ASSESSMENT OF VINCRISTINE MEDICATION ERRORS AND CONTRIBUTING FACTORS IN KENYATTA NATIONAL HOSPITAL

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A thesis submitted in partial fulfilment of requirements for the award of the Degree of Master of Pharmacy in Pharmacoepidemiology and Pharmacovigilance of the University of Nairobi.

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Dedication

I dedicate this work to my wife Norah Kiboko, our children Cherise and Nathan, and my parents, Benjamin Koimur and Esther Koimur. God bless you all abundantly.

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I am grateful to the Almighty God for giving me strength, knowledge and enabling me to write this work.

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List of Abbreviations and Acronyms

ACSQHC	Australian Commission on Safety and Quality in Healthcare
ADRs	Adverse Drug Reactions
AIDS	Acquired Immunodeficiency Syndrome
BSA	Body Surface Area
CNS	Central Nervous System
CPOE	Computerised Physician Order Entry
ERC	Ethics and Research Committee
FMEA	Failure Mode Effect Analysis
HAM	High Alert Medicine
HFMEA	Healthcare Failure Mode Effect Analysis
ID	Identification
IOM	Institute of Medicines
IP	In-patient
ISMP	Institute of Safe Medication Practices
IT	Intrathecal
IV	Intravenous
JCAHO	Joint Commission on Accreditation of Healthcare Organizations
KMTC	Kenya Medical Training College
KNH	Kenyatta National Hospital
MEs	Medication Errors
NCC-MERP	National Coordinating Council for Medication Errors Reporting Programme
NHS	National Health Service
NPSA	National Patient Safety Agency
OP	Out-patient
SHPA	Society of Hospital Pharmacists of Australia
UK	United Kingdom
UoN	University of Nairobi
USA	United States of America

Definitions of Operational Terms

Adults:	Patients aged 13 years and above.
Adverse Drug reaction:	A response to a drug which is noxious and unintended, and which occurs at doses normally used in man for the prophylaxis, diagnosis, or therapy of disease, or for the modifications of physiological function.
Adverse Event:	A medical occurrence during the course of treatment associated with the use of a medicinal product, but not necessarily causally related.
Documentation errors:	Are those that arise due to illegible writing, use of brand names, use of abbreviations, trailing zeroes, and missing contact information of the prescribers.
Dosing errors:	Are errors occurring due to over dosage, under dosage, wrong strength and dose omission.
Failure mode:	Different ways that a process or sub-process can fail to provide the anticipated result.
Hazard analysis:	The process of collecting and evaluating information on hazards associated with the selected process.
Medication Error:	Unintentional errors in prescribing, dispensing, administration or monitoring of medicines while under the control of a healthcare professional, patient or consumer.
Medication order:	A written direction provided by a prescriber and refers to the treatment sheet and prescription.
Monitoring errors:	Include errors due to lack of ordering monitoring parameters and failure to follow up prescribed monitoring.
Omission errors:	Occurs when an action is not performed and includes failure to prescribe a drug.
Opportunities for errors	Sum total of the errors that occurred and errors that could possibly have occurred
Paediatrics:	Patients aged less than 13 years.
Patient safety practice:	A type of process or structure whose application reduces the probability of adverse events resulting from exposure to the health care system

	across a range of diseases and procedures.
Prescribing Error:	The inappropriate selection of a drug (based on indication, contraindications, known allergies, existing drug therapy, and other factors); dose; dosage form; quantity; route of administration; concentration; rate of administration; or inappropriate or inadequate instructions for use of a medication ordered by a physician or other authorized prescriber.
Proactive risk assessment:	Identification and prevention of product and process problems before they occur.
Senior house officer	Medical officer on specialist postgraduate training
Technical errors:	Involve prescribing of vincristine and Intrathecal drugs in one medication order, lack of Tall-Man's lettering.
Timing errors:	Involve either use of wrong duration, wrong frequency, missing duration or frequency.
Therapeutic Index:	Measure used to assess the safety of a drug; it is a ratio of the median lethal dose to the median effective dose.
Route errors:	Are those that arise when information on the route of administration is either incorrect or omitted.

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Abstract

Background: Cancer is the leading cause of death worldwide accounting for 7.6 million deaths annually. Vincristine is a cytotoxic drug used in the management of haematological malignancies and solid tumours in adult and paediatric settings. Vincristine is categorized as a "High Alert" medicine due to its narrow therapeutic index and potential to cause serious morbidity and mortality if not used appropriately. These can be avoided by addressing medication errors. Medication errors are often preventable events with potential adverse outcomes during the course of treatment with medicines.

Objective: The main aim of the study was to determine the prevalence of medication errors among cancer patients receiving vincristine as part of their chemotherapy at Kenyatta National Hospital. The secondary objective was to perform a proactive risk assessment of vincristine use process to identify medication errors contributing factors.

Methodology: The study was carried out in oncology unit of Kenyatta National Hospital (KNH). The study design was descriptive cross sectional-study with two parts, quantitative and qualitative aspects. The quantitative approach involved two phases. First phase involved retrospective review of oncology in-patient non-schedule forms and out-patient cytotoxics summary form to determine vincristine use prevalence among cancer patients attended to in the oncology out-patient clinic and in-patient oncology units between January and June 2016 whereby 2880 records were reviewed. The second phase entailed concurrent review of 241 oncology patients' medical records on vincristine-based regimens attended to in November 2016 and March-May 2017 in the out-patient clinic and in-patient wards to identify vincristine medication errors. Descriptive statistics were used to summarize data using median, range, frequency and percentages. The qualitative component involved proactive risk assessment of vincristine use process to determine hazards to patient safety and appropriate preventive measure using Healthcare Failure Mode Effect Analysis (HFMEA). A failure mode with hazard score of 8 and higher was considered for further analysis to determine if there are any mitigation strategies in place or not. Risk mitigation strategies were developed for failure modes that didn't have any preventive measures in place. Universal and purposive sampling was used for quantitative and qualitative phases of the study respectively.

Results: The overall prevalence of vincristine use in the out-patient department was 4% of which majority (93.4%) of the patients were adults. In the in-patient department, vincristine was administered to 36% of the admitted cancer patients on chemotherapy, most (66.9%) of them were

paediatrics. Most of the patients (62, 25.73%) had acute lymphoblastic leukaemia as the indication for vincristine-based chemotherapy. Based on the Institute of Safe Medication Practices (ISMP) and other international patient safety organisations criteria for medication errors definition and assessment, the prevalence of vincristine medication errors was found to be 99.6% [95% CI 97.1-99.9) in 241 patient medical records reviewed. The prevalence was higher in in-patients (100%) than out-patients (87.5%). Majority (81.7%) of the errors identified did not reach the patients. A medication error rate of 18.6% was also determined.

Healthcare failure mode effect analysis (HFMEA) multidisciplinary team identified 77 failure modes for the vincristine use processes of prescribing, preparation and dispensing, transportation and storage, administration and monitoring. Twelve failure modes were found to be lacking adequate control measures necessitating development of mitigation strategies for the causes.

Conclusion: The prevalence of vincristine medication errors was significantly high based on the criteria set by International Patient Safety Organisations. The hospital system for the management and follow up of oncology patients had weaknesses thus fell short of meeting the criteria hence a high degree of medication errors was observed. Despite the fact that majority of the errors observed were less likely to cause harm, some were potentially fatal thus there is need for strategies to prevent, detect and minimise these errors.

THESIS FORMAT AND PRESENTATION

CHAPTER ONE: INTRODUCTION

1.1 Background

The goal of medication therapy is to achieve defined therapeutic outcomes that lead to improvement of patient's quality of life as it minimizes patient risk (1). Therapeutic use of drugs has inherent risks which are both known and unknown defined as drug misadventures which include adverse drug reactions (ADRs) and medication errors (2). Errors are present in any practice, in medical practice it is frequent due to its human nature and complex processes of medical management.

According to National Coordinating Council for Medication Errors Reporting Programme (NCC-MERP), a medication error is "any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of the health care provider, patient, or consumer. Such events may be related to professional practice, health care products, procedures and systems, including; prescribing, order communication, product labelling, packaging, and nomenclature, compounding, dispensing, distribution, administration, education, monitoring and use" (3). Medication errors are avoidable occurrences which may cause harm or not to a patient at any stage of medication use process (4).

Medication errors due to their avoidable nature lead to increase in healthcare costs and diminish patient confidence in the healthcare system. Medication errors contribute to significant morbidity and mortality of hospitalized patients. According to the Institute of Medicines (IOM) report titled *To Err Is Human,* it is estimated that between 44,000 to 98, 000 patients in America die yearly as a result of medication errors. This is more than mortalities from automobile accidents, breast cancer or AIDS and costs approximately $ 29 billion annually (5).

Therapeutic use of any class of drugs is prone to errors. Cancer chemotherapy is beleaguered by special dangers ranging from narrow therapeutic index, toxicity at therapeutic doses, highly complex regimens and individual vulnerability of cancer patients. This indicates that cancer patients can be adversely affected by medication errors (6).

Vincristine is a vinca alkaloid, obtained from Madagascan Periwinkle (*Catharanthus roseus)*. The drug is used as a cytotoxic medicine in the management of haematological and solid tumours in adult and paediatric settings. Vincristine exerts its action by binding to tubulin and inhibits its polymerization into

microtubules leading to arrest of metaphase in mitotic cycle (7). It is used in combination with other chemotherapeutic agents for the treatment of lymphoblastic leukaemia, myeloma, Hodgkin's lymphoma, non-Hodgkin's lymphoma, Wilm's tumour, some brain tumours and Ewing's tumour (8).

Vincristine is classified as a narrow therapeutic index drug and is administered intravenously. The major side effects are alopecia, hyponatremia and neurotoxicity. Vincristine is a vesicant drug that in the event extravasation occurs, it has the potential to cause local tissue necrosis and injury. Its toxicities are usually dose limited. Peripheral neurotoxicity manifests as both sensory and motor and autonomic neuropathy. Inadvertent intrathecal administration of vincristine causes irreversible neural damage and in vast majority of cases results in death despite vigorous central nervous system (CNS) washout. This error is rare, fatal and often preventable (9–13).

1.2 Problem Statement

Chemotherapy use process is considered as potentially risky for cancer patients due to its complex process, use of agents with narrow therapeutic index, multiple drug use and use of potentially toxic compounds (14). Medication errors can occur at any phase of medication use process from prescription, preparation, dispensing, administration and monitoring of patients. The medication use process involves multidisciplinary approach with physicians, pharmacists and nurses performing various roles (3). Medication errors involving antineoplastic agents may be catastrophic because of the drugs' toxicity and health status of the cancer patients (13,15). In a comparative study in Israel involving several departments, medication errors were reported in 15.6% of patients receiving antineoplastic drugs (16).

Kenyatta National Hospital (KNH) is Kenya's largest teaching and referral hospital where medical care is provided by both qualified staff and students from University of Nairobi (UoN) and Kenya medical training college (KMTC) with oversight of specialists. Oncology unit is served by specialists and medical officers on specialists' training who are tasked with responsibility of prescribing, preparation, administration and monitoring of chemotherapy use. There is no formal induction training for medical officers on specialist' training in the oncology unit. A preliminary audit done at the oncology unit revealed lack of vincristine use protocol and monitoring of processes. These result in enhancement of the potential for medication errors.

1.3 Study Justification

There is upward surge of cancer cases in Kenya and globally which in turn has predisposed many patients to the harmful side effects of the chemotherapeutic agents. Vincristine is listed as one of the

high alert medicines (HAMs) by various patient safety organizations like Institute of Safe Medication Practices (ISMP), Australian Commission on Safety and Quality in Healthcare (ACSQHC), National Patient Safety Agency (NPSA) and Joint Commission on Accreditation of Healthcare Organizations (JCAHO) (10,17–19). In 2003, the Institute for Safe Medication Practices reported that cancer chemotherapy tops the list of high-alert medications, outranking intravenous potassium chloride and insulin as potential threats to patient safety (20) . The risk of medication error is high with vincristine use due to low therapeutic index and increased usage (6). Medication errors associated with vincristine especially inadvertent intrathecal administration have greater potential to cause harm and fatal outcomes (21).

There is limited literature on chemotherapy medication errors among cancer patients in Sub-Saharan Africa and more so in Kenya. Therefore there is need for studies to characterize, highlight the extent and types of vincristine medication errors.

The results will aid in formulation of appropriate mitigation strategies that will help in detection and prevention of the errors. The results of the study can also be applied to other health institutions especially that county governments are setting up cancers centres across the country. The overall achievement will be improvement of patient outcomes and better quality of care.

1.4 Study Questions

1. What is the prevalence of vincristine medication errors in KNH?
2. What is the prevalence of vincristine use among cancer patients in KNH?
3. What are the factors that predispose patients to vincristine medication errors in KNH?
4. What patient safety systems are in place to prevent vincristine medication errors in KNH?

1.5 Objectives of the Study

1.5.1 Main Objective:

To determine the prevalence of vincristine medication errors and assess the contributing factors in KNH.

1.5.2 Specific Objectives:

1. To estimate the prevalence of vincristine medication errors in KNH.
2. To determine vincristine use prevalence among cancer patients in KNH.
3. To identify factors that predisposes patients to vincristine medication errors in KNH.
4. To identify patient safety systems that are in place at KNH to prevent vincristine medication errors.

CHAPTER TWO: LITERATURE REVIEW

2.1 Overview of Cancer

Cancer is a term used for diseases characterized by uncontrolled abnormal cell division that spread and invade other tissues (7). Cancer initiation and progression is dependent on both external or environmental factors (tobacco, radiations, chemicals and infectious diseases) and internal factors in the cell [genetic mutations, immunity and hormones] (22). Risk factors are acquired from the environment or from lifestyle (23).

Cancer is the leading cause of mortality worldwide, in 2008 it accounted for 7.6 million deaths (13%). Close to 70% of these deaths occurred in developing countries. Deaths are projected to hit 13.1 million by 2030. The five most common types of cancer globally are; lung, stomach, liver, colon and breast cancer (23). In Africa, the most common cancers in men are prostate, liver and Kaposi sarcoma while in women are breast and cervical cancer (24). In 2012, 847,000 cancer incidences and 591,000 cancer mortalities were estimated to have occurred in Africa (24).

Cancer ranks third in Kenya as the cause of death only after infectious diseases and cardiovascular disease accounting for 7% of the total national mortality annually (23,25). In 2008, the estimated cancer incidence in Kenya was 129.4/1000 (25). The most common cancers in women in Kenya are breast and cervical cancer while in men are prostate, oesophagus, head and neck cancers (23). In children, the commonest cancers are leukaemias and lymphomas (23).

Cancer management involves three main approaches which are surgical incision of the tumour, radiotherapy and chemotherapy. They are usually applied depending on the type of cancer and stage of disease development (7,26). Cancer management is divided into three phases. Induction (inducing remission), consolidation or intensification (use of drugs of stronger if not equal strength to the induction phase to consolidate what has been achieved) and maintenance (keeping cancer cells from growing again or achieving total elimination) (23,27).

2.2 Indications of Vincristine

Vincristine is used in the management of haematological malignancies and solid tumours. Vincristine indications are summarised in **Table 1** (9,23,27).

