HEALTH PROVIDER FACTORS ASSOCIATED WITH REPORTING OF ADVERSE DRUG REACTIONS IN KENYATTA NATIONAL HOSPITAL

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DEDICATION

To my family, without you, I would be nothing.

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ABSTRACT

Background: Medicines are an important component of public health because they are used to prevent and treat disease; however the use of medicines may cause harm to the patient. An adverse drug reaction is harm that arises from the use of a drug. Adverse drug reactions have a huge impact on the health system since they result in drug-related morbidity and mortality as well as indirect costs such as loss of productivity at work. Reporting of adverse drug reactions to a relevant authority is one of the methods of enhancing medication safety; however under-reporting of adverse drug reactions by health workers is a major challenge in enhancing medicines safety. The factors that affect reporting of adverse drug reactions include health worker factors such as age, specialty, location of practice, knowledge and attitudes about adverse drug reaction reporting; health systems factors such as availability of reporting tools, training and workload; patient factors such as the knowledge of adverse reactions and willingness to discuss them with the health worker and the severity of the adverse reaction.

Objectives: The broad objective of the study was to determine the health provider factors that are associated with reporting of adverse drug reactions in Kenyatta National Hospital. The specific objectives were to determine the socio-demographic factors of the health workers in Kenyatta National Hospital and to determine the knowledge and attitudes of health workers in Kenyatta National Hospital on adverse drug reaction reporting.

Methodology: The study used both quantitative and qualitative techniques. The quantitative component of the study involved the use of a cross-sectional study design. The study population was health workers in Kenyatta National Hospital who were in a position to detect adverse drug reactions. The study population was clustered by cadre then systematic sampling

was used to select the participants. A closed-ended questionnaire was administered to the study participants who consented to participate in the study. The qualitative component of the study involved the use of key informant interviews using open-ended questions. Key informants were selected from the Pharmacovigilance Department of the Pharmacy and Poisons Board.

Analysis: Data from the questionnaire was coded and entered into Stata version 12. Descriptive statistics were used to summarize the socio-demographic characteristics of the study participants. Categorical predictor variables were summarized using frequencies and percentages while the continuous predictor variables were summarized using means and medians. Contingency table analysis using Fischer's exact test was used to determine if there was a statistically significant association between reporting an adverse drug reaction and the categorical predictor variables which are sex, department of the health worker and previous pharmacovigilance training. Student's t test was used to determine if there was a statistically significant association between reporting an adverse drug reaction and the continuous predictor variables age, duration of practice and the knowledge score. Wilcoxon rank sum test was used to determine if there was a statistically significant association between reporting an adverse drug reaction and the overall attitude score. Logistic regression analysis was carried out to determine the effects of all the predictor variables, taken together, on reporting of adverse drug reactions. Analysis of the qualitative data was done by sorting the data into categories and examining the emerging themes.

Results: Previous pharmacovigilance training was found to be significantly associated with reporting of adverse drug reactions ($p=0.000$). Health workers were more likely to report

adverse drug reactions if they had been trained. Health workers' knowledge on adverse drug reactions was significantly associated with reporting of adverse drug reactions (p=0.0021) with reporters having higher mean knowledge scores than the non-reporters. Previous pharmacovigilance training (p=0.000, Odds Ratio 14.04, 95% CI: 3.19-61.76) and knowledge (p=0.033, Odds Ratio 1.19, 95% CI: 1.01-1.40) were found to be the strongest predictors of reporting adverse drug reactions when logistic regression was carried out. The key informants identified several health provider and health systems factors that affect reporting of adverse drug reactions. Lack of knowledge about the adverse drug reaction reporting scheme and poor attitudes were identified as health worker factors that hindered adverse drug reaction reporting. Health systems factors that hindered the reporting of adverse drug reactions were the unavailability of reporting tools, high workloads and the costs incurred when sending a hard copy report to the Pharmacy and Poisons Board.

Conclusion: Health workers' knowledge on adverse drug reaction reporting was a major determinant of reporting of adverse drug reactions. Health workers who had been trained and had more knowledge on adverse drug reaction reporting were more likely to report adverse drug reactions than those who had not been trained nor had less knowledge about adverse drug reaction reporting.

Recommendations: In order to increase reporting of adverse drug reactions by health workers, there is need to train all health workers in order to increase their knowledge, to include all cadres of health workers in reporting and to avail the adverse drug reaction reporting forms in all the wards and clinics of the hospital.

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LIST OF ABBREVIATIONS

ADR	Adverse Drug Reaction
CO	Clinical Officer
ERC	Ethics and Research Committee
EU	European Union
FDA	Food and Drug Administration
GP	General Practitioner
HW	Health Worker
ICSR	Individual Case Safety Report
KNH	Kenyatta National Hospital
MHRA	Medicines and Healthcare products Regulatory Agency
MO	Medical Officer
MoMS	Ministry of Medical Services
MoPHS	Ministry of Public Health and Sanitation
Pharm tech	Pharmaceutical technologist
PPB	Pharmacy and Poisons Board
PV	Pharmacovigilance
RH	Reproductive Health
SSA	Sub-Saharan Africa
UK	United Kingdom
UMC	Uppsala Monitoring Centre
UoN	University of Nairobi
US	United States (of America)
USD	United States dollar
WHO	World Health Organization

CHAPTER 1 INTRODUCTION AND BACKGROUND

1.1 Introduction

Medicines are an important component of public health because they are used to prevent and treat disease. However, the use of medicines is a double-edged sword because in as much as they benefit the patient, they have the potential to cause harm. The thalidomide disaster that occurred in the 1960s highlighted the dangers of medicine use. The medicine thalidomide was marketed to pregnant women as an anti-nausea drug. It was noted that women who used thalidomide during pregnancy later gave birth to children with deformed limbs. Since then, there have been efforts to ensure the safety of new medicines before they are released to the population by conducting clinical trials and after they are released to the population by carrying out post-marketing surveillance (Strom and Kimmel, 2006). Potential types of harm that can be caused by medicines include adverse drug reactions (ADRs), medication errors, the use of sub-standard or counterfeit medicines and the abuse and misuse of medicines.

One of the methods of enhancing medication safety involves reporting of ADRs to a medicines regulatory authority. The ADR reports are then analysed for possible causality and this information is used in decision making; for example the decision to withdraw a medicine from the market may be informed by numerous reports that highlight it as a possible cause of serious ADRs. A major disadvantage of this method is that ADRs are under-reported (Mann and Andrews, 2007).

In many countries, reporting of ADRs is mostly done by the healthcare provider rather than the patient (Herxheimer et al., 2010). Studies have shown that various factors affect the

reporting of ADRs to the national medicines regulatory authority and they include factors related to the health workers, to the health system and to the patient affected by the ADR. Several studies have shown that health provider factors such as age, speciality, duration of practice, the knowledge and attitudes of the health professional towards ADR reporting are strongly related to reporting of ADRs (Lopez-Gonzalez et al., 2009).

The reporting rate of ADRs in Kenya remains low despite the launch of the pharmacovigilance programme in 2007 (Strengthening Pharmaceutical Systems Program, 2011). Since majority of the ADR reports in Kenya are submitted by health workers rather than patients, it is likely that under-reporting of ADRs is associated with certain health worker factors. This study was carried out to determine the health provider-related factors that are associated with reporting of ADRs in Kenyatta National Hospital (KNH). In this study, health provider refers to the health workers. Literature related to reporting of ADRs was reviewed to identify similar studies that have been carried out in other settings and to identify gaps in knowledge or issues that had not been addressed by the other studies. The research problem was described and analysed in detail. The objectives of the study were to determine the health provider factors that are associated with reporting of ADRs in KNH. The quantitative study involved the use of a cross-sectional study design and data was collected using a self-administered questionnaire with closed-ended questions. The qualitative study involved the use of key informant interviews. Analysis of the quantitative study was carried out using contingency table analysis and logistic regression while analysis of the qualitative data was done by sorting the data into categories and examining the emerging themes. The findings of the study were discussed and used to make recommendations on improving the reporting of ADRs by health workers in KNH.

1.2 Background

The increasing use of medicines and the need to ensure medicine safety has led to the emergence of the field of pharmacovigilance (PV), which deals with medicine safety (WHO, 2002).

1.2.1 Pharmacovigilance

i. Definition of pharmacovigilance

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" (WHO, 2002). Although the field of pharmacovigilance initially focused on drugs, the scope has been expanded to include herbals, traditional and complementary medicines, blood products, biological, medical devices and vaccines (WHO, 2002).

Other issues that are relevant to the science of pharmacovigilance include substandard medicines, medication errors, therapeutic ineffectiveness of medicines, interactions of medicines with other medicines or food, use of medicines for indications which are not approved, assessment of drug related mortality, the abuse and misuse of medicines and communication of this information to healthcare professionals and consumers for risk-benefit decision making (WHO 2002; Strengthening Pharmaceutical Systems 2009).

ii. History of pharmacovigilance

It is believed that ADRs were present at the dawn of time when man started using plants as medicines. In the year 2000 BC Emperor Shin Nong, showed that Ma Huang, the ephedra plant caused tachycardia and hypertension. Homer stated, circa 950 BC, that "Many drugs were excellent when mingled and many were fatal". Baltasar Gacian wrote in *The Art of Worldly Wisdom* in 1658, that "Remedies often make disease worse…. It takes a wise doctor to know when not to prescribe". In 1785, William Withering wrote 'Account of the foxglove and some of its medical uses', including "Foxglove when given in large and quickly repeated doses occasions sickness, vomiting, giddiness, confused vision, objects appearing green or yellow" (Talbot and Waller, 2004). In 1789, Wouter van Doeveren, a professor of medicine at Leiden University, gave a public lecture on the diseases and ailments which often affect people as a result of remedies administered to them for therapeutic purposes (Grootheest, 2003).

In 1848, a 15 year old English patient died after receiving the anaesthetic agent chloroform after undergoing surgery for an ingrown toenail. Concerns about the safety of anaesthetics led *The Lancet* journal to set up a commission so that doctors could report anaesthesia-related deaths thus a forerunner of a spontaneous adverse drug reaction system was born (Routledge, 1998). In 1906, the Pure Food and Drug Act was passed in the US, in response to excessive adulteration and misbranding of the foods and drugs that were available at that time (Strom and Kimmel, 2006).

Preclinical toxicity testing was required for the first time in the US in 1938 after the passing of the Food, Drug and Cosmetic Act. This was prompted by the deaths from renal failure of 107

people as a result of the marketing of an elixir of sulfanilamide dissolved in diethylene glycol (Routledge, 1998; Strom and Kimmel, 2006). Chloramphenicol was introduced in 1948, but it was not until the 1950s that it was discovered to cause aplastic anaemia (Talbot and Waller, 2004). In 1960, eight years after the first textbook on adverse drug reactions was published, the Food and Drug Administration (FDA) began to collect reports of adverse drug reactions and to monitor hospital-based drug monitoring programs (Strom and Kimmel, 2006).

In 1961, an Australian obstetrician, William McBride wrote to *The Lancet* to report an increase in the number of congenital malformations associated with the use of thalidomide. At the time, thalidomide was marketed in Europe as a hypnotic drug that was safe to use in pregnancy. The FDA had delayed marketing approval of thalidomide in the US because of concerns about toxicity in acute animal studies (Talbot and Waller, 2004). As a result, the cases of thalidomide-induced phocomelia were fewer in the US than in Europe. West Germany was the most affected because the drug had been sold over the counter (Routledge, 1998).

The thalidomide disaster resulted in regulatory changes that required proof of drug safety. In 1962 the Kefauver–Harris Amendments were passed. These amendments strengthened the requirements for proof of drug safety, requiring extensive pre-clinical pharmacological and toxicological testing before a drug could be tested in humans (Strom and Kimmel, 2006). In 1963 the Committee on Safety of Drugs was formed in the UK to advise whether new drugs should be submitted for clinical trials, whether drugs should be released for marketing and to study adverse reactions to drugs already in use (Talbot and Waller, 2004).

In 1963, the Sixteenth World Assembly adopted a resolution that reaffirmed the need for rapid dissemination of information on adverse drug reactions, and led to the creation of the WHO Pilot Research Project for International Drug Monitoring in 1968. The purpose of this was to develop an international system for detecting previously unknown or poorly understood adverse effects of medicines (WHO, 2002). In that same year, ten countries which supported the spontaneous reporting of ADRs joined the WHO Research Project for International Drug Monitoring. In 1971, a resolution of the Twentieth World Health Assembly laid down the foundations for the WHO International Drug Monitoring Programme, now known as the WHO Medicines Safety Programme (Grootheest, 2003).

The WHO Medicines Safety Programme is supported and co-ordinated by the WHO Collaborating Centre for International Drug Monitoring, commonly known as the Uppsala Monitoring Centre (UMC), which maintains and implements an international database of adverse drug events (Grootheest, 2003). As of October 2013, 117 countries had joined the WHO Medicines Safety Programme and 28 associate members were awaiting full membership status (WHO, 2013a).

iii. Aims of pharmacovigilance

According to the World Health Organization (WHO, 2002), the specific aims of pharmacovigilance are 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,

• contribute to the assessment of benefit, harm, effectiveness and risk of medicines, encouraging their safe, rational and more effective (including cost-effective) use, and

• promote understanding, education and clinical training in pharmacovigilance and its effective communication to the public.

Pharmacovigilance systems safeguard the public through efficient and timely identification, collection, and assessment of medicine-related adverse events and by communicating risks and benefits to support decision making about medicines at various levels of the health care system (Strengthening Pharmaceutical Systems Program, 2011).

iv. Key elements of pharmacovigilance

According to the WHO (WHO, 2004), the key elements of pharmacovigilance in national drug policy are:

• Establishment of national pharmacovigilance systems for the reporting of adverse events, including national and, if appropriate, regional pharmacovigilance centres.

• Development of legislation or regulation for medicine monitoring.

• Development of national policies which includes costing, budgeting and financing.

• Continuing education of health-care providers on safe and effective pharmacotherapy.

• Provision of up-to-date information on adverse reactions to professionals and consumers and

• Monitoring the impact of pharmacovigilance through process indicators and outcome.

v. Consequences of ineffective pharmacovigilance systems

The consequences of weak or absent pharmacovigilance systems include the proliferation of counterfeit medicines which results in significant morbidity and mortality, the occurrence of preventable ADRs, an increase in the cost of healthcare due to adverse drug events, increase in the inappropriate use of medicines, development of resistance to medication, treatment failures necessitating the switch to more expensive medicines and ultimately loss of confidence in the healthcare system (Strengthening Pharmaceutical Systems Program, 2011)

vi. Pharmacovigilance in the developed countries

In the United States of America (US), the FDA is responsible for ensuring safety of all marketed medicinal products. The FDA relies on healthcare professionals and patients to submit voluntary reports and the pharmaceutical manufacturers to submit mandatory reports on adverse drug reactions. Unlike other countries where the adverse drug reaction reports are sent to a national regulatory authority, in the US most healthcare professionals and consumers report to the manufacturer rather than to the FDA (Strom and Kimmel, 2006). In the United Kingdom (UK), the Medicines and Healthcare products Regulatory Agency (MHRA) is responsible for safeguarding public health by ensuring that medicines, healthcare products and medical equipment in the UK market meet appropriate standards of safety, quality, performance and effectiveness, and are used safely. The spontaneous adverse drug reaction scheme in the UK is commonly known as the Yellow Card reporting scheme and is the cornerstone of the adverse drug reaction monitoring system. In the European Union (EU), pharmacovigilance activities are regulated by the corresponding national regulatory authority of each member state. In some member states spontaneous reporting of adverse drug reactions

is mandatory for example France, Austria and Denmark (Mann and Andrews, 2007). An assessment of the EU system of pharmacovigilance showed that in 2004, reporting rates ranged from 23 to 459 reports per million population with the highest reporting rates recorded in Sweden, Ireland, Norway, Denmark, the UK, France, and the Netherlands (European Commission, 2006).

vii. Pharmacovigilance in sub-Saharan Africa

In sub-Saharan Africa (SSA) as of December 2013, out of a total of 46 countries, 23 countries were official member states to the WHO Medicines Safety Programme, 10 were associate members while 13 were non-members. National policies related to pharmacovigilance or medicine safety existed in 19 countries (41 percent). At least 34 countries (74 percent) had a PV centre or unit with a clear mandate and formal organizational structure. All PV centres had ADR reporting forms. However, not all spontaneous reporting systems in countries addressed the full scope of PV, including product quality, medication errors, and treatment failures that could be reported by using the existing ADR form or a separate form. Although 23 countries in SSA were official members of the WHO Medicines Safety Programme with the capacity to collect ADR reports, most of the countries had weak ADR reporting practices (Strengthening Pharmaceutical Systems Program, 2011).

viii. Pharmacovigilance in Kenya

The Department of Pharmacovigilance was set up in 2004 at the Pharmacy and Poisons Board (PPB) with a vision to develop, implement and continuously upgrade an appropriate system for detecting, reporting and monitoring adverse drug reactions (ADRs) and other relevant

problems with medicines in Kenya. The Pharmacovigilance Program was launched in 2007 to monitor both the safety and quality of medicines through voluntary reporting (MoMS and MoPHS, 2009). In 2010, Kenya became the 98th member of the WHO Medicines Safety Programme (PPB, 2010).

The current reporting system involves the use of a Poor Quality Drug Reporting Form ("pink form") to report poor quality medicines and the Suspected Adverse Drug Reaction Notification Form ("yellow form") to report suspected adverse reactions to medicines (MoMS and MoPHS, 2009).

Since 2004, the milestones that have been attained in the national PV system include the development of the national PV guidelines, the establishment of the reporting systems and tools, training of health workers on PV, the development of information and education materials on PV, development of a national strategy on post-marketing surveillance of medicines, regular sending out of safety alerts, and the establishment of the Expert Safety Review Panel which reviews all PV-related reports in order to carry out the necessary follow-up interventions. The weaknesses identified include the lack of a national PV policy, limited capacity to generate signals and manage PV data, a limited scope of PV and the presence of counterfeit medicines (PPB, 2010; Strengthening Pharmaceutical Systems Program, 2011).

The reporting rates for adverse drug reactions remain low despite training of health workers in PV and availing the reporting tools in health care facilities. In 2010, the PPB received 15 reports per million residents (Strengthening Pharmaceutical Systems Program, 2011), which is considerably lower than the WHO-recommended reporting rate of greater than 200 reports per million residents per year (Olsson, 1997).

1.2.2 Adverse drug reactions and adverse drug events

i. Definitions

According to the WHO (WHO, 1972), 'an adverse reaction to a drug is one that is noxious, is unintended and occurs at doses normally used in man.' Edwards and Aronson argue that this definition is inadequate because it precludes minor adverse reactions and error as a source of adverse reactions. They define an adverse drug reaction 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' (Edwards and Aronson, 2000).

