

**KNOWLEDGE, ATTITUDE AND PRACTICE OF PHARMACOVIGILANCE AMONG  
HEALTH CARE PROFESSIONALS AT KENYATTA NATIONAL HOSPITAL**

**FATHIYA SAID ALI HAMUMY**

**U51/68973/2013**

**DEPARTMENT OF PHARMACOLOGY AND PHARMACOGNOSY**

**SCHOOL OF PHARMACY, UNIVERSITY OF NAIROBI**

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**DECLARATION OF ORIGINALITY FORM**

**Name of student:** Fathiya Said Ali Hamumy  
**Registration Number:** U51/68973/2013  
**Faculty/School/Institute:** Pharmacy  
**Department:** Pharmacology and Pharmacognosy  
**Course Name:** Master of Pharmacy in Pharmacoepidemiology and Pharmacovigilance  
**Title of the work:** Knowledge, attitude and practice of pharmacovigilance among health care professionals at Kenyatta National Hospital

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U51/68973/2013

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This Thesis has been submitted with our approval as university supervisors.

**1. DR. ERIC M. GUANTAI**

DEPARTMENT OF PHARMACOLOGY AND PHARMACOGNOSY  
SCHOOL OF PHARMACY, UNIVERSITY OF NAIROBI

Signature..... DATE.....

**2. DR. FRANCIS WAFULA**

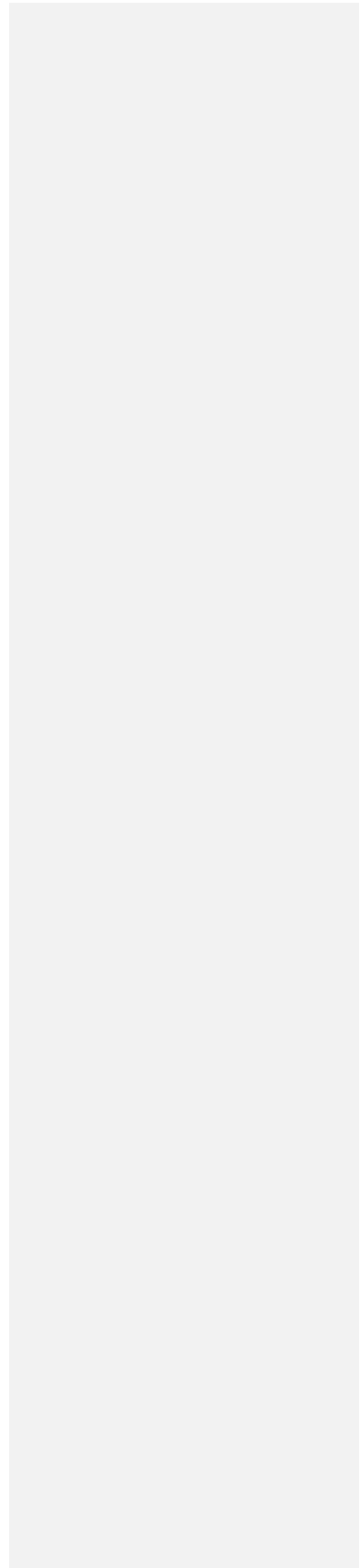
POLICY SPECIALIST,  
WORLD BANK

Signature..... DATE.....

**3. DR. KEFA BOSIRE**

DEPARTMENT OF PHARMACOLOGY AND PHARMACOGNOSY  
SCHOOL OF PHARMACY, UNIVERSITY OF NAIROBI

Signature..... DATE.....



## **DEDICATION**

I dedicate this work to my dear parents for their endless prayers and their belief in me. My lovely husband Ahmed, for being my strong pillar of support and for his constant motivation and to our wonderful children: Abdusalaam, Rayyan, Abdulmun'em and baby Abdulbasit for their patience on the time I have spent away from them.

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**LIST OF ABBREVIATIONS:**

ADR s	adverse drug reactions
CCC	Comprehensive Care Centre
DRPs	Drug related problems
KNH	Kenyatta National Hospital
MRPS	Medication related problems
PPB	Pharmacy and Poisons Board
PV	Pharmacovigilance
W.H.O	World Health Organization

## **ABSTRACT**

### **Introduction:**

Since its inception in 2004, the Pharmacovigilance Department of the Pharmacy and Poisons Board (PPB) in Kenya has been leading efforts to ensure that medicines in circulation are safe to consumers. However, the Department has faced major challenges, among them under-reporting of adverse drug events (ADRs) by healthcare workers and staff shortages, which have severely limited its ability to conduct its duties. It is important that health care workers are aware that reporting ADRs and medication errors can significantly promote patient safety.

### **Aim:**

The study aimed to examine the knowledge, attitudes and practices of healthcare workers on pharmacovigilance at Kenyatta National Hospital, and to identify barriers to effective implementation of pharmacovigilance.

### **Methodology:**

The study was conducted in 2 parts. The first part involved an analysis of adverse drug reactions reports collected at the Kenyatta National Hospital since 2012 to date. All official yellow suspected adverse reaction reporting forms were collected and analysed using Stata version 10. to explore the hospitals' reporting trends and elicit the patterns emerging from them.

The second component involved a qualitative baseline survey of healthcare workers that assessed, in turn, the knowledge, attitude and practice of pharmacovigilance. This entailed conducting structured in-depth interviews with healthcare workers (clinicians, pharmacists and nurses) at Kenyatta National Hospital in Nairobi. Deductive thematic analysis was used to establish, categorize and describe themes and patterns emerging from the qualitative data. Written informed consent was sought from every respondent before the interview. Approval to conduct the study was sought from The University of Nairobi/Kenyatta National Hospital Ethics and Research Committee and The Kenyatta National Hospital.

## **Results**

A total of 27 reports were collected and 48% of all collected reports came from the comprehensive care centre, while 22.3% were from the pharmacy units and the medical wards. Pharmacy personnel submitted the bulk of the adverse reaction reporting forms (85.2%). Forty eight percent of the reported adverse drug reactions were severe in nature, while 35% of the reported reactions affected mainly the skin. Anti retrovirals formed the bulk of the suspected causative agents, while Cotrimoxazole was the most suspected cause of skin reactions. The patient's allergy status ( $P=0.020$ ) and diagnosis ( $p=0.040$ ) were seen to be the major determinants of ADR severity.

The interviews showed that ADRs are a major clinical concern, where healthcare workers testified to encountering ADRs either daily, every one or two admission cycle of patients or once in a while. These ADRs were however, not recorded in the official yellow suspected ADR forms but rather in patient files. Lack of training/awareness of, the tools used and the proper channel of reporting was also observed as a major obstacle of PV implementation among majority of the healthcare workers interviewed.

## **Conclusion**

The study established that adverse drug reactions reporting rates are very low at the Kenyatta National Hospital despite almost 70% of the interviewed healthcare workers acknowledging that ADRs are very common and occur daily. The study found out that only 23.1% of the interviewed healthcare workers (mainly the pharmacists) had been trained on pharmacovigilance and that the larger proportions of healthcare workers were unaware of the pharmacovigilance practices laid out in the hospital and in the country. These findings call for continuous training sessions to be conducted to the healthcare workers so as to integrate pharmacovigilance in their daily practice

## **CHAPTER ONE**

### **1.1: INTRODUCTION**

Drugs may be regarded as dualistic therapeutic tools. On the one hand, drugs cure, prevent, manage or diagnose diseases, but on the other hand improper use of drugs can be the cause of patient morbidity and even mortality (1). Generally, problems related to the use of approved drugs can be summarised using the term drug-related problems (DRPs).

DRPs can be divided into those that result in intrinsic toxicity, and those resulting in extrinsic toxicity. Intrinsic toxicity is caused by the interaction of the pharmaceutical, chemical and/or pharmacological characteristics of the drug itself and the human biosystem. Intrinsic toxicity is therefore synonymous with adverse drug reactions (ADRs). Extrinsic toxicity refers to the problems caused by the handling of the drug either by the healthcare professional or by the patient and this is synonymous to a medication error. Medication errors do not necessarily need to result in harm to the patient. In contrast, ADRs always involve some form of harm (1).

A study undertaken in 2 large hospitals in England by Pirmohamed et al (2004) indicated that the burden of ADRs on the national hospital systems (NHS) is high, and is an important cause of hospital admissions accounting for 1 in 16 hospital admissions and 4% of the hospital bed capacity. Over 2% of patients admitted with an ADR died, further underlining the considerable morbidity, mortality and extra costs associated with ADRs (2, 4).

Most ADRs were predictable from the known pharmacology of the drugs and many represented known interactions and are therefore likely to be preventable. This implies that although many of the implicated drugs have proven benefit, measures need to be put in place to reduce the burden of ADRs and thereby further improve the benefit: harm ratio of the drugs. The study also noted that older drugs continue to be most common implication of such admissions, a finding that was consistent with other studies done earlier(2)

Particular attention therefore needs to be paid to the detection and prevention of ADRs, and ideally this need should be met through pharmacovigilance efforts. The World Health Organization (WHO) defines pharmacovigilance as the science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other possible

drug-related problems (3). It involves the monitoring of the use of conventional medications, herbal preparations, traditional and complementary medicines, blood products and other biologicals, medical devices and vaccines (4) . The concept of pharmacovigilance dates back to 1961, when infants were born with phocomelia after their mothers were exposed to thalidomide, a drug that was marketed as an anti-emetic. This event triggered the creation of systems to monitor medication safety (3).

The exposure of large populations to increasing volumes of medicines, including novel chemical entities used for symptomatic relief and lifestyle modification, as well as the widespread use of medicines in developing countries to curb the prevalence of pandemic diseases such as HIV/AIDS, malaria and tuberculosis further underlined the need for a better and more efficient pharmacovigilance (5).

One of the cornerstones of pharmacovigilance activities is Spontaneous Reporting Systems. These involve the active participation of reporters in the detection and reporting of medication errors and ADRs. In practice, spontaneous reporting is invariably voluntary and presumably based on altruistic motives. Spontaneous reporting is by far the best method of generating signals on new or rare adverse drug reactions (ADRs). Under-reporting is a major drawback of this system (6).

Originally, physicians were the only professionals invited to report their observations and judgment of whether a medicine had caused a certain ADR. It was argued that accepting ADR reports from physicians only would ensure high quality information and minimize the reporting of unrelated, random associations. Studies have shown, however, that different categories of health professionals will observe different kinds of drug related problems, and their reports contribute significantly to successful pharmacovigilance (7). Only by inviting reports from all professionals involved in the care of patients will it be possible to detect the full spectrum of complications related to pharmacotherapy. If, for example, only general practitioners contribute to the pool of information, medicines used primarily by specialists will not be covered (8).

Furthermore, to get a representative picture of the reality, all sectors of the healthcare system need to be involved, such as public and private hospitals, general practitioners, nursing homes, retail dispensaries, and clinics for traditional medicine. Wherever medicines are being used there should be a readiness to observe and report unwanted and unexpected medical events.

Whether or not reporting by patients ultimately adds value is not yet clear but there seems to be general agreement that such reports should be followed-up via the clinician (4). Thus co-operation from clinicians is essential. In Kenya, systems aimed at involving patients in ADR reporting are yet to be implemented.

Pharmacovigilance seeks to improve patient care and safety in relation to the use of medicines and all medical and paramedical interventions, improve public health and safety in relation to the use of medicines, and to contribute to the assessment of benefit, harm effectiveness and risk of medicines. To this end, efforts have been made to promote understanding, education and clinical training in pharmacovigilance and its effective communication to the community (9). This can only be successful through collaboration between various organizations, such as hospitals, regulatory authorities, pharmaceutical industries, national pharmacovigilance centres, and poison control centres.

In Kenya, the National Pharmacovigilance Centre and training institutions are playing an important role in rolling out pharmacovigilance activities through training of healthcare professionals, provision of reporting tools and introduction of online reporting systems. The University of Nairobi has recently included pharmacovigilance as a dedicated discipline in the postgraduate studies offered by the School of Pharmacy. This has given a significant boost to the implementation strategies of pharmacovigilance in Kenya. However, while having taken quite a number of steps to develop pharmacovigilance, Kenya still faces a number of challenges, among them being low number of reports coming from healthcare institutions as well as inadequate reporting tools.



## **CHAPTER TWO: LITERATURE REVIEW**

### **2.1 PHARMACOVIGILANCE: HISTORY AND DEVELOPMENT**

Pharmacovigilance is the science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other possible drug-related problems (3).

The first systematic international efforts to address drug safety issues started in 1961 after the thalidomide disaster. In 1963, the Sixteenth World Health Assembly adopted a resolution (WHA 16.36) (1) that reaffirmed the need for early action in regard to rapid dissemination of information on adverse drug reactions. Later in 1968, A Pilot Research Project for International Drug Monitoring was created by W.H.O so as to develop an international system for detecting previously unknown or poorly understood adverse effects of medicines (4).