Table 1: Indications of Vincristine based drug regimens

	Indication	Drug regimen used
1	Acute lymphoblastic leukaemia.	Vincristine, Doxorubicin/Adriamycin, Methotrexate and Prednisolone
2	Hodgkin's Lymphoma.	Vincristine, Cyclophosphamide, Doxorubicin/Adriamycin, Procarbazine and Prednisolone
3	Multiple myeloma.	Vincristine, Doxorubicin/Adriamycin and dexamethasone
4	Non-Hodgkin's lymphoma.	Vincristine, Cyclophosphamide, Doxorubicin/Adriamycin, Prednisolone and Methotrexate
5	Rhabdomyosarcoma.	Vincristine, Cyclophosphamide, Cis-Platinum, Etoposide, Doxorubicin/Adriamycin and Actinomycin D
6	Neuroblastoma.	Vincristine, Cyclophosphamide , Actinomycin D and Doxorubicin/Adriamycin
7	Ewing's sarcoma.	Vincristine, Cyclophosphamide , Actinomycin D and Doxorubicin/Adriamycin
8	Wilms' tumour.	Vincristine , Actinomycin D and Doxorubicin/Adriamycin
9	Brain tumours.	Vincristine, Nitroso-ureas, Nitrogen mustard, Procarbazine, Methotrexate
10	Trophoblastic neoplasms.	Vincristine, Cisplatin, Cyclophosphamide, Methotrexate and Etoposide
11	Kaposi's sarcoma	Vincristine, Cyclophosphamide and Doxorubicin/Adriamycin
12	Retinoblastoma	Vincristine, Etoposide, Carboplatin/Cisplatin
13	Bladder cancer	Vincristine, Adriamycin, Cyclophosphamide
14	Brain stem Glioma	Vincristine, Actinomycin D, Etoposide, Procarbazine
15	Chronic lymphocytic leukaemia	Vincristine, Cyclophosphamide, Doxorubicin, Prednisolone
16	Gastric Adenocarcinoma	Vincristine, Cyclophosphamide, Mesna, Doxorubicin, Methotrexate, Cytarabine
17	Hepatoblastoma	Vincristine, Adriamycin, Cyclophosphamide
18	High grade sarcoma	Vincristine, Adriamycin, Cyclophosphamide, Cisplatin
19	Nasopharyngeal carcinoma	Vincristine, Ifosfamide, Carboplatin, Etoposide
20	Orbital sarcoma	Vincristine, Adriamycin, cyclophosphamide, Cisplatin
21	Ovarian Dysgerminoma	Vincristine, Actinomycin D, Cyclophosphamide, Cisplatin
22	Pleomorphic sarcoma	Vincristine, Adriamycin, Cyclophosphamide
23	Osteogenic sarcoma	Vincristine, Adriamycin, Cyclophosphamide, Cisplatin, Methotrexate

2.3 Burden of Medication Errors

Medication errors (MEs) occur quite frequently in the medical setting, despite being one of the most preventable cause of patient harm (28,29). The precise magnitude of medication errors is unknown

because of considerable level of under reporting (30). In the United States of America (USA), medication errors are reported in 2-14% of patients admitted to hospitals with 1-2% of patients experiencing harmful effects (29,31). In a study by Harvard medical Practice, medication errors accounted for close to 19% of all events reported (32). In 2006, 2-3% of all hospital admissions in Australia were related to medication errors with old patients being highly at risk (33). A study conducted at Kisii Teaching and Referral Hospital reported a medication error rate of 75.8% among paediatric patients (34). Prescription medication errors are the most prevalent type of errors and it is considered as the source of dispensing and administration errors (35).

2.4 Cancer Chemotherapy Medication Errors

Oncologists just like other physicians do not have greater or lesser chances of committing errors (36). However chemotherapy errors can have devastating effects because of narrow therapeutic index and safety margins (37). Chemotherapy drugs at therapeutic doses are cardiotoxic, carcinogenic and nephrotoxic (38). There are many causes of chemotherapy errors ranging from verbal orders miscommunication, inaccurate patient information, incorrect laboratory data, incomplete patient information, poor labelling and packaging, illegible prescriptions, use of abbreviations and acronyms, "look alike, sound alike" drug names, dose miscalculation to transcription errors (37).

Medication errors were reported among 17.2% of patients on chemotherapy by a study in Spain. The detected errors stratified according to process of use were: prescription 75.7%, preparation 21%, dispensing 1.8%, administration 1.1% and monitoring 0.4% (39).

2.5 Classification of Medication Errors

Medication errors can be classified according to the stage of drug delivery process, degree of harm and psychological approach. With respect to the stage of drug delivery system, errors can be classified as prescription, transcribing, dispensing, preparation and administration, and monitoring errors (40). NCC-MERP (Appendix E) classify the errors according the degree of harm which are: no error; error, no harm; error, harm; and error, death (3). United Kingdom's (UK) NPSA also categorizes errors according to degree of harm caused; no harm, low harm, moderate harm, severe harm and death (41). The psychological approach categorizes errors into two types namely; mistakes and skill based errors (42). Classification of Medication errors according to degree of harm and psychological approach are summarised in **Table 2 and Table 3** respectively.

Table 2: Classification of medication errors according to the degree of harm caused

Degree of harm	Definition by National Patient Safety Agency
No harm	Impact prevented: any patient safety incident that had the potential to cause harm but was prevented, resulting in no harm to the person(s) receiving NHS-funded care.
No harm	Impact not prevented: any patient safety incident that ran to completion but no harm occurred to the person(s) receiving NHS-funded care.
Low harm	Any patient safety incident that required extra observation or minor treatment, and caused minimal harm to the person(s) receiving NHS-funded care.
Moderate harm	Any patient safety incident that resulted in a moderate increase in treatment, and which caused significant but not permanent harm to the person(s) receiving NHS-funded care.
Severe harm	Any patient safety incident that resulted in permanent harm to the person(s) receiving NHS-funded care.
Death	Any patient safety incident that directly resulted in the death of the person(s) receiving NHS-funded care.

Adopted from the UK National Patient Safety Agency (41).

Table 3: Classification of medication errors according to the psychological Approach

Type of error	Explanation	Classifications
Mistakes	Errors resulting from applying wrong plans.	-Knowledge based. -Rule based (applying the rule incorrectly or applying the wrong rule).
Skill based	Errors resulting from applying right plans wrongly.	-Memory based (forgetfulness or inattention). -Incorrect performance or poor technical skill.

Adopted from Ferner *et al*.(42).

2.6 Factors that Contribute to Medication Errors

Medication errors are caused by a combination of human and system factors. Incomplete patient information, inappropriate packaging and labelling of drugs, burn out of healthcare workers, lack of drug information resources and miscommunication of orders are considered as latent causes of medication errors (43). Chemotherapy errors have been attributed to understaffing, poor communication, fatigue, human error and environmental factors (44).

Medication error propagation, detection and reporting are dependent on the system and culture of organization and individuals working in the organization. Lack of expertise and training, lack of

appropriate equipments and technologies, lack of process monitoring contribute immensely to increased incidences of medication errors (45).

2.7 Medication Errors Risk Reduction Strategies

Patient safety involves measures aimed at preventing and avoiding patient injuries or adverse events from healthcare delivery processes. Medication errors have negative outcomes both to the patient in terms of increased healthcare costs and harm while for the healthcare workers it impacts negatively on the confidence the patients have on the healthcare system. Therefore there is need for mitigation strategies to be put in place to deter the occurrence of the errors (46,47).

Chemotherapy errors can be reduced by instituting various strategies. Introduction of computerized prescribing system, pharmacists' participation in drug rounds, and ensuring availability of key reference materials can aid in error reduction (48,49). Cohen *et al* have put forward the following set of recommendations to prevent errors in haematology and oncology (50);

1. Educate health care providers to improve their levels of knowledge about chemotherapy drugs and potential drug errors.
2. Design the drug delivery system to have as many independent checks in it as possible, including independent calculation checks by the prescribing physician, pharmacist and nurse.
3. Establish maximum single and total course dosage limits at each institution. These should be communicated in educational programmes for staff.
4. Standardize the prescribing language by using the full names of drugs and routes (for example, INTRAVENOUS versus INTRATHECAL written out in full and in capital letters rather than abbreviated to IV and IT). All doses should be expressed in milligrams or units, prescriptions should be dated, and the prescriber should use a leading zero but not a trailing zero. The patient's current body surface area should also be written on the prescription.
5. Collaborate with drug manufacturers to eliminate ambiguous dosing information on package inserts and in textbooks.
6. Educate patients and their relatives about their drug regime as they are the last line of defence in the system.
7. Set up an interdisciplinary team that continuously reviews the drug delivery process and feeds back findings to hospital staff.

2.8 Healthcare Failure Mode Effect Analysis

Healthcare is a very complicated system which is predisposed to errors, accidents, near misses, failures, sentinel events and adverse events. Healthcare processes are interdependent and often interlocked. Inconsistencies, various inputs, tight time schedules, culture of hierarchy and dependence on human interventions causes increase in the risk of failures in system processes in the entire organization. Failure Mode Effect Analysis (FMEA) is one of the techniques used for system improvement to enhance human safety. The technique is team-based, proactive, systematic and reasoned-based technique used to prevent process and outcome problems before they happen. It also looks at how severe the effects of the problem will be if it occurs. It helps design preventive measures and if a problem cannot be prevented, FMEA will focus on protective measures that can be designed to deter the failure from reaching the patient or worst still is to mitigate the effects if the failure will cause harm (51).

CHAPTER THREE: METHODOLOGY

The study consisted of two parts. The quantitative phase involved determining the prevalence of vincristine use and medication errors among cancer patients. The qualitative phase aimed at exploring the threats to patient safety and determining the appropriate medication errors mitigation strategies using Healthcare Failure Mode Effect Analysis (HFMEA) technique.

3.1 Quantitative Phase

3.1.1 Prevalence of Vincristine use

3.1.1.1 Study Design

A cross-sectional study seeking to determine prevalence of vincristine use among cancer patients over a 6 months period, 1st January 2016 to 30th June 2016, was undertaken. The study period was chosen to prevent disruption of service provision and capture adequate and representative sample.

3.1.1.2 Study Site

The study site was Kenyatta National Hospital (KNH). It is the oldest and one of the busiest public hospitals in Kenya with a bed capacity of 1,800 and offers specialized healthcare to patients from East and Central African region. The hospital hosts University of Nairobi (UoN) College of Health sciences and Kenya Medical Training College (KMTC), Nairobi Branch. The oncology unit serves at least 1100 cancer patients every month. A wide range of practitioners in various fields of specialisation attend to patients in the unit. An array of equipments for cancer detection and management, dedicated cancer patients wards and treatment centre and a robust patient follow-up system exist. Oncology pharmacies managed by 3 oncology pharmacists offer support to the multidisciplinary team in cancer patients' management and ensure adequate supply of medicines. The study was conducted at the oncology pharmacy of KNH.

3.1.1.3 Study Population

The study entailed review of adults and paediatrics in-patient non-schedule forms, out-patient chemotherapy summary forms and oncology electronic dispensing tool entries.

3.1.1.4 Sample Size

All records entries made, between 1st January 2016 and 30th June 2106, in the in-patient non-schedule forms, out-patient cytotoxic summary forms and oncology electronic dispensing tool which met the inclusion criteria were reviewed.

3.1.1.5 Sampling Method

Universal sampling of all the record entries was done as long as the entries met the inclusion criteria. The sampling frame used was in-patient non-schedule forms and out-patient cytotoxic summary forms.

3.1.1.6 Inclusion and Exclusion Criteria

Record entries for cancer patient on chemotherapy attended to, between 1st January 2016 and 30th June 2016, were included in the study. Record entries where only supportive treatment had been prescribed were excluded from the study. Entries were screened using Screening and Eligibility form (Appendix A).

3.1.1.7 Data Collection Procedure

Chemotherapy summary forms were collected from the oncology pharmacy before commencement of data abstraction. Data abstraction was done with the aid of a pharmacist research assistant. Data was abstracted from 5052 entries made in the summary forms from patients who were attended to in the oncology out-patient clinic and various in-patient oncology units in the hospital. A sample of 2880 patient records was obtained after removing 1800 duplicates and 372 supportive treatment-only record entries.

Data abstracted into a predesigned data collection form (Appendix C) included patient demographics, whether the patient was on chemotherapy or not and prescribed medication.

3.1.2 Determination of prevalence, types and risk factors for Vincristine Medication errors

3.1.2.1 Study Design

A cross-sectional study was conducted to identify medication errors over a 15-week period from November 2016 and March to May 2017. A concurrent review of patient files and medication orders was carried out to identify the medication errors and factors that predispose patients to these errors. A checklist was also used to assess systems and processes that are in place to mitigate against vincristine medication errors. There was a break in data collection period due to disruption of healthcare services by doctors' industrial action.

3.1.2.2 Study Site

The study was conducted at the out-patient oncology clinic, paediatric wards, gynaecology ward 1B and adult's medical wards of KNH that admit oncology patients. Paediatric oncology patients are admitted in wards 1E, 3A, 3B, 3C, 3D and 9D while adult oncology patients are admitted in ward 8C, GFD and gynaecology ward 1B. Patient management in these wards is mainly carried out by senior house officers

with medical specialists attending major rounds twice weekly. Oncology pharmacy at the ground floor (GFC) serves these wards with cancer chemotherapy and allied drugs.

The oncology out-patient clinic is located at ground floor and runs from Monday to Friday every week. Other allied oncology clinics run on Mondays for haematooncology, Wednesday for gynaecology and Thursdays for general medicine at the ground floor as well. The out-patient clinics are served by oncology pharmacy at GFC.

These units were considered appropriate for this study because it is from them those cancer patients who form the target population access care.

3.1.2.3 Study Population

The study population comprised all medical records of oncology patients on vincristine and vincristine-based regimens who were attended to at the oncology out-patient clinic, gynaecology ward 1B, paediatric wards and adult medical wards during the study period.

3.1.2.4 Sample Size

This study had two outcomes; prescription errors and monitoring errors. Prescription errors were the main outcome of interest as the errors originate from the prescribers and are perpetuated by other healthcare workers. In a study in Spain, medication errors were reported in 17.2% of the patients receiving chemotherapy (39). The Cochran formula (52) was used to calculate the sample size as this was a cross-sectional study whose primary objective is to estimate prevalence of vincristine medication errors.

$$n_0 = \frac{z^2 * p(1-p)}{\delta^2}$$

Where:

Z = Z statistic for 95% level of confidence which conventionally is 1.96

P = Estimated prevalence of medication errors

δ = Level of precision to be used in the study set at 5%

n = Sample size

$$n_0 = \frac{1.96^2 * 0.172(1-0.172)}{0.05^2}$$ = 219 patient records

The sample size was enhanced by 10% in order to cushion for any missing information to obtain a final sample size of 241 patient records. A total of 241 patient files were reviewed, of which 8 were from oncology out-patient clinic and 233 from in-patient wards.

3.1.2.5 Sampling Method

Universal sampling method was used to gather the necessary information due to low turnover of cancer patients on vincristine as part of their chemotherapy in both in-patient and out-patient departments, and also short study duration. Therefore, all records accessed were included in the sample as long as they met the inclusion criteria. The sampling frame used was the out-patient oncology attendance register, the in-patient paediatric and adults' admission register. Paediatric patients' records were sampled in the out-patient clinic and the paediatric wards. Adult records were sampled in the oncology out-patient clinic, gynaecology ward and the medical wards until the sample size of 8 for out-patients and 233 for in-patients was achieved.

3.1.2.6 Inclusion and Exclusion Criteria

Patients records with cancer diagnosis and had vincristine prescribed as part of the chemotherapy were included in the study. Illegible records were excluded from the study. Patient records screening was done using Screening and Eligibility form (Appendix B).

3.1.2.7 Data Collection Procedures

Pre-testing of study of tools was conducted in the first week of data collection where patient records from ward 1E and 8C were randomly selected and data abstraction was done. Requisite adjustments were done to ensure validity and reliability of the research instruments before commencement of the study.

3.1.2.7.1 Data Collection in the Out-patient Clinic

Data collection was conducted at the end of each clinic day to prevent disruption of normal running of services. A pharmaceutical technologist was identified as a research assistant to assist in data abstraction due to their daily involvement in dispensing and preparation of drugs at the pharmacy unit level. The oncology clinic attendance register was used to obtain total number of clinic attendants. All records of patients attended to at the clinic were reviewed to identify patients on vincristine-based chemotherapy.

Data from these patient medical records were abstracted into a predesigned data collection form (Appendix D). A list of patient's out-patient numbers already reviewed was confidentially maintained by the investigator to ensure that records were not selected more than once. A sample size of 8 out-patient records was obtained during the study period.

3.1.2.7.2 Data collection in the In-patient Wards

A list of patients admitted in November 2016 and from March to May 2017 with cancer diagnosis was obtained daily from the in-patient admission register for paediatric, adult medical and gynaecology wards. Patient records were retrieved daily and reviewed to identify those that met the inclusion criteria. Data abstraction was done when ward rounds and treatment administration had been completed. A list of patient's in-patient numbers already reviewed was confidentially maintained by the investigator to ensure that records were not selected more than once. A sample size of 233 patient records was obtained during the study period.

Data abstracted into a predesigned data collection form (Appendix D) included; designation of the prescriber, patient's demographics, diagnosis, stage of disease, co-morbidities, prescribed medication, number of co-medication, number of treatment cycles received, most recent full haemogram results and actions taken. Each patient record was reviewed to detect presence of any of the 8 prescription errors and 1 monitoring error or both categories. A brief description of each medication error, error type and category were documented. All medication errors were categorized according to NCC-MERP taxonomy of medication errors (Appendix E). Data was transferred into EpiInfo® version 7 for data storage and analysis.

