf{302+340-1}} = \mathbf{160}$$

Where n is the estimated sample size and N is the population of patients admitted in medical

wards at KNH. The corrected sample size with an additional number for non-responses was adjusted by 10% yielding a total sample of 176 patients. This was the number recruited for study.

3.5.3 Sampling method

Study participants were selected using consecutive sampling from a list of patients admitted to the medical wards. The eight medical wards 7A to 7D and 8A to 8D was categorized into cubes designated as blue, green and white for both males and females. A representative sample was obtained by selecting participants in male and female medical wards who met the eligibility criteria. The list was obtained from nursing officer in-charge or health records information officer. Confidentiality also dictates that you don't use names/bed number.

The pre-selected participants who met the inclusion criteria were recruited in the study. The recruited participants were then taken through the voluntary consenting process as guided in Appendix 1. Only those who consented were allowed to participate in the study.

3.6 Research instruments

A structured questionnaire which was administered by the researcher was used to collect data (Appendix 3a). Helper and Strand form with slight modification was used during data collection. The last part of the form contained information on possible patient associated risk factors (comorbidities) associated with various DTPs present.

3.7 Pre-testing

A pilot study was carried out using 17 patients, that was, 10% of the study sample. The pre-testing of the data collection tool was conducted at KNH medical wards. Improvements was made on discrepancies identified on the questionnaire to enable ease and completeness of the data collection instrument. The data collection tools were submitted to the ERC for approval before using them.

3.8 Validity

External validity was established by ensuring that an appropriate sample size was selected for the study using consecutive sampling. This enabled every participant who met the inclusion criteria to be selected until the desired sample size was attained. The correct

sample size was determined using the Fischer's formula. This was to ensure that the study results are generalizable to the wider population. Internal validity was established by ensuring that the data collection tool was well structured, accurate and complete. Participant's confidentiality and privacy was guaranteed by using unique codes to identify the participant. Data management was under private passwords to secure stored information.

3.9 Reliability

This means that results generated from the study are reproducible. Good reliability will show that the study conducted has satisfied its purpose and the research findings were not due to any extraneous variables. The pre-testing of the research instrument carried out on a subset of the study sample was done to establish reproducibility of the results. Changes were done on the data collection tools to ensure that results reproducible.

3.10 Data collection techniques

Data was collected using interviewer administered tool from recruited participants admitted in the medical wards who consented to participate. The study participants were interviewed by the principal researcher and the tool was filled appropriately. The data not obtained directly from the participants was abstracted from the participants' clinical records. Permission to access the participants' health records was obtained from the administration of KNH. The tool contained; socio-demographic characteristics of the participant, medications part, the type of DTP present and patient associated risk factors associated with various DTPs present. Patient characteristics and type of PPI the patient is using are the independent variables and the types of DTPs are the dependent variables.

Socio-demographic characteristics that were assessed are age, weight, height, BMI, sex, marital status, education level, and occupation, smoking, and alcohol intake. The types of PPIs assessed were omeprazole, esomeprazole, lansoprazole, rabeprazole, and pantoprazole. Patient associated risk factors that were assessed included comorbidities such as diabetes mellitus, hypertension, anemia, human immunodeficiency virus, respiratory disease, liver disease, kidney disease, heart disease, gastrointestinal disease, cancers.

The outcome variables assessed are the seven DTPs and they include:

1. Unnecessary drug therapy- The patient does not have an indication at that time, so the drug therapy is not needed.
2. Additional drug therapy needed- The patient is not receiving a required medication for either treating or preventing a particular disease.
3. Ineffective drug- The drug therapy is not effective hence the desired patient outcomes are not being met.
4. Dosage too low- The dosage is too low hence the desired patient outcomes are not being met.
5. Dosage too high- The dosage of the drug is too high leading to undesirable effects.
6. Adverse drug reaction- The drug therapy causes an adverse reaction to the patient.
7. Non-compliance- The patient is not willing or not able to use the drug as advised by the health care practitioner.

The exposure variables that was assessed are the various causes of the types of DTPs and are shown below:

Table 6: Causes of various types of DTPs

Medical condition absent	Drug interaction leading to ADR
Drug interaction reducing active drug concentration	Drug not approved for the condition
Treating avoidable adverse drug reaction	Drug unsafe for the patient
Additional monitoring required	Dosage form not appropriate
Duplicate therapy	Incorrect administration leading to ADR
Shortened duration of therapy	More effective drug available
Recreational/addictive drug use	Dosage administered increasing too rapidly
Drug interaction increasing active drug concentration	Inappropriate route of administration
Non-drug therapy more appropriate	Forgetfulness of patient to take the drug
Drug dose too high	Poor drug product storage
Untreated condition	Patient prefers not to take the drug
Prolonged duration of therapy	Ineffective dose
Prophylactic therapy	Patient does not understand the instructions
Dosing frequency too short	Dosage interval too infrequent
Synergistic therapy needed	Patient unable to administer/ swallow the drug
Undesirable reaction not due to dose	Drug product not available
Contraindication present	Drug product not affordable to the patient
Allergic reaction	Drug interaction leading to ADR
Refractory condition	Drug not approved for the condition

Adapted from **Linda *et al*,**(14)

The data collected was entered into a Microsoft Excel file with password protection and the computer was secured with a unique password. The patient number was not recorded in the data collection forms since unique codes were generated and known only to the principal investigator. Raw data was safely kept under lock and key and only accessed by authorized personnel. This was to ensure the privacy and confidentiality of the participants' information. Microsoft Excel 2010 was used for data entry, coding and cleaning. Processing was done at the end of each day data collection by the principal investigator and backed up in a separate location away from the computer. Data utilized during the study will be kept for a period of two years after completion of the study before eventually

being permanently destroyed. Data analysis, paper submission and publication should have been done then.

3.11 Data analysis

The data collected was entered into Microsoft Excel 2010 and analyzed using STATA version 13.0. Descriptive statistics was summarized by presenting the data as means with standard deviation for normally distributed continuous variables, and non-normally distributed continuous variables were presented as medians with interquartile range. Frequencies and proportions were used to summarize categorical variables. Chi-square tests was conducted at 5% level of significance to evaluate association between patient risk factors, types of PPIs and DTPs. A logistic model was fitted to evaluate predictors of DTPs

3.12 Logistical and ethical consideration

3.12.1 Quality assurance

All data obtained from patient files was double checked by principal investigator during data entry. Adherence to the Good Clinical Practice (GCP) and International Council for Harmonization (ICH) was maintained throughout the study period.