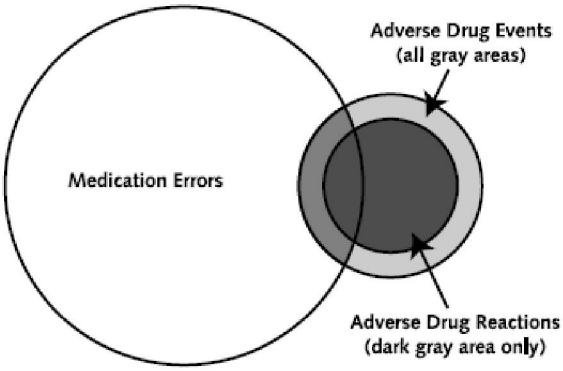
An adverse drug event is an adverse outcome that occurs while a patient is taking a drug, but is not necessarily attributable to it. Therefore, adverse drug events include harm caused by the use of a drug (adverse drug reaction) as well as harm from the use of a drug (Edwards and Aronson, 2000; Nebeker et al., 2004). It may or may not have a causal relation with the drug administered. Adverse events are both preventable and unpreventable. About a quarter of the adverse drug events are due to medication errors (Bates et al., 1995b).

A medication error is defined as "any preventable event that may cause or lead to inappropriate medication use or patient harm while medication is in the control of the health care professional, patient, or consumer" (National Coordinating Council for Medication Error Reporting and Prevention, 2013). Medication errors are more common than adverse events, but they result in harm less than 1% of the time (Bates et al., 1995a). An example of a

medication error is giving a higher or lower dose than required or giving the wrong medicine. ADRs refer to harm caused by a drug at normal doses and it refers to an adverse event with a causal link to a drug (Nebeker et al., 2004).

The relationship of these key terms is represented by Figure 1.1.

Figure 1.1: Relationship between medication errors, adverse drug events and adverse drug reactions



Source: (Nebeker et al., 2004)

From the figure it can be seen that most medication errors do not result in harm to the patient. A few medication errors will cause the patient to experience harm and in this case it will be referred to as an adverse drug event. Some adverse drug events are not caused by medication errors; that is a patient takes a drug correctly but still experiences harm which shows that some adverse drug events cannot be prevented. If a causal link can be established between the drug and the adverse drug event then it is known as an adverse drug reaction.

ii. Classification of adverse drug reactions

Adverse drug reactions were traditionally classified into two main categories: type A reactions and type B reactions. Type A reactions are common, predictable reactions which are dose-dependent and are rarely fatal. They account for the majority of the adverse drug reactions. Type B reactions are normally unpredictable, bizarre reactions to a drug which are independent of the dose and involve relatively high rates of serious morbidity and mortality (Mann and Andrews, 2007; Talbot and Waller, 2004). The classification of adverse drug reactions was expanded into six categories by as shown in Table 1.

Table 1.1 Classification of adverse drug reactions

Type of Reaction	Mnemonic	Features	Examples	Management
A: Dose-related	Augmented	• Common • Related to the pharmacological action of the drug • Predictable • Low Mortality	• Toxic effects: Digoxin toxicity • Side effects Anticholinergic effects of tricyclic antidepressants	Reduce dose or withhold. Consider effects of concomitant therapy.
B: Non dose-related	Bizarre	• Uncommon • Not related to the pharmacological action of the drug • Unpredictable • High Mortality	• Immunological reactions Penicillin hypersensitivity • Idiosyncratic reactions Acute porphyria Pseudoallergy	Withdraw and avoid in future.
C: Dose related and time related	Chronic	• Uncommon • Related to the cumulative dose	Hypothalamus-pituitary-adrenal axis suppression by corticosteroids	Reduce dose or withhold, Withdrawal may have to be prolonged

Type of Reaction	Mnemonic	Features	Examples	Management
D: Time related	Delayed	• Uncommon • Usually dose related • Occurs some time after the use of the drug	• Teratogenesis • Carcinogenesis • Tardive dyskinesia	Often intractable
E: Withdrawal	End of Use	• Uncommon • Occurs soon after withdrawal of the drug	• Opiate withdrawal syndrome • Myocardial ischemia (β blocker withdrawal)	Reintroduce and withdraw slowly
F: Unexpected failure of therapy	Failure	• Common • Dose related • Often caused by drug interactions	Inadequate dosage of an oral contraceptive when used with enzyme inducers	Increase dosage. Consider effects of concomitant therapy

Source: (Edwards and Aronson, 2000)

iii. Management of adverse drug reactions

The management of adverse drug reaction depends on the type of ADR experienced and the severity. Type A reactions generally respond to a reduction in the dose of the drug. Temporary discontinuation of treatment may be necessary if the reaction is severe (Talbot and Waller, 2004). Severe reactions for example those causing anaphylaxis call for the withdrawal of the drug and substitution for another drug. If the drug causing the ADR is essential and substitution is not possible then symptomatic relief is offered for the ADR for example the nausea and vomiting caused by anti cancer drugs is managed using antiemetic drugs (Edwards and Aronson, 2000).

iv. Incidence of adverse drug reactions

Several studies have been carried out to determine the incidence of adverse drug reactions (Abdissa et al., 2012; Acheampong et al., 2012; Aranaz-Andrés et al., 2012; Ma et al., 2012; Obreli-Neto et al., 2012; Ruiter et al., 2012; Shepherd et al., 2012; Tangiisuran et al., 2012). The incidence varied from 0.8 -19.8%. The common findings in these studies was that ADRs were largely preventable (Obreli-Neto et al., 2012; Tangiisuran et al., 2012) and that elderly patients are more at risk of suffering from ADRs (Ruiter et al., 2012; Shepherd et al., 2012; Tangiisuran et al., 2012). A study done at the Kenyatta National Hospital (KNH) revealed that there was a high incidence (48.6%) of adverse drug reactions among the sampled patients on antiretroviral treatment attending the comprehensive care clinic (Mwangangi et al., 2009).

v. Impact of adverse drug reactions on the health system

Adverse drug reactions, medication errors and poor quality medicines have a huge impact on the healthcare system (Strengthening Pharmaceutical Systems Program, 2011). A meta analysis of prospective studies estimated that ADRs represent the fourth to sixth largest causes of death among hospitalized patients in the US (Lazarou et al., 1998). In the US, the cost of drug related morbidity and mortality was estimated to exceed US dollars (USD) 177 billion in 2000 (Ernst and Grizzle, 2001). In the EU, it is estimated that 197,000 deaths per year are caused by ADRs and that the total cost of ADRs to society is 79 billion Euros (European Commission, 2008). A prospective analysis of inpatients in two general hospitals in England revealed that the prevalence of hospital admissions related to an ADR was 6.5% with a projected annual cost of 706 million Euros and an overall fatality of 0.15% (Pirmohamed et

al., 2004). In addition to the direct costs, ADRs also create indirect costs for example the loss of productivity (Goettler et al., 1997).

Several studies have shown the impact of ADRs in Africa (Abdissa et al., 2012; Jaquet et al., 2011; Mehta et al., 2008; Oshikoya et al., 2011). Between 4.5 and 8.4 percent of all hospital admissions were related to ADRs, 1.5–6.3 percent of patients were admitted as a direct result of ADRs; and 6.3–49.5 percent of all hospitalized patients developed ADRs (Strengthening Pharmaceutical Systems Program, 2011).

vi. Monitoring of adverse drug reactions

Monitoring adverse drug reactions is an essential component of ensuring safety of medicines. Before a new drug is released in the market, ADRs are monitored during drug clinical trials. Once the drug has received approval and is released to the market, ADRs can be monitored by using either spontaneous reporting systems or prescription event monitoring. Spontaneous reporting systems are the most commonly used method to monitor adverse reactions, however the major limitation of this method is that ADRs are under-reported (Talbot and Waller, 2004).

1.2.3 Reporting of adverse drug reactions

Reporting of adverse drug reactions is done by health workers, manufacturers of the drug products or by the public. In most countries, health workers are the main source of submitted ADR reports. Spontaneous reporting of ADRs is the most commonly used method of reporting (Herxheimer et al., 2010; Strom and Kimmel, 2006).

i. Adverse drug reaction reporting schemes

Reporting of ADRs can be carried out in two different ways. The first is medical literature whereby many journals publish case reports of patients who have experienced possible ADRs and the second are national pharmacovigilance systems whereby case reports of suspected ADRs are collected by national pharmacovigilance centres mainly through spontaneous reporting systems. Most of the national pharmacovigilance systems are centralized, with voluntary reporting of ADRs done by the health practitioners and/or by patients. Reporting requirements differ depending on the country, however in general most countries require that all suspected ADRs to newly marketed products should be reported (Strom and Kimmel, 2006).

ii. Spontaneous reporting of adverse drug reactions

Spontaneous reporting of adverse drug reactions refers to a system whereby case reports of adverse drug events are voluntarily submitted from health professionals, pharmaceutical manufacturers and the public to the national medicines regulatory authority (MoMS and MoPHS, 2009; Strom and Kimmel, 2006). Healthcare professionals, pharmaceutical manufacturers and the public are provided with forms through which they can notify the national regulatory authority on suspected adverse drug reactions that they detect. Once the reports are received at the national medicines regulatory agency, they are analyzed for possible causality (Mann and Andrews, 2007).

Pre-marketing clinical trials of drugs typically use very small populations of patients, the patients have shorter duration of exposure to the drug and they often exclude patients with co-

morbidities, concomitant medications and special populations such as the elderly, pregnant women and children therefore ADR information obtained from these trials may not be generalized to the general population. Spontaneous reporting systems are therefore a useful method for detecting ADRs in the general population.

The strengths of spontaneous reporting systems are: the method is inexpensive and simple to operate, it covers all drugs during their whole life cycle, it covers the whole patient population including special subgroups such as the elderly, it does not interfere with prescribing habits, it can be used for follow-up studies of patients with severe ADRs to study mechanisms of ADR causation and it can be used to generate hypotheses regarding causation between a drug and an ADR.

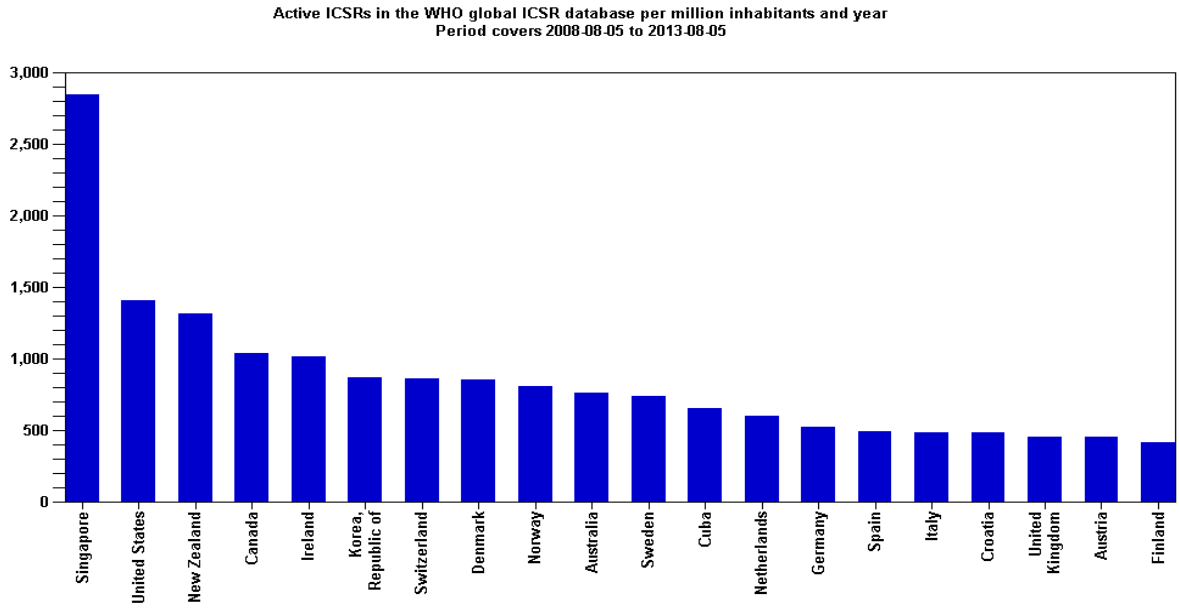
The limitations of spontaneous reporting include limited clinical information to permit a thorough case evaluation, under-reporting which decreases sensitivity and makes the systems sensitive to selective reporting, the reporting rate is rarely stable over time since reporting rates tend to be higher the first few years a drug is released and it does not provide direct information on incidence of ADRs. (Strom and Kimmel, 2006) Spontaneous reporting systems do not provide information on incidence of ADRs because the exposure to the drug (denominator) is usually unknown and there is bias in spontaneous reporting (the numerator). Reporting biases are usually present for drugs that are: in the first few years of marketing, that are vigorously marketed by sales team, used in a population with a high background risk and those that are subject to publicity (Sachs and Bortnichak, 1986).

iii. Trends of ADR reporting

The national pharmacovigilance centre in each member country is responsible for sending individual case safety reports (ICSRs) to the Uppsala Monitoring Centre. ICSRs should ideally be sent once every month, however if this is not possible they should be sent at least once every quarter (WHO, 2013a).

The countries with the highest reporting rates after adjusting for population are shown in Figure 1.2.

Figure 1.2 Graph showing countries with the highest ADR reporting rates

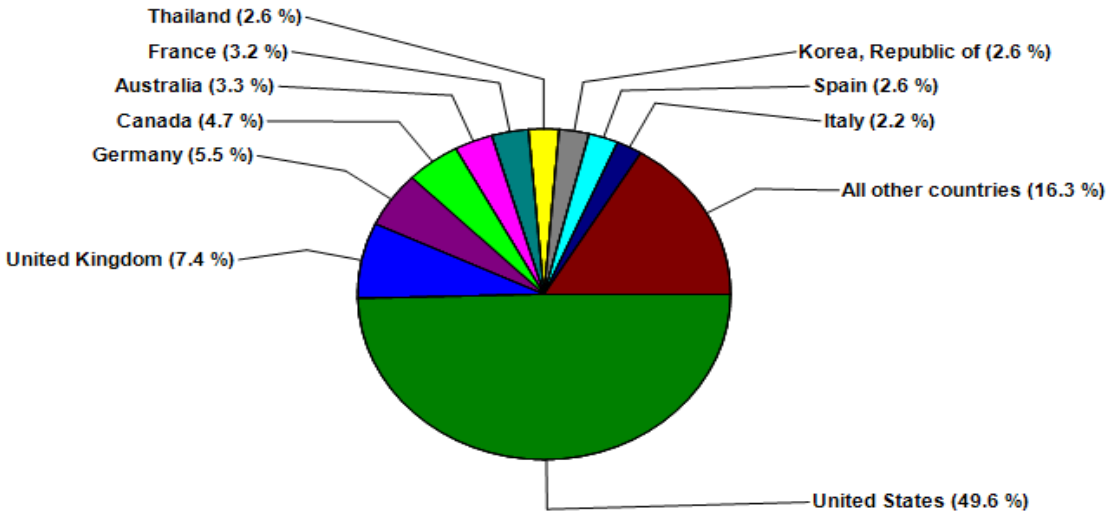


Source: (WHO, 2013b)

The WHO ICSR database has grown since its inception in 1968 and had a cumulative total of 7.6 million reports as at September 2012. The US accounts for approximately half of these

reports and other countries account for the rest of the reports as shown in Figure 2.2 (WHO, 2013a).

Figure 1.3 Distribution of ICSR reports in the WHO database



Source: (WHO, 2013b)

Most countries in sub-Saharan Africa have weak ADR reporting practices. Only 2 countries, Namibia and Burkina Faso submitted more than 100 reports per million population in the year 2010. In 2010, most African countries submitted between 1 and 20 reports per million population (Strengthening Pharmaceutical Systems Program, 2011). This represents a low reporting rate compared to 65% of other low- and middle-income countries which submitted more than 100 reports per million population (Olsson et al., 2010).

CHAPTER 2 LITERATURE REVIEW

Studies have shown that there are several factors that affect spontaneous reporting of adverse drug reactions.

2.1 Factors that affect adverse drug reaction reporting.

Factors that affect ADR reporting can broadly be classified into contextual factors, distal factors and proximate factors.

2.1.1 Contextual factors that affect adverse drug reaction reporting

Contextual factors that affect the reporting of ADRs include the country being studied, country regulatory framework on ADR reporting, media publicity surrounding a particular adverse drug reaction, religion and the year of reporting.

i. Country of reporting

Adverse drug reaction reporting varies across different countries. A study that was done among 9 EU member states showed that the reporting rates and patterns differ between member states (Belton, 1997). A multi-national survey of ADR reporting in clinical trials showed that higher reporting rates of more than 50% were found in countries such as Canada, Sweden, UK and Australia. Denmark, Hong Kong, Netherlands, Norway, France and Finland had reporting rates of 35-45%. The lowest reporting rates of less than 30% were found in Germany, Belgium and Italy.

A survey of ADR reporting in sub-Saharan Africa showed that in 2010, the highest reporting rates were found in Namibia and Burkina Faso (135 and 131 reports per million population respectively). Senegal, Madagascar, Zambia, Kenya, Ghana, Mali, Botswana and Nigeria had ADR reporting rates ranging from 10-34 reports per million population. Countries with the lowest reporting rates were Malawi, Democratic Republic of Congo, Ethiopia, Mozambique, Guinea, Tanzania, Zimbabwe and Uganda which had reporting rates ranging from 1-6 reports per million population and Angola, Benin, Burundi, Côte d' Ivoire, Rwanda and Sudan which did not submit any ADR reports and therefore had a reporting rate of 0 per million population (Strengthening Pharmaceutical Systems Program, 2011).

ii. Country policy, law and regulatory framework

In order for a system that monitors adverse drug events to be effective, an appropriate regulatory framework should exist (Ratanawijitrasin and Wondemagegnehu, 2002). The existence of laws and regulations provide a firm legal basis to ensure that stakeholders comply with the practice of ensuring the safety of medicines. Lack of relevant policy and regulations on pharmacovigilance makes it difficult to enforce the monitoring of safety of medicines which includes the reporting of ADRs (Strengthening Pharmaceutical Systems Program, 2011). In countries such as Sweden and Australia, reporting of ADRs is mandated by law. These countries have higher reporting rates than those in which reporting is not obligatory by law for example Germany (European Commission, 2006).

iii. The year of reporting

ADR reports for a particular drug vary throughout the life cycle of the drug. It has been noted that ADR reports for a drug increase during the first few years of marketing and then decrease gradually thereafter. Weber plotted the mean number of ADR reports for seven non-steroidal anti-inflammatory drugs during the first five years of marketing and noted that the reports peaked at 2 years and then declined rapidly. This is known as the Weber effect (Weber, 1984). The Weber effect has applied to various classes of drugs such as anti-infective, cardiovascular, endocrine and pulmonary drugs (Brodovicz et al., 2001). A survey of 10 drugs in the French market showed that the ADR reports peaked at 1 year and then decreased (Haramburu et al., 1997).

iv. Media publicity

Media publicity surrounding an adverse drug reaction was found in several studies to lead to an increase in reporting. Following the publicity surrounding the neuropsychiatric effects of mefloquine in the UK, the reporting increased six-fold (Bhasin et al., 1997). In the UK, media publicity was associated with marked, short-term peaks in reporting of ADRs suspected to have been caused by paroxetine (Martin et al., 2006). In the US, there was an exponential increase in the number of adverse reports associated with silicone gel breast implants submitted to the FDA following publicity on the lack of safety data on breast implants (Brown et al., 1998).

v. Religion of the area

One study found that countries that had a predominantly Catholic population reported ADRs less than countries that had a predominantly Protestant population. It is thought that this was because of greater literacy among Protestants due to increased study of the Bible (Dukes and Lund, 1979).