A checklist (Appendix G) adapted from JCAHO, ISMP and ACSQHC on recommendations for safe use of vincristine and other vinca alkaloids was administered to unit in-charges and other staff in the 5 paediatric wards, 2 adult oncology wards, gynaecology ward, oncology pharmacy and oncology out-patient clinic. This was done to assess structural and process factors that may contribute to vincristine-related medication errors. The checklist was interviewer-administered to enhance response rate and give clarifications. Data collected from the 11 unit heads were entered into Microsoft Excel for data storage and analysis.

3.2 Qualitative Phase: Proactive Risk assessment of Vincristine use process

3.2.1 Study Design

A focused group discussion with key informants among healthcare workers was carried out to determine possible factors that predispose patients to medication errors. Healthcare Failure Mode Effect Analysis (HFMEA) is a prospective, system-focused clinical risk assessment technique. Observation study was also carried out in each process of vincristine use. The purpose of the observation study was to identify the processes and sub-processes involved in vincristine use and any threats to patient safety. The results obtained were used to develop a tree diagram for processes involved in vincristine use.

3.2.2 Study Area Description

The study was carried out in the out-patient oncology clinic, oncology pharmacy, adult medical ward 8C, and paediatric medical wards 3A, 3B, 3C, 3D and, 9D and paediatric oncology ward 1E of KNH. These sites were selected to identify gaps and best practices in all areas of concern.

3.2.3 Study Population

The study population comprised medical officers, pharmacists, and nurses working at the KNH Oncology unit. These are the healthcare workers involved in the key vincristine use process of prescribing, preparation, dispensing, transportation, storage, administration and monitoring.

3.2.4 Sample Size

Based on the HFMEA criteria healthcare workers were identified, recruited and interviewed once they were taken through the consent process and voluntarily signed the consent form (Appendix F). The recommended size for a HFMEA multidisciplinary team is 6 -10 members (53). Nine healthcare workers participated in the study. The HFMEA guideline requires multidisciplinary team members to be well knowledgeable of the processes to be assessed, be involved in the any of the processes, be trained on the features of the procedure and to have voluntarily given informed consent.

3.2.5 Sampling Method

Purposive sampling method was adopted. The sample included healthcare workers involved in the key vincristine use process of prescribing, preparation, dispensing, transportation, storage, administration and monitoring. Information-rich participants who adequately understood the processes of vincristine chemotherapy use were recruited according to the HFMEA guidelines. Consultations were conducted by the researcher when the staff were done with the procedures while the observations were undertaken

when the procedures were on-going. Unit in-charges in the study site were requested to participate or nominate information-rich officers.

3.2.6 Eligibility Criteria

Healthcare workers were included in the study if they met the inclusion criteria. The sample comprised of healthcare workers stationed in the oncology out-patient clinic, oncology pharmacy, paediatric oncology ward, paediatric medical wards and adult oncology ward.

3.2.6.1 Inclusion Criteria

Healthcare workers were included in the study if they:

1. Have worked or have been working at the oncology unit for at least 1 month at the time of the study
2. Were involved in any of the various processes of vincristine use
3. Gave voluntarily informed consent (Appendix F).

3.2.6.2 Exclusion Criteria

Healthcare workers were excluded to participate in the study if they:

1. Were undergoing internship program

3.2.7 Healthcare Failure Mode Effect Analysis Procedure

The procedure was carried out in the oncology unit of KNH between April and June 2017 in accordance to HFMEA guideline (53). The core processes that were assessed include; prescribing, preparation, dispensing, transportation, storage, administration and monitoring of vincristine. The following steps were undertaken:

Step 1: The scope of the process

Assessment of prescribing, preparation, dispensing, transportation, storage, administration and monitoring of vincristine was carried out.

Step 2: Constitution of the multidisciplinary team

A multidisciplinary team was assembled according to HFMEA guidelines (53). The team comprised 7 regular members and 2 advisors; oncology ward paediatrician and oncology pharmacist. Two senior house officers in paediatrics and internal medicine, 1 pharmaceutical technologist and 1 pharmacist

working in oncology pharmacy, 2 nurses working in paediatric oncology ward and adult oncology ward participated in the study. The investigator, a pharmacist, led the team.

An introductory meeting was held to take the members through the features of the HFMEA process and their roles and responsibilities. A second meeting was held whereby, with the aid of the sample flow diagram (**Figure 8**) adapted from a study by Cheng *et al* (14), the investigator consulted the team members in their respective units to refine processes and sub-processes. He worked with a research assistant during the consultative meetings to record the information given by the members. He also requested members to enumerate potential failure modes and causes for each sub-process they are involved in. A third meeting was held where members determined the likelihood of potential failure mode occurring, the severity of its effects on the patient and process and the chances of it being detected and intercepted before it occurs thereby calculating the hazard score.

A fourth meeting was held to analyse the failure modes and failure mode causes with a hazard score of 8 or higher and those that are single point weakness for which further action were needed. The failure modes and causes were analysed and categorized as eliminate, control or accept. Then on the fifth meeting, the team made recommendations for each failure mode cause(s) that needed to be controlled or eliminated.

Step 3: Processes description

The multidisciplinary team enumerated vincristine use processes and sub-processes and numbered them consecutively. Then a graphical representation was done in a flow diagram (**Figure 8**). An observational study of the entire process was also carried out to verify the processes and sub-process in the flow diagram.

Step 4: Hazard analysis

The multidisciplinary team members brainstormed on all possible failure modes of each sub-process. All potential failure modes identified were then listed and numbered consecutively. Using consensus (53), the severity and probability of the potential failure modes were determined with the aid of severity rating table (Appendix H) and the probability rating table (Appendix I). Hazard scores were calculated for each failure mode using Hazard scoring matrix (Appendix J). A failure mode with a hazard score of 8 or higher was considered for further analysis using HFMEA decision tree to determine if further action was warranted or not based on absence of effective control measure and lack of detectability.

Failure modes with hazard scores less than 8 were further reviewed for criticality to determine if they were single point weaknesses. Criticality, absence of control measures and lack of detectability of a failure mode were used to determine if further actions could be instituted or not. Criticality is the measure of the effect of a single point weakness, which in case it fails, leads to entire system failure while detectability measures the probability of detecting a failure or the effect of the failure before it occurs.

Step 5: Identifying mitigation strategies

The multidisciplinary team analysed the failure mode causes to determine if there were appropriate mitigation strategies in place to deter the failure from occurring using HFMEA worksheet (Appendix K). These failure mode causes were categorized as: eliminate, control or accept. The HFMEA multi-disciplinary team made recommendations for each failure mode cause(s) that was to be either eliminated or controlled. If the failure or the effect of the failure was unlikely to be detected, the team considered: identifying other events that may occur prior to the failure mode that can serve as "alerts" that the failure mode might happen in developing strategies of preventing such failure modes from occurring.

3.3 Study Variables

The main outcome variable was vincristine medication errors. The predictor variables included prescriber cadre, patient age, sex, diagnosis, co-morbidities and number of co-medication. System factors to safeguard patient safety such as availability of process and structural components were also assessed.

3.4 Data Quality Assurance

The data collection tools were pre-tested on 5 randomly selected patient records in paediatric oncology ward 1E and adult oncology ward 8C. Induction training of research assistants on the tools to be used in the study and ethical considerations was done prior to commencement of the study. HFMEA tools were adopted from the Veterans Affairs National centre for patient safety (VA-NCPS) (53). The sample HFMEA flow diagram and observation tool was adapted from JCAHO and Cheng *et al* (14) . Data cleaning was done daily to ensure its completeness and reliability.

3.5 Ethical Considerations

Permission to conduct the study was sought and granted by Kenyatta National Hospital/University of Nairobi Ethics and Research Committee (KNH-UoN-ERC) (Appendix L, Reference number KNH-

ERC/A/317). The permission to collect data was also granted by the various departments where the study was conducted and registered by KNH Research and Programs Department (Appendix M).

Informed consent and voluntary participation was sought from healthcare workers who met the inclusion criteria without coercion or incentives. Participant's identities were concealed by use of serial numbers and any identifier information was not included in the data tool to ensure confidentiality. Completed data collection forms were kept under lock and key while electronic records were password protected for restricted access. Research assistants were trained on ethical considerations before the commencement of the study.

3.6 Data Management

All data collected from the patient medical records and HFMEA process, were entered into EpiInfo® version 7 and Microsoft Excel 2010 respectively. Data cleaning and validation was done thereafter data export to Stata® version 13 was done. Backing up of data was done regularly using a flash disk.

3.7 Data Analysis

Stata® version 13 (Stata Corp, USA) was used to analyse the data. Descriptive data analysis was done first. Variables with skewed distribution were expressed using median and interquartile range. Categorical variables were presented using frequency and percentages with 95% confidence interval. The main outcome of interest, prevalence of various medication errors, was presented as a percentage. The level of significance was set at 0.05.

The prevalence of medication errors was calculated as follows;

$$\text{Prevalence of MEs} = \frac{\text{Number of patient records with medication error}}{\text{Total number of records reviewed during the study period}} \text{ x } 100$$

Medication error rate is determined by calculating percentage of errors. Medication error rate of 5% and above denotes that a facility has system deficiencies. Roy *et al,* 2005 (43) formulae was used to calculate medication error rate as follows.

$$\text{Medication error rate} = \frac{\text{Number of medication errors observed}}{\text{Opportunities for errors}} \text{ x } 100$$

Eight types of medication errors measured; dosing, route, timing, omission, ambiguous or illegible prescription, use of abbreviations, failure to request for monitoring parameters and failure to act on available results. For each of the 241 patient medical records reviewed there were 8 medication errors that could occur hence the opportunities for errors of 1928 errors.

HFMEA method was used to analyse qualitative data. The analyses were descriptive. Each failure mode was analysed independently and recommendations were made accordingly.

CHAPTER FOUR: RESULTS

4.1 Prevalence of Vincristine use among Cancer patients at Kenyatta National Hospital

A total of 5052 patient records for cancer patients on chemotherapy who were attended to in the out-patient oncology clinic and in-patient wards between January and June 2016 were screened for eligibility. Of these, 2880 met the inclusion criteria. The other records (2172) were excluded for the following reason; 1800 records were duplicates and 372 had supportive treatment-only prescribed. This information is summarized in **Figure 2.** Most of these patients included in the study (1884, 65.4%) were attended to in the out-patient clinic and 996 (34.6%) were attended to in the in-patient wards.

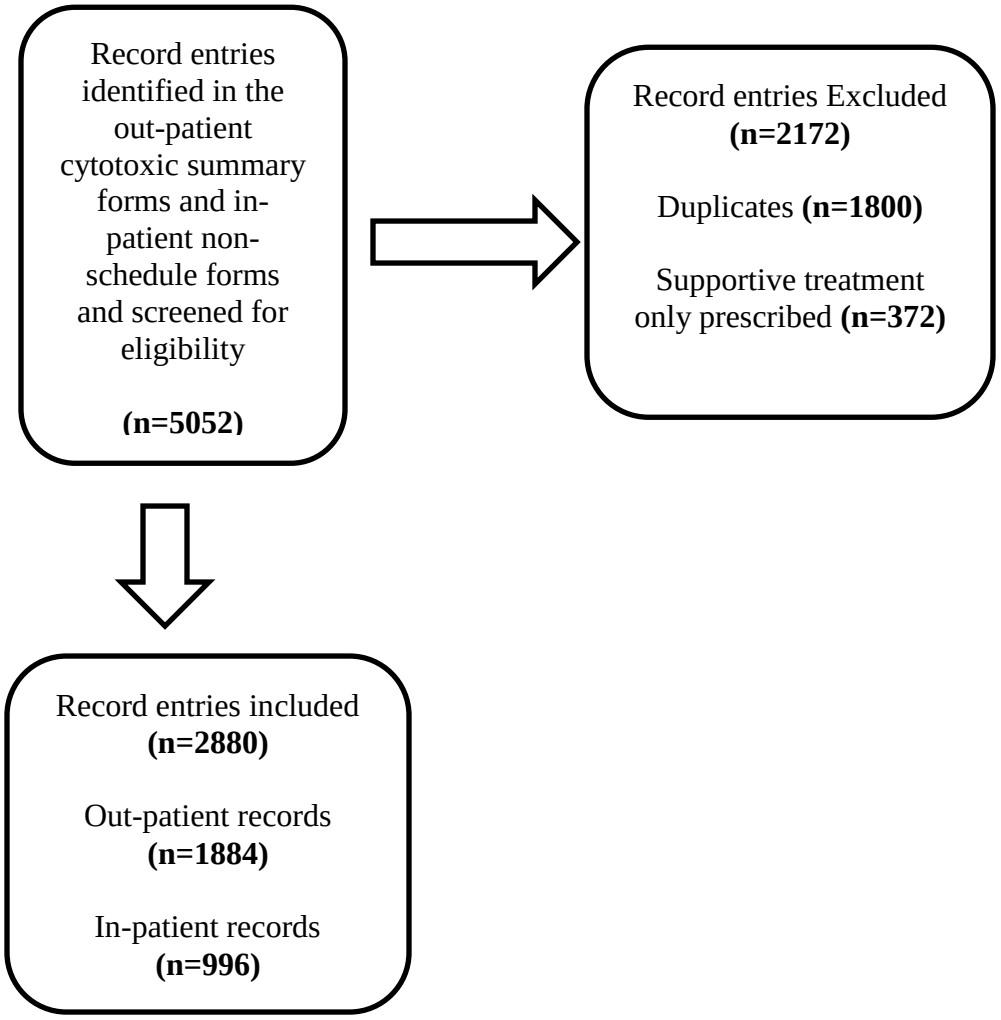


Figure 1: Consort diagram of record entries included in the study

In the out-patient oncology clinic, 1,213 (64.4%) female and 671 (35.6%) male cancer patients were attended to. Of these patients, 18 (1 %) were paediatrics and 1866 (99%) were adults. Vincristine was administered to 4% (76) of patients attended to in the out-patient oncology clinic for cancer chemotherapy administration. Majority of the patients on vincristine were adults (71, 93%).

In the in-patient wards, 561 (56.3%) of the patients admitted for cancer chemotherapy administration were female while 435 (43.7%) were male. Of these patients, 679 (68.2%) were adults while 371 (31.8%) were paediatrics. Vincristine was administered to 36% (360) of the patients admitted in the in-patient wards for cancer chemotherapy treatment. Many of the patients on vincristine were paediatrics (241, 66.9%).

4.2 Characteristics of cancer patients with Vincristine-based prescriptions

A total of 241 patient records were reviewed during the study period of November 2016 and March-May 2017. The desired sample size had been set at 219 thus this gives an overall target achieved at 110%. 233 (96.7%) of the records reviewed were for patients admitted in the in-patient wards while 8 (3.3%) were for patients attended to at the oncology out-patient clinic.

The median age for paediatric patients was 6 years, with an interquartile range of 3-9 years. The minimum and maximum age for paediatric patients was 5 months and 12 years respectively. While for the adult patients, the median age was 37.5 years and an interquartile range of 23-55 years. The minimum and maximum age for adult patients was 17 and 76 years respectively. Most of paediatric patients (116, 54%) and adult patients (7, 26.9%) were in the 6-12 and 18-24 years age bracket respectively. More than half of the patients (149, 61.83%) were male. The baseline characteristics of patients on vincristine-based chemotherapy regimen are summarized in **Table 4.**

Table 4: Baseline characteristics of cancer patients on vincristine-based chemotherapy

	Paediatrics n=215	Adults n=26	Total n=241
Variable	**Frequency (%)**	**Frequency (%)**	**Frequency (%)**
Patient Type			
Out-patient	3 (37.5)	5 (62.5)	8 (3.3)
In-patient	212 (91)	21 (9)	233 (96.7)
Sex			
Female	80 (87)	12 (13)	92 (38.2)
Male	135 (90.6)	14 (9.4)	149 (61.8)
Age Group			
Paediatrics <13 years			215 (89.21)
Adults >13 years			26 (10.79)
Age Category			
< 2 years	11 (5.1)		
2 - 5 years	88 (40.9)		
6 - 12 years	116 (54)		
	Median (IQR) 6 (3,9) years		
	Min - Max 0.43 - 12 years		
13 - 17 years		1 (3.9)	
18 - 24 years		7 (26.9)	
25 - 34 years		4 (15.4)	
35 - 44 years		6 (23.1)	
45 - 54 years		1 (3.9)	
55 - 65 years		5 (19.2)	
> 65 years		2 (7.7)	
		Median (IQR) 37.5 (23,55) years	
		Min - Max 17 - 76 years	

The most common diagnosis was acute lymphoblastic leukaemia (62, 25.7%) of which 59 (95.2%) were paediatric patients. Many of the adult patients were being managed for Non-Hodgkin's lymphoma (12, 46.2%). Anaemia (30, 12.5%) was the most common comorbidity in the patients attended to occurring in 23(10.7%) of the paediatric patients. Disease staging was not done for more than half (129, 53.5%) of the patients attended to. These characteristics are summarized in **Table 5**.