3.12.2 Approval

Clearance was sort from the University of Nairobi and Kenyatta National Hospital- Ethics and Research Committee (Appendix1a). Authorization to carry out the study was also be sort from the Kenyatta National Hospital administration (Appendix1b) after approval from the ethical review board.

3.12.3 Informed consent

Informed consent was obtained from the participant before any information was collected from the patient or their charts. The participants were taken through the consenting process as shown in Appendix 2a. Decision to take part in the study was voluntary and those who declined to participate were not discriminated. All participants who agreed to take part in the study signed an informed consent form.

3.12.4 Risks and benefits

There was no risk to the participants since data was obtained through patient interviews and data abstraction from the patients' health records. No invasive procedure was involved in the study

3.12.5 Confidentiality

The participant was interviewed in a separate room away from other patients in the wards by the principal investigator. Unique code identifier was used during abstracting of data from patient's file to conceal their details.

Data collected was treated confidentially by restricting access to it. Signed copies of the consent forms were kept under lock and key. The principal investigator, supervisors and members of Ethics committee had access to the participants' information and documents.

3.12.5 Dissemination Plan

The study findings will be shared through power point presentations with KNH, MTRH, County governments and Ministry of Health as well as policy implementers. The health workers and patients will be sensitized on the findings through continuous medical education. Finally, the findings will be published in medical journal for wider audience.

CHAPTER FOUR: RESULTS

4.0 Introduction

The results of the study are presented in this chapter. The broad objective of the study was to identify and describe DTPs associated with PPI drug use by patients admitted in medical wards at KNH.

4.1 Socio-demographic characteristics of study population

The total number of patients that participated in the study was 176. The mean age of the patients was 43.6 (SD 16.5) years, while the median age was 39.0 (IQR 30.0 – 57.5) years. The minimum age was 18 years while the maximum age was 82 years. There were slightly more male (95, (54.0%) than female (81, (46.0%). Majority of the patients were of normal BMI (113, (64.2%), 106 (60.2%) were married, and10 (5.7%) were pregnant.

Table 7 Socio-demographic

Age (Years)	**Frequency (n=176)**	**Percentage (%)**
<20	6	3.4
21-29	33	18.8
30-39	50	28.4
40-49	26	14.8
50-59	23	13.1
60-69	24	13.6
>=70	14	8.0
Sex		
Male	95	54.0
Female	81	46.0
BMI		
18.5 and below (underweight)	23	13.1
18.5-24.9 (healthy weight)	113	64.2
25.0-29.9 (overweight)	31	17.6
30 and above (obesity)	9	5.1

Marital status		
Single	59	33.5
Married	106	60.2
Divorced	11	6.3
Pregnancy status		
Yes	10	5.7
No	166	94.3
Religion		
Christian	160	90.9
Muslim	8	4.5
Others	8	4.5
Education		
Primary	56	31.8
Secondary	70	39.8
College/University	30	17.0
None	20	11.4
Tobacco		
Tobacco use	37	21.0
No tobacco use	139	79.0
Number of packs		
0	39	22.2
1	134	76.1
2	2	1.1
3	1	0.6
History of use		
0-1 packs per day	8	4.5
1 pack per day	139	79.0
Previous history of smoking	29	16.5
Alcohol		
Alcohol use	63	35.8

No alcohol use	113	64.2
Drinks/day		
0	41	23.3
1	112	63.6
2	8	4.5
3	3	1.7
4	12	6.8
Previous alcohol history		
<2 drinks per week	7	4.0
2-6 drinks per week	113	64.2
Past alcohol use	53	30.1
None	3	1.7
Caffeine		
Caffeine	81	46.0
No caffeine use	95	54.0
Number of cups		
<2 cups per day	53	30.1
2-6 cups per day	28	15.9
No caffeine use	95	54.0
Occupation		
Formal	15	8.5
Informal	71	40.3
Unemployed	82	46.6
Retired	8	4.5
Income per month (Ksh)		
<5000	96	54.5
5000-10000	42	23.9
10000-30000	28	15.9
>30000	10	5.7
Health insurance		

Yes	93	52.8
No	83	47.2

4.2 PPIs used by the patients

Of the 176 patients, 107 (60.8%) were using omeprazole, while only 69 (39.2%) were using esomeprazole. The most commonly used route for their medication was oral (120, 68.2%), where majority of them were on normal dose (128, 72.7%), and the frequency of use was once a day (127, 72.2%) for most of them. It was indicated for 80 (45.5%) of the patients, and most of the patients were also on other medications (161, 91.5%).

Table 8 PPIs used by the patients

PPI Used	**Frequency (n=176)**	**Percentage (%)**
Omeprazole	107	60.8
Esomeprazole	69	39.2
Route		
Oral	120	68.2
IV	56	31.8
Dose		
Low	10	5.7
Normal	128	72.7
High	38	21.6
Frequency		
1	127	72.2
2	48	27.3
3	1	0.6
Indicated		
Yes	80	45.5
No	96	54.5
Other medications		
Yes	161	91.5
No	15	8.5

4.3 Medical history of the patients

Out of the 176 patients, 96 (54.5%) had previous admissions, where 19 (10.8%) were admitted for Anemia. There were 47 (26.7%) of the patients who had ever done blood transfusion, and 38 (21.6%) who had ever used herbal medications.

Table 9 : Medical history

Previous admission	Frequency (n=176)	Percentage (%)
Yes	96	54.5
No	80	45.5
Condition		
No previous condition	80	45.5
Anemia	19	10.8
Limb fracture	4	2.3
Breast cancer	5	2.8
Delivery	3	1.7
COPD	1	.6
Dermatitis	3	1.7
AML	1	.6
Congenital heart disease	4	2.3
Peritonitis	1	.6
Cancer of oesophagus	1	.6
Malaria	1	.6
Hypertension	4	2.3
Diabetes	6	3.4
Kidney disease	7	4.0
Pulmonary oedema	1	.6
TB	4	2.3
Pneumonia	1	.6
Meningitis	4	2.3
Gastric cancer	2	1.1
Nausea and vomiting	1	.6
Pancreatitis	1	.6
Acute abdominal pain	2	1.1
Sarcoma	1	.6
Upper airway obstruction	2	1.1
Candidiasis	1	.6
Peptic ulcers	3	1.7
Bicytopenia	1	.6
Dehydration	1	.6
Congestive heart failure	1	.6
Liver cirrhosis	2	1.1
Cancer of colon	1	.6
Cellulitis	1	.6
Cancer of the lungs	1	.6
Appendicitis	1	.6
Constipation	1	.6
Psoriasis	1	.6
Asthma	1	.6
Blood transfusion		
Yes	47	26.7
No	129	73.3
Herbs use		
Yes	38	21.6
No	138	78.4

4.4 Other Current Medications

There were other various medications that were being taken by the patients such as Ranferon (17, 9.7%), Phenytoin (12, 6.8%), RHZE (9, 5.1%), TDF/3TC/DTG (9, 5.1%), among others as shown on Table 6.