2.1.2 Distal factors that affect adverse drug reaction reporting

The distal factors that affect ADR reporting are related to health worker, the health systems, the patient and the severity of the adverse drug reaction.

i. Health worker factors

Health worker factors that affect reporting of ADRs include sex, age, years of practice, specialty and the location of practice of the health worker. It is expected that the health workers' age and years of practice are correlated because the older the health worker, the more the years of practice.

Studies have found opposing results with regards to the association between age of the health worker and reporting of ADRs. A number of studies (Tubert-Bitter et al. 1998; Generali et al. 1995) found that health workers who reported ADRs were younger than the non-reporters whereas other studies (Bateman et al., 1992; Cosentino et al., 1999; Irujo et al., 2007) showed that health workers who reported ADRs were older and had more years of practice than non-reporters. One study (Lee et al., 1994) found that there was no relationship between ADR reporting and the duration of practice of the health workers.

A number of studies determined the effect of the health workers' speciality on reporting of ADRs. There was increasing tendency to report ADRs with increasing seniority of the health workers (McGettigan et al., 1997; Sweis and Wong, 2000). Overall, health workers in medical specialities tended to report more than those in surgical specialities (Bateman et al., 1992; Cosentino et al., 1999; Eland et al., 1999; Herdeiro et al., 2005) General practitioners (GPs) submitted more ADR reports compared to doctors working in hospitals and specialists (Belton et al., 1995; Eland et al., 1999). A study carried out in the UK showed that physicians who got speciality through a regulated residence of at least three years in a National Hospital Service (NHS) centre were 2 times more likely to report ADRs than those who did not (Figueiras et al., 1999) Majority of the studies did not show a significant difference in reporting between male and female health workers except one (Figueiras et al., 1999) where the probability of reporting was more than double for male physicians compared to female physicians. Therefore it appears sex of the health worker is not a major determinant of reporting of ADRs.

ii. Health systems factors

Health systems factors that affect the reporting of ADRs include the availability of reporting tools, training of health workers, feedback from the national medicines regulatory authority on adverse drug reactions reported previously and the workload of health workers. Unavailability of reporting tools was found to be a major deterrent to reporting of ADRs (Belton et al., 1995; McGettigan and Feely, 1995; Vallano et al., 2005). Health workers cited lack of feedback from the medicines regulatory authority on previous reports sent as a reason for not sending reports subsequently (Bhatia et al., 2005; Vallano et al., 2005). Training health workers on adverse drug reaction reporting had a positive influence on reporting. There was an increased

tendency to report ADRs if the health worker received training (Green et al., 2001; Sweis and Wong, 2000). Education and training were found to be positive predictors in influencing pharmacists to report ADRs (Green et al., 2001).

Majority of studies have found that there is an association between the health workers' workload and reporting of ADRs with the exception of one (Lee et al., 1994). In several studies, it was found that an increase in workload reduces ADR reporting by health workers (Bateman et al., 1992; Belton et al., 1995; Figueiras et al., 1999; Sweis and Wong, 2000; Vallano et al., 2005). High workload was as a result of writing more prescriptions in the case of general practitioners, spending more time in clinical practice in the case of consultants or other clinical priorities. High workload led to lack of time to report ADRs.

iii. Patient factors

The willingness of patients to discuss ADRs with their health provider affects the reporting of ADRs. In one study (Klein et al., 1984) it was found that 25% of outpatients do not discuss ADR symptoms with their providers. In another study, it was discovered that 42.9% of patients would not consult their GP for serious ADR caused either by conventional medicine or herbal products (Barnes et al., 1998). If a patient does not discuss an ADR with the health worker, then the health worker will not know that the patient experienced the ADR and therefore will not be able to report it.

iv. Severity of the adverse drug reaction

The severity or unusualness of an ADR was stated as an important factor that contributed to health workers reporting an ADR (Belton et al., 1995; Eland et al., 1999; McGettigan et al.,

1997; Williams and Feely, 1999) . Serious or unusual ADRs were more likely to be reported whereas ADRs that were regarded as trivial were not reported.

2.1.3 Proximate factors that affect adverse drug reaction reporting

Proximate factors that affect adverse drug reaction reporting include the knowledge, attitudes and practices of health workers on adverse drug reaction reporting. They are considered proximate factors because all the other factors ultimately affect the knowledge, the attitudes or the practices of the health worker which determine whether or not the health workers report ADRs.

Numerous studies have been carried out to determine the knowledge, attitudes and practices of health workers on adverse drug reaction reporting. Majority of the studies done have been carried out in Europe (UK, Portugal, Spain, Norway, Netherlands, Germany), with few carried out in Asia (India, Thailand and Malaysia), North America (US) and the Middle East (Iran). Sub-Saharan African countries in which studies of this type have been carried out so far include Nigeria and South Sudan. The studies vary with reference to the study population (physicians, medical practitioners and pharmacists), the sample size chosen (7 to 1500), the year in which the study was carried out (1987 to 2013) and the study design (case control studies, cross sectional questionnaire surveys and qualitative studies).

The findings from the studies differ with respect to knowledge and attitudes of the health workers to adverse drug reaction reporting. However, there appears to be consistency across the studies regarding the reasons why health workers do not report ADRs and these include uncertainty that the drug caused the ADR, lack of knowledge about where to report and lack

of time to report ADRs. In general, more favourable attitudes towards ADR reporting were associated with either an intention to report ADRs (compared with non-intention to report) or higher probability of reporting an ADR.

i. Knowledge of health workers on adverse drug reaction reporting

The studies that investigated the knowledge of adverse drug reaction reporting systems investigated four main knowledge areas: the definitions of pharmacovigilance and adverse drug reactions, the awareness of the existence of the adverse drug reaction scheme, the knowledge about the information that should be reported to the ADR reporting scheme and the purposes of the ADR reporting scheme.

a. Knowledge of definitions of pharmacovigilance and adverse drug reactions

A number of studies asked the health workers to correctly define pharmacovigilance or adverse drug reaction. Three of the studies used open-ended questions (Chopra et al., 2011; Oreagba et al., 2011; Toklu and Uysal, 2008), while in one study the questions were multiple choice (Su et al., 2010).

In the studies that used open-ended questions to correctly define pharmacovigilance or adverse drug reactions, smaller proportions of the health workers sampled could actually or conceptually define pharmacovigilance correctly according to the WHO definition (WHO, 2002). In one study 17% and 26% of the health workers could correctly define pharmacovigilance and an ADR respectively (Toklu and Uysal, 2008). In a study carried out in India 38% of the health workers could correctly define pharmacovigilance, 66% could correctly define an ADR and 40% could correctly define a serious ADR (Chopra et al., 2011).

In the study that used multiple-choice question to define ADR, 69.5% of the health workers could correctly identify the definition of an ADR. This higher percentage obtained in the multiple-choice question compared with the results obtained from the open-ended studies is partially explained by the fact that recalling an answer is usually harder than recognizing it (Schuwirth et al., 1996).

From these studies it can be seen that knowledge of the definition of pharmacovigilance is relatively low, however, it has been argued that not knowing the definition of pharmacovigilance does not necessarily mean that the health workers' knowledge on pharmacovigilance is inadequate and that questions about what an adverse event is, what an ADR is, how to determine ADRs, which ADRs should be reported, where ADRs should be reported to and knowledge of the existence of the national pharmacovigilance centres are more pertinent to ascertaining the knowledge of health workers about pharmacovigilance (Adefurin, 2011).

b. Awareness on the existence of adverse drug reaction reporting schemes

Majority of the studies that assessed the knowledge of health workers on ADR reporting schemes assessed whether the workers knew about the existence of an ADR reporting scheme in their country and its functions, where to get the reporting tools and the procedure for reporting. In studies that investigated the awareness of the existence of a national ADR reporting scheme, the proportion of health workers who were aware of the existence of the scheme ranged from as low as 12% in one study (Pérez García and Figueras, 2011) to as high as 99.6% in another (Passier et al., 2009). In majority of the studies more than half of the respondents were aware of the existence of the national pharmacovigilance centre which is

responsible for collecting ADR reports (Chopra et al., 2011; Green et al., 2001; Hasford et al., 2002; Jarernsiripornkul et al., 2009; Passier et al., 2009; Ting et al., 2010; Vessal et al., 2009). A study carried out in Venezuela showed that only 12% of physicians and 20.5% of the pharmacists knew about the existence of the national ADR reporting scheme, and 2.1% of the physicians and 1.3% of the pharmacists knew where to get the ADR reporting tools (Pérez García and Figueras, 2011).

In studies that were determining the correct procedure for reporting ADRs, majority of the health workers knew the correct procedure for reporting ADRs. In a study carried out in China, 78% of the health workers knew the correct procedure for reporting ADRs (Su et al., 2010); similarly the correct procedure for reporting ADRs was identified by 70% of health workers in two studies in Germany and Italy (Cosentino et al., 1997; Hasford et al., 2002) and 97% of health workers in a study that was carried out in Netherlands (Passier et al., 2009). In a Venezuelan study, only 20% of the participants were aware of the correct procedure for reporting ADRs (Pérez García and Figueras, 2011). In a study carried out in the UK, 97% of pharmacists were aware that they could participate in the Yellow Card Scheme (Green et al., 2001).

c. Knowledge about the kind of information that should be reported to the ADR reporting scheme

A number of studies investigated whether health workers have adequate knowledge regarding the kind of information that should be reported to the national pharmacovigilance centres. In a study done on pharmacists in the UK, 97.7% of pharmacists were aware that all adverse reactions for newly marketed agents should be reported, 91.4% were aware that all serious

reactions for established products should be reported and 94% knew that the Committee of Safety of Medicines did not only want reports of only proven ADRs but those where the causality between the drug and the ADR remained unknown. However, smaller numbers of pharmacists knew that all reactions should be reported for vaccines (56.3%) and herbal medicines (36.2%) (Green et al., 2001). A study carried out in India showed that 74.4% of doctors knew that they should report adverse reactions to a new drug. However, only 15% and 10.6% knew that they should report serious reactions and unusual reactions respectively (Chopra et al., 2011).

A study done to compare the knowledge and attitudes of different cadres of doctors (consultants, general practitioners and junior doctors) in high and low reporting areas in northern region in the UK revealed that more than 80% of the doctors knew that all serious ADRs should be reported regardless of whether they were caused by new drugs or well established drugs, all suspected ADRs should be reported for new drugs and any teratogenic adverse effect should be reported. However, fewer doctors (69%) had the correct knowledge about reporting any suspected ADR to a vaccine. A larger proportion (68%) of the doctors believed that all suspected ADRs to well-established drugs should be reported although this was incorrect because according to the UK guidelines, only serious suspected ADRs to well established medicines should be reported (Bateman et al., 1992).

d. Knowledge about the purposes of the ADR reporting scheme

A number of studies investigated whether the health worker had knowledge about the purposes of the ADR reporting scheme (Bateman et al., 1992; Pérez García and Figueras, 2011; Vessal et al., 2009). A study carried out on pharmacists in Iran revealed that knowledge

on the purposes of the ADR reporting scheme was low. Less than half of the pharmacists could correctly identify these purposes of the ADR reporting scheme: to identify factors which may predispose to ADR, to compare ADRs for drugs in similar therapeutic classes and to compare ADRs from the same drug from different manufacturers. Approximately half (49%) of the pharmacists erroneously thought that one of the purposes of the ADR reporting scheme was to enable safe drugs to be identified (Vessal et al., 2009).

A similar study carried out in the UK showed that the knowledge of the purposes of the ADR reporting scheme was high, whereby more than half of the doctors surveyed could correctly identify the purposes of the ADR reporting scheme such as identification of bizarre reactions to drugs and previously unrecognized reactions to drugs and the identification of factors which may predispose to toxicity. However, majority of the doctors erroneously believed that the purposes of the ADR reporting scheme was to enable safe identification of drugs (Bateman et al., 1992).

A study in Venezuela that identified lack of knowledge as a major cause of under-reporting of ADRs showed that less than a quarter of the pharmacists and physicians surveyed could correctly identify pharmacovigilance as associated with the surveillance of ADRs (Pérez García and Figueras, 2011).

ii. Attitudes of health workers to adverse drug reaction reporting

Studies that examined the health workers' attitudes on adverse drug reaction reporting surveyed three broad areas: the health workers' opinions on ADR reporting, the factors and

attitudes that affect ADR reporting (factors that either encourage or hinder ADR reporting) and the health workers' opinions on ways to improve ADR reporting.

a. Health workers' opinions on ADR reporting

In general, health workers' opinions on ADR reporting is positive, with most having the opinion that ADR reporting is a professional obligation (Belton et al., 1995; dos Santos Pernas et al., 2012; Green et al., 2001; Rogers et al., 1988; Su et al., 2010) and that ADR reporting should be compulsory (Green et al., 2001).

b. Factors and attitudes that affect ADR reporting

The studies identify several factors that either encourage or discourage ADR reporting. Health workers are more likely to report ADRs if the reaction is severe (Cosentino et al., 1997; Ekman and Bäckström, 2009; Hasford et al., 2002), unusual (Cosentino et al., 1997; Ekman and Bäckström, 2009) and if the reaction is to a new drug (Cosentino et al., 1997; Ekman and Bäckström, 2009; Hasford et al., 2002). Factors that discourage reporting of ADRs include the reaction being well known (Ekman and Bäckström, 2009), uncertainty about the drug causing the ADR (Gavaza et al., 2010; Hasford et al., 2002; Jarernsiripornkul et al., 2009; Su et al., 2010) and having insufficient clinical knowledge on ADRs (Gavaza et al., 2010; Granas et al., 2007; Oreagba et al., 2011; Su et al., 2010; Toklu and Uysal, 2008).

The factors that discourage ADR reporting are determined by the health workers' attitudes towards ADR reporting. In most of the studies, lack of time was identified as one of the major deterrents to reporting ADRs (Belton et al., 1995; Chopra et al., 2011; Granas et al., 2007; Green et al., 2001; Su et al., 2010). Health workers' perception that there is insufficient time

to report ADRs was described by Inman as lethargy, one of the "seven deadly sins" or attitudes that discourage reporting of ADRs (Inman, 1976).

The attitudes that discourage ADR reporting were proposed by Inman in 1976 and expanded in 1996 (Inman, 1976, 1996). They include:

1. Complacency: the belief that only safe drugs are allowed on to the market.
2. Fear of possible involvement in litigation or investigation of prescribing costs by health departments.
3. Guilt at having administered treatment that may have harmed a patient.
4. Ambition to compile and publish a personal case series.
5. Ignorance of the requirements for reporting.
6. Diffidence at the prospect of appearing ridiculous for reporting merely suspected ADRs.
7. Indifference on the part of an individual doctor to his/her essential role as a clinical researcher who should be contributing to medical knowledge.
8. Lethargy: an amalgam of procrastination, lack of interest or time to find a report card and other excuses.
9. Financial incentives to report.
10. Insecurity: uncertainty about the drug being the cause of the ADR.

A Spanish study that sought to determine the attitudes of physicians to voluntary reporting of ADRs found that the attitudes that were statistically significant include complacency, insecurity, lethargy, the belief that one report does not make a difference to the ADR reporting scheme and the belief that the reporting method was too difficult (Figueiras et al., 2001).

Health workers who had intent to report ADRs had more favourable attitudes towards ADR reporting than those who had no intent to report (Gavaza et al., 2011). Health workers' attitudes have been associated with reporting probability; a decrease in the attitudes complacency, insecurity, diffidence, indifference and ignorance was associated with an increase in reporting probability among physicians in Portugal (Herdeiro et al., 2005).

c. Health workers' opinions on ways to improve adverse drug reaction reporting

The suggested ways to improve ADR reporting include making reporting simpler (Jarernsiripornkul et al., 2009), educating health workers to increase their knowledge of ADR reporting (Green et al., 2001; Hazell and Shakir, 2006; Su et al., 2010), increasing feedback from the pharmacovigilance centres on the reports submitted (Cosentino et al., 1997; Green et al., 2001; Oshikoya and Awobusuyi, 2009), enhancing collaboration with other healthcare professionals (Jarernsiripornkul et al., 2009; Oshikoya and Awobusuyi, 2009), participation in ward rounds (Green et al., 2001; Su et al., 2010) and reminders from the relevant department to submit reports (Green et al., 2001; Oshikoya and Awobusuyi, 2009; Su et al., 2010).

iii. Practices of adverse drug reaction reporting

The studies that looked into the practices of health workers regarding ADR reporting determined whether the health workers had submitted any ADR reports. Other studies determined the practices by presenting health workers using a list of hypothetical ADRs and asking them whether or not they would report the ADRs.

The proportion of health workers who submitted reports to the national pharmacovigilance centre varied across the studies. Adverse drug reactions were reported to the national

pharmacovigilance authority, the pharmaceutical manufacturer or to scientific journals. Health workers encountered more ADRs than they reported (Chatterjee et al., 2006).Generally, more experienced health professionals submitted more reports than the less experienced professionals (Bateman et al., 1992).

The practices of ADR reporting were tested by giving health professionals hypothetical ADRs and asking them whether or not they would report the ADR. The hypothetical ADRs included:

1. Serious ADR for all medicines (both new and established) which should have been reported for example jaundice caused by furosemide, deep vein thrombosis caused by oral contraceptive drugs
2. Any ADRs (both serious and non-serious) for new medicines which should have been reported for example nausea caused by montelukast, headache caused by venlafaxine
3. Non-serious ADRs for established medicines which need not have been reported for example ampicillin-induced rash, cold extremities caused by β adrenoceptor blockers.

More than half of the health workers gave the correct answers regarding the hypothetical ADRs in cases where serious ADRs for both the new and established medicines should be reported and for non-serious ADRs for established medicines need not be reported (Bateman et al., 1992; Green et al., 2001).

However, the use of hypothetical ADRs to assess practices of ADR reporting is not an ideal measure because this method assesses the knowledge of the health worker on ADRs rather than the actual practices of ADR reporting. A more accurate assessment of practices of ADR reporting should be based on past experience for example asking the health workers if they

have ever reported ADRs, the number of times they reported, the types of ADRs they have reported and where they reported the ADRs.

2.2 Knowledge gaps in the determination of provider factors that affect ADR reporting

Many studies have been carried out to determine the factors that affect ADR reporting. The studies that sought to determine the health worker factors that affect ADR reporting examined factors such as age, the specialty of the health worker, their workplace, the health workers' knowledge and attitudes to ADR reporting (Bateman et al., 1992; Cosentino et al., 1999; Figueiras et al., 1999; Herdeiro et al., 2005; McGettigan et al., 1997).