A WHO Technical Report followed based on a consultation meeting held in 1971 (2). The 1971 WHO consultation resolved to advocate establishment of national centres for drug monitoring, to provide guidelines, and to identify the contribution that national centres might make to the international system. Membership of the WHO Programme for International Drug Monitoring which currently has over 65 member countries is coordinated by the WHO Collaborating Centre for International Drug Monitoring, known as the Uppsala Monitoring Centre (UMC).

It was noted that data collection from health practitioners, systematic monitoring of populations, review of health statistics and of drug utilization data, and effective analysis of input data would be necessary for the objectives of pharmacovigilance to be achieved.

From these emerged the practice and science of pharmacovigilance.

International health organizations as well as member states were to contribute to this international pharmacovigilance initiative. According to Article 2 of its constitution, the WHO has a clear mandate to develop, establish, and promote international standards with respect to food, biological, pharmaceutical and similar products. Similarly, the World Health Assembly made a provision in Article 21 of their constitution to adopt regulations concerning standards with respect to the safety, purity and potency of biological, pharmaceutical and similar products moving in international commerce (4). On the other hand, member states would formulate systems for the collection and evaluation of individual case drug safety reports. These reports would later be collected in a central database which would serve the important function of

contributing to the work of national drug regulatory authorities, improve the safety profile of medicines, and help avoid future disasters (3).

## **2.2: SCOPE AND CURRENT PRACTICE OF PHARMACOVIGILANCE**

### **2.2.1 Detection and Reporting of Adverse Drug Reactions**

Pharmacovigilance has been about detecting new Adverse Drug Reactions (ADRs) and, if necessary, taking regulatory actions needed to protect public health. For example, by changing the summary of product characteristics (SPCs) or withdrawing the drug from the market.

An ADR is defined by WHO as any noxious, unintended, and undesired effect of drug that occurs as a result of treatment with a drug at the normal doses used in man for diagnosis, prophylaxis, and treatment (WHO, 1972). ADRs are also described as “an appreciably harmful or unpleasant reaction resulting from an intervention related to the use of a medicinal product, which predicts hazard from future administration and warrants prevention or specific treatment, or alteration of the dosage regimen, or withdrawal of the product (10).

On the other hand, terminologies like “adverse reaction” and “adverse effect” are used in describing adverse drug reactions or side effects and are sometimes used interchangeably. More precisely, an adverse effect (AE) is seen from the point of view of the drug, whereas an adverse reaction is seen from the point of view of the patient. These two terms however, (adverse effect and adverse reaction) must be distinguished from “adverse event”. An adverse effect is an adverse outcome that can be attributed to some action of a drug; an adverse event is an adverse outcome that occurs while a patient is taking a drug, but is not or not necessarily attributable to it (10).

Rohilla and Yadav (11) classify ADRs into six groups in their review of ADRS as shown in Table 1:

**Table 1:** Classification of ADRs

Class	Description	Examples
<b>Type A (Augmented)</b>	ADRs are related to the pharmacological properties of the medicine. Dose related.  The ADR are attributed to genetic variations e.g. hepatic and glomerular disorders	Nephrotoxicity caused by aminoglycosides Anticholinergic effects of tricyclic antidepressants
<b>Type B (Bizarre)</b>	Adverse reactions unforeseen and unpredictable ADRs have less or No relationship with the dosage.	Penicillin induced urticaria.
<b>Type C (Chronic)</b>	The cumulative toxic effects of a drug used over time. Chronic in nature and include the adaptive changes and the withdrawal effects. (dose related and time-related)	Hyperadrenocorticism in chronic corticosteroid use
<b>Type D (Delayed)</b>	Reactions that appear after sometime of the treatment. time-related	secondary cancers caused by use of Alkylating agents e.g. cyclophosphamide
<b>Type E (End of use)</b>	ADRs occurring on sudden termination of treatment	Convulsions as a result of stopping anticonvulsants
<b>Failure of therapy (Failure)</b>		

### 2.2.2 Current scope and practice

Since the thalidomide disaster in 1961 that gave rise to the concept of pharmacovigilance, the field has undergone several steps and has moved from just detecting signals of drug safety to concerns of illegal medicines sale, potentially unsafe donation practices, manufacture and sale of counterfeit and substandard medicines and increasing use traditional medicines outside the

confines of traditional use. All these as a result of high rise in cross border communications, free trade, and internet use that increase access to medicines and information about them (4).

Many other issues that are of relevance to pharmacovigilance include:

- Medication errors
- Lack of efficacy reports
- Use of medicines for indications that are not approved and for which there is inadequate scientific basis
- Case reports of acute and chronic poisoning
- Assessment of drug-related mortality
- Abuse and misuse of medicines
- Adverse interactions of medicines with chemicals, other medicines, and food

Pharmacovigilance is still a rapidly developing field, and faces a number of systemic challenges. For example, little emphasis is currently placed on generating information that can assist a healthcare professional or a patient in the decision-making process of whether or not to use a drug. Gathering and communicating of this information should be an important goal of pharmacovigilance, i.e. being less focused on finding harm and more focused on extending knowledge of safety (12).

Pharmacovigilance methods must also be able to describe which patients are at risk of developing an ADR and what the course of the ADR could be i.e. pharmacogenetics and pharmacogenomics. One approach to achieving this would be to involve patient more as a source of information; this approach will ensure consistency in the system (13).

The WHO Programme for International Drug Monitoring suggests that a successful comprehensive international pharmacovigilance strategy needs to identify and implement feasible systems, governance, infrastructure, human resource, training and capacity building, sustainable methodologies and innovations in pharmacovigilance. A key component of such a strategy would be the dissemination of medicines safety information to policy makers and regulators and knowledge sharing with healthcare professionals through high quality informatics and learning tools, with rational use of medicines and patient safety as the ultimate goal of pharmacovigilance (14). In recent years, regulatory agencies have been reforming their systems

in order to keep pace with the developments in pharmacovigilance, with the focus on being more pro-active (13).

Pharmacovigilance centres are vital in preventing medication errors including informing health-care professionals about the importance of reporting such errors and creating a culture of patient safety. The centres can collaborate with poison control centers to prevent medication errors. Such collaboration allows improved detection and improved preventive strategies. In addition, collaboration with regulatory authorities is important in finalizing decisions. Such collaborations will help avoid duplication of workload (15).

### **2.3: IMPORTANCE OF PHARMACOVIGILANCE**

Pharmacovigilance and all drug safety issues are relevant for everyone whose life is touched in any way by medical intervention.(4)

During medicines development i.e. clinical trials, medicines are strictly observed for their safety and effectiveness. Most of these medicines are tested for short-term safety and efficacy on a limited number of carefully selected individuals. In some cases as few as 500 subjects, and rarely more than 5000, will have received the product prior to its release. However, once marketed, the products are consumed by the large numbers of the general population. It is therefore, crucial that new and evolving treatments are monitored for their effectiveness and safety under real-life conditions. This is because the characteristics of the clinical trial participants do not always wholly represent the characteristics of the population in which it will later be used; consequently, it may be difficult to extrapolate the results obtained from clinical trials to the population at large(16). This is especially true for the elderly, for women or for people belonging to a minority ethnic group (17).

In order to study rare ADRs, ADRs with a long latency and ADRs in specific populations, careful monitoring of the drug in the post-marketing phase is essential. Experience has shown that many adverse effects, interactions (i.e. with foods or other medicines) and risk factors come to light only during the years after the release of a medicine.(13)

The primary method of collecting post-marketing information on the safety of drugs is through Spontaneous Reporting Systems (SRS), a key component of pharmacovigilance. The main function of SRS is the early detection of signals of new, rare and serious ADRs. Reporting of

ADRs enables physicians' pharmacists and patients to report suspected ADRs. This in turn informs stakeholders such as national regulatory centres and policy makers of the potential risk when signals of new ADRs arise. Improving the number of reports and access to the data facilitates a timely evaluation of aggregates of ADR reports, which are often the first signals of a potential problem. A well-known challenge in the spontaneous reporting system is the underreporting of ADRs (18).

A study conducted by Babigumira et al, has outlined that PV systems have the potential to improve health outcomes and to reduce healthcare expenditures related to drug safety by identifying and reducing medication related problems. The study adds that a fully developed tool to assess economic value could assist policy makers and donors in evaluating investments required to increase the capacity of national programs to improve the use, safety, quality, cost effectiveness, and affordability of medicines in low and middle income countries (LMICs) (19).

From an economical perspective, a country's lack of a functional PV system leads to greater costs in terms of the resources used to manage and prevent medication related problems (MRPs), bad health outcomes in terms of medicines-related morbidity and mortality as well as reduction of medicine-related quality-of life (QOL). Comparing these impacts in terms of the opportunity cost of the resources used and the adverse health impacts is important in assessing the potential value of starting or strengthening national PV centers.

The costs of managing different drug AEs and other MRPs include: (1) cost of out-patient (OP) visits, (2) cost of hospitalization, and (3) cost of MRP-related regimen switches including new drugs and consultations. Costs of OP visits and hospitalization for MRPs include direct medical costs (such as healthcare workers time, other medications or antidotes, and laboratory tests), direct non-medical costs (such as patient transportation and upkeep), and indirect costs (which include the opportunity cost of lost productivity during MRP-related illness and convalescence). The above cost minimization studies can assist policy makers and shareholders make informed decisions as involved patient care and pharmacovigilance activities.

A framework has been proposed for the assessment of the economic value of PV programs (19).

## **2.4: IMPACT OF PHARMACOVIGILANCE**

PV plays a vital role in ensuring that prescribers, together with the patient, have enough information to make an educated decision when it comes to choosing a drug for treatment.

The safety of a drug needs to be followed during its whole life cycle. This life-cycle approach includes identifying safety signals, designing studies to confirm them, evaluating benefits as well as risks, using risk–benefit assessments to integrate study results and communicating key findings to patients and physicians (24, 26). This approach to pharmacovigilance has resulted in major decisions about the safety of drugs, including the withdrawal of already approved drugs from the market.

In June 2007 a meta-analysis published, linked the use of rosiglitazone to an increased risk of myocardial infarction and death from cardiovascular causes (20). These results, initiated a new debate on the safety of the drug, it was later concluded that the benefits of rosiglitazone outweigh its risks within the framework of its approved indications (21). However, constant revision/updating of product information and a continued monitoring of this ADR are necessary.

A more recent safety concern is the association between aprotinin and increased mortality. In 2006, a study based on observational data was published by Mangano et al. in which the authors questioned the safety of aprotinin (22). On November 21, 2007, aprotinin was withdrawn from the market in the European Union based on data from the BART clinical trial showing increased mortality for patients receiving aprotinin.

The importance of spontaneous reporting systems cannot be overemphasized in pharmacovigilance practices as a major source of signal detection. Additionally active surveillance and the role of clinical trials play a vital role as methods of collecting ADR data.

Table 2 shows some examples of recent major drug safety issues and the evidence that led to their discovery.

**Table 2:** Drug safety concerns that have arisen in Europe since 1995

Drug	Safety concern	Key evidence	Regulatory action
<b>Trovofloxacin</b>	Hepatotoxicity	Spontaneous ADRs	Withdrawn
<b>Tolcapone</b>	Hepatotoxicity	Spontaneous ADRs	Suspended
<b>Cisapride</b>	QT prolongation; cardiac arrhythmias	Spontaneous ADRs	Patient registration licences subsequently cancelled
<b>Bupropion</b>	Seizures; drug interaction	Spontaneous ADRs	Posology change, Warnings
<b>Cerivastatin</b>	Rhabdomyolysis	Spontaneous ADRs	Withdrawn
<b>Hormone replace therapy</b>	CVS risk; cancer long term	Epidemiological studies	Warnings and restriction of indication
<b>SSRIs</b>	Suicidal behaviour in children	Clinical trials	Warnings accompanied by clinical guidance
<b>COX IIs</b>	CVS risk	Clinical trials	Warnings and clinical guidance
<b>Topical macrolides immunosuppressants</b>	Risk of cancer	Spontaneous reports	Restriction of use, Risk management plan

*SSRI, selective serotonin reuptake inhibitors, CVS, cardiovascular safety; ADR, adverse drug reaction*

Reproduced from J.M Raine (2007): Pharmacovigilance; risk management—a European regulatory view (22)

A pilot project was initiated by the World Alliance for Patient Safety in collaboration with the Uppsala Monitoring Centre, with the Moroccan Pharmacovigilance Centre as project coordinator. The aim of the project was to develop an extended role for national centres of pharmacovigilance, to include the collection of information on the incidence of adverse events related to medication errors, to enable international analysis of these data, and to disseminate the findings (15).



The results (summarized in Table 3) showed the role of pharmacovigilance centres through detecting, identifying, analyzing, and classifying medication errors and carrying out root cause analysis served as important tools in prevention of medication errors. Their duties also included informing health-care professionals about the importance of reporting such errors and creating a culture of patient safety.