Table 10 : Current medications the patients were using

	Yes n (%)	No n (%)
Phenytoin	12 (6.8)	164 (93.2)
Losartan	8 (4.5)	168 (95.5)
Digoxin	2 (1.1)	174 (98.9)
Warfarin	7 (4.0)	169 (96.0)
RHZE	9 (5.1)	167 (94.9)
TDF/3TC/DTG	9 (5.1)	167 (94.9)
Ranferon	17 (9.7)	159 (90.3)
Methotrexate	2 (1.1)	174 (98.9)
Fluconazole	5 (2.8)	171 (97.2)
Cyclosporine	1 (0.6)	175 (99.4)
Carbamazepine	2 (1.1)	174 (98.9)
Atazanavir	2 (1.1)	174 (98.9)
Vitamin K	5 (2.8)	171 (97.2)

4.5 Prevalence of DTPs

This section sought to determine the overall prevalence of DTPs among patients using PPIs admitted in medical wards of KNH. The study results indicate that DTP was present in 76 (43.2%) of the patients.

Table 11 : Prevalence of DTP

DTP Present	Frequency (n=176)	Percentage (%)
Yes	76	43.2
No	100	56.8

4.6 Medication compliance history of the patients

There were 11 (6.3%) of the patients who had allergy to certain medication. On medication experience, 77 (43.8%) patients did not like taking medication, where 12 (6.8%) of them said the drugs did not work, 20 (11.4%) of the patients reported that the drugs did not work for them, and 48 (27.3%) of them found the cost prohibitive.

Table 12 : Medication History

Allergy	**Frequency (n=176)**	**Percentage (%)**
Yes	11	6.3
No	165	93.8
Medication experience	**Yes n (%)**	**No n (%)**
Like taking medication	99 (56.3)	77 (43.8)
If no, (Drugs don't work)	12 (6.8)	164 (93.2)
If no, (Drugs cause more problems)	20 (11.4)	156 (88.6)
If no, (The cost of the drugs)	48 (27.3)	128 (72.7)

4.7 Expectations from medications

Majority of the patients expect that they will be cured (139, 79.0%), and their greatest concern was the side effect of medication (52, 29.5%). Most of them would take medication without being compelled (130, 73.9%), while only 68 (38.6%) would stop taking medication once they feel their condition is under control. Over 70% of the patients had the correct knowledge on dosing, time to take their drugs, duration and reason as to why they are taking the drugs. Only 9 (5.1%) of the patients held cultural or religious beliefs for or against use of certain medications.

Table 13 : Expectations from medications

Expectations	Frequency (n=176)	Percentage (%)
Cure	139	79.0
Relief	37	21.0
	Yes n (%)	No n (%)
Concerns regarding medication	64 (36.4)	112 (63.6)
Number of pills	30 (17.0)	146 (83.0)
Number of times taking drugs	30 (17.0)	146 (83.0)
Side effect of medication	52 (29.5)	124 (70.5)
Take medication without being compelled	130 (73.9)	46 (26.1)
Condition under control (stop medication)	68 (38.6)	108 (61.4)
	Correct n (%)	Incorrect n (%)
Know dose of medication used	130 (73.9)	46 (26.1)
Times taken in a day	131 (74.4)	45 (25.6)
Duration for taking drug	124 (70.5)	52 (29.5)
Know reason for use	135 (76.7)	41 (23.3)
	Yes n (%)	No n (%)
Cultural or religious beliefs against use	9 (5.1)	167 (94.9)

4.8 Family history of chronic conditions

There were 72 (40.9%) patients who indicated there were members of their family who also had chronic conditions.

Table 14 Family History of chronic conditions

Chronic condition	**Frequency (n=176)**	**Percentage (%)**
Yes	72	40.9
No	104	59.1

4.9 Prevalence of various types of DTPs

This section sought to determine the prevalence of various types of DTPs among patients on PPIs therapy in medical wards. There were 28 (15.9%) unnecessary drug therapy, 1 (0.6%) needing additional drug therapy, 2 (1.1%) needing different drug product, 2 (1.1%) dosage was low, 29 (16.5%) adverse drug reactions, 38 (21.6%) dosage was too high, and 2 (1.1%) non adherence.

Table 15 Prevalence of various types of DTPs

Unnecessary drug therapy	**Frequency (n=176)**	**Percentage (%)**
Yes	28	15.9
No	148	84.1
Cause		
No medical condition	27	15.3
Duplicate therapy	1	0.6
No cause	148	84.1
Needs additional drug therapy		
Yes	1	0.6
No	175	99.4
Cause		
Untreated condition	1	0.6
No cause	175	99.4
Needs different drug product		
Yes	2	1.1
No	174	98.9
Cause		
Dosage form inappropriate	1	0.6
Contraindication present	1	0.6
No cause	174	98.9
Dosage too low		
Yes	2	1.1
No	174	98.9
Cause		
Untreated condition	1	0.6
Drug interaction reduces the amount of active drug	1	0.6
No cause	174	98.9
ADR		

Yes	29	16.5
No	147	83.5
Cause		
Unsafe drug for the patient	7	4.0
Drug interaction	20	11.4
Contraindication present	2	1.2
No cause	147	83.4
Dosage too high		
Yes	38	21.6
No	138	78.4
Cause		
Frequency inappropriate	1	0.6
Wrong dose	34	19.3
Drug interaction	2	1.1
Incorrect administration	2	1.1
No cause	138	78.4
Non adherence		
Yes	2	1.1
No	174	98.9
Cause		
Patient forgot to take	1	0.6
Drug product too expensive	1	0.6
No cause	174	98.9

4.10 Summary of comorbidities present

The top five associated risk factors were Anemia (52, 29.5%), followed by hypertension (50, 28.4%), cancer (35, 19.9%), HIV (29, 16.5%), and respiratory diseases (28, 15.9%).