In sub-Saharan Africa, several studies have been carried out to determine the influence of knowledge and attitudes of the health worker to ADR reporting. Most of these studies have been carried out in Nigeria (Fadare et al., 2011; Oreagba et al., 2011; Oshikoya and Awobusuyi, 2009). At the time of carrying out this study, none had been published for similar work in East Africa. The results from the studies done in Nigeria may not be generalised to Kenya because there are key differences between the Nigerian and Kenyan pharmacovigilance programs.

The Nigerian pharmacovigilance system has been in existence since 1993 while the Kenyan system was launched in 2007. As a result, most of the essential components of pharmacovigilance policy and regulations exist in Nigeria but not in Kenya. Components of pharmacovigilance that exist in Nigeria but not in Kenya include the presence of a pharmacovigilance policy, a wider scope of pharmacovigilance which includes the monitoring of ADRs, product quality, medication errors and treatment failure, the use of both active and

passive approaches for pharmacovigilance and well-defined roles and responsibilities for stakeholders .The Nigeria Agency for Food and Drug Administration and Control (NAFDAC) is well staffed and receives regular government budget for operation which is not the case in Kenya (Strengthening Pharmaceutical Systems Program, 2011).

It is therefore possible that ADR reporting by health workers in Nigeria differs significantly from Kenya because the Nigerian pharmacovigilance system is more established compared to that in Kenya. In 2010 the ADR reporting rate in Nigeria (34 reports per million population) was more than double that of Kenya which submitted 15 reports per million population (Strengthening Pharmaceutical Systems Program, 2011). Therefore, research needs to be done in Kenya to determine the factors associated with reporting of ADRs.

Requirements for ADR reporting are not the same across different countries. In countries where ADR reporting is well established such as the US and the UK, health workers are required to report specific categories of ADRs whereas other categories of ADRs are exempt from being reported for example non-serious ADRs to established medicines (Strom and Kimmel, 2006). However in Kenya, the PPB requires health workers to report all suspected ADRs whether the medicine is newly marketed or established and to report even if the health worker has incomplete information regarding the ADR (MoMS and MoPHS, 2009). Due to the differences in ADR reporting guidelines in different countries, it is necessary to carry out a study in Kenya in order to determine the factors affecting reporting in our local setting.

Previous studies that determined the health worker factors associated with reporting of ADRs found conflicting results with respect to certain factors such as age and sex as described in Section 2.1.2. Whereas some studies reported that older health workers were more likely to

report ADRs, others showed the inverse. Whereas some studies showed that sex did not affect reporting of ADRs, others showed that sex was a factor influencing reporting. Due to these differences in the findings, it was necessary to carry out a similar study in Kenya in order to determine the factors that affect ADR reporting.

CHAPTER 3 RESEARCH PROBLEM

3.1 Problem Identification

A major limitation of spontaneous adverse drug reaction reporting systems is that ADRs are under-reported (Talbot and Waller, 2004). Various studies have shown that ADRs are under-reported (Alvarez-Requejo et al., 1998; Conforti et al., 1995; Hallas et al., 1992; Hazell and Shakir, 2006; Hemminki, 1980). In the UK in the four year period between 1992 and 1995, about two-thirds of doctors did not submit an ADR report and it is thought that this is unlikely to be simply because the doctors did not see a patient with an ADR (Mann and Andrews, 2007). It is estimated that under-reporting rates are as high as 94% (Hazell and Shakir, 2006).

Several factors have been suggested as affecting direct reporting of ADRs. They include health worker factors such as the age, duration of practice and specialty (Bateman et al., 1992; Cosentino et al., 1999; Tubert-Bitter et al., 1998); health systems factors such as the availability of reporting tools, training on ADR reporting, feedback from the reporting authority and workload (Belton et al., 1995; McGettigan and Feely, 1995; Vallano et al., 2005); patient factors such as the willingness of the patient to discuss the ADR with the health worker and ADR-related factors such as the seriousness or unusualness of the ADR(Belton et al., 1995; Vallano et al., 2005). Other factors that affect ADR reporting include the length of time the drug has been on the market, the legal implications, the regulations of the country and media publicity surrounding an ADR (Talbot and Waller, 2004).

The true reporting rate of ADRs refers to the number of ADRs reported divided by the number of ADRs that actually occurred. However, it is rare to determine the true reporting rate of an ADR because it is difficult to determine the denominator (number of ADRs that occurred)

because patients often do not tell the healthcare provider of potential ADRs experienced or are unable to distinguish between a potential ADR and the disease symptoms. Therefore, the best estimates of under-reporting are obtained by a study in a sample of the relevant population (Talbot and Waller, 2004).

In Kenya, the PPB received 15 reports per million population in 2010 against the WHO-recommended reporting rate of greater than 200 reports per million population per year (Strengthening Pharmaceutical Systems Program, 2011). Therefore ADRs are significantly under-reported in the country. Core teams from 12 antiretroviral therapy (ART) ADR surveillance sites in Kenya identified lack of awareness at lower cadres, increased workload and limited time to report ADRs as major challenges that were facing the reporting of ADRs (Pharmacy and Poisons Board, 2012).

3.2 Problem analysis

In most countries, the majority of ADR reports are submitted to the national medicines regulatory agency by healthcare providers (Herxheimer et al., 2010). In the US, approximately 70-75% of reports arise from healthcare professionals while the public reports comprise about 15% of the reports submitted (Strom and Kimmel, 2006). In the Netherlands, during a 3 year period from April 2004-April 2007, health worker reports constituted approximately 81% of the reports sent to the National Pharmacovigilance Centre, while the rest were submitted by the patients (de Langen et al., 2008). In Denmark, in 2008, healthcare providers submitted 80% of the reports while patients and their carers submitted 20% of the reports (Herxheimer et al., 2010). In Kenya, most of the ADR reports are submitted by health

workers. Patients can submit ADR reports directly to the PPB but the quality of patient reports has not yet been evaluated (Strengthening Pharmaceutical Systems Program, 2011).

Spontaneous reporting of ADRs in Kenya involves three key players: the patient who consumes the drug, experiences the adverse drug reaction and notifies the health worker; the health worker who is responsible for identifying the ADR and filling in the report, and the PPB which is responsible for collecting and analyzing the reports as well as providing reporting tools and supporting resources. The health worker is an important component of ADR reporting because he is the link between the patient and the PPB. The health worker is responsible for educating the patient on the possible adverse effects that he could experience, and is supposed to encourage the patient to report the ADR. If the patient experiences the ADR and reports it to the health worker, the health worker is responsible for identifying the potential adverse drug reaction and reporting it to the PPB.

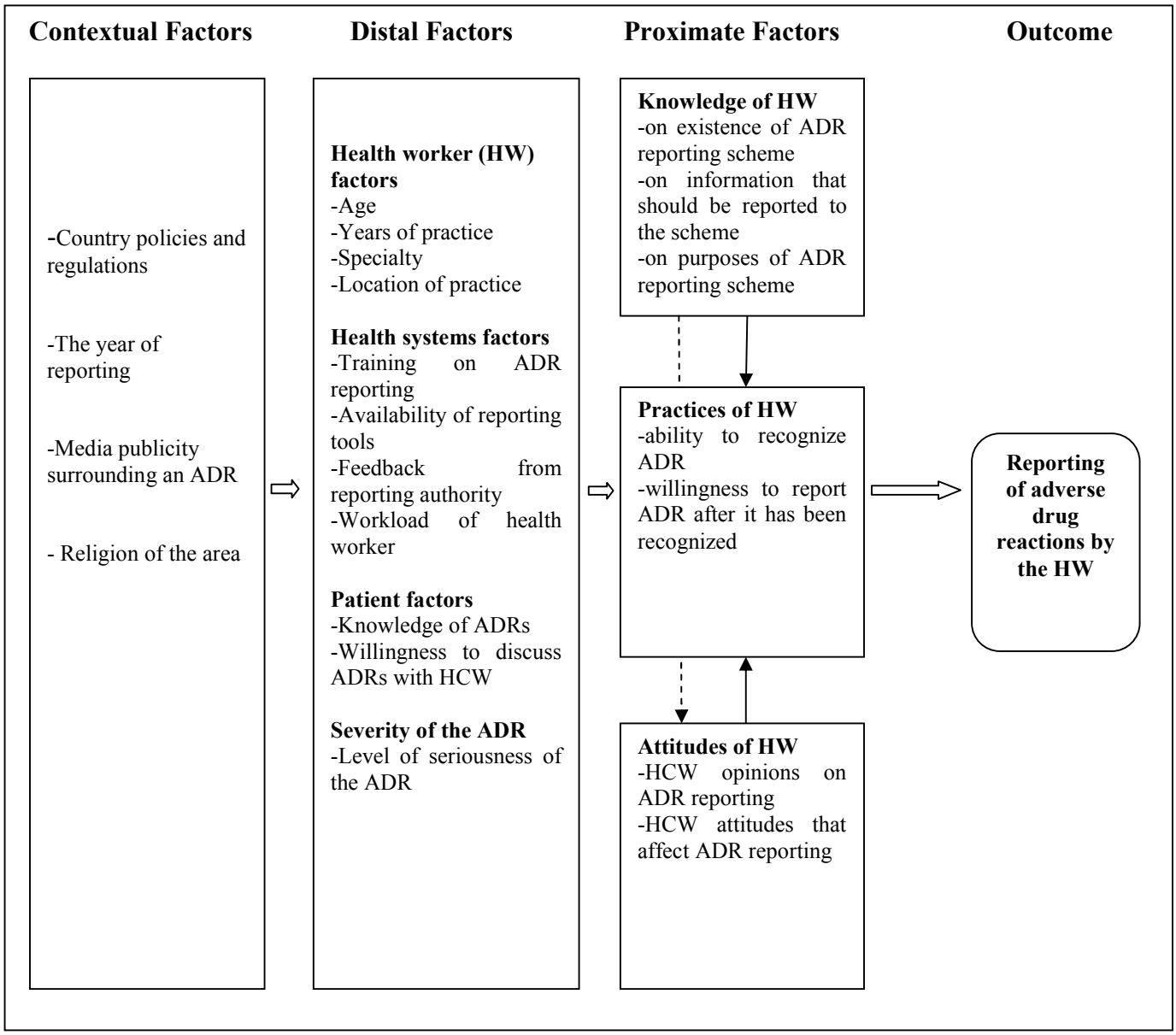
Under-reporting of ADRs may occur if a patient who experiences the ADR does not report it to the health worker, a health worker fails to recognize an ADR reported by the patient or the health worker recognizes the ADR but fails to report it to the national authority (Lopez-Gonzalez et al., 2009). Failure to report a recognized ADR has been attributed to attitudes that were described by Inman as the "seven deadly sins" proposed in 1976 (Inman, 1976).

A systematic review on determinants of reporting of ADRs showed that knowledge and attitudes of health professionals appear to be strongly related with reporting of ADRs in a high proportion of the studies (Lopez-Gonzalez et al., 2009). Health worker factors such as the age, years of practice, specialty and location of practice have been found to affect the reporting of ADRs (Bateman et al., 1992; Belton et al., 1995; Cosentino et al., 1999; Eland et al., 1999;

Generali et al., 1995; Herdeiro et al., 2005). Since health workers are responsible for most of the ADR reporting in Kenya, there is a possibility that health workers' lack of knowledge and poor attitudes to ADR reporting could be contributory factors to the problem of under-reporting of ADRs.

3.3 Conceptual Framework

Figure 3.1 Conceptual framework outlining the factors that affect reporting of ADRs by health workers



The reporting of adverse drug reactions by health workers is affected by numerous factors as described in Section 2.4. These factors can be broadly classified into contextual factors, distal factors and proximate factors. The contextual factors relate to the environment in which ADR reporting is taking place. They include factors such as the country that is reporting, country policies, the year of reporting, media publicity generated and the religion of the area. Distal factors include the health worker factors, health systems factors, patient factors and the ADR factors. The proximate factors are the health workers' knowledge, attitudes and practices of ADR reporting. The contextual factors are the background factors and the distal factors influence the knowledge and attitudes of the health worker, which ultimately affects the practices of the health worker by determining whether the health worker will report or not report the ADR.

Knowledge on adverse drug reaction reporting includes awareness of the existence of adverse drug reaction reporting schemes, knowing the type of information that should be reported to the scheme, the procedure of reporting ADRs, the purposes of the reporting scheme and the importance of reporting ADRs. The attitudes of the health workers towards adverse drug reaction reporting refers to their perceptions and opinions towards adverse drug reaction reporting and the practices of adverse drug reaction reporting refer to the health workers' recognition and reporting of ADRs to the relevant reporting authority.

The level of knowledge of the health worker on ADR reporting determines the adverse drug reaction reporting rate either directly by influencing the practices of adverse drug reaction reporting or indirectly by influencing the attitudes of the health workers, which in turn influences the practices of ADR reporting. A health worker who has inadequate knowledge on

what constitutes an adverse drug reaction is unlikely to recognise an ADR and therefore will not report it, leading to low reporting rates. Health workers may have knowledge on what an ADR is, however, if they do not know the kind of information that should be reported to the ADR reporting scheme, then they might fail to report the ADR despite having identified it correctly. This leads to low reporting rates. Therefore inadequate knowledge affects the practices of ADR reporting either by making the health worker unable to recognise the ADR or by causing an ADR that is correctly identified to go unreported.

Insufficient knowledge on the importance of adverse drug reaction reporting and the impact of ADRs on healthcare may influence the attitudes of the health workers towards ADR reporting. Health workers who have inadequate knowledge on the purposes of the ADR reporting scheme may develop attitudes that discourage ADR reporting. For example, a health worker who is not aware that one of the purposes of an ADR reporting scheme is to identify previously unrecognised reactions to drugs may develop an attitude of complacency whereby he believes that only safe drugs are allowed in the market. If a health worker erroneously believes that the purpose of the ADR reporting scheme is to determine who is responsible for causing ADRs, then he is likely to develop the attitude of guilt and fear possible litigation which will discourage ADR reporting. Lack of knowledge on the significance and impact of ADRs to healthcare is likely to lead to attitudes of indifference and lethargy whereby the health worker comes up with many excuses for not reporting and an attitude of diffidence whereby the health worker fears to appear ridiculous for reporting merely suspected ADRs.

In order to report an ADR, first the health worker needs to be able to recognise an ADR and then report it. Practices that lead to under-reporting of ADRs include the health worker being

unable to recognise the ADR or the health worker choosing not to report an ADR even though they are able to recognise it correctly.

Health worker factors influence the knowledge, attitudes and practices of ADR reporting. Older health workers who have more work experience are likely to have more knowledge on ADRs (Bateman et al., 1992; Irujo et al., 2007) and therefore report ADRs. Health workers in certain specialties are likely to report ADRs more than others. It has been found that health workers in medical specialties report more than those in surgical specialties (Eland et al., 1999; Herdeiro et al., 2005).

Health systems factors affect the health workers' knowledge, attitudes and practices of ADR reporting. Inadequate training on the importance of pharmacovigilance, adverse drug reaction reporting and how to report ADRs leads to poor knowledge of ADR reporting among health workers (Green et al., 2001; Sweis and Wong, 2000). Under-staffing of health facilities leads to greater workload which may affect the attitudes of health workers to ADR reporting negatively since they may perceive that they have inadequate time to fill ADR report forms, resulting in non-reporting. Health workers may be willing to report ADRs, however if the reporting tools are unavailable, ADR reports will not be submitted leading to low reporting rates (Bateman et al., 1992; Sweis and Wong, 2000; Vallano et al., 2005).

Patients may experience ADRs, however if they are not aware what an adverse drug reaction is or if they are unwilling to discuss the ADR with the health worker then the health worker will not be aware of the ADR and will therefore not report it. ADRs that are serious are more likely to be reported by health workers than those that are considered to be trivial (Eland et al., 1999; McGettigan et al., 1997).

The Pharmacovigilance programme was launched in Kenya in 2007 and since then health workers have been trained to report adverse drug reactions and reporting tools have been availed in health facilities. Despite this, reporting rates are still low and the PPB reported that lack of awareness as one of the major impediments of reporting of ADRs. Data from the PPB showed that KNH was submitting few reports despite it being a referral hospital (PPB, 2010). Since health workers are responsible for submitting most of the ADR reports, it is likely that the low reporting rates are being influenced by health worker factors which need to be determined.

Although there are several factors that affect the reporting of ADRs, this study focussed on the health worker factors that affect ADR reporting. The reason for this was that majority of ADR reports are submitted by the health workers rather than by the patients therefore the patient factors were not studied. In addition, time and budgetary constraints made it impossible for the health systems factors and the patient factors to be studied.

3.4 Justification for the research

Adverse drug reactions have a big impact on the health system. A meta analysis of prospective studies estimated that ADRs represent the fourth to sixth largest causes of death among hospitalized patients in the US (Lazarou et al., 1998). Several studies have shown the impact of ADRs in Africa (Abdissa et al., 2012; Jaquet et al., 2011; Mehta et al., 2008; Oshikoya et al., 2011). Between 4.5 and 8.4 percent of all hospital admissions were related to ADRs, 1.5–6.3 percent of patients were admitted as a direct result of ADRs; and 6.3–49.5 percent of all hospitalized patients developed ADRs.

A study showed that the adverse drug events increased monthly costs among patients with metastatic breast cancer by between $854 and $5,320. The costs related to adverse events were primarily driven by increased inpatient, outpatient, and pharmacy costs (Hurvitz et al., 2014). Adverse drug events were shown to be the cause of hospital admissions or increased hospital stay among paediatric patients in New Zealand (Kunac et al., 2009). In Africa between 4.5 and 8.4 percent of all hospital admissions were related to ADRs, 1.5–6.3 percent of patients were admitted as a direct result of ADRs; and 6.3–49.5 percent of all hospitalized patients developed ADRs (Strengthening Pharmaceutical Systems Program, 2011). A high incidence of ADRs (48.6%) was reported among patients who were attending the comprehensive care clinic in KNH (Mwangangi et al., 2009).

Due to the high incidence of adverse drug reactions and the significant impact that they have on the health systems both in terms of direct and indirect costs, it is necessary to ensure adverse drug reactions are reported early in order to avoid significant costs to the health system. It was therefore necessary to carry out a study to determine the factors that affect reporting of ADRs in order to design targeted interventions to improve reporting of ADRs among health workers in KNH.

3.5 Research objectives and questions

3.5.1 Research objectives

Broad objective

To determine the health worker factors associated with adverse drug reaction reporting in Kenyatta National Hospital

Specific objectives

1. To determine the socio-demographic factors of the health workers in Kenyatta National Hospital.
2. To determine the knowledge of health workers in Kenyatta National Hospital on adverse drug reaction reporting.
3. To determine the attitudes of health workers in Kenyatta National Hospital on adverse drug reaction reporting.
4. To explore the health systems factors that affect reporting of adverse drug reactions by health workers.

3.5.2 Research questions

1. Is there an association between the socio-demographic factors of the health worker and adverse drug reaction reporting?
2. Is there an association between the knowledge of the health worker and adverse drug reaction reporting?
3. Is there an association between attitudes of the health worker and adverse drug reaction reporting?

3.5.3 Null hypotheses

1. There is no association between the socio-demographic factors of the health worker and reporting of adverse drug reactions.
2. There is no association between the knowledge of the health worker and reporting of adverse drug reactions.