**Table 3 :** Examples of actions taken after detection of medication errors by the Moroccan Pharmacovigilance Centre during 2002–2005

Product	Type of error	Details	Action
<b>BCG vaccine</b>	Route of administration and dose	Intramuscular instead of intradermal administration; 10 times the recommended dose given, because BCG vaccine contains 10 doses in one bottle	Letter to physicians
<b>Methyl-ergometrine</b>	Wrong patient	Drug prescribed for the mother but given to the neonate because of the use of one prescription sheet for the mother and the neonate	Letter from the Ministry of Health to all gynecologists and all maternity hospitals in the country
<b>Corticosteroid</b>	Wrong indication	Drug given for weight gain	Letter to the pharmacist
<b>Cypro-heptadine</b>	Wrong indication	Drug given as an appetite stimulant	Letter to the pharmacist
<b>Dontomycin</b>	Erroneous publicity	Described as an analgesic instead of an antibiotic	Letter to the manufacturer
<b>Rinomycin</b>	Lack of specific warning	No warning for people with hypertension due to phenylephrine	Modification of the SPC
<b>Indomethacin calcium pentahydrate</b>	Erroneous publicity	Described as a coxib instead of an NSAID	Letter to the manufacturer
<b>Flucloxacillin Injection</b>	Wrong dilution	Lack of information on dilution in the SPC; sterile water for injection not included in the drug package	Modification of the SPC

*BCG: bacille Calmette–Guérin; NSAID: nonsteroidal anti-inflammatory drug; SPC: Summary of Product Characteristics; Bencheikh et al. 2009 (15)*

## **2.5: BARRIERS TO PHARMACOVIGILANCE**

Several studies conducted around the world have identified reasons why it is challenging to implement pharmacovigilance. A recent systematic review conducted by Abubakar et al, related outcomes of different studies that identified gaps in pharmacovigilance. They found that there was poor knowledge of ADR reporting by doctors even though some were aware of pharmacovigilance. Lack of awareness of reporting procedures and difficulty of filling forms were also seen by many as obstacles. The study also found that doctors had little knowledge on ADR reporting centres and that many doctors did not know exactly what to report given that majority of ADRS seen were well known (23).

Elsewhere, doctors reported that they did not receive adequate training to report ADRs. In a survey done in Nigeria, 89.6% of the doctors who responded said they need training on ADR reporting (24). Majority of doctors also felt reporting ADRs was a professional obligation and that awareness needed to be raised to change the mindsets of the reporters.

A study done by Biriell and Edwards identified closer contact between them and the pharmacovigilance centre and the feedback of pharmacovigilance activities as ways of improving spontaneous reporting by hospital doctors (6). Another study also reported similar findings (25).

It is worth noting however, findings of this study cannot be generalized to all doctors majorly because many countries have not been represented in the review role of healthcare workers.

## **2.6: PHARMACOVIGILANCE IN KENYA**

In Kenya, the Department Of Pharmacovigilance which is housed at the Pharmacy and Poisons Board (PPB) was set up in the late 2004 with a vision of developing, implementing and continuously upgrading an appropriate system for detecting, reporting and monitoring adverse drug reactions (ADRs) and other relevant problems with medicines in Kenya. The department also carries out routine post market surveillance on all medicines in Kenya. (26)

The department has been actively involved in designing tools and guidelines for detection and reporting of ADRs. In December 2007, the Guidelines for the National Pharmacovigilance System were developed followed by sensitization of healthcare workers through a national

sensitization workshop in Nairobi and through *ad hoc* meetings. They have recorded over 10,000 trained healthcare workers. Several other tools were also developed concurrently including the form for reporting poor quality medicinal products, suspected ADR reporting form and ADR Alert Card, which are currently in use. The department reports recording over 8,000 ADRS in their database and 4000 poor quality medicines reports. It has also advanced to incorporate online reporting of ADRS, and is currently working on consumer reporting.

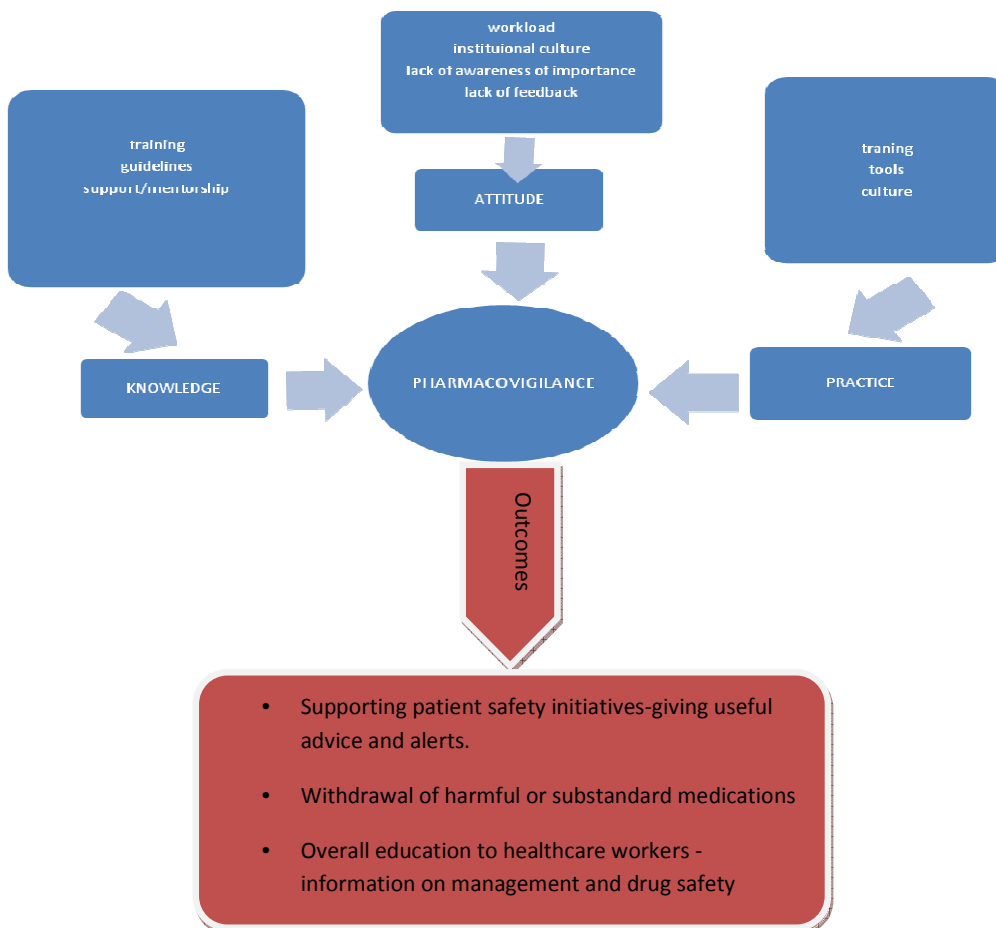
Antiretroviral therapy (ART) has greatly improved the survival of People infected with the HIV-virus. However, ART is associated with immediate and long-term adverse events. With increased access comes a greater need to monitor and promote the safety and effectiveness of these essential medicines (5). In Kenya the rise in vertical programmes and their focus on patient safety has enabled the set up of the pharmacovigilance system and this was used as an entry point into and training of identification and reporting of ADRs i.e. The HIV/AIDS programme. Today majority of the ADR reports collected come from those programmes.

In Kenya, reports from the PPB reveals some of the challenges faced are: inadequate funding seen as a major drawback to many of the pharmacovigilance activities and Post Marketing Surveillance activities, underreporting of cases of ADRs, sustaining the reporting culture, problems with developing and implementing Medication Error Reporting System and major issues with the culture of self medication (without considering possibility of ADR). Additionally, problems of herbal medicine/over the counter prescriptions (OCPs) have also been cited - users rarely report that they are on these types of medications.

There are also plans of develop Medicines Information Centres to promote consumer reporting for suspected ADRs and Poor Quality Medicines.

## 2.7: CONCEPTUAL FRAMEWORK

The outcomes of PV can be realized by addressing 3 main aspects: knowledge (training and giving constant information to practitioners), attitude (addressing culture and attitude change), and practice (availing tools and mentorship), as illustrated below.



## **2.8: PROBLEM STATEMENT**

Medicines are like double edged swords, they can alleviate disease but also have potential of causing harm no matter how skillfully they are used. Other than the active ingredients, excipients such as coloring agents, lubricants, preservatives, etc. have a potential for producing adverse or unwanted effects. ADRs may be unexpected, unknown and/or rare. They are in some cases life-threatening, and can be major determinants of treatment outcomes.

This therefore necessitates continuous monitoring of known and unknown ADRs, emphasizing the need for pharmacovigilance. Proper monitoring of ADRs requires an effective and efficient pharmacovigilance system to guarantee the safety of medicines at all times.

In Kenya, like many other countries in Africa, pharmacovigilance activities are being faced with a number of challenges such as underreporting of cases of ADRs, sustaining the reporting culture, problems with developing and implementing Medication Error Reporting Systems, amongst others.

Ignoring the importance of documenting and reporting ADRs by healthcare workers leads to recurrence of preventable drug-related morbidity and mortality. As noted in previous studies, most ADRs causing hospital admissions are due to commonly used medications and are mainly preventable (27).

## **2.9: JUSTIFICATION OF STUDY**

Knowledge Attitude and Practice (KAP) studies on pharmacovigilance have been done around the world but none has been done in Kenya. This study aimed to establish quantitatively the extent of practice of ADRs reporting in KNH as well as assess qualitatively, information on the knowledge, attitudes and practices of hospital healthcare professionals on pharmacovigilance activities.

This is mainly because the success of pharmacovigilance activities is heavily reliant on the participation of healthcare workers as they perform their daily duties of diagnosis, prescribing, dispensing, and administration of medication and monitoring of patients. Their opinions and attitudes on the barriers they encounter with the spontaneous reporting of ADRs and their

suggestions of ways to solve them are very important to gain insights on what can be done to improve the existing structures and systems of pharmacovigilance.

### **2.10: STUDY HYPOTHESIS**

There exists a lack of knowledge, indifferent attitude and inadequate practice of pharmacovigilance among healthcare workers in Kenya.

### **2.11: OBJECTIVES**

#### **Main Objective**

The study aimed to examine the knowledge, attitudes and practices of healthcare workers on pharmacovigilance at Kenyatta National Hospital, and to identify barriers to effective implementation of pharmacovigilance.

#### **Specific objectives**

1. To determine the scope and extent of pharmacovigilance activities at KNH through the examination of the sources, contents and trends of ADR reports generated at KNH.
2. To identify gaps in the knowledge of healthcare workers regarding the importance, requirements, tools and processes of pharmacovigilance in Kenya.
3. To determine the factors that influence the opinions and practices of healthcare workers at KNH regarding pharmacovigilance

### **2.12: SIGNIFICANCE OF THE STUDY**

Information from this study will assist in identifying shortcomings and refining the pharmacovigilance practices in the hospital with a view to fully integrating them into the day to day activities of healthcare workers involved in drug use in the hospitals.

This will in turn prevent or reduce harm to patients and thus improve public health by assisting healthcare workers make informed decision with regards to medication use in clinical practice.

The ultimate beneficiaries of an improved pharmacovigilance system are the patients, as knowledge of drug safety issues can improve the manner in which healthcare workers manage patients.

## **CHAPTER THREE: METHODOLOGY**

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### **3.1 STUDY DESIGN**

This was a cross sectional study with two components. The first component was a quantitative arm that analyzed all ADR reports collected at the KNH since 2012 to date, exploring reporting trends and describing characteristics of the pharmacovigilance aspects. The second arm was the qualitative component which involved in-depth interviews with nurses, doctors and pharmacists to assess their knowledge, attitude and practice. The study was carried out between May and September 2015 at Kenyatta National Hospital.

### **3.2 STUDY SITE**

This study was conducted at the Kenyatta National hospital (KNH) in Nairobi. Kenyatta National Hospital is the oldest hospital in Kenya. It is also the largest National Referral and Teaching Hospital in East Africa with a bed capacity of 1800. KNH serves as a teaching hospital for the University of Nairobi and the Kenya Medical Training College. The hospital services are provided across its 50 wards, 22 outpatient clinics, an Accident and Emergency Centre, and 24 theatres of which 16 are specialized. It covers an area of 45.7 hectares and within the KNH complex are College of Health Sciences (University of Nairobi); the Kenya Medical Training College; Kenya Medical Research Institute and National Laboratory Service (Ministry of Health).

This hospital was selected because, as the largest public hospital in Kenya, it provides an excellent entry point to the assessment of pharmacovigilance in the public sector hospitals in Kenya, and will give a generalized idea of pharmacovigilance practices in government hospitals in Kenya.

### **3.3 STUDY POPULATION**

In the quantitative arm, all available pharmacovigilance (ADR) reports filled at KNH were considered for analysis.

The qualitative aspect of the study covered in depth interviews of healthcare workers. These included physicians, nurses and pharmacists who were currently offering services at the medical wards of the hospital in the study period (May – September 2015). These cadres of healthcare

workers are directly involved in the use of pharmaceutical products in the management of patients, and are therefore expected to be aware of, and contribute actively to, pharmacovigilance activities.

### **3.4 ELIGIBILITY CRITERIA**

#### **3.4.1 Eligibility criteria for quantitative component**

All available ADR reports from all the departments within KNH were considered eligible.