Table 16 Summary of comorbidities present

Category	Yes n (%)	No n (%)
Diabetes	17 (9.7)	159 (90.3)
Hypertension	50 (28.4)	126 (71.6)
Anemia	52 (29.5)	124 (70.5)
HIV	29 (16.5)	147 (83.5)
Respiratory disease	28 (15.9)	148 (84.1)
Liver disease	11 (6.3)	165 (93.8)
Kidney disease	26 (14.8)	150 (85.2)
Heart disease	9 (5.1)	167 (94.9)
Gastrointestinal disease	20 (11.4)	156 (88.6)
Cancer	35 (19.9)	141 (80.1)
Others	16 (9.1)	160 (90.9)

4.11 Association between comorbidities with DTPs

This section sought to investigate the association between the comorbidities and various DTPs among patients using PPIs in medical wards of KNH. Pearson Chi-square tests was used to test the association between each of the risk factors with DTP. There were no significant associations found, though the results indicated that patients with hypertension, anemia, kidney disease, heart disease, and cancer were more at risk of DTP, while those with diabetes, HIV, respiratory disease, liver disease, and GI disease were less likely to be at risk of DTP.

Table 17 Association between the patients associated risk factors with DTPs

		DTP			
Variable	**n**	**Yes**	**No**	**OR (95% CI)**	**p-value**
Diabetes					
Yes	17	7 (41.2)	10 (58.8)	0.9 (0.3 – 2.5)	0.861
No	159	69 (43.4)	90 (56.6)		
Hypertension					
Yes	50	23 (46.0)	27 (54.0)	1.2 (0.6 – 2.3)	0.635
No	126	53 (42.1)	73 (57.9)		
Anemia					
Yes	52	26 (50.0)	26 (50.0)	1.5 (0.8 – 2.8)	0.238
No	124	50 (40.3)	74 (59.7)		
HIV					
Yes	29	12 (41.4)	17 (58.6)	0.9 (0.4 – 2.1)	0.830
No	147	64 (43.5)	83 (56.5)		
Respiratory disease					
Yes	28	10 (35.7)	18 (64.3)	0.7 (0.3 – 1.6)	0.386
No	148	66 (44.6)	82 (55.4)		
Liver disease					
Yes	11	2 (18.2)	9 (81.8)	0.3 (0.1 – 1.3)	0.104
No	165	74 (44.8)	91 (55.2)		
Kidney disease					
Yes	26	14 (53.8)	12 (46.2)	1.7 (0.7 – 3.8)	0.237
No	150	62 (41.3)	88 (58.7)		
Heart disease					
Yes	9	5 (55.6)	4 (44.4)	1.7 (0.4 – 6.5)	0.446
No	167	71 (42.5)	96 (57.5)		
GI disease					
Yes	20	6 (30)	14 (70)	0.5 (0.2 – 1.4)	0.212
No	156	70 (44.9)	86 (55.1)		
Cancer					
Yes	35	16 (45.7)	19 (54.3)	1.1 (0.5 – 2.4)	0.736
No	141	60 (42.6)	81 (57.4)		

CHAPTER FIVE: DISCUSSION, CONCLUSIONS AND RECOMMENDATIONS.

5.1 Introduction

This chapter entails the discussion of the research findings as well as the conclusion and recommendations.

5.2 Discussion

The representation of study participants were almost equal, where male and female was 54% and 46 %percent. This is comparable to study done in Switzerland where 53% and 47% were male and female respectively (17). Similarly, another study in UK had almost the same participants 55.4 %& and 44.6% respectively. However, the mean ages of the two studies were 65.5 and 68 years respectively. The difference in the mean ages could be associated with good health systems those countries. This was in contrast with the mean age of the study participants. A study in India had a comparable mean age of 45.38 years(24). Another study Australia had almost the same ratio(37).

The prevalence of DTPs associated with PPI use among patients admitted in medical wards from this study is 43.2%.This is comparable to studies done in Nigeria and Australia (34) (37). However this is inconsistent with the findings done in the same facility but in a different setting (33).The difference could have been as a result of the study design used. From other studies in Jordan, Malaysia and Ireland the prevalence was high (38) (39)(10).These variations could possibly be as a result of drug utilization, the sample size and the study designs used in those countries. Some of the studies were either multi-centered or multi- regional studies.

On the prevalence of the various types of DTPs, the findings of this study showed that Drug Therapy Problem associated with high dose, the prevalence was at 21.6%. This is comparable to findings in Malaysia(39). However, these results were not consistent with findings in India where a high number of patients were on prolonged PPI use than expected (25). Also in India, the prevalence was high as a result of patients receiving Intravenous administration as opposed to oral administration (24). In India, pantoprazole IV was widely used as opposed to our findings where omeprazole was widely used. In the Malaysian case, the use of omeprazole IV was commonly used as in our case. The reasons for varied use

could be as a result of physicians' choice, drug availability, cost of drug, and the drug's pharmacokinetic profile.

The second most prevalent DTP in our study was the existence of drug interaction at 16.5%. This drug interaction could be occasioned by other medications on which the patient is on apart from the PPIs. Some of the drugs which were used by the patients include digoxin, warfarin methotrexate, atazanavir and losartan. All these drugs have a potential of causing undesirable effect to the patient. For example, a combination of omeprazole and digoxin, may increase digoxin toxicity. Likewise, to omeprazole and warfarin which leads to high concentration of warfarin. In the case of losartan, omeprazole reduces the amount of losartan and may predispose the patient to increased blood pressure. The other drug was oral ferrous sulphate where omeprazole inhibits its absorption (25). Also in some instances the patient may be having a condition where use of PPI may worsen for example liver cirrhosis which PPI may precipitate hepatic encephalopathy (40). Use of PPI combined with other antibiotics in advanced age may cause and desirable effect as was in the Taiwan case (28).