3. There is no association between the attitudes of the health worker and reporting of adverse drug reactions.

CHAPTER 4 METHODOLOGY

The study used both quantitative and qualitative techniques. The reasons for the addition of the qualitative component to the quantitative study were two fold; to help understand the results of the quantitative study and to generate new ideas regarding the other factors related to the health systems or the patients that affect the reporting of adverse drug reactions.

4.1 Quantitative Study

4.1.1 Study design

The study design was determined by the specific objectives of the research. In order to achieve the specific objective which sought to determine the knowledge of ADR reporting among health workers, a cross sectional study design was chosen because knowledge of any subject tends to change over time and therefore determination of knowledge has to be done at a particular point in time. A cross-sectional study was suitable because it assessed knowledge at a particular point in time. Similarly, in order to achieve the specific objective which sought to determine the attitudes of health workers to adverse drug reaction reporting, a cross sectional study design was used since attitudes tend to change over time and therefore determination of attitudes needed to be done at a particular point in time.

4.1.2 Study area

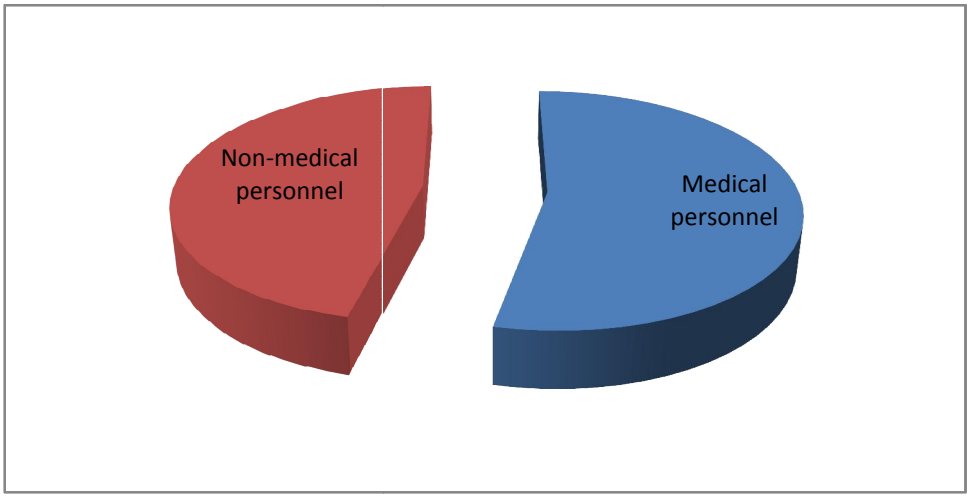
The study site chosen was Kenyatta National Hospital, a level six referral hospital in Nairobi. The reason for choosing this facility as the study site is because the pharmacovigilance program in Kenya was first introduced in the level five and six referral institutions. It is assumed that the use of a wider range of therapeutic classes of medicines and the presence of

patients with various levels of disease severity in this institution greatly increases the probability that patients with an adverse drug reaction are seen by the health workers.

4.1.3 Study population

The study population were the health workers in KNH. According to a report outlining Kenya's human resources for health (Capacity Kenya, 2010), at the end of 2010 KNH had a total of 4638 workers of whom 53.4% were medical personnel for example doctors, dentists, pharmacists, clinical officers, nurses, lab technicians, radiographers, nutritionists and medical records staff while 46.4% were non-medical personnel for example workers in administration, finance, security and support staff as shown in Figure 4.1.

Figure 4.1 Distribution of personnel in KNH in 2010



Source: (Capacity Kenya, 2010)

Medical personnel are most likely to identify ADRs in patients. However, certain cadres of medical personnel may not be in a position to detect ADRs because they do not interact

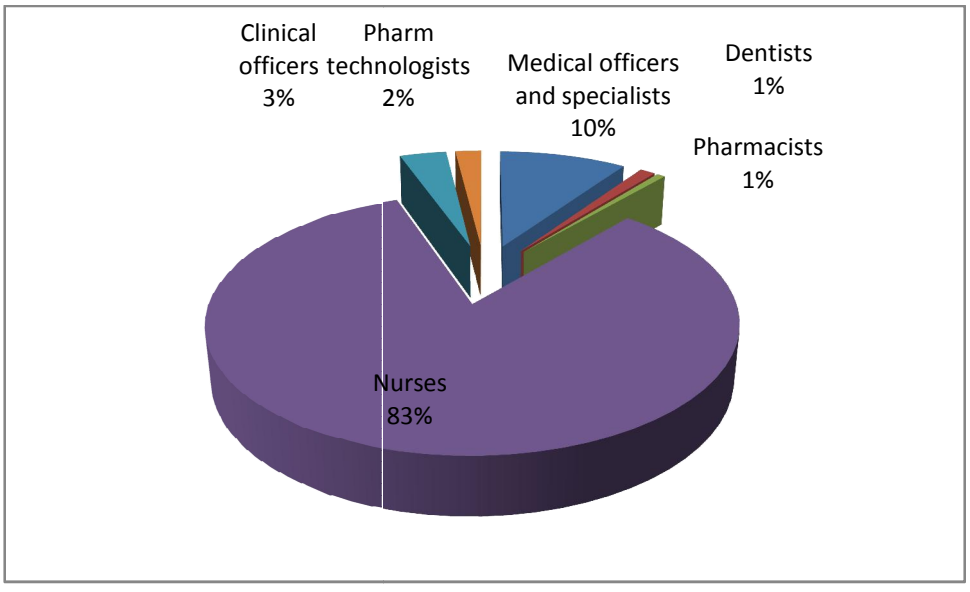
directly with patients for example medical records officers and laboratory technologists. Therefore, the study population was limited to cadres that directly interacted with patients and were in a position to detect ADRs such as doctors, pharmacists, dentists, nurses, pharmaceutical technologists and clinical officers. The distribution of these personnel at the end of 2010 is as shown in Table 4.1 and Figure 4:2.

Table 4.1: Distribution of selected cadres of health workers in KNH in 2010

Cadre	Staff in post 2010	Percentage %
Medical officers and specialists	196	9.5
Dentists	24	1.2
Pharmacists	13	0.6
Nurses	1709	83.2
Clinical officers	72	3.5
Pharmaceutical technologists	40	1.9
Total	2054	100.0

Source: (Capacity Kenya, 2010)

Figure 4.2 Distribution of certain cadres of health workers in KNH in 2010



Inclusion criteria:

- Health workers who were directly involved in clinical patient care.
- Health workers who were in a position to detect adverse drug reactions for example nurses, clinical officers, pharmaceutical technologists, medical officers, dentists and pharmacists.

Exclusion criteria:

- Health workers who were not directly involved in the clinical care of patients.
- Health workers who were not in a position to detect adverse drug reaction for example laboratory technologists.
- Health workers who declined to participate in the study.

4.1.4 Sampling

i. Sample size calculation

The sample size was determined using the formula for calculating the sample size based on estimates of a single proportion (Cochran, 1963):

$$n = \frac{(Z_{1-\frac{\alpha}{2}})^2[p(1-p)]}{d^2}$$

where:

Z is the reliability coefficient at the 95% confidence level or 1.960

p is the estimated proportion of health workers who have ever reported an adverse drug reaction. Since there were no published studies in Kenya showing the proportion of health workers in Kenya who had reported adverse drug reactions, p=0.5 was used. When p=0.5, the value p(1-p) generates the most conservative or largest sample size.

d is the margin of error selected to be 5%

Using this formula, the sample size calculated was 384.

The sample size was corrected for a finite population (population less than 50000) using the formula (Cochran, 1963):

$$new\ sample\ size = \frac{sample\ size}{1 + \frac{(sample\ size - 1)}{population\ size}}$$

This gave a corrected sample size of 324.

A similar study done in Nigeria (Okezie and I, 2008) showed a non-response rate of 9% therefore a ten percent increase in the sample size was added to cater for those who would decline to participate in the study. Therefore the calculated sample size was 356.

ii. Sampling technique

Cluster sampling method was used.

The study population was clustered by cadre of the health workers in order make the data more representative of the overall population. Based on the distribution of health workers in

KNH in 2010 as shown in Table 4.1 above, the health workers sampled in each cadre was as shown in Table 4.2.

Table 4.2: Selection of sample by cadre of health worker

Cadre	**Staff in post 2010**	**Percentage %**	**Sample size per cadre**
Medical officers and specialists	196	9.5	34
Dentists	24	1.2	4
Pharmacists	13	0.6	3
Nurses	1709	83.2	296
Clinical officers	72	3.5	12
Pharmaceutical technologists	40	1.9	7
Total	2054	100	356

An assumption made was that the distribution of different cadres of health workers in KNH had not changed significantly since 2010.

Six sampling frames corresponding to each of the cadres above were sourced from the KNH Human Resources Department. Each sampling frame consisted of all the names of the health workers belonging to a specific cadre. Each sampling frame was in the form of a Microsoft Excel spreadsheet and was first randomly arranged by name. Selection within each cluster was done using systematic sampling whereby every *k*th person on the list was chosen to participate in the study where *k* was the sampling interval obtained by dividing the total population within each cluster by the sample size calculated within each cluster. Selection was done to reflect the different proportions of health workers in each department.

For example, in selecting the clinical officers to participate in the study:

$$k = \frac{total\ population}{sample\ size} = \frac{72}{12} = 6$$

The starting point on the list was obtained by randomly selecting a number between 1 and *k* (which in this case is 6) and thereafter selecting every 6th name on the list.

In certain cases the sampling interval *k* was not an integer for example in the case of pharmaceutical technologists:

$$k = \frac{total\ population}{sample\ size} = \frac{40}{7} = 5.7$$

In this case, *k* was rounded down to 5. The starting point was obtained by randomly selecting a number between 1 and 5 and thereafter selecting every 5th pharmaceutical technologist on the list until 7 were selected. The same method was applied in selecting the respondents from the other cadres.

4.1.5 Variables

Outcome variable:

The outcome variable was reporting an adverse drug reaction.

Predictor variables:

The predictor variables were the demographic factors of the health workers which include age, sex, duration of practice, the department of the health worker, having received pharmacovigilance training previously; the knowledge of the health worker on ADR reporting and the attitudes of the health worker towards ADR reporting.

The conceptual framework in Section 3.3 outlines the factors that affect the reporting of ADRs. In this case, reporting of an ADR is the outcome and is therefore selected as the outcome variable. The predictor variables such as the age, duration of practice and department of the health worker were identified from previous studies as common health worker factors that were associated with reporting of ADRs and were therefore selected as predictors. Knowledge and attitudes of the health worker to ADR reporting are proximate factors that affect reporting of ADRs and were therefore included as predictor variables. In order to objectively assess the knowledge and attitudes, the health workers were asked a series of questions which were then scored. This score was used as the predictor variable.

4.1.6 Data collection tools

Data was collected from July to September 2013 using a structured self-administered questionnaire containing closed-ended questions that were administered to randomly selected participants. A self-administered questionnaire offered the advantage of anonymity which was more likely to result in honest answers because the questions that assessed attitudes of health workers on adverse drug reaction reporting were of a personal nature.

Knowledge of ADR reporting was assessed using a number of questions that sought to determine if the health worker was aware of the existence of an adverse drug reaction reporting scheme, the kind of information that should be reported to the scheme and the purposes of the scheme. The attitudes of health workers to adverse drug reaction reporting was determined using a Likert scale where the questions were based on attitudes that affect ADR reporting as described by Inman (Inman, 1996). The outcome variable was determined by asking the health worker if he/she had ever reported an ADR.

4.1.7 Data analysis

Data from the questionnaire was coded and entered into a spreadsheet. The data was imported to Stata version 12 which was used for data analysis. Descriptive statistics were used to summarize the demographic details of the study respondents. Categorical predictor variables such as sex and department were summarised using frequencies and percentages whereas the continuous predictor variables such as age were summarised using the means and standard deviation for normally distributed data and using the median and interquartile range for skewed data. Contingency table analysis using Fischer's exact test was used to compare if there was a statistically significant difference between the reporters and non-reporters with respect to the demographic characteristics of the health worker. Student's t test and Wilcoxon rank sum test were used to determine if there was an association between the health workers' knowledge and attitude scores respectively and reporting of ADRs. Logistic regression was used to determine the magnitude of association between the predictor variables and reporting of ADRs.

4.2 Qualitative study

4.2.1 Key informant interviews

The health worker is part of the health system therefore the reporting of adverse drug reactions is affected by contextual factors within the health system. Semi-structured face-to face interviews of key informants were conducted to explore further the possible factors within the health system that affect reporting of ADRs by health workers.

4.2.2 Selection of the key informants

The key informants were selected based on their extensive knowledge on adverse drug reaction reporting. The key informants were selected from the Pharmacovigilance Department of the Pharmacy and Poisons Board. The Pharmacovigilance Department of the PPB is responsible for co-ordinating the national adverse drug reaction reporting system. Three key informants were selected from this department on the basis of their expertise in each of the key areas of ADR reporting namely the Head of the Pharmacovigilance Department, the pharmacist responsible for co-ordinating pharmacovigilance training for health workers and the pharmacist responsible for reviewing ADR reports sent in from the health facilities. However, the head of the pharmacovigilance department had left the post and one of the other key informants had taken his place, therefore two key informants were interviewed.

4.2.3 Data collection tools

Data from the key informant interviews was collected using a semi-structured questionnaire containing open-ended questions. The questions sought to get insights on the factors within the health system that encouraged and deterred the reporting of adverse drug reactions by health workers. The participants' responses to the questions were noted down.

4.3 Ethical consideration

The study was approved by the University of Nairobi/Kenyatta National Hospital (UoN/KNH) Ethics and Research Committee with the reference P170/4/2013. Informed consent was obtained from all the study participants. Sampled health workers who declined to participate

in the study were excluded. To ensure confidentiality of the participants' responses, no names were collected on the questionnaires.

4.4 Pre-testing of questionnaires

Pre-testing of the questionnaires was carried out to identify potential problems with the research, to ensure that the questions were well understood and to determine the response time of the participants to the questionnaire. The questionnaire was modified slightly to edit two questions that were similar and to include a question that asked the health workers if they had ever seen a patient with a suspected adverse drug reaction. The results from the pre-test were not included in the final analysis of the data since the questionnaire was modified slightly afterwards.

4.5 Minimization of errors and biases

Errors and biases were minimized by quality assurance procedures that sought to maintain the integrity of the data collected: These included the proper selection of the study participants based on the inclusion criteria, randomization of study participants, the use of a structured questionnaire for data collection and pre-testing of the questionnaire before beginning the actual data collection to ensure that the questions were well understood.

CHAPTER 5 RESULTS

5.1 Quantitative Study

The questionnaires were administered to 356 health workers in various departments in the hospital. Two hundred and eighty nine health workers consented to participate in the study, giving a response rate of 81.2%. Sixty seven health workers declined to consent and were therefore excluded from the study. The distribution of study participants by cadre is shown in the table below.

Table 5.1: Distribution of study participants by cadre

Cadre	Number	Percentage (%)
Medical officers and specialists	27	9.4
Dentists	3	1.0
Pharmacists	3	1.0
Nurses	241	83.4
Clinical officers	9	3.1
Pharmaceutical technologists	6	2.1
Total (N)	289	100

5.1.1 Demographic characteristics of the study participants

i. Distribution of study participants by sex

Three study participants did not indicate their sex in the questionnaire. Of the 286 who did, the majority (n=210, 73.4%) were female. The distribution of the participants by sex is shown in Table 5.2.

Table 5.2 Distribution of study participants by sex

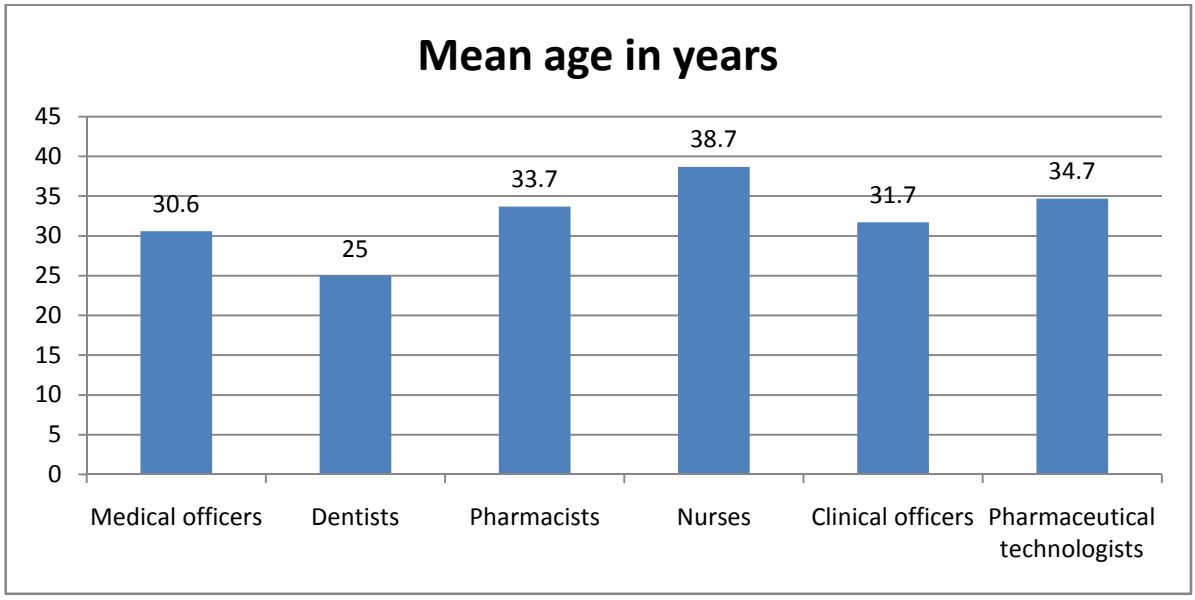
Sex	Number	Percentage (%)
Male	76	26.6
Female	210	73.4
Total	286	100

ii. Age of participants

A number of participants (n=35, 12.1%) did not indicate their ages on the questionnaire. The mean age of the 254 participants (87.9%) who indicated their age was 37.3 years with a standard deviation of 8.1 years.

The mean age of the participants by cadre is shown in Figure 5.1.