#### **3.4.2 Eligibility criteria for qualitative component**

##### **a) Inclusion Criteria for qualitative component**

All physicians, nurses and pharmacists; who were working at the medical wards at KNH, during the study period and who consented to be interviewed.

##### **b) Exclusion criteria for qualitative component**

Healthcare workers who did not consent to be interviewed.

### **3.5 SAMPLE SIZE DETERMINATION AND SAMPLING TECHNIQUES**

#### **3.5.1 Quantitative component**

Universal sampling was applied, whereby all available official yellow suspected ADR reporting forms filled at the Kenyatta National Hospital were collected from all the pharmacy units and the medical wards. In 2009 pharmacovigilance activities were initiated in Kenya and KNH staffs were beneficiaries of the training. It is assumed therefore that healthcare workers are practicing pharmacovigilance and using the appropriate tools for recording of ADRs.

#### **3.5.2 Qualitative component**

The sample was drawn from three cadres of healthcare workers working in the medical wards and pharmacy. The study participants were from the medical ward because of the wide range of diseases managed in these wards - the range of diseases covered in medical wards is higher than any other ward, including both infectious and non-communicable diseases. Furthermore, the range of drugs used to manage diseases in the medical wards is very broad, a consequence of the



wide variety of diseases and conditions being managed in these wards. Also, severe ADRs requiring admission are likely to be in medical wards.

Convenient and purposive sampling methods were applied, whereby the heads of the various healthcare cadres in the medical wards were approached and asked to participate in the interview and/or also designate members of their teams whom they thought could take part in the interview. This allowed recruitment of participants who were readily available to give information of the pharmacovigilance practices in the hospitals. A total of 26 healthcare workers from the hospital were conveniently sampled in this way. These 26 healthcare workers consisted of 11 clinicians, 8 pharmacists and 7 nurses from six wards and four pharmacy outlets. Preliminary analysis of the data was carried out on the initial sample, and no further recruitment of participants was done as theme saturation was observed to have been achieved, i.e. no new information was being generated from continued interviews from the healthcare workers. The process of thematic analysis is described in Section 3.9.

**Assumption:** that the knowledge, attitudes and practices of each cadre of healthcare workers (physicians, pharmacists and nurses) is uniform throughout the institution, and does not vary within and between departments/wards or specializations, and therefore the findings from the healthcare workers in the medical wards and pharmacies will be representative of those in other departments/wards within the institution.

## **3.6 RESEARCH INSTRUMENTS**

### **3.6.1 Quantitative data**

A data collection tool was devised using Microsoft Excel (2010) to input the details of the data extracted from the yellow suspected adverse drug reaction reporting forms collected from the institution. A copy of each of the data collection tool is attached (Appendix C).

### **3.6.2 Qualitative data**

An Interview Guide (Appendix A) was used for collecting the qualitative data from the identified healthcare workers. The Interview Guide was initially pretested on 5 health professionals and refined accordingly.

## **3.7 DATA COLLECTION TECHNIQUE**

### **3.7.1 Quantitative**

All pharmacy units and six medical wards were visited. The head of each pharmacy unit/medical ward was approached and asked to retrieve any suspected ADR yellow form that they or their members of staff had ever filled. Details such as baseline characteristics of those affected by ADRs, source of reports, suspected drugs causing ADRs, common affected organs and severity and outcomes of ADRs were extracted from each report and recorded on Microsoft Excel (2010) data collection form (Appendix C).

### **3.7.2 Qualitative**

The heads of the various healthcare cadres in the medical wards and pharmacy units were approached and asked to participate in the interview and also designate members of their teams whom they thought had some time to take part in the interview. An informed consent was then sought from the designated participants. The purpose of the interview as well as the methods that were to be used in recording the information sought were explained clearly, and the participants who consented did so by signing the Informed Consent Form (Appendix B). The healthcare workers who could not take part immediately were then requested to select an interview date time and venue that will be convenient to them.

The interview was recorded by digital audio recording and supplemented manually by pen and paper. The Interview Guide (Appendix A) was moderated and recorded by the principal investigator. Each interview on average lasted about 30- 40 minutes. The responses were transcribed verbatim within 48 hours into Microsoft Word (2010) Document.

## **3.8 DATA MANAGEMENT AND QUALITY ASSURANCE**

All data from the in depth interviews was transcribed into MS Word (2010) documents. Data was entered and cross checked by the investigator to ensure accuracy and completeness. Interviews were transcribed within 48 hours of the interview so as to capture all verbal interactions during

the interview and to avoid loss of information. The hand written notes were compared to the transcribed version and any supplementary information was incorporated.

The names of the interviewees were kept confidential by the investigator. Hard and soft copies of data were stored under lock and key by investigator.

All data from the ADR reports and the in depth Interviews from Microsoft word was later entered into Microsoft Excel 2010 worksheets. Data cleaning and validation was performed and the data exported into STATA version 10.0. Backing up of files to compact discs and flash sticks was done regularly to avoid loss. Confidentiality of the data was ensured by storing all data in password controlled files and directories, which were only accessible to the principal investigator.

### **3.9 DATA ANALYSIS**

Data from the reports was analysed using Stata version 10.0. Descriptive statistics were generated and determinants of ADR severity were explored using Fischer's exact statistic against all variables.

Deductive thematic analysis was used to structure analysis of the interviews manually. The major themes were generated from the subsections of the interview guide. The major ideas emerging from the participants' responses to the interview questions were then aligned along the themes that were established which depicted each participant's context and perspective. Themes emerging from the interviews were generated in this way until theoretical saturation was achieved. This process involved identifying patterns in the data: recurring ideas, perspectives and descriptions. This was done for each professional group. The final analysis for this study focused on the development of connections, comparison and narratives around the key emergent themes from each professional group.

### **3.10 ETHICAL CONSIDERATIONS**

Ethical approval was granted by Kenyatta National Hospital/University of Nairobi, Ethics Review Committee (KNH/UoN-ERC) reference number – KNH-ERC/A/268. Institutional approval was also sought from The Kenyatta National Hospital reference number – KNH/SAD-MED/42B/VOL.1/88.

Informed consent was sought from all the key informants from whom qualitative data was collected after adequate explanation of the study requirements. The participants were informed that they were free to withdraw from the study at any stage of the interviews. An informed consent form was used for this purpose (Appendix B).

There were no direct benefits to the participants. However, the findings will be communicated to the healthcare workers and information will assist in establishment and development of pharmacovigilance activities in the hospitals.

The names of the respondents were concealed and confidentiality of information upheld. Electronic records were password protected, while digital recordings were destroyed after transcribing and verification of the data was done.

### **3.11 DISSEMINATION PLAN**

Final copies of the finished dissertation book will be submitted to the medical library of the University of Nairobi, the Department of Pharmacology and Pharmacognosy for accessibility to other students and university staff, the Kenyatta National Hospital and the Pharmacy and Poisons Board for implementation. A manuscript will be prepared and published in a peer reviewed, open access biomedical journal, ensuring that the study findings can be accessed worldwide through internet.

## **CHAPTER 4: RESULTS AND DISCUSSION**

The results of the 27 analysed reports (the quantitative component) and the 26 healthcare workers interviews (the qualitative component) are presented and discussed in this chapter.

### **4.1: ANALYSIS OF ADVERSE DRUG REACTION REPORTS**

Twenty seven yellow suspected ADR reporting forms were collected and analysed for their basic characteristics (age, gender, allergy status and diagnosis), source of reports and type of reactions commonly seen, suspected ADR causative agents and type of organ system commonly affected by adverse drug reactions, the severity of reactions seen in the institution and the impact or outcomes of the drug reactions.

#### **4.1.1: Baseline Characteristics**

A total of 27 ADR reports were collected since 2012, and the reporting rate has been seen to increase over the four years with a sharp decrease in reporting noted in 2014. Of those reports 25.9% were adults as opposed to children (22.2%). More than 50% of the reports had the age of patients unfilled. Reports from female patients were more (59.3%) compared to male patients (37%). Only one report had the sex unspecified.

The characteristics of the reports are summarized in Table 4 below.

Table 4: Baseline characteristics of the analysed reports

<b>PARTICULARS</b>	<b>NUMBERS (n)</b>	<b>PERCENTAGE (%)</b>
<b>DATE</b>		
<b>2012</b>	4	14.8%
<b>2013</b>	6	22.2%
<b>2014</b>	2	7.4%
<b>2015</b>	14	51.9%
<b>unspecified</b>	1	3.7%
<b>AGE</b>		
<b>Adult</b>	7	25.9%
<b>Children</b>	6	22.2%
<b>unspecified</b>	14	51.8%
<b>SEX</b>		
<b>female</b>	16	59.3%
<b>male</b>	10	37.0%
<b>unspecified</b>	1	3.7%
<b>ALLERGY</b>		
<b>not allergic</b>	16	59.3%
<b>allergic</b>	3	11.1%
<b>unspecified</b>	8	29.6%

### Discussion

The results of this study showed that most (59.3%) of the reported ADRs occurred in women. This could suggest that women are more prone to report ADRs than men, which would concur with previous studies (28). This could also be attributed to the health seeking behaviors of women enabling their ADR concerns to be captured. However, the fact that the study sample size was very low and that all ADRs occurring at KNH were not reported, means that these results cannot conclusively show that indeed women suffer from ADRs more than the men.

However, it is worth noting that other studies done show that women are more prone to ADRs than men. An example is the study done by David Amacher in the USA which indicated that a

number of prospective, multicenter studies have confirmed a higher risk of ADRs in general among female subjects compared to a male cohort (29,30).

#### 4.1.2: Sources of the reports

Almost half the reports (48.2%) come from the Comprehensive Care Centre (CCC) clinic; the inpatients reports were at 22.3% while the source could not be established for 18.5% of the reports. Pharmacy personnel submitted more ADR reports (85.2%) than any other cadre of healthcare workers. Nurses and doctors on the other hand were at 3.7% reporting rate each. These findings are summarized in Table 5 below.

Table 5 : Sources of reports

SOURCE OF REPORT	NO OF REPORTS (N)	PERCENTAGE (%)
<b>MEDICAL WARD/CLINIC</b>		
Wards	8	22.3%
MOPC	3	11.1%
CCC	13	48.2%
Unspecified	5	18.5%
<b>REPORTER</b>		
Nurses	1	3.7%
Medical doctors	1	3.7%
Pharmacy personnel	23	85.2%
Unspecified	2	7.4%

#### Discussion

This study showed that fewer reports were received from the wards. This is contrary to the expectation that ADRs would be more commonly and easily identified in the inpatient clinical areas, where majority of the acute cases of ADRs come to the attention of the caregivers. This indicates that healthcare workers in the wards are probably unaware of the systems in place for reporting ADRs or are not equipped with the appropriate tools for recording these events.

The largest proportion of reports (48.2%) came from the CCC. This is most likely because the staff has been trained on pharmacovigilance and they therefore follow the official procedures of reporting of suspected adverse drug reactions. The nature of the CCC clinic is such that the patients are followed up regularly and chances of identifying or reporting an ADR are higher than in any other clinic or ward. In addition to that the nature of the diseases treated at the CCC exposes one to consumption of many drugs increasing the chances of drug–drug interactions and adverse drug reactions (29,31,5).

The analysis also indicates that 85.2% of the reports were filled and submitted by pharmacy personnel (pharmacists 48.1%, pharmaceutical technologists 37%). This could be due to the fact that majority of the pharmaceutical personnel have been trained on pharmacovigilance as opposed to their counterparts. This is consistent with the interviews done where 7 out of the 8 pharmacists had been trained on PV. This therefore affirms that training and awareness are indeed strong factors affecting reporting of ADRs.

#### **4.1.3: Classes of drugs recorded**

ARVs were present in 55.6% of the ADR reports; this is majorly because about 48.2% of the reports come from the CCC clinic. Antibiotics on the other hand were present in 69.3% of all the reports. This is most likely because most of the reports that reported ARVs use, had at least one antibiotic along with it. Some of the CCC reports had a combination of ARVs together with 2 antibiotics (mainly Cotrimoxazole and Anti-TBs). CVS drugs were present in 37% of all the reports.

The recorded drugs are summarized in Table 6.



Table 6: Number of ADR reported per drug class

THERAPEUTIC CLASS	SPECIFIC DRUGS	NO.OF CASES REPORTED
<b>ARVS</b>	Zidovudine/lamivudine/efavirenz	3(11.1%)
	Zidovudine/lamivudine/nevirapine	1 (3.7%)
	Abacavir/ lamivudine/nevirapine	2(11.1%)
	Abacavir/lamivudine/efavirenz	1 (3.7%)
	Tenofovir/lamivudine/efavirenz	6 (22.2%)
	Tenofovir /lamivudine/nevirapine	1 (3.7%)
	Zidovudine/lamivudine/lopinavir	1 (3.7%)
	Unspecified	2 (7.4%)
<b>CVS DRUGS</b>	Amlodipine	2 (7.4%)
	Nifedipine	1 (3.7%)
	Amlodipine/hydrallazine	1 (3.7%)
	Losartan	3 (11.1%)
	Atenolol	2(7.7%)
	Dopamine	1(3.9%)
	Unspecified	1 (3.7%)
<b>ANTIBIOTICS</b>	Ceftriaxone	1 (3.7%)
	Amoxycillin &Ceftriaxone	1 (3.7%)
	Isoniazid	2 (7.4%)
	Cotrimoxazole	8 (29.6%)
	Cotrimoxazole & Anti-TBs	5(18.5%)
	Gentamycin & Benzyl penicillin	1(3.7%)
	Unspecified	1 (3.7%)
<b>OTHER DRUGS</b>	Pyridoxine	6 (22.2%)
	Quinine	1 (3.7%)
	Magnesium Sulphate	1 (3.7%)
	Atorvastatin	2 (7.4%)
	Salbutamol inhaler	1 (3.7%)
	Combination- Ranitidine,Phenytoin,Tramadol	2 (7.4%)
	Unspecified	2 (3.7%)

NOTE: some reports had an overlap of 2 or more therapeutics classes.