The third common DTP from our findings was use of unnecessary drugs which was at 15.9%. Our findings were in agreement with those of France (18). However, these results were not consistent with findings in another study in France where majority of the adults were using PPIs with no indication (17). Findings in Ireland also disagreed with our findings, where majority of PPI users had no valid indication (19). Also contrasting findings were found in Spain, where majority of those on PPI use had no valid indication (41). In another study in Italy, findings were way higher than ours, with the main finding being that majority of the prescriptions had no valid indications (20).The possible reasons may be perceived intention to prevent stress ulcers ,trying to treat a condition resulting from co-administration with NSAIDs. The other one could possibly be treating a condition occasioned by use of recreational drugs or substances.

The following DTPs; Needs a different drug product, dosage too low, and non- adherence were all ranked fourth, all equally at 1.1%. The drug therapy associated with low dosage was in contrast with the findings in a UK study, where majority of the patients had low dosage (25). It was also in contrast with another study in Switzerland, where the occurrence of low dosage was high (21). The probable causes could be associated with low dose of the

drug being administered or the duration of use of the drug being shortened than it is supposed to be used or indicated. The difference in our findings with the UK and Switzerland studies could be beyond the scope of this study. On needs different drug product, the cause was a result of the dosage form being inappropriate, whereby the patient was able to take oral medication, but there was use of IV medication. However the same findings in an Indian study showed that a high percentage of patients were on using IV medication unnecessarily, whereas they could take the medication orally (24). These differences could be as a result of the preference in the physicians' prescribing patterns.

On non-adherence, the cause was a result of the patient forgetting to take medications. However, these findings were in contrast with another study in US where majority of the patients were unable and unwilling to adhere to the medication regimens (14) Other causes for this could be directions of medications not being understood by the patients, or inability of the patients to administer or swallow the medication. The DTP of needs additional drug therapy came in last with a prevalence of 0.6%. On the findings of needs additional drug therapy, the cause being untreated condition in the patient. This could either be due to the patient having an underlying condition not yet treated or the drug product was required for synergism. For example, in H. Pylori infection, PPI use is required in addition with other drugs for synergism. However, there were no comparable studies to associate with these findings.

On the association between the comorbidities and various DTPs among patients using PPIs in medical wards of KNH, there were no statistically significant associations found. There are so far no studies that have looked into the association between comorbidities and the different types of DTPs associated with use of PPIs. But in a different context, some studies have found a cause-specific mortality associated with prolonged use of PPIs especially patients with cardiovascular problems (9).

5.3 Summary

The overall prevalence of DTPs among patients using PPIs admitted in the medical wards of KNH is 43.2%. The individual prevalence of the different types of DTPs varied from one to another. The prevalence of DTP presence where the dosage was too high stands at 21.6%. The prevalence as a result of drug Interaction is 16.5% DTP presence as a result of use of unnecessary drugs is 15.9%. The DTP presence due to low dosage, non-adherence,

and the need of a different drug stand equally at 1.1%. The least prevalent DTP is the need of additional drug therapy which is 0.6%

The association between the DTPs presence among the patients and comorbidities is statistically insignificant. The p-values range from 0.104 to the highest of 0.861 among the different comorbidities present. The comorbidities in study were Diabetes, Hypertension, Anemia, HIV, Respiratory disease, Liver disease, Kidney disease, Heart disease, Gastrointestinal disease and Cancers.

5.4 Conclusion

From the study findings, the DTPs among patients using PPIs admitted in the medical wards of KNH is high. This necessitates immediate action to address this problem. This will improve the patients' therapeutic outcomes and safety and also reduce the cost of treatment. The findings also show the disproportionate misuse of PPIs which may lead to comorbidities and mortality.

To address this problem, the prescribers should be enlightened on the need to strictly adhere to the guidelines while prescribing PPIs. It also requires the involvement of a multi-disciplinary team especially the clinical pharmacists to be involved in reviewing treatment sheets and monitoring PPI use in the wards. This will assist in detecting, resolving and preventing the occurrence of DTPs associated with PPI use.

5.4 Recommendations

5.4.1 Recommendations for Policy and Practice

This being the first study in Kenya that highlighted prevalence of DTPs associated with the use of PPIs in medical wards of KNH, and concerns that arise thereof on the dangers it poses on morbidity, mortality, and costs of healthcare, there is need to consider the following recommendations;

1. The need for prescribers in the hospital to strictly adhere to the guidelines on proper use and administration of PPIs, both for in-patient and outpatients.

2. There is need for proper sensitization of prescribers, clinical officers and other healthcare providers on proper prescription of PPIs and their magnitude of inappropriate use.
3. Involvement of clinical pharmacists in reviewing treatment sheets and monitoring PPI use in the medical wards of KNH. This will be beneficial in identifying, resolving and preventing possible occurrences of DTPs associated with PPI use.

5.4.2 Recommendations for Research

Since there was no association between patient risk associated factors (comorbidities) and occurrence of DTPs with the patients using PPIs, further research and studies is recommended.

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APPENDICES

Appendix 1a ETHICS APPROVAL

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Ref: KNH-ERC/A/232

21st July 2020

APPROVED
21 JUL 2020
KNH/UoN-ERC

Robert Kiprop Saina
Reg. No.U56/11175/2018
Dept. of Pharmaceutical and Pharmacy Practice
School of Pharmacy
College of Health Sciences
University of Nairobi

Dear Robert

RESEARCH PROPOSAL – DRUG THERAPY PROBLEMS AMONG PATIENTS ON PROTON PUMP INHIBITORS IN THE MEDICAL WARDS OF KENYATTA NATIONAL HOSPITAL (P85/02/2020)

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 21st July 2020 – 20th July 2021.

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. Clearance for export of biological specimens must be obtained from KNH- UoN ERC for each batch of shipment.
f. 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*).
g. 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.

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: Dr. Sylvia Opanga, Dept.of Pharmaceutics and Pharmacy Practice, UON
Dr. Tom Menge, Chief Pharmacist, KNH

Appendix 1b INSTITUTIONAL APPROVAL LETTER

Appendix 2A: Consent form

Title of the Study: Drug therapy problems among patients on proton pump inhibitors in the medical wards of Kenyatta National Hospital.

The purpose of the study: The study aims at determining the prevalence and types of Drug Therapy Problems associated with PPI use among patients admitted in medical wards at KNH. The study will also determine the patient's factors that are associated with these Drug Therapy Problems. The finding of the study will help minimize the adverse effects.