Figure 5.1 Mean age of participants by cadre

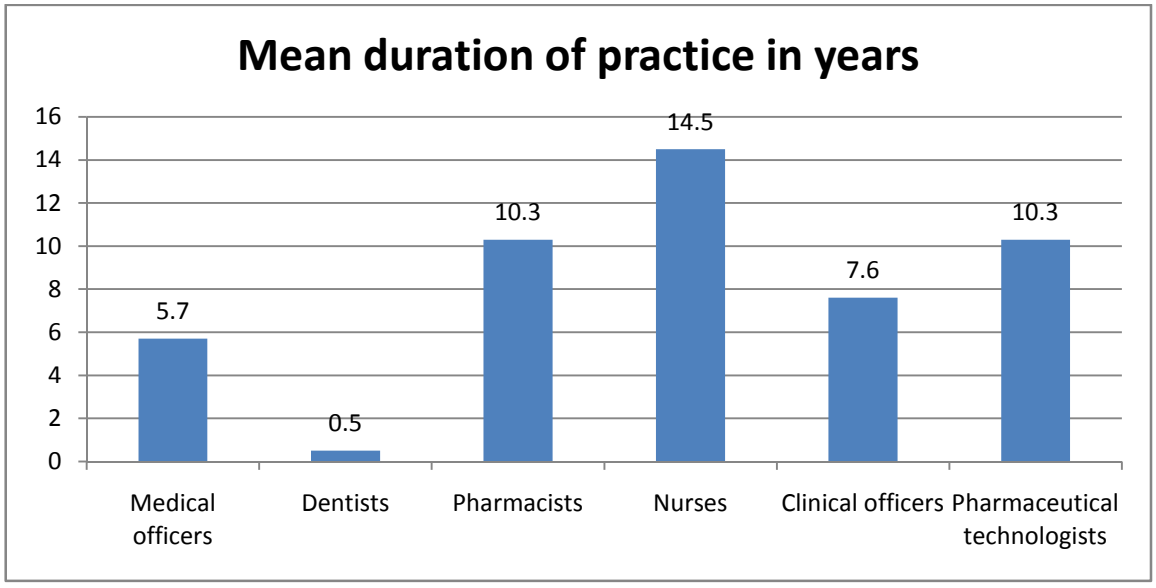


5.1.2 Occupational characteristics of the study participants

i. Duration of practice of the participants

The mean duration of practice of the 287 (99.3%) participants who answered the question was 13.2 years with a standard deviation of 8.1 years. The mean duration of practice for each cadre is shown in Figure 5.2.

Figure 5.2 Mean duration of practice of participants by cadre



ii. Distribution of study participants by department

The distribution of participants by department is shown in Table 5.3.

Table 5.3 Distribution of study participants by department

Department	Number	Percentage (%)
Surgery	77	26.64
Medicine	50	17.30
Paediatrics	45	15.57
Reproductive Health (RH)	42	14.53
Private Wing	22	7.61
Orthopaedic Surgery	21	7.27
Anaesthesia	20	6.92
Pharmacy	9	3.11
Dental	3	1.04
Total	289	100

iii. Distribution of study participants by cadre and department

The distribution of health workers by cadre and department is shown in Table 5.4.

Table 5.4 Distribution of study participants by cadre and department

	MO	Dentist	Pharmacist	Nurse	CO	Pharm. technologist	Total
Surgery	9	0	0	67	1	0	77
Medicine	7	0	0	41	3	0	50
Paediatrics	3	0	0	42	3	0	45
Reproductive Health	5	0	0	33	0	0	42
Private Wing	1	0	0	22	0	0	22
Orthopaedics	0	0	0	20	0	0	21
Anaesthesia	2	0	0	16	2	0	20
Pharmacy	0	0	3	0	0	6	9
Dental	0	3	0	0	0	0	3
Total	27	3	3	241	9	6	289

iv. Previous pharmacovigilance training of participants

Health workers were asked if they had ever received any training or on-the-job sensitization on pharmacovigilance. The majority of health workers (n=210, 72.7%) had not received any training on pharmacovigilance as shown in Table 5.5.

Table 5.5 Previous pharmacovigilance training of study participants

Previous PV training	Number	Percentage (%)
Yes	79	27.3
No	210	72.7
Total	289	100

An analysis of the previous pharmacovigilance training by cadre showed that pharmacists and pharmaceutical technologists had the highest percentage of health workers trained at 100% each (n=3 and n=6 respectively) followed by clinical officers (n=3, 33.3%), nurses (n=61, 25.3%), medical officers (n=6, 22.2%) and dentists (n=0, 0%).

5.1.3 Knowledge of health workers on adverse drug reaction reporting

Knowledge of ADR reporting was assessed through a series of questions that were designed to determine the awareness of the existence of an ADR reporting scheme in the country, knowledge on who should report ADRs and what should be reported to the scheme and the purposes of the ADR reporting scheme.

The questions were scored as shown in the questionnaire in Appendix 4. The maximum knowledge score was 25 points. The mean knowledge score for all the health workers was 13.7 points with a standard deviation of 4.4 points.

i. Awareness on the existence of the ADR reporting scheme

The awareness of the health workers on the existence of the ADR reporting scheme was determined using three questions with a maximum possible score of 3. The mean score for awareness for all the health workers was 0.53 points with a standard deviation of 0.85 points. Health workers had low awareness on the existence of the ADR reporting scheme.

ii. Awareness of the existence of a national PV centre for ADR reporting

Awareness of the existence of the national pharmacovigilance centre was low. Sixty eight participants (23.6%) were aware of the existence of the centre while the majority (n=220, 76.4%) of the participants were unaware of its existence. One participant did not answer the question. Whereas 68 (23.6%) of all the participants said that they were aware of the existence of a national centre for reporting ADRs, only 30 (10.4%) could correctly identify the location of the centre as the Pharmacy and Poisons Board. Majority of the health workers left the response blank (n=233, 80.6%) while others erroneously gave the location of the national PV centre as the University of Nairobi, Department of Pharmacovigilance (n=18, 6.2%) or the Ministry of Health headquarters at Afya House (n=8, 2.8%).

iii. Awareness of the Suspected Adverse Drug Reaction reporting form

Most participants reported that they had never seen the Suspected Adverse Drug Reaction reporting form. Fifty five (19.1%) of the study participants had seen the Suspected Adverse Drug Reaction reporting form while 233 (80.9%) health workers had never seen the ADR form. One participant did not answer the question.

Awareness of the existence of the reporting form varied across the cadres. All of the pharmacists (n=3, 100%) and pharmaceutical technologists (n=6, 100%) sampled had seen the reporting form. A minority of the medical officers (n=9, 33.3%), dentists (n=1, 33.3%) and clinical officers (n=3, 33.3%) and nurses (n=46, 19.2%) reported to having seen the reporting form.

iv. Knowledge about who should report ADRs and what should be reported

This was assessed using a series of questions to determine whether the health workers knew who should report ADRs and the information that should be reported to the ADR reporting scheme. This information is contained in the National Pharmacovigilance Guidelines for health workers for detecting and reporting ADRs and poor quality medicinal products (MoMS and MoPHS, 2009). The questions that assessed this aspect of knowledge had a maximum possible score of 17 points. The mean score for all the health workers was 10.7 points with a standard deviation of 4.0 points.

The health workers' responses to the questions that sought to find out the information that should be reported to the scheme is shown in Table 5.6.

Table 5.6 Responses to the questions asking the information to be reported to the ADR reporting scheme

Information to be reported *	Total responses	Correct responses (%)	Incorrect responses (%)
All suspected ADRs whether serious or not (yes)	281	258 (91.8)	23 (8.2)
Suspected ADR to a medical device (yes)	266	180 (67.7)	86 (32.3)
Suspected ADRs to vaccine (yes)	258	242 (93.8)	16 (6.2)
Suspected ADRs to traditional (herbal) medicines (yes)	263	147 (55.9)	116 (44.1)
When health worker is not sure that the drug caused the ADR (yes)	279	117 (41.9)	162 (58.1)
When health worker has incomplete details regarding the patient or the ADR (yes)	279	99 (35.5)	180 (64.5)

**the correct answer to each question is shown in the brackets*

v. Knowledge on the purposes of the ADR reporting scheme

A series of questions were asked to determine the knowledge of the health workers on the purposes of the ADR reporting scheme. The maximum possible score was 5. The mean score for all the participants was 2.5 points with a standard deviation of 0.8 points.

The health workers' responses to the questions that sought to find out the purposes of the ADR reporting scheme is shown in Table 5.7.

Table 5.7 Responses to the question on the purposes of the ADR reporting scheme

Purpose of ADR reporting scheme*	Total responses	Correct responses (%)	Incorrect responses (%)
To determine the incidence of ADRs (No)	280	5(1.8)	275(98.2)
To identify factors that predispose patients to ADRs (Yes)	278	249(89.6)	29(10.3)
To enable safe drugs to be identified (No)	273	15(5.5)	258(94.5)
To identify previously unrecognised ADRs (Yes)	279	248(88.9)	31(11.1)
To identify bizarre reactions to drugs (Yes)	270	208(77.0)	62(23.0)

**the correct answer to each question is shown in the brackets*

5.1.4 Attitudes of health workers to adverse drug reaction reporting

The attitudes to ADR reporting were assessed using a Likert scale with three choices: "agree", "not sure" and "disagree". Each question assessing attitude was scored as shown in the questionnaire in Appendix 4. The maximum possible score was 10. The higher the score, the more positive the health workers' attitudes were towards ADR reporting. The attitude scores for all the health workers exhibited left skew with a median score of 7 (interquartile range 6-8).

Generally, most health workers had positive attitudes to ADR reporting with most of the health workers having the opinion that ADR reporting is a professional obligation. The percentage response of the health workers to each question assessing attitude is shown in Table 5.8.

Table 5.8 Responses to the questions assessing attitudes to ADR reporting

Statement that assesses attitude	Total responses	Agree (%)	Disagree (%)	Not sure (%)
Reporting adverse drug reactions is a professional obligation	288	276 (95.9)	11 (3.8)	1 (0.3)
It is difficult to know whether or not an adverse drug reaction has occurred based on my clinical knowledge.	283	44 (15.5)	212 (75.0)	27 (9.5)
Reporting just one case of a suspected adverse drug reaction will not have a significant effect on the national database for adverse drug reactions	283	48 (17.0)	199 (70.3)	36 (12.7)
There is not enough time in my work schedule to report adverse drug reactions	284	34 (12.0)	237 (83.5)	13 (4.5)
I would only report an adverse drug reaction if I am sure that the drug caused it.	282	119 (42.2)	140 (49.6)	23 (8.2)
Most of the serious adverse drug reactions have been described before the drug is released in the market	282	152 (53.9)	74 (26.2)	56 (19.9)
If a patient experiences an adverse drug reaction it means I may have administered treatment that harmed him/her.	284	56 (19.7)	207 (72.9)	21 (7.4)
Reporting adverse drug reactions might result in legal action taken against health workers	285	40 (14.0)	204 (71.6)	41 (14.4)
It is nearly impossible to determine if a drug is responsible for causing a particular adverse drug reaction	285	27 (9.5)	209 (73.3)	49 (17.2)
Filling in an adverse drug reaction report generates extra work.	285	68 (23.9)	208 (73.0)	9 (3.1)

5.1.5 The association between health worker factors and ADR reporting

Most health workers (n=257, 89.9%) reported that they had seen a patient with a suspected ADR while a minority (n=29, 10.1%) reported that they had not seen a patient with an ADR.

Although most health workers reported that they had seen a patient with a suspected ADR, only a minority (n=15, 5.3%) had ever reported an ADR while the majority (n=270, 94.7%) had never reported an ADR.

i. Association between sex and reporting of ADRs

There was no significant association between the participants' sex and reporting an ADR (Fischer's exact test, p=0.554). Since p=0.554, the null hypothesis that there is no association between the sex of the health worker and the reporting of ADRs failed to be rejected. Therefore the male and female health workers are equally likely to report ADRs.

Table 5.9 Cross tabulation between ADR reporting and sex

Sex	Reported	Not reported	Total
Male	5	70	75
Female	10	197	207
Total	15	267	282

ii. Association between the department of the health worker and reporting of ADRs

The relationship between the department of the health worker and reporting of ADRs was confounded by the cadre of the health worker because some departments did not have certain cadres for example the pharmacy department did not have clinical officers, medical officers, dentists or nurses. To control for confounding, stratification was done along the cadres that cut across different departments namely medical officers, clinical officers and nurses and the relationship between the departments and reporting an ADR was examined. Since no medical officer or clinical officer had reported an ADR, an association between the department and reporting could not be determined when data was stratified along these 2 cadres therefore an

examination of the association between department and reporting of ADRs was carried out for nurses.

Table 5.10 Cross tabulation between ADR reporting and department of the health worker

Department	Reported ADR	Not reported ADR	Total	% reporting
Medicine	1	39	40	2.5
Reproductive Health	2	31	33	6.1
Private Wing	1	21	22	4.5
Paediatrics	2	40	42	4.8
Orthopaedic Surgery	1	19	20	5.0
Surgery	3	61	64	4.7
Anaesthesia	0	16	16	0
Total	10	227	237	4.2

There was no significant association between the department of the health worker and reporting an ADR when data was stratified along cadre of the health worker (Fisher's exact test, p=0.997). Since p=0.997, the null hypothesis that there is no association between the department of the health worker and the reporting of ADRs failed to be rejected. As shown in Table 5.10, reporting rate was highest among the nurses in the Reproductive Health department (n=2, 6.1%), followed by Orthopaedic Surgery (n=1, 5.0%), Paediatrics (n=2, 4.8%), Surgery (n=3, 4.7%), Private Wing (n=1, 4.5%), Medicine (n=1, 2.5%) and Anaesthesia (n=0, 0%).

iii. Association between previous pharmacovigilance training and reporting of ADRs

There was a statistically significant association between the participants' previous pharmacovigilance training and reporting an ADR (Fischer's exact test, p=0.000). Since

p=0.000, the null hypothesis that there is no association between previous pharmacovigilance training and the reporting of ADRs was rejected. Participants who were trained were more likely to report ADRs than those who were not trained.

Table 5.11 Cross tabulation between ADR reporting and previous PV training

Previous PV training	Reported	Not reported	Total
Trained	12	65	77
Not trained	3	205	208
Total	15	270	285

iv. Association between duration of practice of the health worker and reporting of ADRs

Some participants (n=35, 12.1%) did not indicate their age on the questionnaire. A simple linear regression analysis of the relationship between the duration of practice as an outcome variable and age as a predictor variable showed that the two variables were highly correlated and this correlation was statistically significant (R squared=0.89, p=0.0000). The R squared or coefficient of determination is the proportion of variance in the duration of practice that can be explained by the age. The higher the value of R squared the better the model fits the data. Since the R squared obtained in this model is high (0.89 or 89%), it means the duration of practice can be better predicted from age of the health worker. In this study, the older the participant, the more the years they had practiced. The relationship between the duration of practice and age is represented by the equation

Duration of practice = 0.95 age - 22.95

Since the two variables are highly correlated, the variable age was therefore dropped from the analysis and duration of practice used instead since more respondents had indicated their duration of practice (n=283, 97.9%).

A Student's t-test was used to determine the association between the duration of practice of the health worker and reporting an ADR. There was no significant association between the mean duration of practice of the health worker and reporting an ADR (p=0.595). Since p=0.595, the null hypothesis that there is no association between the duration of practice of the health worker and the reporting of ADRs failed to be rejected. As shown inTable 5.12, the 95% confidence intervals of the mean duration of practice of the reporters and the non-reporters overlap which shows that there is no statistically significant difference in the mean duration of practice between the health workers who reported ADRs and those who did not report ADRs.

Table 5.12 Comparison of mean duration of practice between reporters and non-reporters

	Number	**Mean duration of practice in years**	**95% CI: Lower**	**95% CI: Upper**
Reporters	15	12.65	7.19	18.12
Non-reporters	268	13.17	12.20	14.14
Combined	283	13.15	12.19	14.10

v. Association between knowledge of the health worker and reporting of ADRs

A Student's t-test analysis showed that there was a statistically significant association between the health workers' ADR knowledge score and reporting of ADR (p=0.0021). Since p=0.0021, the null hypothesis that there is no association between the knowledge of the health worker

and the reporting of ADRs was rejected. Reporters had a higher mean knowledge score than non-reporters as shown in Table 5.13.

Table 5.13 Comparison of the mean knowledge score in reporters and non-reporters

	Number	Mean knowledge score	95% CI: Lower	95% CI: Upper
Reporters	15	16.93	14.34	19.53
Non-reporters	270	13.57	13.05	14.10
Combined	285	13.75	13.23	14.27

Three areas of knowledge were tested: the awareness of the existence of the reporting scheme, knowledge of the information that should be reported and knowledge of the purposes of the reporting scheme. Student's t test analysis showed that there were statistically significant associations between two areas of knowledge and reporting of ADRs. These two areas were the awareness of the existence of the reporting scheme and knowledge of the purposes of the ADR scheme.

There was a significant association between the health workers' awareness of the reporting scheme and reporting of ADRs (p=0.0000). Health workers who had reported an ADR had a higher mean awareness score than those who had never reported an ADR. There was no statistically significant association between the health workers' score of the knowledge of the information that should be reported and the reporting of ADRs (p=0.0802). Therefore, the knowledge score of the information to be reported in the ADR scheme was not significantly different between health workers who had reported ADRs and those who had not reported ADRs. Health workers who reported ADRs had a higher mean knowledge score on the purposes of the ADR reporting scheme than non-reporters and this difference was statistically

significant (p=0.0226). Table 5.14 shows a summary of the comparison of the mean scores for each of the three areas of knowledge between health workers who reported ADRs and those who did not.

Table 5.14 Summary of the association between each of the areas of knowledge and ADR reporting

Knowledge Area	Categories	Total	Reporters	Non-reporters	P value
Awareness of the existence of the ADR scheme	Mean [95% CI]	0.53 [0.43-0.63]	1.87 [1.28-2.45]	0.46 [0.36-0.55]	0.0000
Information to be reported to the ADR scheme	Mean [95% CI]	10.71 [10.24-11.18]	12.13 [9.92-14.35]	10.63 [10.15-11.11]	0.0802
Purposes of the ADR reporting scheme	Mean [95% CI]	2.51 [2.41-2.61]	2.93 [2.68-3.19]	2.49 [2.39-2.59]	0.0226

vi. Association between the health workers' attitudes and reporting of ADRs

The Wilcoxon rank sum test was used to determine if there was an association between the health workers' attitudes and reporting of an ADR. There was no significant association between the health workers' overall attitude score and reporting of ADRs (p=0.4153). Since p=0.4153, the null hypothesis that there is no association between the attitudes of the health worker and the reporting of ADRs failed to be rejected.

Fischer's exact test analysis was used to determine if there was a significant association between each of the attitudes and ADR reporting. For each of the attitudes assessed, there was

no significant difference in attitudes between the reporters and non- reporters as shown in Table 5.15. Therefore, the attitudes of the health workers did not have an effect on the reporting of ADRs.