Table 5: Characteristics of diagnosis and management of cancer patients per age group

	Paediatrics n=215	Adults n=26	Total n=241
Variable	**n (%)**	**n (%)**	**n (%)**
Diagnosis			
Acute Lymphoblastic Leukaemia	59(95.2)	3(4.8)	62(25.7)
Wilm's Tumour(Nephroblastoma)	53(100)	0(0.0)	53(22.1)
Non-Hodgkin's Lymphoma	10(45.4)	12(54.6)	22(9.2)
Hodgkin's Lymphoma	18(90)	2(10)	20(8.3)
Neuroblastoma	18(100)	0(0.0)	18(7.5)
Rhabdomyosarcoma	17(100)	0(0.0)	17(7.2)
Retinoblastoma	11(91.7)	1(8.3)	12(5)
Burkitt's Lymphoma	6(100)	0(0.0)	6(2.5)
Osteogenic Sarcoma	6(100)	0(0.0)	6(2.5)
Bladder Cancer	3(100)	0(0.0)	3(1.2)
Diffuse Large B-Cell Lymphoma	0(0.0)	3(100)	3(1.2)
Hepatoblastoma	3(100)	0(0.0)	3(1.2)
Orbital Sarcoma	3(100)	0(0.0)	3(1.2)
Brainstem Glioma	2(100)	0(0.0)	2(0.8)
Choriocarcinoma(High Risk GTN)	0(0.0)	2(100)	2(0.8)
Meduloblastoma	2(100)	0(0.0)	2(0.8)
Chronic Lymphocytic Leukaemia	0(0.0)	1(100)	1(0.4)
Gastric Adenocarcinoma	0(0.0)	1(100)	1(0.4)
High Grade Sarcoma	0(0.0)	1(100)	1(0.4)
Kaposi Sarcoma	1(100)	0(0.0)	1(0.4)
Nasopharyngeal Carcinoma	1(100)	0(0.0)	1(0.4)
Ovarian Dysgerminoma	1(100)	0(0.0)	1(0.4)
Pleomorphic Sarcoma	1(100)	0(0.0)	1(0.4)
Co-Morbidity			
Anaemia	23(76.7)	7(23.3)	30(12.5)
Sepsis	9(90)	1(10)	10(4.1)
Neutropenia	5(100)	0(0)	5(2.1)
Others*	17(81)	4(19)	21(8.7)
None	161(92)	14(8)	175(72.6)
Staging			
Done	107(95.5)	5(4.5)	112(46.5)
Not Done	108(83.7)	21(16.3)	129(53.5)

*Pancytopenia, HIV/AIDS, malnutrition, sickle cell disease, congenital heart disease, chicken pox, tonsillitis, meningitis and hypertension

4.3 Prescriber characteristics

The characteristics of prescribers responsible for cancer chemotherapy prescriptions are show in **Table 6**. Senior house officers generated most of the prescriptions both in the in-patient wards and oncology out-patient clinic accounting for 215 (89.2%) of the total prescriptions. This could be attributed to the fact that KNH is a teaching and referral hospital. Almost half of the patients (120, 49.8%) were prescribed for 4-6 chemotherapy drugs other than vincristine.

Table 6: Characteristics of prescribers of Vincristine in Kenyatta National Hospital

Variable	Frequency (Percentage) n=241
Prescriber	
Medical specialist	7 (2.9)
Senior house officer	215 (89.2)
Medical officer	2 (0.83)
Clinical officer RH	10 (4.15)
Clinical officer PAEDS	7 (2.9)
*****RH- Clinical officer specialised in Reproductive Health	
* PAEDS- Clinical officer specialised in Paediatrics	
Number of Co-medication prescribed per patient	
0	1 (0.4)
1 – 3	116 (48.1)
4 – 6	120 (49.8)
7 – 9	4 (1.7)

4.4 Prevalence of Vincristine Medication Errors

A high proportion of patients attended to had medication errors in their prescriptions. A total of 240 out of 241 patient records were found to have at least 1 vincristine medication error, yielding a prevalence of 99.6% [95% CI 97-99.9). The prevalence was higher in in-patients (100%) than out-patients (87.5%). In the out-patient department only one medical record didn't have any error according to the criteria used while in the in-patient all records reviewed had at least one medication error. The difference in prevalence was statistically significant (p <0.001). **Figure 3** shows the frequency and prevalence of vincristine medication in the out-patient and in-patient during the study period.

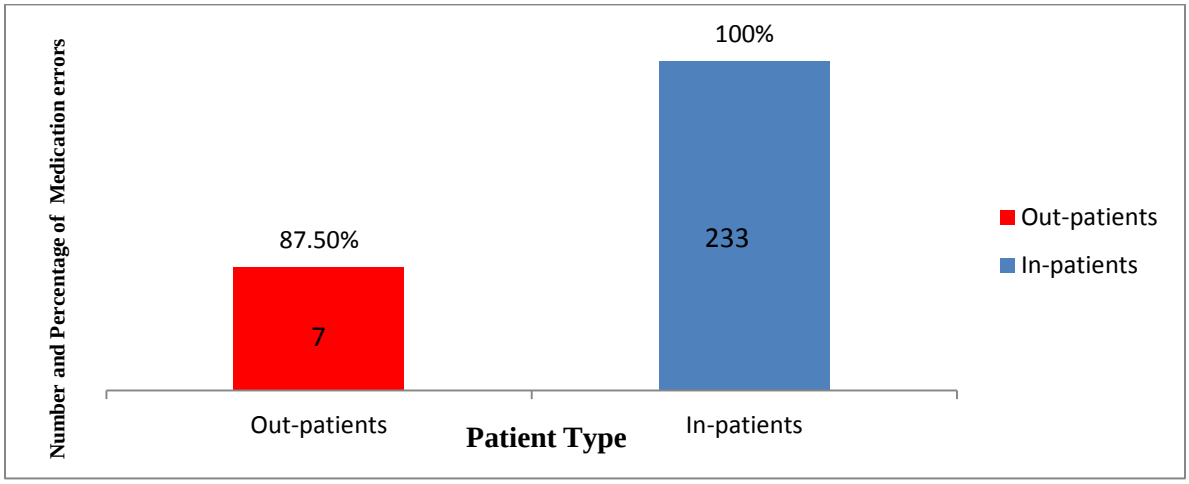


Figure 2: Frequency and prevalence of vincristine medication errors in cancer patients at KNH

More than half (54.4%) of the patients' record reviewed during the study period had 1 medication error. There was no medication error in only 1(0.41%) patient file reviewed. **Table 7** summarizes the episodes of vincristine medication errors identified per patient record reviewed.

Table 7: Episodes of vincristine medication errors identified per patient record reviewed

Number of Vincristine medication errors identified per patient	Frequency (Percentage) n=241
None	1 (0.4)
1	131 (54.4)
2	99 (41.1)
3	10 (4.1)

4.5 Types of Vincristine Medication Errors Identified

Eight types of medication errors were identified during the review of patient medical records. A total of 359 medication errors were encountered which were then classified into 8 types as shown in **Figure 4.**

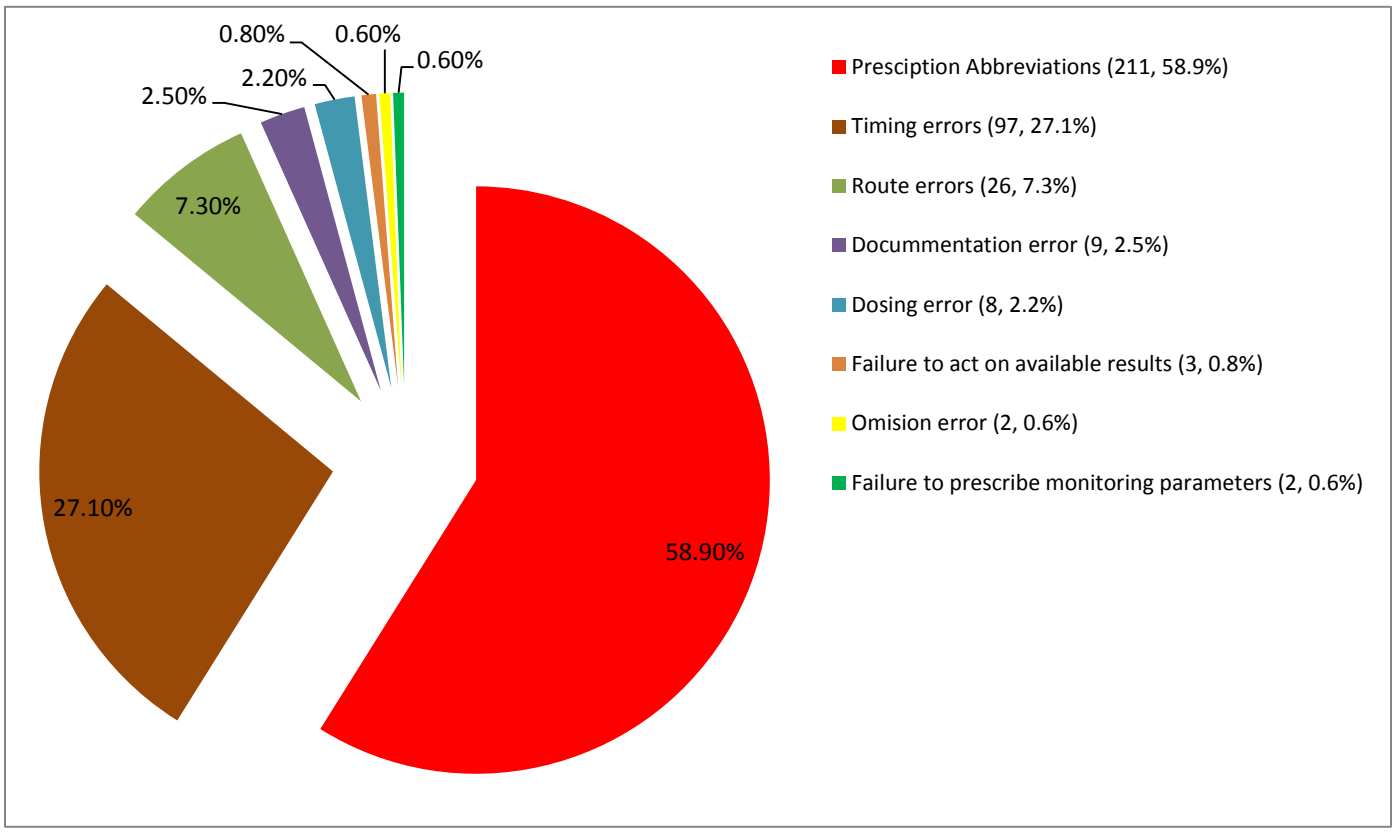


Figure 3: Types of Vincristine Medication Errors identified during the study

The most common type of error was the use of abbreviations (211, 58.9%) in prescribing where "IV" was used instead of "Intravenous" and "VCR" instead of "Vincristine". Timing error was the second leading type of error depicted by failure to indicate the frequency of administration and indication of schedule of administration rather than frequency of administration.

The errors identified were classified according to the NCC-MERP system (Appendix E). The identified errors were assigned to error category B, C and D. **Figure 5** illustrates the distribution of vincristine medication errors according to NCC-MERP system of classification. 196 (81.7%) errors were assigned to category B, 42(17.5%) category C and 2 (0.8%) category D. Category D error was encountered in 2 patients, one 6 years old patient was prescribed and administered 4 milligrams of vincristine yet the maximum dose of vincristine is 2 milligrams. This necessitated interventions and monitoring of the patient to preclude harm while another patient with osteosarcoma had haemoglobin level of less than 5mg/dl however blood transfusion was not done for more than a week. In this case there was failure to act on the available results.

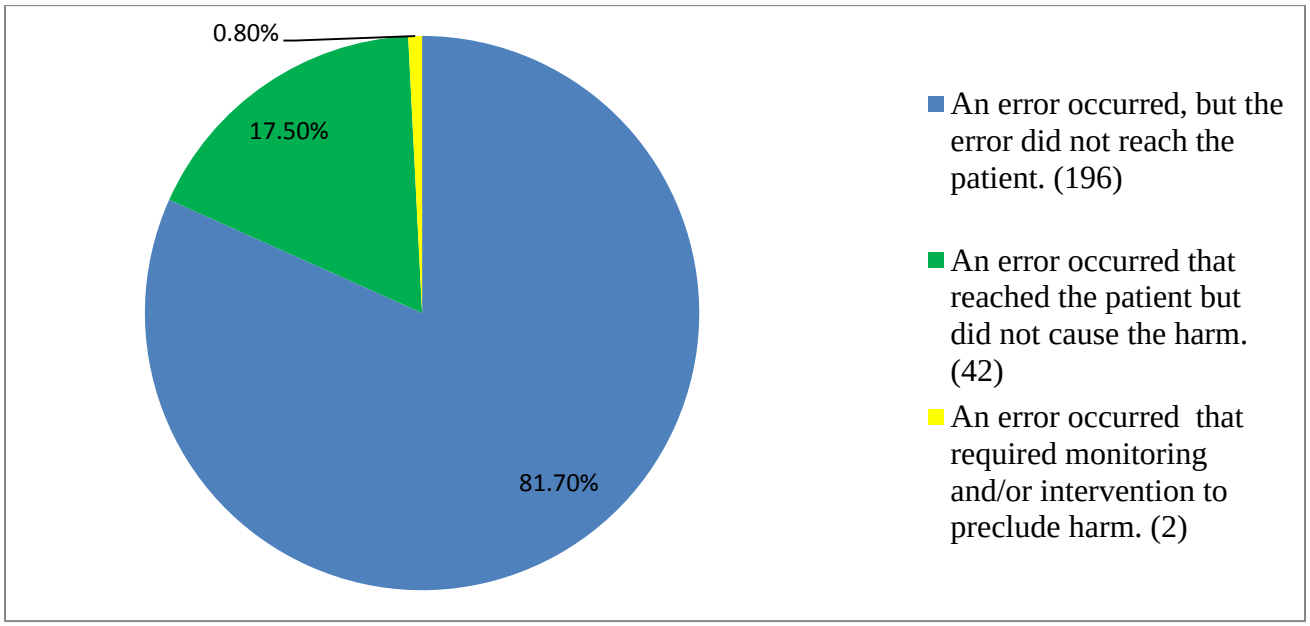


Figure 4: NCCMERP system error category classification of identified medication errors

The medication error rate calculated using Roy *et al*, 2005 formula was found to be 18.6%. A medication error rate of >5% is an indication of system failures (43). **Figure 6 and 7** represents examples of prescriptions with various types of errors encountered during the study. In **Figure 6** underdose of vincristine was prescribed due to body surface area (BSA) miscalculations, use of

abbreviations and frequency of administration not clear. Patient regimen was also confused for cycle of treatment.