## Discussion

This analysis showed that antibiotics are the most reported class among the drug classes. This compares to other studies done in different parts of the world (30, 31,35) ARVs on the other hand have been shown in many different studies to be highly associated with various ADRs. This is primarily due to the number of drugs each patient takes, the low immunity status of the patients coupled with the overriding co morbidities (32, 31). In Kenya and many other countries in the world, the close follow up of patients taking ARVs and the knowledge healthcare workers have on the reporting coupled with active probing of ADR manifestation in patients with HIV, has helped the realization of these figures. It has also been proven that patients with chronic illnesses are more prone to ADRs by virtue of their illnesses and that fact that they are on many drugs (5,31,35).

### 4.1.4: Number of ADR reactions per report

Most (63%) of the reports had only one recorded ADR. The reports had a minimum of one reaction to a maximum of 6 reactions per report recorded (Figure 1).

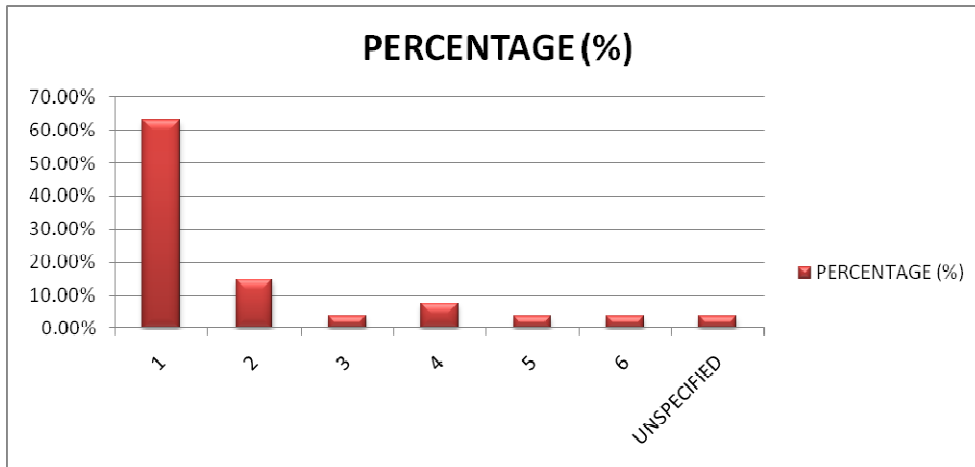


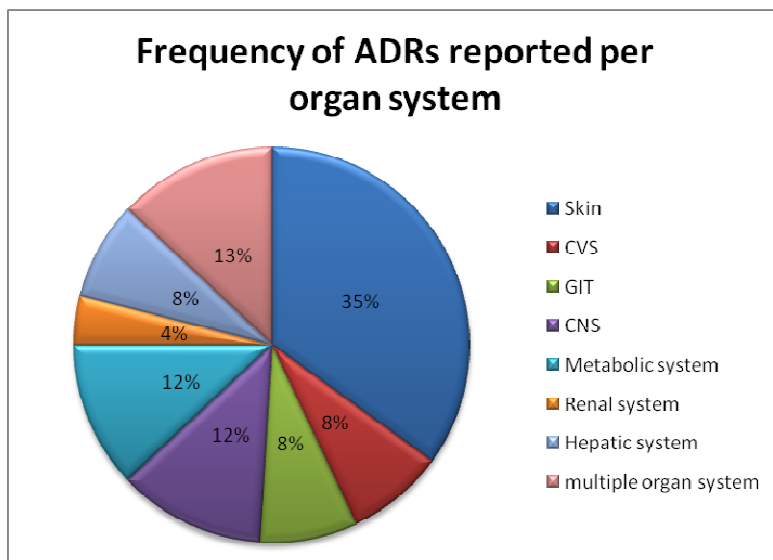
Figure 1 : Number of ADRs reactions per report

## **Discussion**

The study showed that a patient can experience one or more ADRs from the drugs they are taking at a given time. This depends on how many drugs they are taking, disease status and perhaps the mechanism of action of any particular drug. This therefore means that any drug taken can affect one or multiple systems. For example a patient can take Cotrimoxazole and get a rash that constitutes one reaction from one drug. Another patient on the other hand can take Cotrimoxazole and suffer from nausea, pruritis and even interstitial nephritis constituting three types of reactions from one drug. An example of such cases can be seen in many studies where more than one ADR can be reported by patients for one or many drugs taken (37, 38).

### **4.1.5: Adverse drug reactions reported and organ systems affected**

The study has shown that drugs affect all organs in the body with the skin being the most affected organ at 35% of the reports, followed by CNS (12%) and metabolic reactions at (12%). The hepatic, GIT and CVS systems constituted 8% of the reported cases each. Only 4% of the reported cases had renal involvement. A total of 13% of the reports had multiple organ involvement for example: manifestations of the skin (SJS), CVS (palpitations) and CNS (confusion). These findings are summarized in Figure 2.



**Figure 2:** Organ systems affected by adverse drug reactions

**Discussion:**

Several studies done around the world indicate that the skin is the most affected organ in the body (32, 33, 35 ). Some of these literature reports have argued that this is because skin reactions are the most likely ADRs to pick because of their obvious manifestation. The current study concurs with the mentioned studies as skin was mostly affected at 35%. The CNS system, metabolic system and the GIT have also appeared in the same studies as common ADR target systems with vomiting just like in this study cited as the most common GIT occurrence(33).

**4.1.6: Adverse drug reactions reported and drugs implicated**

The drugs implicated in the reported ADRs are analyzed in Table 7 below. From the analysis, Cotrimoxazole, Nevirapine, Phenytoin and Isoniazid seem to be the notorious suspected causative agents of most skin reactions. CNS reactions seem however, to be caused by a broad array of drug classes as shown in the table above. Interestingly noted that drugs used for treatment of cardiovascular reactions are the same ones that cause cardiovascular ADRs an example is Losartan and Amlodipine reported to have caused palpitations and accelerated heartbeats. GIT ADRs on the other hand are caused by a variety of drugs. ARVs in this analysis seem to have affected the metabolic, renal and hepatic system with Zidovudine and Stavudine being the suspected causative agent of Lipodystrophy.

**Table 7 :** Specific types of ADRs and drugs implicated

SYSTEM	TYPE OF ADR	NO OF CASES REPORTED	SUSPECTED CAUSATIVE AGENT
<b>SKIN</b>	TENS	3 (%)	Cotrimoxazole/Phenytoin/nevirapine
	SJS	3	Cotrimoxazole/Isoniazid/Nevirapine/Abacavir
	rashes	4	Cotrimoxazole/Isoniazid
	Extravasations at injection site	1	Phenytoin
<b>CNS</b>	psychosis/aggressive behaviour/suicidal attempts	2	Efavirenz
	Severe headaches	1	Losartan/Amlodipine
	Restlessness and confusion	1	Magnesium sulphate
	Cortical blindness and bilateral paralysis	1	Quinine
	dizziness	1	Losartan/Amlodipine
	<b>CVS</b>	palpitation	2
leg swelling	1	Amlodipine	
shortness of breath	2	Abacavir/Cotrimoxazole, Nevirapine	
accelerated heartbeat	1	Losartan Amlodipine	
<b>GIT</b>	Vomiting	2	Lopinavir/ritonavir /Magnesium Sulphate
	Stomach cramps	1	Amlodipine
	Impaired swallowing	1	Cotrimoxazole /nevirapine
<b>METABOLIC REACTIONS</b>	Lypodystrophy	3	Zidovudine/Stavudine
	<b>OTHER SYSTEMS</b>		
	liver	2	Isoniazid/Nevirapine
	Renal	1	Tenofovir
	<b>MULTIPLE ORGANS INVOLVEMENT</b>		

NOTE: some reports had more than one reaction reported.

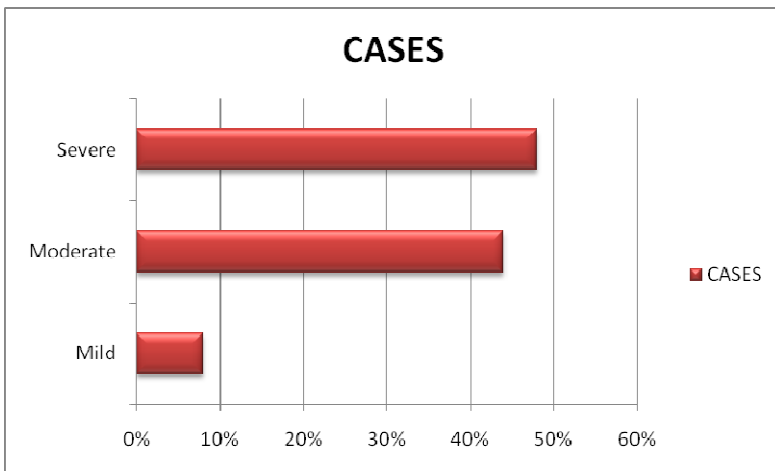
**Discussion:**

The analysis of implicated causative agents seems to be consistent with findings from various previous studies. Classic examples are those of skin reactions attributed to use of antibiotics like the Sulphonamide class (Cotrimoxazole) and ARVs (nevirapine) (34) .

The ARVs have equally been widely studied and this study concurs with others that relate the causes of the ADRs such as rashes to the use of nevirapine, Lypodystrophy to the use of Stavudine and CNS disorders associated with efavirenz use (32, 36,38). GIT and metabolic reactions are implicated in many ADRs studied in literature as well (31, 33).

**4.1.7: Severity of the reported ADRs**

About half (48%) of the reports submitted rated the ADRs as severe in nature, another 44% were moderate reactions while a small proportion (8% ) of the reports recorded mild reactions (Figure 3).



**Figure 3 :** Severity of reported ADRs

## **Discussion**

The analysis could mean that healthcare workers record mainly moderate and severe reactions that come to their attention which is consistent with the interviews carried out that indicated some healthcare workers felt only severe or new or certain ADRs should be recorded as opposed to recording all ADRs. The reactions that don't seem to have caused much harm may go unreported. This concurs with a study done in Spain by Alvarez et al (1998) who stated in his findings that "Under-reporting seems to be positively selective, as it involves mainly the less severe and better-known effects, preserving the value of spontaneous reporting for signal detection"(28).

### **4.1.8: Determinants of the severity of reactions**

Statistical analysis using Fischer's exact test was performed to establish the determinants of severity of reaction. Analysis of the basic patient characteristics done revealed that a patient's allergy status ( $p=0.020$ ) and diagnosis ( $p=0.040$ ) were the major determinants of ADR severity. The results showed that patients with no allergies to drugs have a higher likelihood of severe reactions to drugs as opposed to those with known allergies (Table 8).

The results also indicated that children were more prone to severe ADRs as opposed to the adults, although the results were not statistically significant ( $p=0.242$ ). The adults were seen to experience more moderate reactions. Severity of reactions however, did not vary with the sex of the patient, source of report or even the number of reactions the patient had.

Particular organ systems, number of medications taken per patient and the drug classes recorded in the reports were not significantly associated with severity of reactions.

**Table 8:** Determinants of the severity of reactions

	VARIABLE	P-VALUES
<b>BASIC CHARACTERISTICS</b>	Age	0.242
	Sex	0.588
	Ward	0.556
	Allergy status	<b>0.020</b>
	Diagnosis	<b>0.04</b>
	No of reactions	0.666
<b>ORGAN SYSTEM</b>	Skin	0.281
	CNS	0.70
	CVS	0.073
	GIT	0.443
	Metabolic reactions	1.000
<b>MEDICATION USED</b>	No. of drugs used	0.506
	ARVS	0.585
	Antibiotics	0.930
	CVS drugs	
	GIT drugs	0.520
	Other drugs	0.304

**Discussion:**

This study associates diagnosis and allergy status to severity of ADR, possibly because healthcare workers are keener when administering medication to patients with known allergies as opposed to patients without allergies and therefore would not exercise precaution when dealing with non-allergic patients. For example, to encourage patients to report any suspected itchiness or unusual rashes. This consequently may leads to patients ignoring such symptoms and experiencing severe reactions later in the course of drug consumption.