Table 5.15 Health workers attitudes to ADR reporting

Attitude statement	Responses	Reporters	Non-reporters	Total	p value
Adverse drug reaction reporting is a professional obligation	Agree	15	259	274	1.000
	Disagree	0	9	9	
	Not sure	0	1	1	
	No response marked	0	1	1	
It is difficult to know whether or not an adverse drug reaction has occurred based on my clinical knowledge	Agree	2	41	43	0.858
	Disagree	11	199	210	
	Not sure	2	25	27	
	No response marked	0	5	5	
Reporting just one case of a suspected adverse drug reaction will not have a significant effect on the national database for adverse drug reactions	Agree	3	45	48	0.943
	Disagree	10	187	197	
	Not sure	2	34	36	
	No response marked	0	4	4	
There is not enough time in my work schedule to report adverse drug reactions	Agree	4	30	34	0.214
	Disagree	10	224	234	
	Not sure	1	12	13	
	No response marked	0	4	4	
I would only report an adverse drug reaction if I am sure that the drug caused it	Agree	4	112	116	0.587
	Disagree	10	130	140	
	Not sure	1	22	23	
	No response marked	0	6	6	
Most of the serious adverse drug reactions have been	Agree	10	141	151	0.098
	Disagree	4	70	74	
	Not sure	0	54	54	

Attitude statement	Responses	Reporters	Non-reporters	Total	p value
described before the drug is released in the market	No response marked	1	5	6	
If a patient experiences an adverse drug reaction it means I may have administered treatment that harmed him/her	Agree	5	49	54	0.371
	Disagree	10	196	206	
	Not sure	0	21	21	
	No response marked	0	4	4	
Reporting adverse drug reactions might result in legal action taken against health workers	Agree	1	39	40	0.925
	Disagree	12	189	201	
	Not sure	2	39	41	
	No response marked	0	3	3	
It is nearly impossible to determine if a drug is responsible for a particular adverse drug reaction	Agree	0	26	26	0.621
	Disagree	12	195	207	
	Not sure	3	46	49	
	No response marked	0	3	3	
Filling in an adverse drug reaction report generates extra work	Agree	5	63	68	0.374
	Disagree	9	196	205	
	Not sure	1	8	9	
	No response marked	0	3	3	

A summary of the health worker factors that are associated with reporting of ADRs is shown in Table 5.16.

Table 5.16 The correlates of ADR reporting among health workers in KNH

Health worker factor	Categories	Total	Reporters (n=15)	Non-reporters (n=270)	p value
Sex	Male Female	75 207	5 10	70 197	0.554
Duration of practice years	Mean [95% CI]	13.15 [12.19-14.10]	12.65 [7.19-18.12]	13.17 [12.20-14.14]	0.595
Department*	Medicine Reproductive Health Private Wing Paediatrics Orthopaedics Surgery Anaesthesia	40 33 22 42 20 64 16	1 2 1 2 1 3 0	39 31 21 40 19 61 16	0.997
Previous PV training	Yes No	77 208	12 3	65 205	0.000
Knowledge on ADR reporting	Mean [95% CI]	13.75 [13.23-14.27]	16.93 [14.34-19.53]	13.57 [13.05-14.10]	0.0021
Attitudes towards ADR reporting	Rank sum [Expected rank sum]	40755 40755	2392 2145	38363 38610	0.4153

**the department was stratified along cadre of health workers, the figures shown are for nurses*

From this table, it can be seen that the health worker factors that are associated with reporting of ADRs are having received previous pharmacovigilance and the knowledge on ADR reporting since the p values obtained for these predictor variables are less than 0.05, the chosen level of significance.

vii. Modelling the predictor and outcome variables

Logistic regression was carried out to determine the strength of the association between the outcome variable which is reporting an ADR and the predictor variables which are sex, age duration of practice, department, previous PV training, knowledge score and attitude score. The null hypothesis to be tested in the logistic regression model was that there was no effect of the predictor variables, taken together, on the outcome variable. The outcome of the logistic regression model is shown in Table 5.17.

Table 5.17 Logistic regression analysis between ADR reporting and predictor variables

Number of observations = 249
Likelihood Ratio $chi^2(8)$ = 30.44
Probability > chi^2 = 0.0002
Pseudo R^2 = 0.2685

Predictor Variable	Coefficient	Odds ratio	95% CI Lower	95% CI Upper	p value
Sex	-0.21	0.81	0.21	3.20	0.767
Age	-0.15	0.86	0.64	1.16	0.321
Duration of practice	0.16	1.17	0.87	1.58	0.309
Training	2.64	14.04	3.19	61.76	0.000
Department	-0.09	0.92	0.71	1.18	0.492
Knowledge score	-0.17	1.19	1.01	1.40	0.033
Attitude score	-0.34	0.71	0.48	1.06	0.086
Constant	-0.77	0.46	0.00006	3575.57	0.866

Since the p value obtained (p=0.0002) is less than 0.05, the null hypothesis is rejected and the conclusion is that the predictor variables, when taken together, have an effect on reporting of ADRs.

An analysis of the effects of the predictor variable on the outcome variable revealed that when the predictor variables were taken together, previous pharmacovigilance training and

knowledge score were significantly associated with reporting an ADR (p values 0.000 and 0.033 respectively). When the other predictor variables are kept constant, there was an increase in odds of reporting by 1.19 times for each unit increase in the knowledge score and an increase in odds of reporting by 14.04 times for health workers who had been trained. The odds ratios were calculated from the regression coefficients that are used in the model.

The logistic regression model is summarized using the equation:

Log odds of reporting an ADR = 0.12 designation – 0.21 sex - 0.15 age + 0.16 duration of practice + 2.64 training – 0.09 department – 0.17 knowledge score - 0.34 attitude score – 0.77

5.2 Qualitative study

Content analysis of the qualitative data from the key informant interviews was carried out. The interview notes were read through and data was classified into categories. Once all the data had been sorted into categories, the categories were examined to determine the emerging themes.

5.2.1 Trends of ADR reporting in Kenya

i. Reporting rates

The common theme identified was that although ADR reporting had improved since the launch of the pharmacovigilance program, the reporting rates were not at the ideal levels. The ideal reporting rate was identified by one key informant to be at least 200 reports per million population per year.

One key informant reported that, “Ideally we should be getting 8000 reports per year, but last year we got 2000 reports which represents about a quarter of the ideal reporting rate.”

ii. Reporting by region

The regions with the highest reporting rates were those in which there were large health facilities for example North Rift which has the Moi Teaching and Referral Hospital (MTRH), the Coast which has the Coast Provincial General Hospital and South Nyanza which has the St Camillus Mission Hospital. An unusual finding was that KNH was submitting relatively few reports considering that it is a national referral hospital; the other level 6 facility MTRH had submitted about 7 times the number of reports that KNH had submitted despite the fact that it is a smaller referral facility than KNH.

One key informant reported that “More reports are received from the areas with the big hospitals, North Rift, Coast and South Nyanza; these areas are where the big referral hospitals are. Compared to other referral facilities, we have received few reports from KNH. KNH so far have submitted about one hundred reports but MTRH have submitted about seven hundred reports which is unusual; given the patient numbers it is expected that KNH would submit many ADR reports but they do not.”

iii. Cadres of health workers that were reporting ADRs

The key informants reported that all cadres of health workers had reported ADRs. Nurses, clinical officers and pharmaceutical technologists had submitted more reports than pharmacists and medical officers. However, a comparative analysis of the reporting rate per

cadre had not been carried out therefore it was not possible to compare reporting rates per cadre.

As one key informant said, “Nurses and COs are the ones who report the most, maybe because they are the ones who number more especially in the smaller health facilities.” Another reported “The COs, nurses and pharm techs [pharmaceutical technologists] have so far been the ones who send the most reports, more than the MOs and pharmacists... we haven’t done an analysis to compare the reporting rates per cadre so maybe they submit more reports simply because they are more than the MOs and pharmacists.”

5.2.2 Factors that hindered ADR reporting by health workers

The categories that were identified are health worker factors and health systems factors.

i. Health worker factors

The themes that were identified were the health workers’ attitudes and knowledge. The attitudes that were mentioned to be hindering ADR reporting were fear of submitting an ADR report because doing so is seen as an admission of guilt of wrong doing by the health worker, the belief that ADR reporting is too much work, the belief that ADRs have already been described in literature and so there is no need to report the same ADRs. Lack of knowledge on the existence of the ADR scheme and where to report ADRs was identified as one of the factors that hindered reporting of ADRs.

A key informant reported, “Some health workers don’t report ADRs because they are afraid that they will be blamed for causing it, others complain of the high workload in their facilities

and others simply don't care. Some of them believe that ADR reporting is the work of the pharmacist and they should not be involved in it."

ii. Health systems factors

The unavailability of reporting tools, high workload for health workers and the incurring of extra expenses to send an ADR report were identified as health systems factors that were hindering ADR reporting by health workers.

5.2.3 Factors that encourage reporting of ADRs by health workers

The factors that encourage ADR reporting by health workers are health systems-related factors. The presence of Medicines and Therapeutics Committees in hospitals was identified as a factor that encourages ADR reporting since committees sometimes discuss patients with ADRs. Training of health workers through continuous medical education (CME) sessions was reported to encourage ADR reporting by health workers. The online ADR reporting system was reported to have encouraged the submission of ADR reports since it does not incur the costs of sending a hard copy report. It was reported that in the 6 month period since its launch, approximately 1000 reports or 15% of the total reports had been submitted through the online reporting system.

A key informant reported: "Whenever we hold a training, we see an increase in the number of reports submitted to the Board, but after sometime the reports reduce, until we hold a training again, then we see the reports increase."

5.2.4 Challenges encountered in implementing the ADR reporting scheme

The challenges encountered in implementing the ADR reporting scheme fell in two categories: health worker-related and health systems related which formed the bulk of the challenges. The health worker-related challenge that was identified was the negative attitudes of the health workers namely the resistance to report ADRs and fear of reporting ADRs. The health systems factors that were identified were inadequate finances to carry out trainings of health workers, inadequate staffing at the PV department of the PPB, high turnover of staff in the health facilities due to regular transfers of health workers leading to the disbandment of the facility PV teams and the inaccessibility of far-flung facilities such as those in the north eastern parts of Kenya.

One key informant said, "A major challenge that we find in reporting is the high turnover of staff. You may spend time and money training staff and then they get transferred and then you have to start all over again. Other challenges are lack of sufficient funds to conduct trainings for all health workers, accessing health facilities in areas that are far such as those in North Eastern."

5.2.5 Interventions to increase ADR reporting among health workers

i. Interventions targeting the health worker

These interventions were aimed at increasing the knowledge of the health worker on ADR reporting. Training of healthcare workers was carried out in order to increase awareness on the existence of the ADR reporting scheme and to encourage reporting. Training was not only carried out for the health workers who are already qualified and working in health facilities

but also for those who are about to graduate from universities and tertiary level colleges. The pharmacovigilance newsletter was distributed to various facilities as a way of increasing awareness of ADR reporting and providing updates for example informing health workers about medicines that have been recalled.

ii. Interventions targeting the health system

The launch of the online ADR reporting system was done to overcome the one of the challenges that was deterring reporting of ADRs namely the high costs incurred in printing and sending the hard copy reports. The key informants reported that the online reporting system had been well received by health workers and about 15% of the total reports had been submitted online within a period of 6 months since its launch.

5.2.6 Resources to increase ADR reporting

The key informants identified the following resources that were needed to increase reporting of ADRs:

i. Increasing awareness of ADR and ADR reporting

There is need to educate the public on ADRs and the importance of reporting them to health workers. Pharmacovigilance should be introduced in the training curricula for health workers. Health workers should be trained on ADR reporting including the use of the online reporting form.

ii. Technical support

These interventions included an increase in the staffing for the pharmacovigilance department and the purchase of infrastructure required to launch the online ADR reporting system in the entire country.

5.3 Summary of results

Knowledge about the ADR reporting scheme was low, with most health workers unaware of the existence and the purposes of the ADR reporting scheme. These findings were similar to those reported by the key informants. Most of the health workers sampled had positive attitudes to ADR reporting. Contingency table analysis and Student's t test was used to determine if there was an association between the predictor variables and reporting an ADR. Age of the health worker, sex, duration of practice, and the department of the health worker were not found to be associated with reporting of ADRs. Although attitudes were not found to be associated with reporting of ADRs in the quantitative study, the key informants reported that attitudes such as fear and complacency were hindrances to reporting of ADRs. Knowledge of the health worker and previous pharmacovigilance training were found to be significantly associated with reporting of ADRs. When logistic regression was carried out, knowledge of the health worker and previous pharmacovigilance training were found to be the significantly associated with reporting an ADR.

CHAPTER 6 DISCUSSION

This study sought to determine the demographic characteristics of health workers in KNH, their knowledge and attitudes to ADR reporting and the health worker factors that are associated with reporting of ADRs. The factors that were studied were the health workers' age, sex, the duration of practice, department, previous PV training, knowledge on ADR reporting and attitudes on ADR reporting. Three areas were tested under knowledge of ADR reporting: the awareness of the existence of the ADR reporting scheme, knowledge of who should report and what should be reported and knowledge about the purposes of the ADR reporting scheme. The qualitative part of the study sought to determine the factors that hinder ADR reporting by health workers and ways in which ADR reporting can be improved.

6.1 Socio-demographic characteristics of the study participants

6.1.1 Age

The nurses had the highest mean age followed by pharmaceutical technologists, pharmacists, clinical officers, medical officers and dentists. The trends are similar to those reported when a survey was carried out to assess the human resources for health in the ministries of health (Capacity Kenya, 2010). The survey reported the mean age of nurses to be higher than the mean ages of pharmacists and medical officers. Health workers working in KNH tend to be younger than those in the ministries of health. The medical officers in KNH have a lower mean age than that in the ministries for health because most of the medical officers in KNH are registrars (medical officers undergoing postgraduate training) who complete postgraduate training at an average age of 34 years (Ndetei et al., 2008).

6.1.2 Duration of practice

The mean duration of practice per cadre followed a similar pattern to the age with nurses having the longest mean duration of practice followed by pharmaceutical technologists and pharmacists, clinical officers, medical officers and dentists. The age and duration of practice are related are highly correlated which explains why the patterns of duration of practice are similar to those of age. The equation relating the age and duration of practice suggests that the average age at which the health workers sampled started to practice was approximately 23 years.

A survey on the mean years of service of health workers in the ministries of health revealed that nurses had a mean duration of practice of 17 years, clinical officers and pharmaceutical technologists 14 years, dentists 11 years, medical officers 10 years and pharmacists 5 years (Capacity Kenya, 2010). The trends in duration of practice for health workers in KNH are similar to those of health workers in the ministries of health; nurses tend to have practiced for longer periods than medical officers, pharmacists and dentists. The duration of practice varies across all cadres and it was found not to be associated with reporting of ADRs.

6.1.3 Sex

Most of the study participants (73.4%) were female because most of the health workers sampled were nurses (83.4%) and nursing is a predominantly female profession in Kenya (Capacity Kenya, 2010).

6.1.4 Previous pharmacovigilance training

Majority of the health workers had not received any training on pharmacovigilance. An analysis of the training per cadre revealed that all the pharmacists and pharmaceutical technologists had been trained whereas less than half of the other cadres had received training. The possible explanation for this observation is that the pharmacovigilance training begun with these two cadres before being rolled out to the other cadres and therefore not all the workers in the other cadres had received training. The National Pharmacovigilance Guidelines are provided to all health facilities in order to supplement the education of health workers on reporting of ADRs. It contains information on how to detect and classify ADRs, the reporting system and the expected outcomes. In addition the PPB uses a standard training curriculum to train all cadres of health workers on ADR reporting (MoMS and MoPHS, 2009). However, it is unlikely that all the health workers in KNH had read these guidelines given that most of them were unaware of the existence of the ADR reporting scheme.

The key informants identified inadequate training as one of the challenges in the implementation of the ADR reporting scheme. It was noted that the training curricula for health workers were deficient in imparting knowledge of pharmacovigilance and therefore steps were being taken to include pharmacovigilance in the curricula through the efforts of the PPB.

6.2 Knowledge of the health workers on ADR reporting

Awareness of the existence of the ADR reporting scheme was generally low among the health workers. Awareness on the information to be reported to the scheme and the purposes of the

scheme was fairly good. Studies done in other countries revealed that the knowledge on the existence of an ADR reporting scheme varied widely, from as low as 12% to as high as 99% of the health workers sampled (Chopra et al., 2011; Green et al., 2001; Hasford et al., 2002; Jarernsiripornkul et al., 2009; Passier et al., 2009; Ting et al., 2010; Vessal et al., 2009).

Countries where health workers had high awareness of the ADR reporting scheme for example European countries and the US had launched their pharmacovigilance systems much earlier (in the 1960s and 1970s) than those where the health workers had low awareness such as the countries in Latin American and Africa where the pharmacovigilance systems were launched later (in the 1990s and 2000s).

6.3 Attitudes of the health workers to ADR reporting

The health workers' attitudes to ADR reporting were generally positive. Almost all of the health workers believed that ADR reporting was a professional obligation. This finding is similar to results from other studies that showed that health workers believe that ADR reporting is a professional obligation (Belton et al., 1995; dos Santos Pernas et al., 2012; Green et al., 2001; Rogers et al., 1988; Su et al., 2010).

Most studies found that the time taken to fill and submit a report was a major deterrent to reporting (Bateman et al., 1992; Belton et al., 1995; Green et al., 2001) which differ with the findings from this study where most of the health workers felt that ADR reporting does not generate extra work. A study done in Portugal found that the attitudes of complacency and diffidence were common among the respondents (dos Santos Pernas et al., 2012).

These findings differ from those obtained by the qualitative study. The key informants reported that some of the reasons that health workers do not report ADRs include fear since reporting an ADR may be taken as an admission of guilt on the part of the health care worker, the belief that reporting an ADR is too much work and having an attitude whereby they simply do not care to report ADRs. Others exhibit an attitude of complacency; they believe that the adverse drug reactions have already been documented so they see no need to report.

6.4 Health worker factors that affect ADR reporting

Using contingency table analysis and logistic regression analysis the factors that were found to be significantly associated with reporting of ADRs were previous PV training and knowledge on ADR reporting. Previous PV training affects the knowledge of the health worker on ADRs which in turn affects reporting ADRs.

Previous PV training was found to be significantly associated with reporting ADRs. Training is a form of imparting knowledge therefore it is expected that health workers who are trained on ADR reporting have higher levels of ADR knowledge than those who are not trained. The information from this study confirms this; health workers who were trained had higher mean knowledge scores (14.7 points, 95% CI: 13.6-15.7) than those who were untrained (13.4 points, 95% CI: 12.8-14.0) and this difference was statistically significant (p=0.015). Knowledge affects the practices of the health workers; those who are aware about the existence of the scheme and the procedures for reporting are more likely to report than those who are not. The finding that training is associated with reporting ADRs is supported by the information supplied by the key informants who reported that there is a tendency for reporting rates to increase after health workers are trained on ADR reporting.

For each of the three areas of knowledge, there was a statistically significant association between reporting of ADRs and two of the knowledge areas namely the awareness of the existence of the reporting scheme and the knowledge of the purposes of the reporting scheme. The non-reporters had lower mean knowledge scores than the reporters meaning that health workers who report ADRs are more aware of the existence of the reporting scheme and its purposes than those who do not report ADRs. The findings are consistent with the information provided by the key informants who reported that increased knowledge of the health worker on ADR reporting lead to a better understanding on the benefits of reporting ADRs and led to higher reporting rates.

The PPB reported that in 12 adverse drug reaction surveillance sites, the main challenges that were facing the reporting of ADRs were lack of awareness, increased workload, similarity in ADRs reported leading to monotony in reporting and limited time to report ADRs (Pharmacy and Poisons Board, 2012). The findings from this study support the PPB reports that lack of awareness is a major impediment to the reporting of ADRs. Lack of knowledge, increased workload and limited time to report ADRs were identified by the key informants as some of the factors that affect ADR reporting negatively.