Institution: Department of Pharmaceutics and Pharmacy Practice, School of Pharmacy,

University of Nairobi, P.O BOX 30197-00400, Nairobi

Principal Investigator: Dr. Robert Saina Kiprop- Postgraduate student (Clinical

Pharmacy) University of Nairobi, P.O BOX 30197-00400, Nairobi

Supervisors:

1. Dr. Sylvia Opanga, Senior Lecturer, Department of Pharmaceutics and Pharmacy Practice, University of Nairobi.
2. Dr. Tom Menge, Chief Pharmacist, Kenyatta National Hospital.

I am Dr. Robert Saina Kiprop, a postgraduate student at the University of Nairobi, School of pharmacy. I am carrying out a study to partly fulfill requirements for the Master Degree in Clinical Pharmacy.

Voluntary participation: Participation in the study will be voluntary and participant will be expected to provide honest information to the questions asked in the questionnaire. Participants will not be forced to answer any questions they are not uncomfortable answering and all information provided by the will be treated with the confidence it deserves.

Confidentiality: Patient's name will be coded and their information will be entered in a

computer with password protection. Signed copies of the consent forms will be kept under lock and key. This will ensure their identity is concealed.

Risks and harm: One of the risks that you may encounter is lack of privacy. The collected information will be treated with confidentiality and restricted for access using password protected electronic medical records. Signed copies of your consent participation forms will be kept in a locked office file cabinet. Only the principal investigator, supervisors and members of KNH-UoN ERC will access the documents. 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.

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. Robert Saina Kiprop. Telephone Number 0721-748169. Email: rocyner@gmail.com or Prof M.L Chindia, Secretary Kenyatta National Hospital-University of Nairobi Ethics 44 and Research Committee, Telephone No: **2726300** Ext: **44102** Email: *uonknh_erc@uonbi.ac.ke.*

Participant's Statement

I have read this consent form or had the information read to me. I have had the chance to discuss this research study with a study counselor. I have had my questions answered in a language that I understand. The risks and benefits have been explained to me. I understand that my participation in this study is voluntary and that I may choose to withdraw 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.

Have you understood **YES** **NO**

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

Participant printed name: _____

Participant signature / Thumb stamp _____

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 2B: 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. Robert Saina Kiprop, Mwanafunzi uzamili (utabibu dawa), Chuo kikuu cha Nairobi, SLP 30197-00400, Nairobi.

Wasimamizi:

1. Dr. Sylvia Opanga, Mhadhiri, Chuo Kikuu cha Nairobi
2. Dkt. Menge, Idara ya Pharmacy, Hospitali Kuu ya Kenyatta.

Mimi ni Dkt. Robert Saina Kiprop, 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.

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: 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 pekee ndiye atakaye 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: rocyner@gmail.com. Simu: 0721-748169 au Prof M.L Chindia Kabitu Simu.: **2726300** ongezo: **44102** Tovuti: *uonknh_erc@uonbi.ac.ke.* Utarudishiwa ada ya mazungumzo kupitia laini hizi kama mazungumzo yenyewe yanahusu utafiti huu.

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.

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

Jina la Mshiriki: _____

Sahihi / Kidole _____

Tarehe _____

Taarifa ya Mtafiti

Mimi, ninayetia sahihi hapo chini, nimeelezea maswala muhimu ya utafiti huu kwa mshiriki aliyetajwa 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: _____

Appendix 3a: QUESTINNAIRE

STUDY TITLE: Drug Therapy Problems among patients on Proton Pump Inhibitors admitted in the medical wards of Kenyatta National Hospital

SECTION A: Socio-demographic characteristics.

Date…../…../….

Code number of the participant…….

I BIODATA

1. Age_____ years Date of birth_____
2. Sex Male___(0) Female ___(1)

3. Weight _____kg Height in cm_____

4. BMI_____

Marital status Single (0) Married (1) Divorced (2)

5.
6. Pregnancy status **Yes (0) No (1)** Due date_____

Religion Christian (0) Muslim (1) Others (2)

Level of education: Primary (0) Secondary (1) College/University (2) None (3)

Recreational drug use status.

Substance	History of use	Substance	History of use
Tobacco use (0) No tobacco use (1)	(0) 0-1 packs per day (1)> 1 pack per day (2) Uses other forms of tobacco (e.g. chewing, e-cigarettes) (3) Previous history of Smoking (4) Interested in quitting	Alcohol use (0) No alcohol use (1)	(0) <2 drinks per week (1)2-6 drinks per Week (2)> 6 drinks per Week (3) Past alcohol use
Caffeine (0) No caffeine use (1)	(1) <2 cups per day (2) 2-6 cups per day (3) >6 cups per day	Recreational drug use (include substance and frequency of use)	(1) Yes (2) N0 (3) Other

II OCCUPATION

What is your employment status? Formal (1) informal (2) unemployed (3) retired (4)

On average how much do you make per month? _____

12.Category of monthly income (Ksh) <5000 (0) 5000-10000 (1) 10000-30000 (2) >30000(3)

13.Do you have a health insurance policy? **Yes (0) No (1)**

III MEDICAL HISTORY

Have you ever been admitted in hospital? **Yes (0) No (1)**
If Yes what was the condition? .....
Have you ever had a blood transfusion? **Yes (0) No (1**)
22Have you ever used any complementary or alternative medicine **Yes (0) No (1)**

IV MEDICATION HISTORY
23. Do you have allergy to any medication?
Yes (0) No (1) Other (2)

Medication Experience
24. Do you like taking medications? **Yes (0)No (1)**

25. If No to question **24** above, what is the reason?

Drugs don't work **Yes (0)No (1)**

Drugs cause more problems **Yes (0)No (1)**

The cost of drugs **Yes (0)No (1)**

Availability of drugs **Yes (0) No (1**)

26. What do you expect from the medications you use? Cure (0) Relief (1)

27. Do you have any concerns regarding your medications? **Yes (0) No (1)**
28. If yes to question **27** above what are your
Concerns?