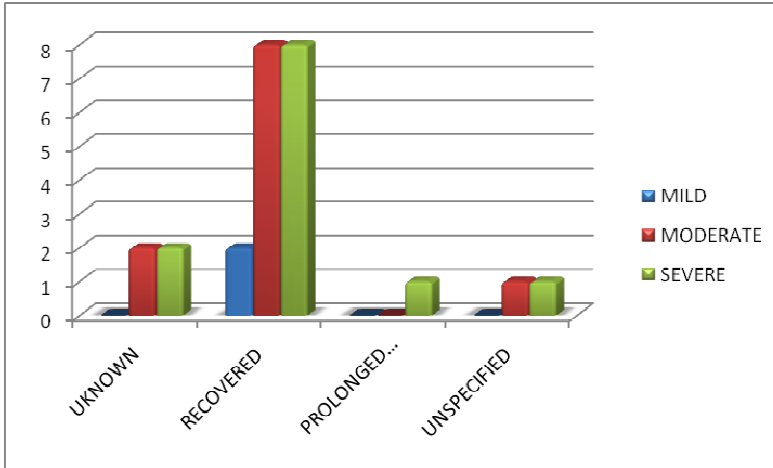


Several studies of analysis of ADRs have indicated that children experience mild, moderate or severe reactions in different proportions. However, a study done by Morales (20000), indicated that ADRs are not common in children but explained that evidence is missing because of lack of clinical trials on children and reliance on epidemiological studies (40) . The sample size in this study limits it from concluding that children suffer severe ADRs more frequently than adults but such an observation might be explained by the fact that doses used in children are usually not precise and this could therefore put them at greater risks to ADRs than the adults. Additionally, children have their organs less developed putting them at greater risk of harm due to medication errors and ADRs.

Our study shows no gender associations to severity of ADRs. Furthermore this study did not show strong associations between severity of disease with any particular organ system as well as medications the patient was put on, possibly because of the small sample size of the reports collected. These therefore are not determinants of ADR severity in this study.

#### **4.1.9: Effect of severity of the ADRs on the treatment outcomes**

64% of the ADRs recorded recovered from the reaction, 4% required prolonged hospitalization, and 12% did not recover from the ADR. One out of the twelve severe cases of the ADRs reported did not recover upon treatment (Figure 4). The analysis therefore indicate that the association between severity of the ADRs on the outcome of treatment of the ADR recorded not statistically significant ( $P=1.000$ ).



**Figure 4:** Effect of severity of the ADRs on the treatment outcome

### Discussion

Severity of ADR did not appear to be a determinant of treatment outcome. This could mean that if the patient receives medical attention and the offending drug is withdrawn from use, the recovery chances are high. This lays a strong argument that medication errors and ADRs have reduced mortality and morbidity if they are reported and receive medical attention. However it is of importance to note also that the more severe an ADR the higher the costs incurred in its management as has been looked at by Pandit et al in a study conducted to assess severity and cost associated with ADRs(40)

## **4.2: QUALITATIVE RESULTS**

Twenty six healthcare workers from 6 different medical wards participated in the interviews. Among them; 8 pharmacists (the pharmacist in charge of Kenyatta National Hospital and 7 other pharmacists working in different pharmacy units, 11 doctors (7 resident doctors and 4 interns) and 7 nurses participated. The findings of the interviews are divided into three major domains: knowledge, attitude and practice.

### **4.2.1: Knowledge of pharmacovigilance:**

#### **Knowledge of concept of pharmacovigilance**

Almost all the healthcare workers seemed to be aware of the pharmacovigilance concept although most of the interviewees had not heard of the term “pharmacovigilance”. All the interviewees could explain what ADRs and medication errors are and were able to give a few details including some examples of ADRS they have encountered in their fields of practice.

#### **Challenges in identification of ADR**

Almost all the healthcare workers shared similar concerns as far as challenges faced in identification of adverse reactions were concerned. However, almost all interviewees claimed that obvious ADRs such as sedation caused by Chlorphemiramine, rashes caused by Cotrimoxazole and even vomiting associated with tramadol use, among many examples were fairly easy to identify. There were others that were challenging and harder to even relate to any particular medication a patient is taking. These challenges were classified as patient factors, system factors or nature of the ADRs factors (Table 9).

**Table 9:** Challenges in identification of ADRs

Patient factors	Nature of the ADR	System factors
ADRs become difficult to identify if patients take OTC self-medications	The more the drugs prescribed the more challenging it is to know which drug has offended the system (polypharmacy)	Inaccessible records for proper follow up,
Failure of patients to disclose e.g. spells of dizziness. Mild cases don't turn up for reporting and are dismissed as normal occurrences.	Skin reactions sometimes indistinguishable from skin diseases.	Challenging to identify if healthcare worker does not work in clinical areas e.g. the pharmacy.
Unknown medication history	Distinguishable if ADR is immediate and much harder if the ADR is delayed.	Some drugs are given in combination e.g. Anti TBs and is therefore difficult to pick out the single molecule that might have caused the ADR.

**Awareness of the National Pharmacovigilance centre**

Slightly more than half of the interviewed healthcare workers had not heard of the National Pharmacovigilance centre at the Pharmacy and Poisons Board, majority of these being nurses and medical doctors. All except one of the pharmacists knew of the National Pharmacovigilance centre and their role in the health sector.

**Awareness of Pharmacovigilance tools**

Almost a half of the healthcare workers interviewed did not know that there are tools available to record ADRs and very few had heard that there are forms to record ADRs. A few have heard of the forms but have never seen them or used them before. Of all the interviewed healthcare

workers mainly pharmacists and one of the doctors have seen and used the forms (tools). Two of the doctors said they have come across alert cards in their practice.

### **Knowledge of ADRs to be reported**

Some of the interviewed healthcare workers believed only new and / severe ADRs should be recorded, while very few of them felt only ADRs that one is certain about should be recorded. However, the majority of those interviewed felt that all ADRs should be reported.

.....”*I think all the ADRs should be reported, because all ADRs are important...*”

Interviewee (19)

### **Training on Pharmacovigilance**

All the pharmacists except 2 have received either national or institutional training on pharmacovigilance. A very small number of all healthcare workers interviewed have been trained while the majorities have not received any form of pharmacovigilance training.

All the interviewed pharmacists knew the channel of reporting the ADRs. Many of the interviewees also thought sending regular reminders would strengthen the practice.

Availing tools and educating the healthcare workers on the use was also viewed as a good start to encourage reporting of ADRs.

One of the doctors stated that...” *presence of tools is a reminder by itself to ADR reporting .ADR forms should be attached to patient file or to the t-sheets*”. Interviewee (06)

Incorporating ADR reporting into the day to day practice, making it part of the job description was seen as a good option to encourage reporting by 2 of the interviewees. Others suggested that it should be made an agenda in departmental meetings to discuss pharmacovigilance practices.

“*..Make reporting of ADRs part of job description*” Interviewee (04)

#### **4.2.2: Attitude towards Pharmacovigilance:**

##### **Responsibility of recoding ADRs,**

When asked on who should be responsible for recording ADRs, of healthcare workers many believed recording of ADRs is every healthcare workers responsibility, however, a small number of the interviewees thought the responsibility should be with nurses and doctors because they are in direct contact with patients and would be the first to recognize the presence of a reaction. One of the nurses said she thinks the responsibility of recording should be with everyone including the patients.

*“ I think ADRs can be recorded by any healthcare worker as long as they are the ones who saw it, even the patients themselves should be able to record ADRs...”*interviewee (24)

##### **Importance of a Pharmacovigilance centre**

All the interviewees except one thought it was extremely important to start a PV centre within the KNH, primarily because ADRs are not pleasant and should be prevented, to reduce mortalities and morbidities, to improve quality of care and most importantly to save lives.

One interviewee felt having a PV centre would really help in decision making.

*“...having a PV centre would really help in decision making”*. Interviewee (01)

Along with that, others thought it was needful for responsible, official and organized collection of data, facilitation of faster responses and reporting of more adrs reports and eventually better management of ADRs and prevention.

One of the pharmacists said that establishing a PV centre will create a culture of reporting in the institution.

*“.....I believe establishing a PV centre will create a culture of reporting”*. Interviewee (04)

Two of the interviewees suggested that the PV centre can serve as a call in centre that eventually encourages more healthcare workers to report cases.

Some doctors thought a PV centre will inform of new ADRS and help in management of complicated ones and also give information on better use of appropriate drugs.

One of the interviewees believed that having a system is sufficient to handle the pharmacovigilance practices and did not see the need for a PV centre.

#### **4.2.3: Practice of pharmacovigilance**

Majority of the healthcare workers could not quantify accurately how often they came across ADRs, however, many of them mentioned they come across ADRs daily in their practices depending on where one was working. For example healthcare workers working at the oncology unit would come across ADRs daily because chemotherapeutic agents are associated with a lot of ADRs. On the contrary Pharmacists working in outpatient departments would see ADRs less frequently as they said most patients just pick their medication and go.

*“Here at pharmacy 40 I come across ADRs once in a while “interviewee (01)*

A few of the interviewee said they see ADRs at least one case every admission or every 2 admissions in a week.

#### **How to prevent ADRs**

A practice to prevent ADRs. Half of interviewees said that they gave pre-medication to anticipated ADRs to patients, .e.g. laxatives when giving opiates, anti emetics when giving tramadol, hydration when using Amphotericin B. Two of the doctors thought using drugs only when needed would help prevent ADRs.

*“....That’s why I believe it is important to use drugs only when necessary”. Interviewee (08)*

A number of the interviewees also counsel patients to warn them of anticipated ADRs. Some said they would give clear instructions to patients for example drink lots of water, other interviewees believed counterchecking medicines before administration prevents administration errors.

Sharing of the identified cases of ADRs during ward rounds to other colleagues and senior supervisors is also a common practice by many doctors and nurses in KNH.

A few pharmacist and clinicians said they ask for history of drug allergies to avoid problems with medication.

One pharmacist mentioned that there is a panel of experts who oversee careful drug selections at pharmacy level to ensure good quality drugs are being used in the hospital.

**Challenges in reporting of ADRs**

When probed on the reasons why there are not able to report ADRs several common concerns came up and are listed below (Table 10). These concerns seem to be shared across all cadres.

**Table 10:** Challenges in reporting of ADRs in KNH

FACTORS	REASONS
<b>SYSTEM</b>	Lack of knowledge/ lack of awareness  Lack of tools to record ADRS  Punitive nature of institution  Lack of proper tools to record medication errors, No feedback after reporting....” <i>report then what....</i> ” Interviewee (02) .....” <i>Reporting is not a culture...</i> ” Interviewee (05)
<b>HEALTHCARE WORKER</b>	Heavy workload, Time consuming, Priority is treating all patients....  <i>“I’d rather treat the patient and record it in file, then move on the next patient than look for forms that are unavailable”.</i> Interviewee (19)

**Preferred way of reporting**

More than half of the interviewees would prefer online reporting because it would be faster since KNH has created a database for each patient. Incorporating the ADR information within this system would be simpler. The other few preferred manual reporting giving reasons such as: manual will be faster as u don’t have to go logging into a computer, others thought when something is done manually it would create more awareness as people will begin seeing the



forms around. One said manual is evidence based. Others preferred manual reporting but did not explain their preference.

On the other hand, a small number of the interviewees were indifferent and said any mode of recording available will be satisfactory and would be embraced.

### **Future outlook for PV in KNH**

Several suggestions were given on how to improve the current PV system of the hospital.

Of utmost importance was the training of personnel that was suggested by all interviewees. Training and increasing manpower would greatly shape the PV practice and would be an essential ingredient in accomplishing PV goals. All the interviewees thought defining the actual channel of reporting ADR is essential for proper flow of information and feedback. One of the doctors also suggested that pre practice training of PV would equip healthcare workers with the technical knowledge to incorporate proper practice in their clinical years.

*“..Pre practice training of pharmacovigilance will equip healthcare workers effectively to handle PV activities”*. Interviewee (05)

Healthcare workers felt that after awareness; there should be constant reminders to the healthcare workers on the dangers of ADRs and the importance of reporting them. Encouraging of the healthcare workers should be done through acknowledgements and feedback as suggested.

*“..ADR reporting should be put as part of job description and make reporting of ADRS to be Made a way of measuring performance”*. Interviewee (04)

The interviewees thought that Pharmacovigilance activities should be an agenda in the departments and that organized forums should be conducted to discuss and analyze ADRs, as this would greatly impact on the PV practice. Interdisciplinary communications should be strengthened among all departments and information collected should be disseminated regularly. The inputs could only work with the great support of the management of the hospital as suggested by some of the pharmacists.

*“..... There should be support from top management and Kenya to formulate a policy on ADRs and own it”*. Interviewee (16)

Most medical doctors felt that deploying pharmacist to the wards would be very beneficial in discussing and reporting of ADRs. Additionally there should be a PV champion in all wards whose work will be to strengthen PV practices.

Majority also added that the PV centre should be established and work should begin.