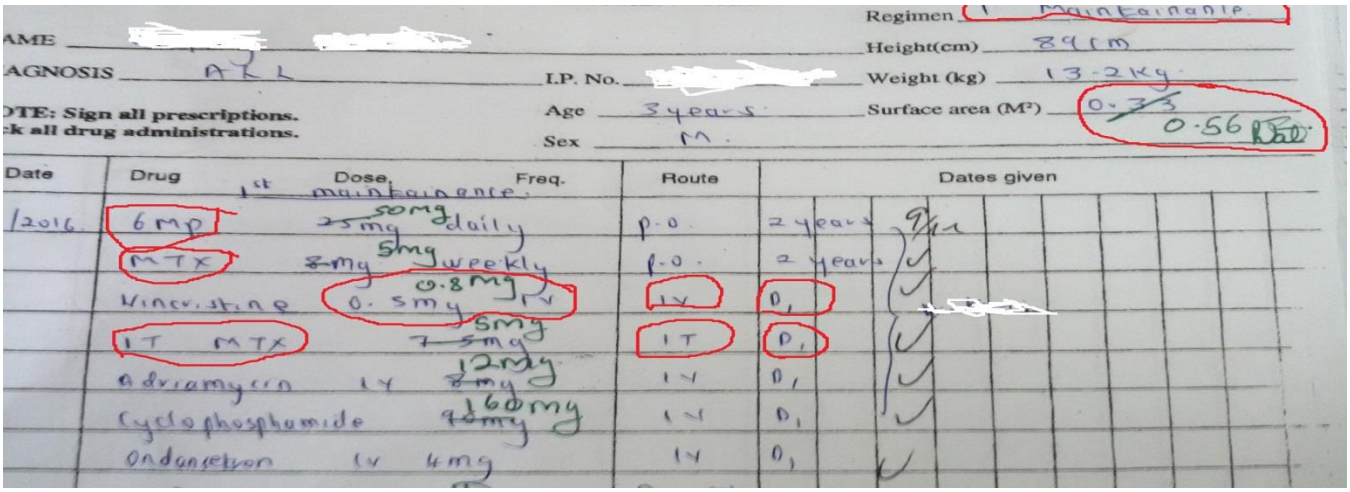


Figure 5: An in-patient chemotherapy prescription with dosing, timing errors and use of abbreviations

Figure 7 depicts an ambiguous prescription whereby the dose can be confused as 102mg instead of the intended 1.2mg. The route of administration is not indicated while the schedule of treatment has been indicated rather than the frequency of administration.

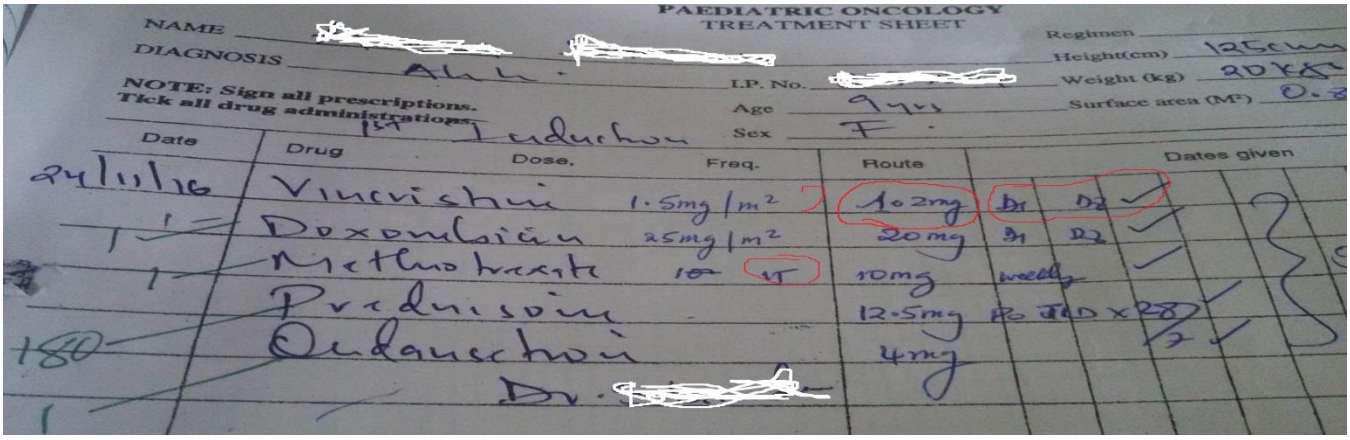


Figure 6: An ambiguous in-patient chemotherapy prescription with route and timing error

4.6 Assessment of Structural and Process components of patient safety system

Eleven units where vincristine is utilized were visited to assess the existence of structural and process components of patient safety system. The units were 6 paediatrics wards, adult oncology ward, gynaecology ward, oncology pharmacy and 2 oncology out-patient clinics.

Table 8 summarizes structural components in place to minimize or prevent vincristine medication errors. Eight units mainly paediatric wards reported the presence of a guideline related to chemotherapy use namely "Kasili's synopsis of the management of paediatric Cancers in Kenya". Staff in 9 out of 11 units were encouraged to report medication errors as part of the hospital staff appraisal system however 4 units reported presence of a documented procedure of reporting the errors. Nine units recognized the relevance of the contributions that pharmacists make in their units. None of the units reported presence of formal induction training of new staff but rather on job training is done. Moreover none of the units reported availability and accessibility of all staff to a list of high alert medications and a list of abbreviations to avoid in chemotherapy.

Table 8: Structural components in place to minimize or prevent vincristine medication errors

	Variable n=11	**Frequency**	**Percentage**
1	Presence of a guideline related to cancer chemotherapy use	8	72.7
2	Presence of a protocol specifically on vincristine use	0	0
3	Guideline includes education and competency requirements for all staff involved	2	18.2
4	Guideline readily accessible to staff	8	72.7
5	Presence of a team that guides and monitor implementation of the guideline	2	18.2
6	Presence of a documented procedure of reporting medication errors	4	36.4
7	Staff encouraged to report medication errors	9	81.8
8	Presence of medication errors reporting tools	9	81.8
9	Medicine information resources available to staff	8	72.7
10	List of High-alert medicines available and accessible to staff	0	0
11	Vincristine recognized as a High-Risk medicine	0	0
12	List of abbreviations to be avoided in chemotherapy available and readily accessible to staff	0	0
13	Presence of a formal process for approving guidelines, prescription order forms and Oncology treatment sheets before use	7	63.3
14	Presence of formal induction training of new staff	0	0
15	Presence of defined responsibilities for pharmacists in the management of patients receiving chemotherapy	9	81.8

Table 9: Process components in place to minimize or prevent vincristine medication errors

	Variable n=11	Frequency	Percentage
1	Presence of a defined oncology treatment sheet for prescribing chemotherapy	9	81.1
2	Presence of a list of authorized chemotherapy prescribers with sample signatures	0	0
3	Chemotherapy orders authorized by a medical specialist for new patients	10	90.9
4	Presence of a clear process or procedure for communicating with prescriber when questions arise	10	90.9
5	Prescribers are contacted to verify medication orders before dispensing or administration	11	100
6	Patients/guardians actively participate in the management of their condition	4	36.4
7	Patient' consent sought before chemotherapy administration	7	63.6
8	Presence of a procedure for handling verbal orders	0	0
9	Presence of a strategy to prevent chemotherapy errors e.g. Double-checks	3	27.3
10	Chemotherapy administration done on Weekdays between 8:30AM and 5:00PM	8	72.7
11	Pharmacists review the medical records of patients on chemotherapy in the unit	3	27.3
12	Chemotherapy monitored for success and adverse drug reactions	6	54.5
13	Vincristine use process monitored and reviewed regularly	0	0

Table 9 summarizes process components in place to minimize or prevent vincristine medication errors. Nine units reported use of a defined sheet for prescribing chemotherapy while adult medical ward 8C and gynaecology ward 1B use the standard treatment sheet. Four units reported that patients or their guardians actively participate in the management of theirs conditions but only limited to well-knowledgeable patients. Informed consent is sought for in patients in 7 units, however only verbal consent is usually given. Pharmacists review patient records in the wards in only 3 wards regularly and occasionally in the other units.

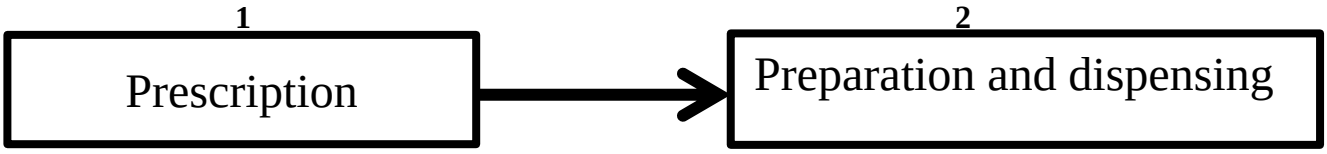
A strategy to reduce and prevent chemotherapy medication errors was reported in 3 of the 11 units which include double-checks in pharmacy and ward rounds. Monitoring of vincristine-based therapy for adverse drug reactions and success was reported to be done in 6 of the 11 units. It was also noted that there is no specific vincristine use protocol in all units thus the process couldn't be monitored and reviewed regularly.

4.7 Proactive risk assessment of vincristine use process using HFMEA method

At the beginning of the study, an introductory meeting of 1 hour was held whereby the team members were taken through the various aspects of the HFMEA process and their roles and responsibilities in the study. Five meetings in total were held lasting on average 1.5 hours each. Due to difficulty in having all team members in one meeting, some meetings were held per department.

The process was sub-divided into 6 phases: prescribing, preparation, dispensing, transportation, storage, administration and monitoring. Each process step and sub-step was enumerated and numbered consecutively.

Chemotherapy prescriptions in KNH are done by medical specialists and Senior house officers; Dispensing and preparation for Out-patient oncology clinics, Ward 1E, GFD and some days 8C is done by pharmaceutical technologists and pharmacists while preparation for the other wards is done by Senior house officers; Transportation and storage is done by Nurses while administration and monitoring is done by Senior house officers. Preparation process was analysed as one being cognizant of the two preparation areas. **Figure 8** illustrates vincristine use processes and sub-processes.



Sub-processes;

A. Checking patient's medical record
   a. Diagnosis type of malignancy and staging
   b. Hypersensitivity history
   c. Co-morbidities and contraindications
   d. Chemotherapy schedule
   e. Relevant laboratory results
B. Patient routine assessment
   a. Ordering appropriate tests
   b. Sample collection
C. Dosing
   a. Measuring height and weight
   b. Calculating Body surface area
   c. Dose calculation
D. Prescription Detailing
   a. Patient biodata (Name, age, sex, weight, height, IP/OP No., BSA)
   b. Diagnosis, staging and regimen
   c. Date of prescription and cycle number
   d. Drugs to be given(generic name(FU dose, route(FULL), frequency and c duration of administration)
   e. Days, dates when each drug is to be given
   f. The prescriber's name, designation and signature
E. Medication order sent to Pharmacy
   a. Prescription duplicated into Non-Schedule form and S11
   b. Medication order and patient file taken to pharmacy

Sub-processes;

A. Verifying the prescription
   a. Checking for completeness
      i. Patient's basic information (IP/OP number, date, doctor's information, medicine quantity)
      ii. Checking administration information(date, medicine name, dosage, days and frequency)
B. Prescription Validation
   a. Checking for protocol adherence
   b. Confirm test results are optimal
   c. Dose Re-calculation
   d. Checking drug interactions, side effects profile and hypersensitivity
   e. Authorization by Oncology pharmacist
C. Medicine Retrieval
   a. Control on the S11
   b. Charge, issue and record in the HMIS
   c. Checking for medicine availability
   d. Medicine retrieval
   e. Labelling of medicine bag
   f. Labelling of the medication
   g. Packing the medicine in a medicine bag
   h. Transportation to the Chemotherapy preparation room
D. Medicine Preparation
   a. Staff don Personal protective equipments
   b. Checking if the patient identifiers(name, IP/OP No.), prescription, medicine, and label correspond with the original prescription
   c. Confirming the dosage, volume, and administration date
   d. Checking that medicine in vial is clear and without any foreign matter
   e. Syringe selection
   f. Drawing the medicine into a syringe
   g. Labelling of the syringe
E. Packing the medicine
   a. Packing the medicine into a medicine bag
   b. Sealing the medicine bag
   c. Filling the S11
   d. Calling for transport

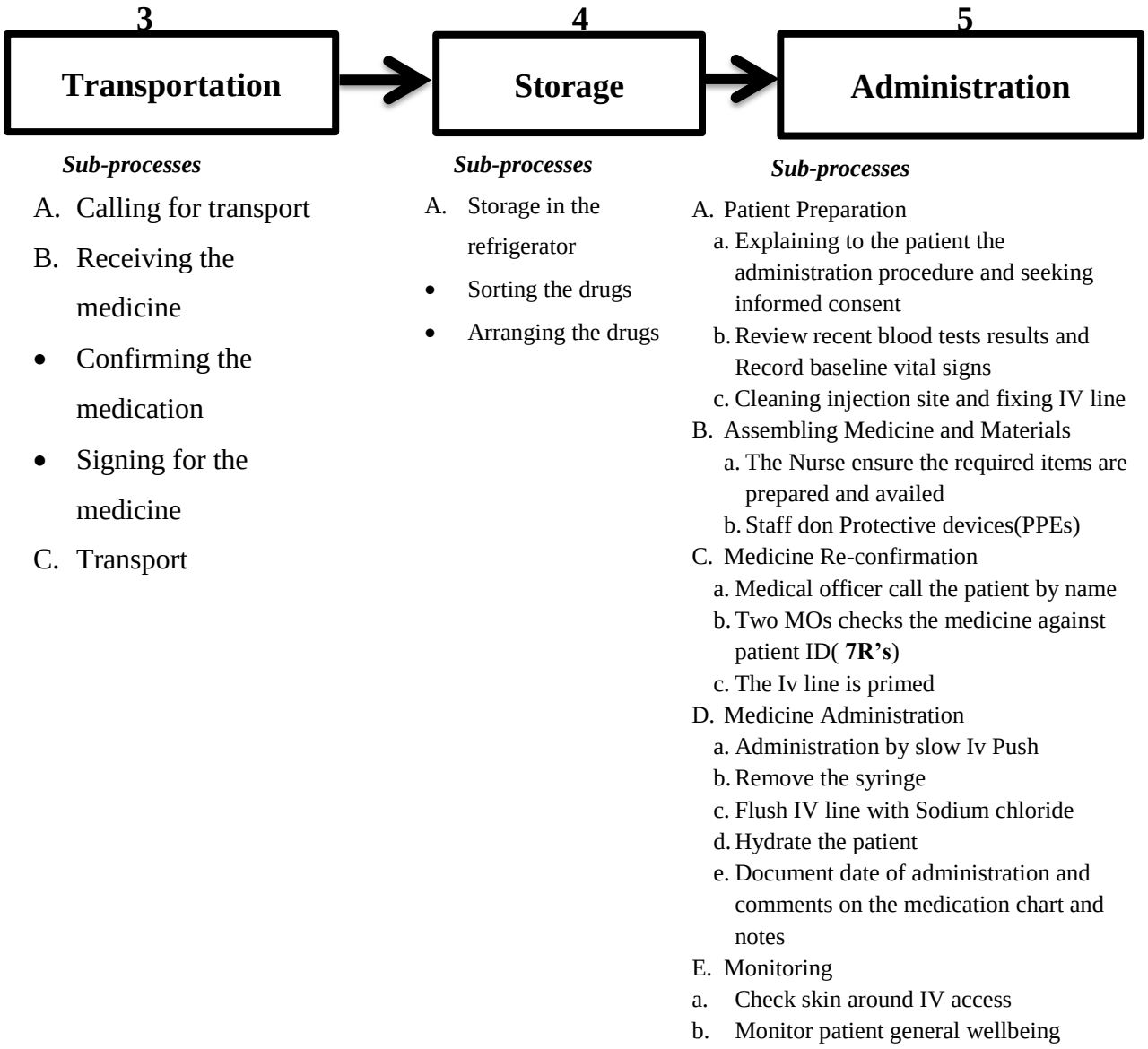


Figure 7: Healthcare Failure Mode Effect Analysis Process Flow Diagram

Seventy seven (77) failure modes were identified, from which 19 were classified as high risk using hazard scoring matrix (Appendix J). **Table 10** shows number of major steps, sub-steps and failure modes identified for 5 phases of vincristine use process analysed. Six (6) other failure modes were identified to be single point weaknesses in the process. For each failure mode, failure mode causes were identified and hazard scores determined. Twelve (12) of the 25 failure modes identified were not adequately covered by existing control measures. **Table 11** illustrates the 12 failure modes and failure mode causes determined by the HFMEA team using the decision tree to be lacking adequate control measures. Recommendations for these failure mode causes were made to militate against the failure

modes. Transportation and storage of vincristine were considered as low risk steps by the multidisciplinary team.