Previous training on ADR reporting was found to be associated with reporting of ADRs. This finding is similar to those in other studies which showed that training health workers on adverse drug reaction reporting has a positive influence on reporting. There was an increased tendency to report ADRs if the health worker received training (Green et al., 2001; Sweis and Wong, 2000). In a study done in the UK, education and training were found to be positive predictors in influencing pharmacists to report ADRs (Green et al., 2001).

A finding from this study that is consistent with other studies that were carried out previously is the presence of a discrepancy between the number of health workers who report to seeing patients with suspected ADRs and the number of those who have reported an ADR. Whereas 89.9% of health workers reported to seeing a patient with a suspected ADR, only 5.3% had ever reported an ADR. In a Venezuelan study, 90% of the health workers reported to seeing a patient with at least one suspected ADR, but only 22.7% had ever filled in an ADR report (Pérez García and Figueras, 2011). Studies carried out in Nigeria had similar findings; in one study more than 81% of the health workers had observed at least one episode of an ADR but less than half (42.7%) had ever reported it (Fadare et al., 2011), whereas in another study 92.4% of the health workers had observed ADRs while only 25.5% of cases were reported (Ohaju-Obodo and Iribhogbe, 2010). From these studies it appears that most health workers are able to recognize ADRs; however the presence of other factors such as lack of awareness about ADR reporting, poor attitudes to ADR reporting and health systems factors such as unavailability of reporting tools lead to low reporting.

The age, sex, department and duration of practice of the health workers were not found to be significantly associated with reporting of ADRs. This finding is consistent with findings from other studies which show that the personal and professional factors have a weaker influence on ADR reporting than the knowledge and attitudes of the health worker (Lopez-Gonzalez et al., 2009). A study carried out among pharmacists in Hong Kong showed that there was no relationship between duration of practice and ADR reporting (Lee et al., 1994).

One key finding of this study differs from other studies that have been carried out before is the association between the attitudes of the health workers towards ADR reporting and the

reporting of ADRs. The findings from this study show that there is no statistically significant association between the health workers' attitudes and ADR reporting. This finding is inconsistent with several studies that have been carried out which showed that health workers' attitudes affect ADR reporting.

A study that was done in the US that found that the pharmacists who had an intention to report ADRs had more favourable attitudes than those who did not intend to report ADRs (Gavaza et al., 2011). In a study carried out among physicians in Portugal, a decrease in the attitudes complacency, insecurity, diffidence, indifference and ignorance was associated with an increase in reporting probability (Herdeiro et al., 2005). The attitude insecurity was found to affect reporting of ADRs in the UK, most health workers did not report ADRs unless they were sure that the drug was the cause (Belton et al., 1995). Physicians in Sweden tended not to report ADRs if they felt that the reaction was well known (Ekman and Bäckström, 2009).

A systematic review that examined the determinants of under-reporting of ADRs found that the attitudes that were most commonly associated with not reporting ADRs were ignorance, diffidence, lethargy, indifference and insecurity, complacency and fear (Lopez-Gonzalez et al., 2009).

A possible explanation for the finding that there is no significant difference in the attitude score between reporters and non-reporters in this study is that the knowledge of ADR reporting affects the attitudes. In this study, most of the health workers were not aware of the existence of the ADR reporting scheme, had never seen the reporting form and had never reported an ADR; therefore their responses to the attitude questions are not based on the actual

experience of reporting an ADR but on hypothetical situations of what they perceive ADR reporting to be.

Adverse drug reaction reporting is an important method of ensuring medicine safety. The findings from this study are important because they show that lack of knowledge is a major impediment to reporting of ADRs by health workers in KNH.

6.5 Limitations of the study

A limitation of this study is that the results obtained may not be generalized to other public hospitals in Kenya. The reason for this is because KNH is a large teaching and referral hospital, which contains cadres of health workers that may be absent in other lower level facilities, for example doctors undergoing postgraduate training (registrars) are found in referral hospitals and certain cadres of health workers for example medical specialists do not practice in the lower level facilities such as dispensaries and health centres. Another limitation of the study was that the use of self-administered questionnaire may limit the accuracy of information that was obtained; however, this was mitigated by using qualitative methods to complement the data collected from the quantitative study and to provide more information on the health systems factors that affect the reporting of ADRs by health workers.

CHAPTER 7 CONCLUSION AND RECOMMENDATIONS

7.1 Conclusion

This study sought to find out the knowledge and attitudes of adverse drug reaction reporting among health workers in KNH as well as the factors that are associated with adverse drug reaction reporting. The findings from the study showed that although most of the health workers had seen a patient with a suspected adverse drug reaction, only a few had ever reported ADRs.

i. Knowledge of health workers on adverse drug reaction reporting

The findings from the study show that the knowledge on the existence of the reporting scheme was generally low. Most health workers scored poorly on the awareness of the existence of the ADR reporting scheme, but had average scores on the awareness of the information that should be reported to the scheme and the purposes of the scheme. Most health workers had never seen the ADR reporting form.

ii. Attitudes of health workers on adverse drug reaction reporting

The attitudes of health workers to ADR reporting were generally positive. Most felt that adverse drug reaction reporting was a professional obligation.

iii. Factors associated with adverse drug reaction reporting

Health worker's knowledge and previous pharmacovigilance training were found to be significantly associated with reporting of ADRs.

In summary, the health workers were not reporting ADRs because they were unaware of the existence of the ADR reporting scheme.

7.2 Recommendations

Spontaneous reporting of adverse drug reactions is one of the methods used to enhance medicine safety. Based on the findings of this study, the following recommendations are made to improve reporting of adverse drug reactions in Kenyatta National Hospital.

i. Training of health workers on ADR reporting

Previous pharmacovigilance training was found to be significantly associated with the reporting of adverse drug reactions (p=0.000). It is recommended that the health workers should receive training on ADR reporting. The training should provide health workers with information on the existence of the national scheme for reporting adverse drug reactions and the importance of reporting as well as provide information on who should report ADRs and the information that should be reported.

The PPB should consider the development of online training modules on ADR reporting. One advantage of online modules would be reduced costs of training each health worker since there would be cost savings on accommodating health workers and production of printed training materials. Another advantage would be flexibility since health workers could learn during a time that is convenient for them. PPB could then liaise with the other health professional associations such as the Kenya Medical Association, Nursing Council of Kenya and the Clinical Officers Council such that the health workers who complete these modules earn continuous professional development points.

Since the age, sex and the duration of practice of the health worker are not significantly associated with reporting of ADRs, all the health workers should be considered for training regardless of their sex and the number of years they have practiced.

ii. Availing the ADR reporting forms in the wards and increasing awareness of the online reporting form

Most health workers reported that they had never seen the Suspected ADR reporting form. There was a statistically significant association between seeing the ADR form and reporting an ADR ($p=0.000$). The ADR reporting form should be availed in all wards and clinics in the hospital in the same way as the other hospital forms such as the laboratory request form and radiology request form. The ward in-charges could order the ADR forms from the pharmacy department regularly as they do with the other ward stationary. Each ward and clinic should have a file where the ADR reports that are filled in are kept before they are forwarded to the PPB at the end of every month.

Health workers should be made aware of the existence of the online reporting forms as an alternative to the paper-based reporting form for submitting reports because the online reporting system has more advantages such as the immediate receipt of the form by the PPB and the cost savings since no postage or printing costs are incurred when sending the online report.

iii. Rebranding of the national pharmacovigilance system

The results showed that most health workers were unaware of the existence of the national ADR reporting scheme and most had never seen the reporting form. There was a statistically

significant association between the awareness of the ADR reporting scheme and the reporting of ADRs (p=0.000). In addition to training health workers, another method of increasing awareness is to have an identifiable brand for the National Pharmacovigilance system that makes it easy for the health worker to identify the scheme. Examples of well branded pharmacovigilance systems are the US system named MedWatch and the UK and Nigerian systems named the Yellow Card Scheme. It is possible that the use of the name the National Pharmacovigilance Centre may be a contributing factor for the non-pharmacy related cadres from reporting ADRs because the word "pharmacovigilance" may be erroneously interpreted as relating only to pharmacists or pharmaceutical technologists. A well-branded system with a catchy name that is easy to remember would also make it easier when implementing patient reporting of ADRs in the future.

iv. Further research on ADR reporting

There is need to carry out further research to other facilities in the country to determine if the factors associated with reporting ADRs are similar to those that have been found in this study. Additional research is needed to determine the effect of the other factors on adverse drug reaction reporting for example the health systems factors and patient factors, as well as effective interventions for improving reporting of adverse drug reactions.

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APPENDICES

Appendix 1: Informed consent form for health workers in Kenyatta National Hospital

INFORMED CONSENT FORM

Title of the study:

Health worker factors associated with reporting of adverse drug reactions in Kenyatta National Hospital.

Introduction

You are invited to participate in a research conducted by Dr Clare Obonyo, a student at the University of Nairobi, School of Public Health. This research is part of the Master of Public Health degree. Your participation in this study is voluntary. Please feel free to ask any questions or to seek clarification if you do not understand. If you decide to participate, you will be asked to sign this form and you will be given a copy of the form to keep.

Purpose or objectives of the study

The purpose of this study is to determine the health worker factors associated with reporting of adverse drug reactions in Kenyatta National Hospital. The study is for research purposes only and the information collected will be used to help design interventions that will improve the reporting of adverse drug reactions by health workers.

Study Procedures

If you decide to participate in the study, you will be asked to fill in a questionnaire.

Participant selection

The participants in this study are the health workers who are directly involved in patient care in Kenyatta National Hospital. You have been randomly selected from a list of health workers in Kenyatta National Hospital to participate in the study.

Benefits of participating in the study

By participating in the study, you will provide information that will help us understand reporting of adverse drug reactions in Kenyatta National Hospital. This information will help

us take necessary actions to make it easier for you to report adverse drug reactions and therefore increase the reporting rates.

Voluntarism

Your participation in this study is voluntary. You may choose not to participate in the study. You may withdraw consent at any time and decide not to continue participating in the study.

Confidentiality

No names or personal information will be collected at any stage during the study. Any information that will be collected during the study will be kept confidential. The data collected from the study will be stored in the personal computer of the researcher Dr Clare Obonyo and presented as a thesis towards the Master of Public Health degree.

Information on researchers

If you require any additional information regarding the researcher, please contact:
Dr Clare Obonyo
Email address: aceobonyo@gmail.com

or

The Director,
School of Public Health
University of Nairobi
Telephone number: 020 272 6300
Email address: director-sph@uonbi.ac.ke

Information on the UoN/KNH Ethics and Research Committee

If you would like to contact of the University of Nairobi/Kenyatta National Hospital Ethics and Research Committee regarding any aspects of this study, the contact details are:

University of Nairobi/Kenyatta National Hospital Ethics and Research Committee
Telephone 2726300 Ext 44355

The study proposal has been reviewed and approved by the University of Nairobi/Kenyatta National Hospital Ethics and Research Committee under the reference number P170/4/2013.

Signature of Research Participant

I have read the above information. I have been given the opportunity to ask questions and the questions have been answered satisfactorily. I agree to participate in the study.

Signature of participant: _____

Date:_____

Signature of Investigator

I have explained the research to the participant and answered his/her questions to the best of my ability. I confirm that consent has been given freely.

Signature of Investigator: _____

Date: _____

Appendix 2: Informed consent form for key informants

INFORMED CONSENT FORM

Title of the study:

Health worker factors associated with reporting of adverse drug reactions in Kenyatta National Hospital.

Introduction

You are invited to participate in a research conducted by Dr Clare Obonyo, a student at the University of Nairobi, School of Public Health. This research is part of the Master of Public Health degree. Your participation in this study is voluntary. Please feel free to ask any questions or to seek clarification if you do not understand. If you decide to participate, you will be asked to sign this form and you will be given a copy of the form to keep.

Purpose or objectives of the study

The purpose of this study is to determine the health worker factors associated with reporting of adverse drug reactions in Kenyatta National Hospital. The study is for research purposes only and the information collected will be used to help design interventions that will improve the reporting of adverse drug reactions by health workers.

Study Procedures

If you decide to participate in the study, you will be interviewed.

Participant selection

The participants in this study are the health workers who are directly involved in patient care in Kenyatta National Hospital and those who are working in the Pharmacovigilance Department in the Pharmacy and Poisons Board (PPB). You have been selected to participate in the study because of your experience in the PPB; you are likely to provide more information on the reporting of adverse drug reactions and some of the challenges that health workers experience in the reporting of adverse reactions.

Benefits of participating in the study

By participating in the study, you will provide information on health workers' reporting of adverse drug reactions and factors that may encourage or discourage adverse drug reaction

reporting by health workers. This information will be useful in designing and implementing strategies of improving adverse drug reaction reporting rates.

Voluntarism

Your participation in this study is voluntary. You may choose not to participate in the study. You may withdraw consent at any time and decide not to continue participating in the study. You have a right to refuse to answer certain questions.

Confidentiality

No names or personal information will be collected at any stage during the study. Any information that will be collected during the study will be kept confidential. Some of your comments may be quoted in the final report; however you will not be identified by name or any other potentially identifying information such as your designation. The data collected from the study will be stored in the personal computer of the researcher Dr Clare Obonyo and presented as a thesis towards the Master of Public Health degree.

Information on researchers

If you require any additional information regarding the researcher, please contact:
Dr Clare Obonyo
Email address: aceobonyo@gmail.com

or

The Director,
School of Public Health
University of Nairobi
Telephone number: 020 272 6300
Email address: director-sph@uonbi.ac.ke

Information on the UoN/KNH Ethics and Research Committee
If you would like to contact of the University of Nairobi/Kenyatta National Hospital Ethics and Research Committee regarding any aspects of this study, the contact details are:
University of Nairobi/Kenyatta National Hospital Ethics and Research Committee
Telephone 2726300 Ext 44355

This study has been reviewed and approved by the University of Nairobi/Kenyatta National Hospital Ethics and Research Committee Reference number P170/4/2013.

Signature of Research Participant

I have read the above information. I have been given the opportunity to ask questions and the questions have been answered satisfactorily. I agree to participate in the study.

Signature of participant: _____

Date:_____

Signature of Investigator

I have explained the research to the participant and answered his/her questions to the best of my ability. I confirm that consent has been given freely.

Signature of Investigator: _____

Date: _____

Appendix 3: Questionnaire

Health provider factors associated with reporting of adverse drug reactions in Kenyatta National Hospital.

Please answer the questions as accurately as you can. The information submitted will be treated in confidence.

Questionnaire Number: _____

1. Age: _____ years
2. Gender
   - Female
   - Male
3. What is your designation? (tick one)
   - Clinical Officer
   - Clinical Pharmacist
   - Consultant Doctor
   - Consultant Dentist
   - Dentist
   - Dentist Intern
   - Medical Officer
   - Medical Officer Intern
   - Nurse
   - Pharmaceutical technologist
   - Pharmacist
   - Pharmacist Intern
   - Registrar
4. For how long have you practiced as a healthcare provider?
   _____ years
   If less than 1 year: _____months
5. Department: _____
6. Have you ever received any training or on-the-job sensitization on adverse drug reaction reporting?
   - No
   - Yes

7. Are you aware of the existence of a national pharmacovigilance centre in Kenya for reporting adverse drug reactions? [yes= 1 point]
    - No
    - Yes
8. If you answered yes to question 7, where is the national pharmacovigilance centre located? (tick one) [PPB= 1 point]
    - Ministry of Health headquarters (Afya House)
    - Pharmacy and Poisons Board
    - Department of Pharmacovigilance in the School of Pharmacy, University of Nairobi
9. Have you ever seen the Suspected Adverse Drug Reaction reporting form? [yes=1 point]
    - No
    - Yes
10. Who should report suspected adverse drug reactions? (tick **all** that apply) [each choice=1 point, maximum score 11 points]
    - Consultant doctors
    - Registrars
    - Medical officers/ Medical officer interns
    - Dentists/ Dentist interns
    - Pharmacists/ pharmacist interns
    - Nurses
    - Pharmaceutical technologists
    - Clinical Officers
    - Traditional medicine practitioners
    - The patient affected by the adverse drug reaction
    - The next of kin of the patient affected by the adverse drug reaction

11. When would you fill an adverse drug reaction report?
(Please tick one response for each choice)

		Yes	**No**	**Not sure**
i.	All suspected adverse drug reactions, whether they are serious or not	[1 point]		
ii.	A suspected adverse reaction to a medical device	[1 point]		
iii.	Suspected adverse drug reactions to vaccines	[1 point]		
iv.	Suspected adverse drug reactions to traditional (herbal) medicines	[1 point]		
v.	When you are not sure that the drug caused the adverse drug reaction	[1 point]		
vi.	When you have incomplete details regarding the patient or the adverse drug reaction	[1 point]		

12. What are some of the **purposes** of the adverse drug reaction reporting scheme?
(Please tick one response for each choice)

		Yes	No	Not sure
i.	To determine the incidence of all adverse drug reactions		[1 point]	
ii.	To identify factors that predispose patients to adverse drug reactions	[1 point]		
iii.	To enable safe drugs to be identified		[1 point]	
iv.	To identify previously unrecognized adverse drug reactions	[1 point]		
v.	To identify bizarre reactions to drugs	[1 point]		

13. Do you **agree** or **disagree** with each of the following statements?
(Please tick one response for each choice)

		Agree	**Not sure**	**Disagree**
i.	Reporting adverse drug reactions is a professional obligation	[1 point]		
ii.	It is difficult to know whether or not an adverse drug reaction has occurred based on my clinical knowledge.			[1 point]
iii.	Reporting just one case of a suspected adverse drug reaction will not have a significant effect on the national database for adverse drug reactions			[1 point]
iv.	There is not enough time in my work schedule to report adverse drug reactions			[1 point]
v.	I would only report an adverse drug reaction if I am sure that the drug caused it.			[1 point]
vi.	Most of the serious adverse drug reactions have been described before the drug is released in the market			[1 point]
vii.	If a patient experiences an adverse drug reaction it means I may have administered treatment that harmed him/her.			[1 point]
viii.	Reporting adverse drug reactions might result in legal action taken against health workers			[1 point]
ix.	It is nearly impossible to determine if a drug is responsible for causing a particular adverse drug reaction			[1 point]
x.	Filling in an adverse drug reaction report generates extra work.			[1 point]

14. Have you ever come across a patient who had a suspected adverse drug reaction?
    - ☐ Yes
    - ☐ No
15. Have you ever filled in an adverse drug reaction report?
    - ☐ Yes
    - ☐ No

Thank you for taking time to participate in the study.

Appendix 4: Key informants' interview guide

Health provider factors associated with reporting of adverse drug reactions in Kenyatta National Hospital

Designation of key informant: _____

1. What are the trends of adverse drug reaction reporting by health workers in Kenya?

2. In your opinion, why do the health workers fail to report ADRs?

3. Are there factors within the health system that encourage health workers to report ADRs?

4. What are the challenges that you have encountered in implementing the ADR reporting scheme among health workers?

5. What interventions have been made so far by the PV dept to increase ADR reporting among health workers?

6. In your opinion, what additional resources would be required to increase ADR reporting among health workers to the ideal levels?