*“...Establish a PV centre with a team leader and pharmacovigilance will come to life”.*

Interviewee (07)

*“.... institute the practice try put bottlenecks e.g. patients should not leave hospital until they are assessed for allergies or ADRs...”* Interviewee (22)

#### **4.3: DISCUSSION**

Studies have shown that the practice of PV is known to many health professionals but reporting rates remain low in most developing countries. This is true for most studies undertaken to assess the knowledge and practice of PV in most countries in the world (25,37,38). In Kenya PPB acknowledges receiving over 8000 reports in their database. However, PPB confirms that, the numbers of reports are much lower than what is expected because the ADRs seen in practice are much higher but not reported. This study concurs with the literature and PPB findings where healthcare workers come across many ADRs but very few reports are submitted of the same (43).

From the interviews it was discovered that healthcare workers come across ADRs either on daily basis, once or twice every admission cycle of patients or at least once in a while. However, their practices were not in keeping with the stipulated official PV procedures and channels of reporting. As a practice in KNH, majority of the interviewees (nurses and doctors) record an ADR that has occurred in the patients file, they then manage the ADR, and they later verbally report their observations to their senior colleagues. The nurses would highlight it in their “CARDEX” (daily records card) and must handover written findings to their senior colleagues or during handover sessions. This practice can make an excellent entry point to upgrade reporting of ADRs if nurses were to be trained to use the official tools. Such a practice can be developed through the use of the yellow suspected ADR reporting form and reporting and collection of ADRs can be much more organized.

This practice has also been highlighted in a study conducted by Fadare et al in 2008 in Northern Nigeria where they highlighted the role the nurses can play in reporting of ADRs if properly trained (44).

A study conducted in Saudi Arabia noted that pharmacists were the most knowledgeable cadre of health professionals (45). Similarly, our study also showed that pharmacists knew about pharmacovigilance because of either receiving a formal training or on the job experiences from senior colleagues on pharmacovigilance. This is so because of the perceptions that ADRs are drug related and pharmacists are specialized in drugs making them inevitably aware of all matters concerning drugs. In addition to this the pharmacovigilance centre in Kenya is housed under the Pharmacy and Poisons Board making pharmacists the first beneficiaries of trainings and tools to collect information on ADRs. It is also worth noting that the proportion of doctors to pharmacists in Kenya is big and therefore for every pharmacist trained the impact would be felt more compared to the doctors who are many. Most of the healthcare workers (mainly the doctors and the nurses) were not trained and therefore were not aware of the reporting tools and the reporting procedure of ADRs. This was evident from the major mismatch between their testimonies of how often they come across ADRs (very often) versus the number of ADR reports collected in the hospital which was low. This was however very similar to several observational studies conducted around the developing countries (25,37,38 ,40).

A study to establish obstacles and solutions for spontaneous reporting of adverse drug reactions in the hospital by Vallano et al (2005) found that the usual clinical activities and lack of time for filling in records, lack of knowledge of the pharmacovigilance system in the hospital, uncertainty of the ADR diagnosis and the potential conflicts derived from reporting ADRs and unavailability of yellow cards were the major reporting obstacles (6). These findings are very similar to this study that has described the major challenges to ADR reporting as heavy workload, lack of time, ignorance of the PV system in place, lack of feedback and tools. Other studies around the world have analysed these challenges and given similar findings (24,46).

Most interviewees felt that ADRs were an important clinical aspect and felt they should be reported to avoid future tragedies caused by medication, prevent avoidable ADRs. They however, acknowledged that due to the heavy workload they faced in their day to day practice and any additional work might not be very welcomed but nevertheless agreed to be reporting

when training is done and tools are given to them. This was a positive response for the future activities of PV that will be undertaken in the hospital.

Most doctors and nurses felt the responsibility of recording ADRs lies with them. They however suggested that pharmacists should oversee the affairs of ADR reports and they should be seconded to the wards to strengthen the PV practice. Pharmacists on the other hand were quite aware of the PV practices but said forgetfulness, heavy workload and lack of a reporting culture are the main reasons they do not actively report. Interestingly, these reasons are shared by many healthcare workers worldwide in observational studies conducted to find out reasons for under reporting of ADRs, (6,43,44).

Pre medication and reassuring patients of anticipated ADRs were the 2 common practices of preventing ADRs among the interviewees in KNH. However upon probing all the interviewees felt that a lot can be done to prevent ADRs and medication errors. Among them being: regular trainings and continuous sensitization of staff, sending reminders to report, organizing forums to discuss ADRs and organized and regular feedback. Modification of current ways of reporting to simpler ways e.g. attaching forms to discharge summaries, smaller notification forms amongst many. This seems to be the cornerstone of all measures taken to enhance PV practices as the same solutions have been cited by various studies done across the globe (6,23,28,42,45,46).

## **CHAPTER FIVE: CONCLUSION, LIMITATIONS AND RECOMMENDATIONS**

### **5.1: CONCLUSION:**

Pharmacovigilance and ADR reporting have been seen without a doubt to have a very significant clinical role both analytically and practically in this study. The analysis of KNH ADR reports and the in-depth interviews conducted have showed that the healthcare workers have inadequate knowledge and practice of pharmacovigilance. Although, the interviewees knew of the general concept of pharmacovigilance, the term “pharmacovigilance” and appropriate practice was unknown to many.

Major gaps were highlighted and continuous trainings and provision of tools along with giving feedback on reports were the main missing ingredients in the practice of pharmacovigilance. Healthcare workers however, displayed positive attitude towards integrating pharmacovigilance in their daily activities to set ground for detection of preventable ADRs, previously unknown ADRS and ultimately to make informed choices on patient management and drug use safety.

This study was intended to give an overview of the extent of reporting and ADR trends so as to establish the level of practice in the hospital. This could give an indication of the situation in the other government facilities and the country as well. This will eventually assist in crafting of appropriate strategies to improve ADR reporting in institutions and strengthen the PV practice at large.

### **5.2: STUDY LIMITATIONS**

The study was successfully carried out as planned. However, there were some limitations which could affect the generalizability of these results.

ADR reports collected between 2009 and 2011 had been archived and could not be accessed, thereby lowering the available sample size. It is acknowledged that a larger sample size would be more precise and provide more information.

The responses from the interviewees could have been influenced by reporting bias.

The interviews were only conducted to healthcare workers at the medical wards and the assumption is that the information given is uniform with all healthcare workers in the hospital.

### **5.3: RECOMMENDATIONS:**

#### **Recommendations for practice**

1. The pharmacy department through the chief pharmacist should make a presentation on pharmacovigilance to the management of KNH in order to create a buy in and support for the discipline of PV.
2. Archived information should be accessible for review or research purposes subject to approval
3. Regular trainings should be conducted at KNH and all hospitals with the help of the Pharmacy and Poisons Board.
4. The Pharmacy and Poisons Board (ministry of health) should liaise with the college of health sciences to offer pre practice sensitization trainings to health sector students.
5. The Pharmacy and Poisons Board should avail tools to every hospital or find simpler ways of creating notification forms for easy capture of ADR information.
6. The Pharmacy and Poisons Board should analyze, compile all ADR reports and provide feedback to the reporting institutions.
7. A pharmacovigilance centre should be established in Kenyatta National Hospital to serve as a central place for all pharmacovigilance activities within the hospital.
8. Deploy a pharmacist to each and every ward in the hospital to strengthen pharmacovigilance and pharmaceutical practices.
9. The pharmacy department /PV centre should make PV activity forums regular for disseminating updates and new findings to create a culture of reporting and to get the healthcare workers constantly updated on PV events.

### **Recommendations for future research**

1. Further studies should be conducted to establish the pharmacovigilance practices carried out after implementation of the above recommendations.
2. A study to be conducted to cover all the wards and clinics in the hospital to give a more holistic finding on the knowledge attitude and practice of pharmacovigilance.
3. Baseline studies should also be conducted to compare pharmacovigilance practices across all hospitals in Kenya to lay a foundation for harmonization of the discipline.

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## **APPENDIX A: INTERVIEW GUIDE**

**TITLE:** KNOWLEDGE, ATTITUDE AND PRACTICES OF PHARMACOVIGILANCE AMONG HEALTH CARE PROFESSIONALS AT THE KENYATTA NATIONAL HOSPITAL.

### **Introduction:**

My name is Dr Fathiya Said Hamumy; I am doing a qualitative baseline study on knowledge attitude and practice of pharmacovigilance among health care professionals at the Kenyatta National Hospital.

### **Purpose of interview:**

Pharmacovigilance is a relatively new concept in Kenya. It is a very broad field and is important as it ensures safety of medication use and in turn safety of patients with regards to drug use.

The main aim of my study will be to identify gaps in the knowledge of healthcare workers regarding the importance, requirements, tools and processes of pharmacovigilance in Kenya, as well as to determine the factors that influence the opinions and practices of healthcare workers in Kenya regarding pharmacovigilance.

As part of this study, I am interested in getting your views on various aspects of pharmacovigilance. It would be very useful if we could spend some time together to discuss this issue.

**General background:**

1. *Respondents code* \_\_\_\_\_ *Profession*\_\_\_\_\_
2. Sex: Male \_\_\_\_\_ Female\_\_\_\_\_
3. Age: 20-30 ( )      30-40 ( )      40-50 ( )      50-60( )      *Tick as appropriate*
4. Years of practice: \_\_\_\_\_
5. Department: \_\_\_\_\_
6. Highest educational level: \_\_\_\_\_
7. Brief description of current responsibilities \_\_\_\_\_

**Interview topics:**

**A) KNOWLEDGE**

1. What is your understanding of the concept of pharmacovigilance (PV)?

*(Probe.....)*

Can you define PV?

Can you tell me what an Adverse drug reaction (ADR) is?

Can you explain what medication errors are?

2. Kindly explain what challenges you go through in identification of an ADR?

*(Probe.....)*

Can you distinguish an ADR from the manifestation of disease easily?

3. Is there a pharmacovigilance centre in this institution?

*(Probe.....)*

Where is it located?

Who is in charge of it?

What goes on in that department?

4. Have you heard of the National Pharmacovigilance Centre?

*(Probe.....)*

Do you know where it is located?

Do you know their functions?

Are you aware of their responsibilities towards you as a healthcare worker and vice versa?

5. Do you know of the pharmacovigilance reporting tools?

*(Probe.....)*

The (yellow) ADR reporting form?

The (pink) Poor Quality Medication Form?

The Alert Cards?

Online reporting systems in existence?

Are they available in this institution?

6. What do you use to report adverse drug reactions?

*(Probe.....)*

7. Kindly explain to me the processes Involved in reporting an ADR in this institution

*(Probe.....)*

8. Do you know what is to be reported as ADRs?

*(Probe.....)*

New ADRs? Common ADRs? All ADRs? Only ADRs that you are certain about?

9. Have you been trained on pharmacovigilance?

*(Probe.....)*

National training? Institutional training? On the job training?

Give a short overview of what was taught during this training.

## **B) ATTITUDE**

1. Do you think it is necessary to have pharmacovigilance established in hospitals?

*(Probe.....)*

Is it important to the medical field?

|

2. How do you find the process of reporting an ADR or medication error?

*(Probe.....)*

Do you think it is time consuming?

Do you think it is convenient?

|

3. What are the challenges faced in reporting medication errors and ADRs by the healthcare workers?

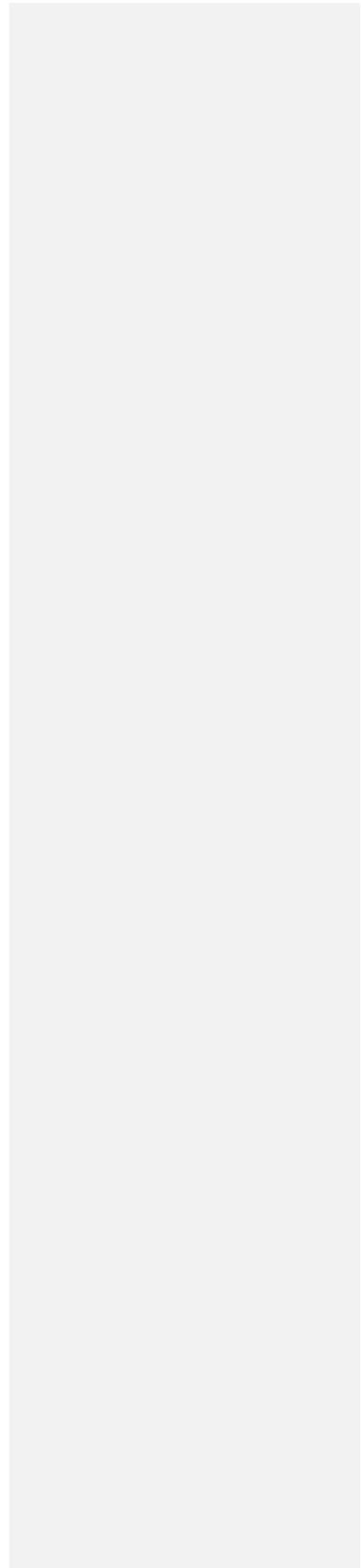
*(Probe.....)*

Heavy workload?

Lack of interest?

Lack of knowledge?

|





4. In your opinion, what should be done to facilitate reporting of ADRs and medication errors?

*(Probe.....)*

5. To whom do you think the responsibility of reporting ADRs lie?

Why?