Table 10: Number of process steps and failure modes identified

	Major Steps		Major and Sub-steps		Failure Modes		High Risk Failure Modes and Single point Weaknesses	
Stage of medicine use process	**No.**	**%**	**No.**	**%**	**No**	**%**	**No.**	**%**
Prescribing	4	25	16	23.5	15	19.5	10	40
Preparation and Dispensing	5	31.3	28	41.2	31	40.3	10	40
Transport	1	6.3	2	2.9	3	3.9	0	0
Storage	1	6.3	2	2.9	2	2.6	0	0
Administration	5	31.3	20	29.4	26	33.8	5	20
Total	16		68		77		25	

4.8 Failure modes and Recommendations

Failure Mode 1: Out-dated weight and height measures indicated on the treatment sheet

It was observed by the HFMEA multi-disciplinary team that majority of the patients especially in the wards do not have latest weight and height measures in their treatment sheets. This has the potential of patients getting underdose or overdose. The team recommended the amendment of the chart to provide for space for twice monthly charting of the patient weight and height.

Failure Mode 2: Past history inconclusive in determining last date of administration

The treatment chart doesn't provide adequate space to indicate the date of administration which makes it difficult for the prescribers to schedule the next course of treatment. Amendments on the treatment sheet to provide space for affixing the date and sensitization of prescribers on the difference between scheduled day of treatment and date of administration were recommended.

Failure Mode 3: Dose Miscalculation

Dose calculations by prescribers were considered to be a source of errors which can translate to patients receiving underdose or overdose of medications. Double-checks in the wards and in the pharmacy, development of job aids with formulas and dose limits were recommended for adoption

Failure Mode 4: Obscure prescription/medication order

The use of handwritten medication orders and abbreviations were considered as the main causes of the obscure orders. The clinicians reported restrictive size of the medication order as the cause of using abbreviations. It was recommended that the chart be redesigned to provide adequate space, sensitization of staff on abbreviations to avoid and possible adoption of Computerised Physician Order Entry (CPOE) System in chemotherapy prescribing.

Failure Mode 5-7: Inadequate Labelling

Labels affixed on the medicine bag, vial/box, and syringe were found to be wanting in providing adequate safeguards for the patients in terms of identity of drug and patient, storage conditions, directions of use and warnings. Vincristine being a high-alert medication should have appropriate labels including warning which is lacking in the unit. The multidisciplinary team recommended that the standard operating procedure (SOP) for handling cytotoxics should be amended to provide for labelling requirements, procurement of labelling machine and development of standard colour-coded labels with clear warning labels.

Failure Mode 8: Medication Spillage

Medication spillage especially during preparation is a preventable hazard that can cause serious harm to both handlers and patients. Inadequate working space both in the pharmacy chemotherapy preparation room and ward procedure rooms and heavy workload pose a greater risk of the event occurrence. Recommendations for sensitization or formal induction training of new staff in the various service departments, centralizing preparation of cytotoxics in pharmacy department to be done exclusively by pharmacy staff, adequately equipped with Biologic safety cabinet/Externally ducted Negative pressure isolators and adequate working bench to aid in curtailing the risk were made.

Failure Mode 9: Failure to adequately confirm vital information before administration

Heavy workload and inadequate staffing level predisposes the patients to the risk of various errors due to staff burnouts. Proper checks of all aspects (right medication, right patient, right dose, right time, right administration route, right sequence and right administration duration) need to be done regularly by at least 2 pharmacy staff. Independent bedside double-checks by 2 nurses before administration or by the senior house officers need to be instituted and ensure that medication administration is done by at least 2 staff.

Failure Mode 10: Extravasation

Veins are some of the most important assets of a patient which need to be safeguarded at all costs(27). Vincristine is a vesicant medication which can cause tissue burns and necrosis if administered

inappropriately. The team observed that cancer patients in KNH were predisposed to extravasation due to repeated use of peripheral intravenous access for administration of vincristine and other drugs. Staff sensitization on prevention and management of extravasation as well as provision of extravasation kits in all chemotherapy administration areas were recommended. Vincristine dilution using Sodium chloride 0.9% should be done to 10ml for patients aged less than 10 years and 20ml for greater than 10 year old patients(27).

Failure Mode 11: Inadvertent intrathecal administration of vincristine

Inadvertent intrathecal administration of vincristine has fatal ramifications on the patients. The multidisciplinary team assessed the predisposing factors and found that there are inadequate control measures to prevent this event. For instance vincristine is prepared in small volume syringes which could be confused for intrathecal use; vincristine and intrathecal medications are prescribed and administered on the same day, vincristine and intrathecal medications are stored in the same refrigerators and lack of adequate warning labels on the syringe. The team recommended that vincristine be diluted in large volume syringes (Minimum10ml) using Sodium chloride 0.9% or adopt the use of minibags (20ml for paediatrics and 50ml for adults). Schedule administration of intravenous drugs different from intrathecal drugs, intravenous drugs should be administered first. Adequate labelling of the medication including warning labels and proper sensitization of staff on proper handling of cytotoxics was also recommended.

Failure Mode 12: The doctor fails to notice exosmosis has occurred

Post-administration monitoring of patients is very vital especially after administering vesicant drugs like vincristine. The team noted that sometimes due to heavy workload the senior house officers leave the room immediately after medication administration which could lead to delayed detection of adverse events. It was recommended that chemotherapy administration should be done by at least two staff between 8:30AM and 5:00PM on weekdays so that if there is need for medical specialists' review they can be accessed with ease.

Table 11: Vincristine use process failure modes and recommendations

FAILURE MODE First Evaluate failure mode before determining potential causes	POTENTIAL CAUSE	SCORING			DECISION TREE ANALYSIS		
		Severity	Probability	Hazard score	Single point weakness (Y/N)	Action Type (Control, Accept or Eliminate)	Recommendations
1. Out-dated patient height and weight measures indicated	→	3	3	9			
	1. Poor documentation	3	3	9		Control	Twice monthly charting of weight and Height be documented on the Treatment sheet/Chemotherapy chart
	2. Lack of space to fix latest measures	3	4	12		Control	Amend the Chemotherapy chart to provide for the provision of twice monthly charting of weight and height
2. Previous history inconclusive in determining last date of Vincristine administration	→	3	3	9			
	1. Misinterpretation between schedule day and date of administration	3	3	9		Control	Update prescribers on the difference between the schedule day and Date of administration
	2. Inadequate space to affix the date on the Treatment sheet	3	4	12		Eliminate	Redesign the Chemotherapy treatment chart to provide adequate space to affix the date
3. Dose miscalculation	→	4	3	12			Ensure double-checks in wards and pharmacy.
	1. Non-adherence to treatment protocol	3	3	9		Control	Develop job aids for calculations of BSA, dosages and determine minimum and maximum doses
	2. Use of inaccurate BSA	4	3	12		Control	Amend the Chemotherapy chart to provide for the provision of twice monthly charting of weight and height
4. Medication order is obscure	→	4	2	8		Redesign the Treatment chart to give provision for stage of treatment and schedule	
	1. Use of non-standard abbreviations	3	3	9		Eliminate	Sensitize prescribers on non-standard abbreviations to avoid.
	2.Handwritten medication orders	3	3	9		Eliminate	Adopt the use of CPOE. Computerised Physician Order Entry System in chemotherapy prescribing
5. Incomplete labelling of the primary packaging material (Name/IP No., Route administration, Warnings, Storage conditions)	→	3	3	9			
	1.Label on medicine bag misconstrued as appropriate label	3	4	12		Eliminate	Design and print (purple) Colour-coded labels with Predesigned Warnings (BOLD) and Route of Administration. Name and IP/OP No. space provided
	2. Lack of adequate space to affix the label	3	3	9		Eliminate	Print labels or Use Ziplock dispensing envelopes with space for patient name, IP/OP No,

FAILURE MODE First Evaluate failure mode before determining potential causes	POTENTIAL CAUSE	SCORING			DECISION TREE ANALYSIS		
		Severity	Probability	Hazard score	Single point weakness (Y/N)	Action Type (Control, Accept or Eliminate)	Recommendations
6. Incomplete label affixed on the syringe((Name, IP/OP No, Preparation date, Expiry date, Medication name, dose and route of administration)	→	3	4	12		Print label and affix on plastic Ziplock bag/ Purchase infusion minibags or use large volume syringes >20cc	
	1. Lack of clear guidelines on what to affix on the label	3	4	12		Control	Develop clear policy guidelines on what to affix on the label and disseminate to staff in the unit
	2. Lack of adequate space to affix the label	3	3	9		Control	Design colour-coded label, purchase labels printer and print with required items((Name, IP/OP No, Preparation date, Expiry date, Medication name, dose and route of administration)
7. Failure to affix WARNING label (INTRAVENOUS USE ONLY, FATAL IF ADMINISTERED VIA OTHER ROUTES)	→	2	4	8			
	1.Lack of clear guidelines/SOP	2	4	8		Eliminate	Design a clear warning label and affix on the syringe(INTRAVENOUS USE ONLY, FATAL IF ADMINISTERED VIA OTHER ROUTES)
	2.Lack of awareness on what to affix on the label	2	4	8		Control	Sensitize staff on the necessity of affixing warning labels
8. Medication spillage	→	4	2	8			
	1. Lack of adequate working space	4	2	8		Accept	Ensure all areas where production, storage and administration of cytotoxics have spill kits
	2. Production in an inappropriate environment	4	2	8		Control	Centralize production of cytotoxics at the pharmacy to be done exclusively by pharmacy staff
	3. Poor handling of cytotoxics	4	2	8		Control	Sensitize staff on how to handle cytotoxics especially new Senior house officers
9. Failure to adequately confirm vital information before administration (7R's)	→	4	1	4	YES	Enforce training and education to ensure Independent double checks are done by a Nurse or by two Senior house officers before administration at bedside	
	1. Heavy workload	4	1	4	Yes	Accept	Ensure at least 2 staff perform medication administration
10. Vincristine leaks to adjacent tissues(extravasation)	→	4	3	12			Provision of extravasation kits
	1. IV line fixed adjacent to recently used venepuncture	4	3	12		Control	Staff training on prevention of extravasation
	2. Improper administration rate	4	3	12		Control	Ensure administration is by slow IV for at least 2 minutes and flush with 10Ml of Sodium chloride after administration
	3. IV line not fixed properly	4	2	8		Control	Flushing of IV line before administration.
	4.Nonadherance to guidelines	4	2	8		Control	Sensitize staff on the guidelines on prevention of extravasation. Dilute vincristine to 10ml volume for <10 years patients and 20ml for >10 years using Sodium chloride

FAILURE MODE First Evaluate failure mode before determining potential causes	POTENTIAL CAUSE	SCORING			DECISION TREE ANALYSIS		
		Severity	Probability	Hazard score	Single point weakness (Y/N)	Action Type (Control, Accept or Eliminate)	Recommendations
11. Inadvertent intrathecal administration of vincristine	→	4	1	4	YES		
	1.Use of small volume syringes that can be confused for intrathecal route use	4	4	16		Eliminate	Dilute Vincristine with 0.9% Sodium chloride using large volume syringes; for paediatrics less 10 years use 10Ml syringes, more than 10 years 20Ml or 20ml Minibags for paeds and 50Ml minibags for adults
	2.Prescribing vincristine and Intrathecal medication to be administered same day	4	4	16		Eliminate	Prescribe vincristine and other intravenous drugs to be administered on a different day and time from Intrathecal medications. Intravenous medications be administered first
	3.Transportation and storage of Vincristine and Intrathecal medication in the same place	4	3	12		Control	Vincristine and Intrathecal preparations should be packaged separately in colour-coded adequately labelled plastic bags. They should also be stored in separate refrigerators.
	4.Lack of Warning label	3	4	12		Eliminate	Ensure warning label is affixed black coded label.(INTRAVENOUS USE ONLY, FATAL IF ADMINISTERED VIA OTHER ROUTES)
	5.Lack of clear guidelines	3	3	9		Control	All staff designated to prescribe, prepare, dispense, transport and administer vincristine should be adequately trained on how to handle cytotoxics
12.The doctors fails to notice exosmosis has occurred	→	4	2	8		All units should have (Fully Kitted) extravasation kits. Chemotherapy administration be done strictly on weekdays between 8:30 AM and 5:00 PM	
	1. The doctor was in a hurry due to heavy workload thus patient monitoring wasn't done after administration	4	2	8		Accept	Enforce training on the importance of post-administration monitoring and ensure medication administration is done by at least 2 officers
	2. The patient turned around in bed	4	2	8		Accept	Ensure that the patient remains in bed still after administration

CHAPTER FIVE: DISCUSSION

5.1 Conceptual Framework

The Donabedian model for quality improvement was used to determine the contributing factors of vincristine medication errors. The structure is divided into three components which are structure, processes and outcomes. The structure components examined the individual, physical and organizational aspects in which the care is provided. This includes equipments, facilities, personnel, patients and operational processes that support care. The process component is reliant on the structure component for resources and mechanisms of which healthcare workers provide patient care activities in order to improve patient health outcomes (54).

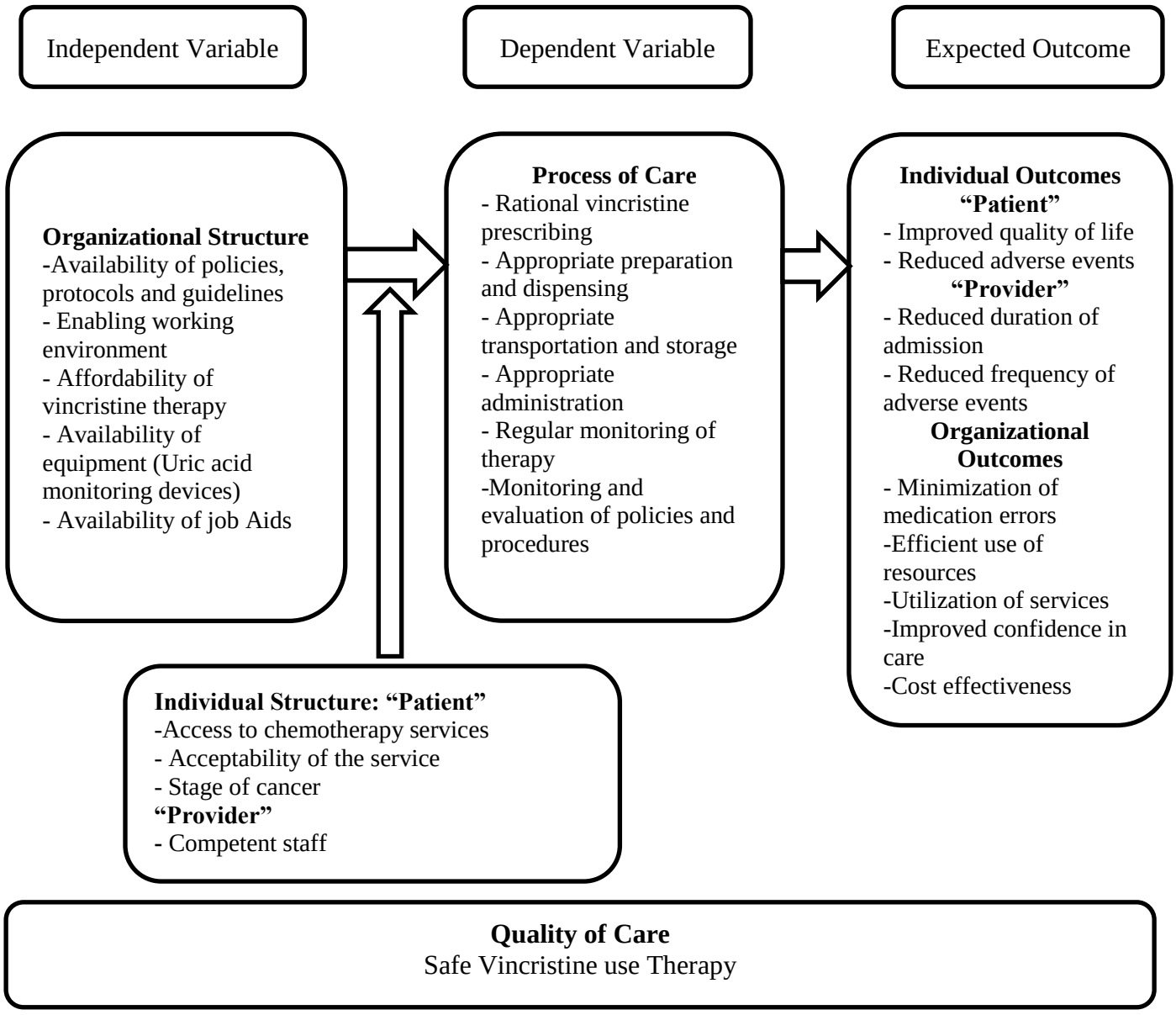


Figure 8: Conceptual Framework adapted from Donabedian Model

5.2 Vincristine use in Kenyatta National Hospital

Vincristine is used in both in-patient and out-patient settings of KNH to manage various paediatric and adults cancers. The out-patient clinics usually serve most of the adult patients and a few paediatrics. Vincristine was found to be commonly used in paediatric in-patient setting than in the out-patient. The overall use of vincristine was 4% and 36% in the out-patient and in-patient respectively. Most of the cancer patients on vincristine-based chemotherapy were aged between 6-12 years. The most common indication of vincristine in this study was management of acute lymphoblastic leukaemia accounting for 25.7% of all cases. This is one of the most common paediatric cancers accounting to 85% of all leukaemias (23,27). Anaemia was the most common co-morbidity in the study population. This could be as a result of bone marrow suppression by chemotherapy drugs and/or general disease progression (27).