The number of pills **Yes (0) No (1)**

The number of times you take the drugs **Yes (0) No (1)**

Side effect of the medication **Yes (0**) **No (1)**

29. Do you currently suffer from any side effects of the medication? **Yes (0) No (1)**

30. Do you choose to take medications without being compelled? **Yes (0) No (1)**

31. Do you choose to refill your prescriptions? **Yes (0) No (1)**

32. When you feel that your condition is under control do you sometimes stop taking the Medications for a while? **Yes (0) No (1)**

33. Do you know the dose(s) of the medication(s) you are using? _____

Yes (0) No (1)

34. How many times do you take in a day?_____
i)once
ii) twice
iii) thrice
Yes (0) No (1)

35. Do you know the duration within which you should take your drugs?_____

Yes (0) No (1)

How should you take this medication with regard to food? With food (0) After food (1) Before food (3) I don't know (4)

Do you know why you are using this medication? _____

Yes (0)No (1)

Do you hold any cultural or religious beliefs for or against the use of certain medications? Yes (0) No (1)

39. The list of PPIs currently being used by the participant:

PPI	CODE	DOSAGE FORM	DOSE	FREQUENCY	INDICATION
Omeprazole	1				
Esomeprazole	2				
Lansoprazole	3				
Rabeprazole	4				
Pantoprazole	5				

40. Other current medication(s) the participant is currently using.

Medication including strength and dosage form	Indication	Drug Class
1		
2		
3		
4		
5		
6		

VI FAMILY HISTORY

41. Is there any member of your family who also has a chronic condition? Yes (0) No (1)

VII REVIEW OF SYSTEMS

A. General system

42 Fever**? Yes (0) No (1)**

43 Malaise? **Yes (0) No (1)**

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

45 Do you have any weight change**? Yes (0) No (1)**

B. Special senses

Eyes

46 Do you have any problem with the eyes**? Yes (0) No (1)**
If **yes** which problem?

47 Impaired visual acuity? **Yes (0) No (1)**

48 Pain in the eyes**? Yes (0) No (1)**

49 Itching? **Yes (0) No (1) Other (2)**

50 Swelling? **Yes (0) No (1)**

51 Do you have any problem with your ears? **Yes (0) No (1)**
If **yes**, which is the problem?

52 Loss of hearing**? Yes (0) No (1)**

53 Loss of balance? **Yes (0) No (1)**

54 Ringing in the ears? **Yes (0) No (1)**

55 Do you have any problem with your throat? If **yes** which is the problem?

56 Pain while swallowing food? **Yes (0) No** (1)

D. Respiratory System

57Do you have any problem with your respiratory system? **Yes (0) No (1)**

If **yes**, which is the problem?

59Chest pain? **Yes (0) No (1)**

60 Shortness of breath? **Yes (0) No (1)**

61 Wheezing? **Yes (0) No (1)**
62 Coughing? **Yes (0) No (1)**

E. Digestive system

63 Do you have any problem with your digestive system? **Yes (0) No (1)**
If **yes**, which is the problem?

64 Pain in the abdomen? **Yes (0) No (1)**

65 Poor appetites? **Yes (0) No (1)**

66 Heart burn? **Yes (0) No (1)**

67 Difficulty in swallowing? **Yes (0) No (1)**

68 Diarrheas? **Yes (0) No (1)**

69 Hard stools? **Yes (0) No (1)**

70 Nausea? **Yes (0) No (1)**

F. Genitourinary system
71 Do you have any problem with your genitourinary system? **Yes (0) No (1)**
If **yes**, which is the problem?

72Pain when urinating? **Yes (0) No (1)**

73 Decreased sexual drive? **Yes (0) No (1)**

74 Increased frequency of urination? **Yes (0) No (1)**

75 Irregular menses? **Yes (0) No (1)**

76 Painful menses? **Yes (0) No (1)**

77 Heavy menses? **Yes (0) No (1)**

G. Neurologic system
78 Do you have any problem with your neurologic system? **Yes (0) No (1)**
If **yes**, which is the problem?

79 Feeling dizziness? **Yes (0) No (1)**

80 Feeling drowsiness? **Yes (0) No (1)**

81 Experiencing memory loss? **Yes (0) No (1)**

82Experiencing mood changes? **Yes (0) No (1)**

83Lack of sleep? **Yes (0) No (1)**

84 Headache? **Yes (0) No (1)**

H. Musculoskeletal System

85 Do you have any problem with your musculoskeletal system? **Yes (0) No (1)**
If **yes**, which is the problem?

86 Back aches? **Yes (0) No (1) Other (2**)

87 Joint pain? **Yes (0) No (1)**

88 Joint stiffness? **Yes (0) No (1) O**

89 Difficulty in walking? **Yes (0) No (1)**

90 Swelling of joints? **Yes (0) No (1)**

91 Do you have any problem with your skin? **Yes (0) No (1)**

If **yes**, which is the problem?

Itchiness **Yes (0) No (1)**

Rashes **Yes (0) No (1)**

94 Dry skin Yes **(0) No (1)**

SECTION 2 MEDICAL RECORDS REVIEW

The following data should be abstracted from the medical records.

Lab parameter	Current reading	**Status**		
		Low (0)	Normal (1)	High (2)
Heart rate				
Pulse rate				
Hb				
Creatinine				

Sodium				
Potassium				
Calcium				

96 Summary of prescribed drugs, indications and identified DTPs.

Condition	Drugs	Dosage	Goals	Current Results	Outcome status	Drug therapy problem	Cause

ON 3 EVALUATIONS OF DTPs

97. Did the patient have any DTP? **Yes (0)** **No (1)**

98 If yes to question 97, classify the DTP according to the table shown below

DTP	CAUSE	**CODE**	COMMENT
Unnecessary Drug Therapy	No medical condition	0	
	Duplicate therapy	1	
	None drug therapy indicated	2	
	Treating avoidable ADR	3	
	Addictive or recreational	4	
	Drug		
Needs Additional Drug Therapy	Untreated condition	**5**	
	Preventive /prophylactic	**6**	
	Synergistic/potentiating	**7**	
	More effective drug	**8**	
Needs Different Drug Product	Available		
	Dosage form inappropriate	**9**	
	Condition refractory to the	**10**	
	Drug		
	Contraindication present	**11**	
	Drug not effective for the	**12**	
	Condition		
Dosage too low	Wrong dose	**13**	
	Frequency inappropriate	**14**	
	Drug interaction reduces the amount of active drug	**15**	
	Duration inappropriate	**16**	
ADR	Undesirable effect	**17**	
	Unsafe drug for the patient	**18**	
	Drug interaction	**19**	
	Dosage administered or	**20**	
	changed too soon		
	Allergic reactions	**21**	
	Contraindication present	**22**	
Dosage too High	Wrong dose	**23**	
	Frequency inappropriate	**24**	