### **C) PRACTICE**

1. How often do you come across ADRs in your practice? *(Probe...)*

Kindly give me an example of the latest one you have come across and tell me what you did about it?

2. What do you do when you encounter an ADR?

*(Probe.....)*

3. Identification of ADRs is not usually straightforward. How do you go about establishing a causal relationship?

*(Probe.....)*

Do you rely on your knowledge of side effect profiles of prescribed drugs?

Do you consider ADRs when taking medication history?

Do you take history of herbal /alternative therapies used?

Do you explore self medication?

4. What measures do you take to prevent adverse drug reactions as a person and as an institution?

*(Probe.....)*

Do you share reported cases in any forum e.g. Continuous Medical Education (CMEs)?

Do you warn patients of potential ADRs when giving medication?

5. What do you think can be effective if implemented to avoid ADRs and medication-related problems (MRPs)?

*(Probe.....)*

6. What is your preferred way of reporting medication errors and ADRS?

*(Probe.....)*

Would you prefer an online or the manual system?

What additional features would you suggest for your preferred method of reporting?

7. What do you think should be done to improve the current pharmacovigilance practices in this hospital?

*(Probe.....)*

**Wrap-up**

Thank you for your time and willingness to participate in this study. Do you have anything to add to what was already discussed or were there important topics which were not covered?

## **APPENDIX B: INFORMED CONSENT FORM**

**Title of the study:** KNOWLEDGE, ATTITUDE AND PRACTICES OF PHARMACOVIGILANCE AMONG HEALTH CARE PROFESSIONALS AT THE KENYATTA NATIONAL HOSPITAL.

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

**Investigator:** Dr Fathiya said Ali Hamumy, P.O BOX, 00506-3436, Nyayo Stadium, Nairobi.

**Supervisors:**

Dr Eric .M. Guantai, Department of Pharmacology and Pharmacognosy;

Dr Francis Wafula, Policy specialist World Bank.

Dr Kefa Bosire, Department of Pharmaceutics and Pharmacy Practice.

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

Permission is requested from you to enroll in this medical research study. You should understand the following general principles which apply to all participants in a medical research:

- i. Your agreement to participate in this study is voluntary.
- ii. You may withdraw from the study at any time without necessarily giving a reason for your withdrawal.
- iii. After you have read the explanation please feel free to ask any questions that will enable you to understand clearly the nature of the study.

**Introduction:** In this study am assessing the knowledge, Attitude and practice of health professional in pharmacovigilance.

**Purpose of the study:** The purpose of the study is to establish the baseline knowledge, attitude and practice that healthcare professionals have towards pharmacovigilance in Kenya.

**Importance of the study:** the information obtained will assist in filling the gaps that healthcare workers are currently experiencing as far as reporting of ADRs and pharmacovigilance practices in Kenya are concerned and establishing the best way forward in the field of medication safety and patient safety.

**Procedure to be followed:** With your permission, I will engage you in a discussion about pharmacovigilance which I will record using a voice recorder. I will also take some notes on pen and paper where necessary. All information obtained will be handled with utmost confidentiality.

**Risks:** There will be no risks involved in this study.

**Benefits:** There will be no direct benefits to you but the findings of this study will be useful in improving the science and practice of pharmacovigilance in Kenya and worldwide.

**Assurance of confidentiality:** All information obtained from you will be kept in confidence. At no point will your name be mentioned or used during data handling or in any resulting publications. Codes will be used instead.

**Contacts:** In case you need to contact me, my academic department or the Kenyatta National Hospital/ University of Nairobi Ethics and Research Committee concerning this study please feel free to use the contacts provided above. I now request you to sign the consent form attached.

**CERTIFICATE OF CONSENT**

I have read and understood the information provided regarding the study and my questions regarding the study have been addressed. I willingly consent to participate in this study.

NAME OF PARTICIPANT:.....

SIGNATURE:.....

DATE:.....

**Statement by the researcher:**

I have provided all relevant information to the participant and answered all questions asked regarding the study. I have explained to the participant that his/her responses will be recorded in a note book and will be taped. I confirm that information requested has been provided voluntarily.

A copy of this informed consent has been provided to the participant.

NAME OF RESEARCHER:.....


SIGNATURE:.....

DATE:.....

In case of any questions or concerns, feel free to contact any of the following:

- The principal investigator Dr. Fathiya Said Hamumy on 0722359470,
- The lead supervisor Dr. E. M. Guantai on + 254 20 272509, or
- KNH/UON ethics committee on 2726300 extension 44102
-

APPENDIX C: QUANTITATIVE DATA COLLECTION MATERIAL



**MINISTRY OF HEALTH  
THE PHARMACY AND POISONS BOARD**  
P. O. Box 27663-00506 NAIROBI  
Tel: (020)-2716905 / 6 Ext 114 Fax: (020) 2713431/2713409  
Email: pv@pharmacyboardkenya.org

PV 1

**IN CONFIDENCE**

Initial Report  
 Follow-up Report

**SUSPECTED ADVERSE DRUG REACTION REPORTING FORM**

NAME OF INSTITUTION: ..... INSTITUTION CODE: .....

ADDRESS: ..... CONTACT: .....

---

PATIENT'S NAME/ INITIALS: ..... I.P.O.P. NO.: ..... D.O.B: .....

PATIENT'S ADDRESS: ..... WARD/CLINIC: ..... GENDER:  Male  Female  
(Name/Number)

ANY KNOWN ALLERGY:  No  Yes (specify) ..... PREGNANCY STATUS:  Not Pregnant  1st Trimester  2nd Trimester  3rd Trimester WEIGHT (kg): ..... HEIGHT (cm): .....

DIAGNOSIS: (What was the patient treated for).....

BRIEF DESCRIPTION OF REACTION: .....

LIST OF ALL DRUGS USED IN THE LAST 3 MONTHS PRIOR TO REACTION (include OTC and herbal)(see rear side of this form for additional drugs)	DOSE	ROUTE AND FREQUENCY	DATE STARTED	DATE STOPPED	INDICATION	TICK (✓) SUSPECTED DRUG(S)
1						
2						
3						
4						
5						

**SEVERITY OF THE REACTION:** (Refer to scale overleaf)

Mild  
 Moderate  
 Severe  
 Fatal  
 Unknown

**ACTION TAKEN:**

Drug withdrawn  
 Dose increased  
 Dose reduced  
 Dose not changed  
 Unknown

**OUTCOME:**

Recovering / resolving  
 Recovered / resolved  
 Requires or prolongs hospitalization  
 Causes a congenital anomaly  
 Requires intervention to prevent permanent damage  
 Unknown

**CAUSALITY OF REACTION:** (Refer to scale overleaf)

Certain  
 Probable / Likely  
 Possible  
 Unlikely  
 Conditional / Unclassified  
 Unassessable / Unclassifiable

ANY OTHER COMMENT: .....

NAME OF PERSON REPORTING: ..... DATE: .....

E-MAIL ADDRESS: ..... PHONE NO. ....

DESIGNATION: ..... SIGNATURE: .....



**You need not be certain ... just be suspicious !**

Your support in this Pharmacovigilance program is appreciated.  
Submission of a complaint does not constitute an admission that medical personnel or manufacturer or the product caused or contributed to the event.  
Patient's identity is held in strict confidence and programme staff is not expected to and will not disclose reporter's identity in response to any public request.  
Information supplied by you will contribute to the improvement of drug safety and therapy in Kenya. Once completed please send to:  
The Pharmacy and Poisons Board on the above address

**EXPLANATORY NOTES**

**CONFIDENTIALITY**

All information collected in this form, identities of the reporter and patient, will remain confidential

**WHAT TO REPORT**

An Adverse Drug Reaction (ADR) is defined as a reaction that is noxious and unintended, and occurs at doses normally used in man for prophylaxis, diagnosis or treatment of a disease, or for modification of physiological function.

**Report all suspected adverse experiences with medications,**

especially those where the patient outcome is:

- Death
- Life-threatening (real risk of dying)
- Hospitalization (initial or prolonged)
- Disability (significant, persistent or permanent)
- Congenital anomaly
- Required intervention to prevent permanent impairment or damage

**Report even if:**

- You are not certain if the drug caused the reaction
- You do not have all the details

**WHO CAN REPORT**

All healthcare professionals (clinicians, dentists, nurses, pharmacists, physiotherapists, community health workers etc) are encouraged to report. Patients (or their next of kin) may also report.

*Please use the space provided below for any further information. You may attach more pages to this form if required.*

**WHAT HAPPENS TO THE SUBMITTED INFORMATION**

All information submitted is handled in strict confidence. The Pharmacy and Poisons Board will assess causality and statistical analysis on each form. Data will periodically be used for review and suggest any interventions that may be required to the Ministry of Health. Data will also be submitted periodically to the Uppsala Monitoring Centre - the WHO Collaborating Center for International Drug Monitoring in Sweden.

**SUBMISSION OF INITIAL OR FOLLOW-UP REPORTS**

It is important to tick the appropriate box on the top-right corner of the front page to indicate whether the report is an initial (original) report or is a follow-up (subsequent) report.

It is very important that follow-up reports are identified and linked to the original report.

**WHERE TO REPORT**

After completing this form, please forward the same to your Pharmacy Department for onward submission, or mail directly, to:

**THE PHARMACY AND POISONS BOARD**

Lenana Road,  
P. O. Box 27663-00506 NAIROBI  
Tel: (020)-2716905 / 6 Ext 114 Fax: (020)-2713431/2713409  
E-mail: pv@pharmacyboardkenya.org

LIST OF ALL DRUGS USED IN THE LAST 3 MONTHS PRIOR TO REACTION (include OTC and herbals)	DOSE	ROUTE AND FREQUENCY	DATE STARTED	DATE STOPPED	INDICATION	TICK (6 SUSPECTED DRUGS)
6						
7						
8						
9						
10						

Criteria for Assessment of Severity of an ADR	
<b>Mild</b>	<ul style="list-style-type: none"> <li>• The ADR requires no change in treatment with the suspected drug</li> <li>• The ADR requires that the suspected drug be withheld, discontinued or otherwise changed. No antidote or other treatment is required</li> <li>• No increase in length of stay.</li> </ul>
<b>Moderate</b>	<ul style="list-style-type: none"> <li>• The ADR requires that the suspected drug be withheld, discontinued or otherwise changed, and/or an antidote or other treatment is required.</li> <li>• Increases length of stay by at least one day</li> <li>• The ADR is the reason for admission.</li> </ul>
<b>Severe</b>	<ul style="list-style-type: none"> <li>• The ADR requires intensive medical care</li> <li>• The ADR causes permanent harm to the patient</li> </ul>
<b>Fatal</b>	<ul style="list-style-type: none"> <li>• The ADR either directly or indirectly leads to the death of the patient</li> </ul>

WHO-UMC Causality Assessment Scale	
Causality Term	Assessment
<b>Certain</b>	<ul style="list-style-type: none"> <li>• Event of laboratory test abnormality, with plausible time relationship to drug intake</li> <li>• Cannot be explained by disease or other drugs</li> <li>• Response to withdrawal plausible (pharmacologically, pathologically)</li> <li>• Event definitive pharmacologically or phenomenologically (i.e. an objective and specific medical disorder or a recognized pharmacological phenomenon)</li> <li>• Rechallenge satisfactory, if necessary.</li> </ul>
<b>Probable / Likely</b>	<ul style="list-style-type: none"> <li>• Event or laboratory tests abnormality, with reasonable time relationship to drug intake</li> <li>• Unlikely to be attributed to disease or other drugs</li> <li>• Response to withdrawal clinically reasonable</li> <li>• Rechallenge not required</li> </ul>
<b>Possible</b>	<ul style="list-style-type: none"> <li>• Event or laboratory tests abnormality, with reasonable time relationship to drug intake</li> <li>• Could also be explained by disease or other drugs</li> <li>• Information on drugs withdrawal lacking or unclear</li> </ul>
<b>Unlikely</b>	<ul style="list-style-type: none"> <li>• Event or laboratory tests abnormality, with a time to drug intake that makes a relationship improbable (but not impossible)</li> <li>• Disease or other drugs provide plausible explanations</li> </ul>
<b>Conditional/ Unclassified</b>	<ul style="list-style-type: none"> <li>• Event or laboratory test abnormality</li> <li>• More data for proper, assessment needed or</li> <li>• Additional data under examination</li> </ul>
<b>Unassessable/ unclassifiable</b>	<ul style="list-style-type: none"> <li>• Report suggesting an adverse reaction</li> <li>• Cannot be judged because of insufficient or contradictory information</li> <li>• Data cannot be supplemented or verified.</li> </ul>

Your support in this Pharmacovigilance program is appreciated.  
 Submission of a report does not constitute an admission that medical personnel or manufacturer or the product caused or contributed to the event.  
 Patient's identity is held in strict confidence and programme staff is not expected to and will not disclose reporter's identity in response to any public request.  
 Information supplied by you will contribute to the improvement of drug safety and therapy in Kenya.  
 Once completed please send to: The Pharmacy and Poisons Board on the above address