Senior house officers generated majority (89.2%) of the chemotherapy prescriptions in the oncology out-patient clinics and the in-patient wards. They are the major prescriber workforce in the hospital as KNH is a teaching and referral hospital for both basic and specialised training. This is also the practice in many hospitals in many parts of the world for instance a study in a France hospital indicated that residents were the main (64.9%) prescribers(55).

5.2 Prevalence of Vincristine medication errors and contributing factors

Almost all patients' medical records reviewed during the study had at least one vincristine medication error. Medication errors are not uncommon with cytotoxic drugs and are potentially fatal (36,56). However data that dwells specifically on the prevalence of vincristine medication errors are scare especially local or regional studies. Comparison with other international studies cannot be easily made as vast setting difference exists. In this study the criterion for assessing and defining medication errors was borrowed from various international patient safety organisations (ISMP, NCC-MERP ACSQHC, JCAHO and NPSA) which are aimed at minimising risks to patient safety. The demerits of these criteria is that it doesn't cater for challenges and organisational routines and culture of a resource-limited setting like KNH thus a high medication error rate was expected. These patient safety organisations are recognised by World health organisation (WHO) for their effort in addressing issues around medication errors (57). Guidelines and tools set by international patient safety organisations can be used to assess levels of patient safety by the virtue of WHO acknowledging these institutions.

In this study we found that 99.6% of patients had been exposed to at least one medication error and 45.4% of these patients had 2 or more errors. This is consistent with other KNH studies by Aywak *et al,* 2015(58) and Nyakiba *et al,* 2012 (59) *(*Un-published works), where 98.5% and 96.7% of the patients

experienced at least one medication error respectively. The prevalence of medication errors in the in-patient population was higher at 100% compared to 87.5% in the out-patient population. The difference in the prevalence could be associated first with the prevalence of use as vincristine is commonly used in the in-patient than the out-patient setting. Secondly, patient workload for cancer patients on vincristine-based regimens is heavier in the in-patient than out-patient setting. Majority (81.7%) of the medication errors identified did not reach the patient thus did not cause harm however, in the event that some of these errors had reached the patients there was a possibility of patient harm. Pharmacists played a big role in intercepting the errors especially dosing errors. Double checks and protocol adherence assessment is done at the pharmacy level.

The hospital being a teaching facility cares of the patients in majorly done by senior house officers on training. Lack of formal induction training of these officers could contribute immensely on the high error rate prevalence. Lack of a standard protocol for cancer management in paediatric and adults' settings with qualifications and competencies of the officers involved in the various processes on patient management could also contribute to the errors observed. Lack of the list of high alert medicines and abbreviations to avoid in chemotherapy was identified as one of the key contributors of the errors as abbreviations contributed to 58.9% of all errors observed which is comparable with Aywak *et al*, 2015 findings where use of abbreviations accounted for 62% of the errors observed(58). Abbreviations are commonly used to make work easier however some abbreviations can be misread or misinterpreted to mean something totally different which can lead to improper use of a drug and possible patient harm or even death. These said documents were under development during the study period and have since been disseminated to all units. Use of abbreviations can also be explained by lack of monitoring of vincristine use process, lack of standard system of handling medication errors and knowledge gap. These errors can be reduced by the use of computerized physician order entry (60).

The 359 medication errors identified in the 241 medical records reviewed during the 15-week study period can be compared to that reported at a hospital in France where 449 medication errors were identified in 6,607 medical records of patients on antineoplastics over a period of 1 year (61). However of the 359 medication errors identified, only 2 errors which reached the patients necessitated intervention and monitoring to preclude harm. One 6 years old patient was prescribed and administered 4 milligrams of vincristine yet the maximum dose of vincristine is 2 milligrams. This necessitated interventions and monitoring of the patient to preclude harm while another patient with osteosarcoma had haemoglobin level of less than 5mg/dl however blood transfusion was not done for more than a

week. In the France hospital study, 436 of the errors identified were intercepted before it reached the patient and 2 of the errors that reached the patients required enhanced monitoring (61).

Prescription errors represented 98.8% of the errors while monitoring errors accounted for 1.2%. In a study in Spain chemotherapy medication errors were reported in 17.2% of the patients attended to with prescription errors accounting for 75.7%, preparation 21%, dispensing 1.8%, administration 1.1% and monitoring 0.4% (39). While in France hospital study, prescription errors represented 91% of the errors followed by preparation and dispensing (8%) and administration (1%) (61). Prescription errors can be associated with lack of a standard protocol for cancer management, heavy workload, use of handwritten medication orders and lack of formal induction training of new prescribers. These errors can also be explained by the practice in the hospital especially in the wards whereby senior house officers are tasked with prescribing, preparation and administration of chemotherapy. This task shifting act makes them complacent to write complete prescriptions as they are expected to follow their own instructions. This contributes to a greater degree of the use of abbreviations, failure to indicate route and frequency of administration. While overdose on chemotherapy drugs can results in permanent damage or fatality to the patient, underdose can also compromise therapy success (55). Although dosing error rate was low (2.2%), overdose with vincristine can result in permanent neurological damage or death (62). Lack of vincristine use protocol, use of out-dated weight and height measures, lack of clear guideline on maximum dosage and lack of formal induction training of new prescribers contribute to perpetuation of this error. Antineoplastic dosing errors were reported in 59.3% of prescriptions in a study in France. These errors were associated with improper calculation of body surface area and lack of maximum dosage of vincristine (55).

The 18.6% medication error rate determined in the study which is comparable with Aywak *et al*, 2015 of 19.2% (58) indicated to weaknesses in the patient safety systems in the management of patients on vincristine-based chemotherapy. Medication error rate of 5% and above denotes that a facility has system deficiencies. Medication errors are caused by a combination of human system factors (43). Evaluation of structural and process components of patient safety system identified inadequacies in the safeguards against vincristine medication errors. Lack of guideline, lack of team that guides implementation of guidelines, heavy workload and knowledge gap have been reported as key contributors of medication errors (4).

Care provided by pharmacists in the hospital for prevention, detection and management of medication errors provide multiple levels of patient protection (28). Pharmacists in KNH are involved in preparation and dispensing of vincristine in the medication use cycle. It was reported that clinical pharmacists are involved in reviewing of patient files regularly in the wards in 3 of the 11 units surveyed and occasionally in the other units. Understaffing is a major hindrance for the clinical pharmacists to participate in ward rounds in all the 11 units. This has been mitigated by ensuring that all patient files are reviewed in the oncology pharmacy before medications are prepared or dispensed. However this has not adequately prevented perpetuation of medication errors due to various institutional cultures and practices.

5.3 Proactive risk assessment of vincristine use process

"Anything that can go wrong will go wrong" ~Murphy's Law (63). The aim of this part of the study was to assess the vincristine use process and determine all possible failure modes and causes then evaluate existing control measures and develop mitigation strategies for high risk failure modes. Twelve high risk failure modes and single point weaknesses without adequate preventive measures were identified by the HFMEA multidisciplinary team. These failure modes are summarised in **Table 11.**

Use of out-dated weight and height measures to calculate patient's body surface area to be used in dose calculation of vincristine was highlighted by the team as a failure mode that can lead to underdose or overdose. This can be attributed to the restrictive nature of the oncology treatment sheet whereby there is no space to affix latest measures. Use of inaccurate body surface area has been noted as one of risk factors to dosing errors (55). The team recommended that the treatment sheet be redesigned to provide space for at least twice monthly charting of weight and height to ensure that current weight, height and BSA is indicated in the medication order (37). Another documentation-related failure mode was the inability to determine the last date of administration using past history on the oncology treatment sheet. This was ascribed to the fact that there is no adequate space on the oncology treatment sheet to indicate the date of administration. Redesigning of the oncology treatment sheet and sensitisation of prescribers to distinguish between scheduled day of treatment and date of administration were recommended.

Dose miscalculations leads to dosing errors (55). This was noted by the team as a salient cause of underdosing and overdosing in KNH. Institution of double-checks in the wards and pharmacy as well as preparation of job aids with formulas and dose limits should be adopted (34,54). Obscure prescriptions or medication orders can lead to misinterpretation of the same. This is usually caused by use of non-

standard abbreviations and handwritten prescriptions(14). The team recommended redesigning of the oncology treatment sheet to provide for adequate space to write all drug details in full, sensitisation of staff on abbreviations to avoid and adoption of CPOE in chemotherapy prescribing. CPOE system has been attributed to reduction in error rate and elimination of illegibility (60).

Mislabelling or lack of labels have been noted as risk factors for medication errors in chemotherapy (64,65). Labels affixed on the medicine bag, vial/box and syringe were found to be inadequate in providing the necessary safeguards. This can be attributed to lack of clear guidelines on the contents of the labels and the necessity of labels. Some adverse drug events have been linked to inadequate labelling(46). The team recommended development of clear guidelines on labelling requirements, procurement of labelling machine and development of colour-coded labels with clear warnings (37). Antineoplastic agents can cause acute and chronic problems on patients and handlers due to their mutagenic, teratogenic and carcinogenic effects (66,67). Medication spillage can happen due to improper handling of cytotoxics and due to accidental failures. This can be precipitated by inadequate working space, preparation in an inappropriate environment for instance procedure rooms in the wards, task shifting between pharmacy staff and senior house officers in preparation and heavy workload. The team recommended centralising preparation in an adequately equipped pharmacy chemotherapy preparation room, formal induction training of new staff on handling of cytotoxics, increasing staffing in the pharmacy department to ensure preparation of cytotoxics is exclusively done by pharmacy staff and provision of spill kits in all places where cytotoxics are used. Centralisation of chemotherapy preparation has been found to reduce preparation errors (66). Failure to adequately confirm vital information before medication administration caused by heavy workload and inadequate staffing predispose patients to harm. Medication administration needs to be done by at least 2 staff and bedside independent double-checks before administration needs to be instituted. Involvement of patients or guardians in verification of medication is also encouraged (68).

Vincristine is a vesicant drug. In case extravasation occurs it can result in tissue injury and necrosis (13). Use of peripheral intravenous line, continuous use of same IV access to administer various drugs and lack of proper drug post-administration monitoring predisposes patients to the risk of extravasation. KNH guidelines recommend dilution of vincristine with Sodium chloride 0.9% to a volume of 20ML before administration (27). This is however not adhered to as vincristine is prepared in 2ML syringes undiluted. It is internationally recommended to use mini-bags to prevent extravasation (69). ISMP considers use of mini-bags as a best practice for hospitals in their 2016-2017 Targeted Medication

Safety best practices for Hospitals (70). Chemotherapy administration should also be done by at least two staff on weekdays within official working hours to ensure proper monitoring and quick remedial actions in case of adverse events.

Inadvertent intrathecal administration of vincristine is a rare event but majorly results in catastrophic consequences (46). Despite various recommendations to prevent this catastrophic event over 120 cases have been reported worldwide with the latest fatality occurring in 2011, however underreporting of this cases is common (65,69). Assessment of preventive measures of this event in KNH was found to be wanting. For instance use of small volume syringes administration of intrathecal and intravenous medications on the same day and lack of warning labels on prepared medications. Most of these predisposing factors are system-related. The team recommended use of mini-bags for vincristine preparation, scheduling different days of intrathecal and intravenous medication administration, adequate labelling of medication and sensitisation of staff on proper cytotoxics handling. A study by Gilbar *et al* 2015 (65), revealed various shortcomings in the implementations of the recommendations to prevent this event and provided a critical role that oncology pharmacists need to play to ensure that the event is deterred.

CHAPTER SIX: CONCLUSION AND RECOMMENDATIONS

6.1 Conclusion

The prevalence of vincristine medication errors was significantly high based on the criteria set by International Patient Safety Organisations. The hospital system for the management and follow up of oncology patients had weaknesses thus fell short of meeting the criteria hence a high degree of medication errors was observed. Despite the fact that majority of the errors observed were less likely to cause harm, some were potentially fatal thus there is need for strategies to prevent, detect and minimise these errors.

6.2 Recommendations

6.2.1 Recommendations for policy and practice

The following recommendations are made to KNH management based on the study finding;

1. Hospital MTC to develop and disseminate protocols on safe use of high risk medications and ensure there is a team that guides and monitors implementation.
2. Director of clinical services should ensure formal induction training of new staff especially senior house officers on the use and handling of cytotoxics as well as proper transitioning during staff turnovers is initiated.
3. The pharmacy department coordinator of continuous professional development should ensure regular continuous medical education sessions are held to update staff on drug doses, medication errors and adverse drug events.
4. Job description of pharmacists must include working in clinical areas, including wards and clinics to help intercept and prevent medication errors.
5. Centralise preparation of cytotoxics in adequately equipped pharmacy and adopt the use of mini-bags in the administration of vincristine.
6. The hospital MTC and paediatric oncology protocol development team should update the paediatric oncology treatment sheet and customise it for use in the adult oncology wards.

6.2.2 Recommendations for future research

1. Larger prospective studies are recommended to determine incidence, predictors and outcomes of antineoplastic medication errors.
2. A clinical audit of deceased cancer patients' records to determine if antineoplastic medication errors could have contributed to the mortality.

3. A similar study to determine the prevalence of vincristine medication errors should be done after implementation of the above said recommendations.

Study Limitations

Due to poor documentation it was not possible to collect some information such as diagnosis from the in-patient non-schedule forms and out-patient cytotoxic summaries. Side effects of vincristine were not assessed in this study. Logistic regression to identify predictors of vincristine medication errors could not be done as almost all medical records reviewed had medication errors. Some respondents may not have given accurate response to the interview-administered questionnaire. HFMEA team members were expected to have biased personal opinions depending on the unit they work, however this was minimised by having a multidisciplinary team.

Study findings dissemination plan

Efforts will be made to disseminate the findings of this study to the relevant authorities in KNH for this research to have an impact. Presentation at the KNH Medicines and Therapeutics Committee (MTC) meeting and pharmacy department continuous professional development sessions avenues will be explored for study findings dissemination.

Opportunities for oral presentations at symposiums and conferences, such as Pharmaceutical Society of Kenya (PSK) annual conference, Hospital Pharmacists Association of Kenya (HOPAK) annual symposium and KNH/UoN conference shall be explored.

Copies of this thesis will be availed to the School of Pharmacy and College of Health Sciences Libraries as well as the Department of Pharmacology and Pharmacognosy for access of students and faculty of the University of Nairobi. A study report will also be made to the Department of Research and Programs of KNH. In addition, study findings will be published in a peer-reviewed journal.

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Appendices:

Appendix A: Screening and Eligibility form (Vincristine use Prevalence)

All subjects enrolled must meet the eligibility criteria detailed in the application approved by the KNH/UoN Ethics and Research Committee.

I. Study Information

Study Title: Assessment of vincristine medication errors and contributing factors in KNH

Principal investigator: Emmanuel Kipkurui Kurgat

Signature……..

Date of Screening…….

II. Patient Information

Patient code…….

Gender: Male ☐ Female ☐ (Tick Appropriately)

III. Eligibility criteria(Tick appropriately)

Inclusion Criteria (Items in 1-3 to be answered **YES** for eligibility)	**Yes**	**No**
1. Oncology patient either male or female		
2. Oncology patient either adult or paediatric		
3. Oncology patient attended to or admitted between 1st January 2016 and 30th June 2016		
Exclusion Criteria (Item in 1 to be answered **NO** for eligibility)	**Yes**	**No**
1. Supportive treatment only prescribed		

Appendix B: Screening and Eligibility form **(Vincristine Medication errors prevalence)**

All subjects enrolled must meet the eligibility criteria detailed in the application approved by the KNH/UoN Ethics and Research Committee.