	Wrong dose	**23**	
	Duration inappropriate	**25**	
	Drug interaction	**26**	
	Incorrect administration	**27**	
Non-adherence	Directions not understood	**28**	
	Patient prefers not to take	**29**	
	Directions not understood	**28**	
	Patient forgets to take	**30**	
	Drug product too expensive	**31**	
	Cannot swallow/ administer	**32**	
	Drug product not available	**33**	

99 Develop a final analysis of DTPs present in this patient and summarize them in the table below.

NO	DTP	STATUS	
1	Unnecessary drug therapy	**Yes (0)**	**No (1)**
2	Needs additional drug	**Yes (0)**	**No (1)**
3	Different drug needed	**Yes (0)**	**No (1)**
4	Dosage too low	**Yes (0)**	**No (1)**
5	Adverse drug event	**Yes (0)**	**No (1)**
6	Dosage too high	**Yes (0)**	**No (1)**
7	Non-compliance	**Yes (0)**	**No (1)**

Patient-associated risk factors

Category	**Code**	**Response**	
Diabetes	0	Yes (0)	No (1)
Hypertension	1	Yes (0)	No (1)
Anemia	2	Yes (0)	No (1)
Human immunodeficiency virus	3	Yes (0)	No (1)
Respiratory disease	4	Yes (0)	No (1)
Liver disease	5	Yes (0)	No (1)
Kidney disease	6	Yes (0)	No (1)
Heart disease	7	Yes (0)	No (1)
Gastro-intestinal disease	8	Yes (0)	No (1)

Cancer	9	Yes (0)	No (1)
Others	10		
Total tally of comorbidities			

Appendix 3b: REVIEW OF SYSTEMS AND LAB VALUES

Most the patients experienced malaise (120, 68.2%), 111 (63.1%) of them had pain, 94 (53.4%) experienced changes in their weight, while only 46 (26.1%) had fever. On special senses, 36 (20.5%) had eye problems, and only 3 (1.7%) had ear problems. Respiratory problems were experienced by 67 (38.1%) of them, while 127 (72.2%) had digestive problems, and on the genitourinary system only 38 (21.6%) had problems. Neurologic system problems were experienced by 80 (45.5%) of the patients, and problems with musculoskeletal system had 80 (45.5%) patients. On skin, 22 (12.5%) patients experienced problems.

Table 6.0 Review of Systems

General system	**Yes n (%)**	**No n (%)**
Fever	46 (26.1)	130 (73.9)
Malaise	120 (68.2)	56 (31.8)
Pain	111 (63.1)	65 (36.9)
Weight change	94 (53.4)	82 (46.6)
Special senses		
Eye problem	36 (20.5)	140 (79.5)
Impaired acuity	31 (17.6)	145 (82.4)
Eye pain	11 (6.3)	165 (93.8)
Eye itching	7 (4.0)	169 (96.0)
Eye swelling	2 (1.1)	174 (98.9)
Ear problem	3 (1.7)	173 (98.3)
Hearing loss	0 (0.0)	176 (100.0)
Balance loss	1 (0.6)	175 (99.4)
Ringing ears	2 (1.1)	174 (98.9)
Throat problem	0 (0.0)	176 (100.0)
Pain while swallowing	0 (0.0)	176 (100.0)
Respiratory		
Respiratory problem	67 (38.1)	109 (61.9)
Chest pain	47 (26.7)	129 (73.3)

Shortness of breath	36 (20.5)	140 (79.5)
Wheezing/Coughing	15 (8.5)	161 (91.5)
Digestive system		
Problem with digestive system	127 (72.2)	49 (27.8)
Pain in the abdomen	66 (37.5)	110 (62.5)
Poor appetite	93 (52.8)	83 (47.2)
Heart burn	69 (39.2)	107 (60.8)
Difficulty in swallowing	19 (10.8)	157 (89.2)
Diarrhea	20 (11.4)	156 (88.6)
Hard stool	23 (13.1)	153 (86.9)
Nausea	58 (33.0)	118 (67.0)
Genitourinary system		
Problem with genitourinary system	38 (21.6)	138 (78.4)
Pain when urinating	9 (5.1)	167 (94.9)
Decreased sexual drive	9 (5.1)	167 (94.9)
Increased frequency of urination	23 (13.1)	153 (86.9)
Irregular menses	6 (3.4)	170 (96.6)
Painful menses	3 (1.7)	173 (98.3)
Heavy menses	3 (1.7)	173 (98.3)
Neurologic system		
Problem with neurologic system	80 (45.5)	96 (54.5)
Dizziness	38 (21.6)	138 (78.4)
Drowsiness	26 (14.8)	150 (85.2)
Memory loss	8 (4.5)	168 (95.5)
Mood changes	24 (13.6)	152 (86.4)
Head aches	60 (34.1)	116 (65.9)
Musculoskeletal system		
Problem with musculoskeletal system	80 (45.5)	96 (54.5)
Back ache	36 (20.5)	140 (79.5)
Joint pain	51 (29.0)	125 (71.0)
Joint stiffness	17 (9.7)	159 (90.3)

Difficulty in walking	37 (21.0)	139 (79.0)
Swelling of joints	19 (10.8)	157 (89.2)
Skin		
Problem with skin	22 (12.5)	154 (87.5)
Itchiness	14 (8.0)	162 (92.0)
Rashes	12 (6.8)	164 (93.2)
Dry skin	16 (9.1)	160 (90.9)

4.9 Medical records review

Majority of the patients had normal values for HB (94, 53.4%), creatinine (125, 71.0%), sodium (90, 51.1%), potassium (133, 75.6%), and calcium (140, 79.5%).

Table 7: Medical Records Review

	Low n (%)	**Normal n (%)**	**High n (%)**
HB	79 (44.9)	94 (53.4)	3 (1.7)
Creatinine	12 (6.8)	125 (71.0)	39 (22.2)
Sodium	73 (41.5)	90 (51.1)	13 (7.4)
Potassium	31 (17.6)	133 (75.6)	12 (6.8)
Calcium	32 (18.2)	140 (79.5)	4 (2.3)

Appendix 4: PLIAGIARISM REPORT

DRUG THERAPY PROBLEMS AMONG PATIENTS ON PROTON PUMP INHIBITORS IN THE MEDICAL WARDS OF KENYATTA NATIONAL HOSPITAL

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