I. Study Information

Study Title: Assessment of vincristine medication errors and contributing factors in KNH

Principal investigator: Emmanuel Kipkurui Kurgat

Signature……..

Date of Screening…….

II. Patient Information

Patient code…….

Gender: Male ☐ Female ☐ (Tick Appropriately)

III. Eligibility criteria(Tick appropriately)

Inclusion Criteria (Items in 1-3 to be answered **YES** for eligibility)	**Yes**	**No**
1. Oncology patient either male or female		
2. Oncology patient either adult or paediatric		
3. Vincristine prescribed as part of chemotherapy regimen		
Exclusion Criteria (Item in 1 to be answered **NO** for eligibility)	**Yes**	**No**
1. Illegible records		

Appendix C: Data Collection Form (Vincristine Use Prevalence)

Serial number…….. Date of collection……

Code Number of participant……

I. BIODATA

1. **Date of birth:** Day….. Month…….. Year……..Age……
2. **Sex:** Male ☐ Female ☐ (Tick Appropriately)

II. CHEMOTHERAPY HISTORY

1. Date of Admission: Day……. Month…….. Year……..
2. Was chemotherapy prescribed? YES ☐ NO ☐
3. What chemotherapy was prescribed?

Table 1. Summary of prescribed chemotherapy

Medication name, formulation and strength.	Prescribed dose	Route of administration	Frequency of administration	Duration of treatment.

Appendix D: Data Collection Form (Medication Errors Prevalence)

Serial number…….. Date of collection……

Code Number of participant……

I. BIODATA

1. Participant code number……
2. Date of birth: Day….. Month…….. Year……..Age……
3. Sex: Male ☐ Female ☐ (Tick Appropriately)
4. Weight: …….
5. Height: ……..
6. Body surface area (BSA m^2)……..

II. PARTICIPANT MEDICAL RECORD REVIEW

1. In-patient ☐ Out-patient ☐

2a.Diagnosis…….

2b. Stage of diagnosis……..

3. Number of cycles prescribed…….

4. Co-morbidities if any……

5a. Is complete blood count monitoring done? YES ☐ NO ☐

5b. Are the results acted upon appropriately? YES ☐ NO ☐

Table 1: Summary of Complete blood Count Results

Date of Review	Blood Count Done (Y/N)	Was Count Low (Y/N)	Action Taken

Table 2. Summary of prescribed chemotherapy

Date medication prescribed	**Medication name, formulation and strength.**	**Prescribed dose**	**Route of administration**	**Frequency of administration**	**Duration of treatment.**	**Designation of prescriber**

II. CATEGORIZATION OF MEDICATION ERROR(S)

1. Medication error(s) identified if any, give brief description of the error

_____

_____

_____

2. Tick appropriately type of error identified above

Error code	Description of error	Tick if present(√)
1.	Dosing error (dose not indicated, overdose or under-dose)	
2.	Route error (wrong route, failure to indicate route)	
3.	Timing error (wrong frequency, no frequency indicated)	
4.	Omission error (failure to prescribe or administer the drug)	
5.	Documentation error (Ambiguous or illegible prescription)	
6.	Use of abbreviations (use of "IV" instead of " Intravenous", "IT" for intrathecal	
7.	Failure to request monitoring parameter (such complete blood count) or place the request	
8.	Failure to act on available results	

2. Indicate the NCCMERP category for the error identified above_____

Appendix E: NCC-MERP Medication Error Categories

Error category	Definition
A	Circumstances or events that have the capacity to cause error
B	An error occurred, but the error did not reach the patient.
C	An error occurred that reached the patient but did not cause the patient harm.
D	An error occurred that reached the patient and required monitoring to confirm that it resulted in no harm to the patient and/or required intervention to preclude harm.
E	An error occurred that may have contributed to or resulted in temporary harm to the patient and required intervention.
F	An error occurred that may have contributed to or resulted in temporary harm to the patient and required initial or prolonged hospitalization
G	An error occurred that may have contributed to or resulted in the patient's permanent disability
H	An error occurred that required intervention necessary to sustain life
I	An error occurred that may have contributed to or resulted in the patient's death

Appendix F: Informed Consent Form for Healthcare Workers.

APPENDIX 3: INFORMED CONSENT FORM FOR HEALTHCARE WORKERS.

Study Title: Assessment of vincristine medication errors and contributing factors in Kenyatta National Hospital.

Institution: Department of Pharmacology and Pharmacognosy, School of Pharmacy, University of Nairobi. P.O. Box 30197-00400, Nairobi.

Principal Investigator: Dr. Kurgat Emmanuel Kipkurui, P. o. Box 4343-30100, Eldoret. Mobile +254716-304-727.

Supervisors: Prof. Anastasia N. Guantai, Department of Pharmacology and Pharmacognosy, School of Pharmacy, University of Nairobi.

Dr. Irene Weru, Clinical Pharmacist, Pharmacy department, Kenyatta National Hospital.

Dr. David Wata, Clinical Pharmacist, Pharmacy department, Kenyatta National Hospital

Introduction

I am Dr. Kurgat Emmanuel Kipkurui conducting the above stated study to partly fulfill requirements for a Master Degree of Pharmacy in Pharmacoepidemiology and Pharmacovigilance of the University of Nairobi. I would highly appreciate your contribution to this study should you agree to participate.

Ethical Approval: Kenyatta National Hospital/University of Nairobi Ethics and Research Committee, P.O.BOX 20723-00100, Nairobi. Tel 2726300 / 2716450 Ext 44102/44355.

What is the purpose of the study?

The study aims to assess vincristine medication errors and determine their contributing factors among cancer patients in Kenyatta National Hospital. It further intends to develop mitigation strategies for the identified gaps in patient safety.

Why have I been invited to participate?

You have been approached to participate in the study based on your knowledge, experience and expertise in chemotherapy at Oncology unit in KNH.

What is expected of me as a participant?

Should you agree to participate in the study, your expertise will be sought as a member of Healthcare failure Mode Effect Analysis (HFMEA) multidisciplinary team. The team will identify the processes and sub-processes of vincristine use in oncology unit of KNH to develop a detailed process flow

diagram. The flow diagram will be subjected to hazard analysis to determine the different ways that a process or sub-process can fail to provide the anticipated result and the possible outcomes for each failure mode.The multidisciplinary team will thereafter categorize the severity (how serious the outcome of the failure is likely to be) and probability (how often the failure is likely to occur) of each failure mode using severity scale and probability rating table respectively.

HFMEA Hazard Scoring Matrix shall then be used to assign a hazard score to each potential failure mode based on its severity and probability. Any failure mode with hazard score of 8 and above will be subjected to decision tree analysis to determine whether the failure mode warrants further action based on criticality, absence of control measure and detectability. The HFMEA multidisciplinary team finally will recommend mitigation strategies on the failure modes causes that do not have effective control measures in place.

Who will have access to the collected data?

All the information obtained from you will be kept in confidence and at no time will it be released to anyone apart from UoN/KNH Ethics and Research Committee upon request. The information will be coded and entered in a password protected computer only accessible to the principal investigator. Digital recordings will be masked and destroyed within 72 hours after transcription of the information.

Must I participate?

Your participation is completely voluntary. You may withdraw from the study at any time without necessarily giving a reason for your withdrawal.

Are there any benefits for participating?

There are no financial incentives or other direct benefits to you. However, the findings will be very instrumental in improving the quality of care of cancer patients on vincristine-based therapy through detection and prevention of medication errors before they occur.

Are there any risks associated with my participation?

There are no risks anticipated in this study. All information will be handled in confidence.

What do I do in case of a concern?

You are free to contact me, my academic department or the Kenyatta National Hospital/ University of Nairobi Ethics and Research Committee using the contacts provided above.

STATEMENT OF CONSENT

Respondent's statement

I _____ willingly give consent to the investigator to interview me and use the information obtained in his study. Dr. Kurgat Emmanuel has explained to me the nature of the study.

Respondent Signature_____ Date_____

I_____ give consent to the investigator to use digital voice recorder for the purpose of data collection.

Signature_____ Date_____

Investigator statement

I confirm that I have explained the nature and effect of the study. I am adequately convinced that the participant fully understands all aspects of the research as discussed.

Signature_____ Date_____

In case of any concern, you may contact the principal investigator on E-mail: manuhkurui@yahoo.com mobile No.: +254716304727 or KNH-UoN Ethics and Research Committee Secretary: Prof. Mark Chindia Tel +254 207 726300 ext. 44355 or 44102, E-mail uonknh_erc@uonbi.ac.ke

Appendix G: System and Process Factors Audit Tool

Department: Out-patient ☐ In-patient ☐ (Tick one)

Clinic/Unit/Ward:……..

A: Demographic characteristics

Age		
Gender	Male ☐	Female ☐
Cadre	Nurse	
	Pharmaceutical Technologist	
	Pharmacist	
	Medical Officer	
	Registrar	
	Consultant	
Level of Education	Diploma	
	Higher Diploma	
	Degree	
	Postgraduate Diploma	
	Masters	
	Doctorate	

A. Structural Component		**Yes/No**	**Comment**
1	Is there any Chemotherapy use policy, protocol, or guideline that is in this unit? Name …		
2	Is there any policy, protocol, or guideline that is specifically related to Vincristine use in this unit?		
3	(If yes in Q1) Does the policy, protocol or guideline include education and competency requirements for all involved staff?		
4	(If yes to Q1) Is the policy, protocol or guideline readily accessible to staff?		

5	Is there a team that guides implementation of the policy, protocol or guideline?		
6	How often is the protocol updated?		
7	Is there a documented procedure for reporting of medication errors?		
8	Are staff encouraged to report medication errors?		
9	Are chemotherapy medication errors reporting tools available in KNH?		
10	Are there any medicine information resources available to staff?		
11	Is a list of high alert medicines available to staff?		
12	Does KNH promote Vincristine as a High Risk medicine?		
13	Is a list of abbreviations to be avoided in Chemotherapy available and accessible to staff?		
14	Is there a formal process for approving guidelines, prescription order forms and Oncology treatment sheets before use in KNH?		
15	Is there formal induction training for new staff in the unit?		
16	Are there defined responsibilities for pharmacists in the management of patients receiving chemotherapy?		

B. Process component		Yes/No	Comment
1	Is there a defined Oncology treatment sheet for prescribing chemotherapy?		
2	Is there a list of Authorized chemotherapy prescribers with sample signatures?		
3	Are chemotherapy orders authorized by an Oncologist especially for new patients?		
4	Is there any clear process or procedure for communicating with prescriber when questions arise?		
5	Are prescribers contacted to verify medication orders before dispensing or administration?		
6	Do patients/Guardians actively participate in management of their Condition?		
7	Is patient' consent sought before chemotherapy administration?		
8	Are there cases of chemotherapy orders done by telephone?		
9	Is there a procedure for handling verbal orders?		
10	Is there any strategy in place to prevent chemotherapy errors?		
11	Do pharmacists review the medical records of patients on chemotherapy in the unit?		
12	Is Chemotherapy administration done on Weekdays between 8:30AM and 5:30PM?		
13	Is Vincristine therapy monitored for success and adverse drug reactions?		
14	Is Vincristine use process monitored and reviewed regularly?		

Appendix H: HFMEA Outcome Severity Rating Scale

Rating	Outcome Category	Description
4	Catastrophic	Resident experiences death or major permanent loss of function (sensory, motor, physiologic, or intellectual)
3	Major	Resident experiences permanent lessening of bodily function (sensory, motor, physiologic, or intellectual), disfigurement, surgical intervention required, or increased level of care for 3 or more days.
2	Moderate	Resident experiences an event, occurrence, or situation which could harm the resident but will not cause permanent injury or lessening of bodily function or require the delivery of additional healthcare services
1	Minor	Resident may experience a minor injury, but most likely would not be affected by the failure and it would not cause any changes in the delivery of care.

Appendix I: HFMEA Failure Probability Rating Scale

Rating	Description	Definition
4	Frequent: failure is most inevitable	1 failure in 5 attempts
3	Occasional: repeated failures	1 failure in 50 attempts
2	Uncommon: infrequent failures	1 failure in 200 attempts
1	Remote: relatively few failures	1 failure in 5000 attempts

Appendix J: HFMEA Hazard Scoring Matrix

Probability	Severity of effect			
	Catastrophic	**Major**	**Moderate**	**Minor**
Frequent	16	12	8	4
Occasional	12	8	6	3
Uncommon	8	4	4	2
Remote	4	3	2	1

Appendix K: HFMEA Worksheet

FAILURE MODE **First Evaluate failure mode before determining potential causes**	**POTENTIAL CAUSE**	**SCORING**						**DECISION TREE ANALYSIS**		
		Severity	**Probability**	**Hazard score**	**Single point weakness**	**Existing control measure (Y/N)**	**Detectable (Y/N)**	**Proceed (Y/N)**	**Action Type (Control, Accept or Eliminate)**	**Recommendation**
	→									
	1.									
	2.									

Appendix L: Ethical Approval Letter

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

KENYATTA NATIONAL HOSPITAL APPROVED 17 AUG 2016 KNH/UoN-ERC P.O. Box 20723-00202

KNH-UON ERC
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Twitter: @UONKNH_ERC https://twitter.com/UONKNH_ERC

KENYATTA NATIONAL HOSPITAL
P O BOX 20723 Code 00202
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Ref: KNH-ERC/A/317

17th August, 2016

Emmanuel Kipkurui Kurgat
Reg. No.U51/81931/2015
Dept.of Pharmacology and Pharmacognosy
School of Pharmacy
College of Health Sciences
University of Nairobi

Dear Emmanuel

Research Proposal- Assessment of Vincristine medication Errors and Contributing factors in Kenyatta National Hospital (P580/05/2016)

This is to inform you that the KNH- UoN Ethics & Research Committee (KNH- UoN ERC) has reviewed and **approved** your above proposal. The approval period is from 17th August 2016 – 16th August 2017.

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

"Protect to discover"

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

Yours sincerely,

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

c.c. The Principal, College of Health Sciences, UoN
The Deputy Director, CS, KNH
The Assistant Director, Health Information, KNH
The Chair, KNH- UoN ERC
The Dean, School of Pharmacy, UoN
Supervisors: Prof. A.N. Guantai, Dr. Irene Weru, Dr.David Wata

"Protect to discover"

Appendix M: KNH Study Registration Certificate

KNH/R&P/FORM/01

RECEIVED 27 OCT 2016 CHIEF PHARMACIST

KENYATTA NATIONAL HOSPITAL
P.O. Box 20723-00202 Nairobi
Tel.: 2726300/2726450/2726565
Research & Programs: Ext. 44705
Fax: 2725272
Email: knhresearch@gmail.com

Study Registration Certificate

1. Name of the Principal Investigator/Researcher
   EMMANUEL KIPKURUI KURGAT
2. Email address: MANUHKURUI@YAHOO.COM Tel No. 0716-304-727
3. Contact person (if different from PI).....
4. Email address: ..... Tel No. .....
5. Study Title
   ASSESSMENT OF VINCRISTINE MEDICATION ERRORS AND CONTRIBUTING FACTORS IN KENYATTA NATIONAL HOSPITAL
6. Department where the study will be conducted PHARMACY, PAEDIATRICS, MEDICINE AND REPRODUCTIVE HEALTH.
   (Please attach copy of Abstract)
7. Endorsed by Research Coordinator of the Department where the study will be conducted.
   Name: Dr. I. Were Signature ..... Date 31/10/2016
8. Endorsed by Head of Department where study will be conducted.
   Name: Dr. T. B. Menge Signature ..... Date 31.10.2016
9. KNH UoN Ethics Research Committee approved study number P580/08/2016
   (Please attach copy of ERC approval)
10. I EMMANUEL K. KURGAT commit to submit a report of my study findings to the Department where the study will be conducted and to the Department of Research and Programs.
    Signature ..... Date 14/10/2016
11. Study Registration number (Dept/Number/Year) Pharmacy / 18 / 2016
    (To be completed by Research and Programs Department)
12. Research and Program Stamp .....

KENYATTA NATIONAL HOSPITAL H.O.D. RESEARCH & PROGRAMS P.O. Box 20723 NAIROBI

All studies conducted at Kenyatta National Hospital **must** be registered with the Department of Research and Programs and investigators **must commit** to share results with the hospital.

Version 2: August, 2014