The University Of Sheffield.

PHARMACOVIGILANCE AND ADVERSE DRUG REACTION REPORTING PRACTICES AMONG GHANAIAN HEALTHCARE PROFESSIONALS

by

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DEDICATION

To my family, for their inspiration and unconditional support.

DECLARATION

I, Walter-Rodney Nagumo hereby declare that this thesis is an original piece of work. No part of the work referred to in this thesis has been submitted in part or entirety to any other university or institution of learning, other than the University of Sheffield, for the award of an academic degree or qualification similar.

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ABSTRACT

Background - Under-reporting of adverse drug reactions (ADRs) is a challenging medication safety problem globally. Even though ADRs are associated with significant morbidity and mortality, poor reporting among healthcare professionals (HCPs) persists, particularly in resource-limited settings. This study aimed to explore HCP experiences and factors influencing ADR reporting in the Ghanaian hospital setting.

Methods - A concurrent mixed methods design was undertaken using face-to-face semi-structured qualitative interviews, focus groups and a survey. Nursing, pharmacy and medical staff were sampled using a stratified random sample from five hospitals in Tamale, Ghana coupled with purposive sampling for interviews. Survey data were analysed descriptively using SPSS and in-depth interviews and focus group discussions analysed using a six-stage thematic analysis using NVivo.

Findings - 386 HCPs (86% response rate) participated in the survey. Pharmacovigilance (PV) knowledge was low (19%) with the majority being unaware of the national PV centre (68%) and basic information on reporting forms (65%). Pharmacy staff were however more knowledgeable compared to nursing and medical staff. Only 13% of HCPs reported to have observed an ADR at least once in a year and another 14% had completed a form. The majority (92%) of HCPs agreed that patient safety could improve if they reported ADRs and disagreed that litigation (82%) and lethargy (81%) were a hindrance. Pharmacists were perceived to have a key ADR reporting role. Use of verbal reporting was perceived to reduce ADR reporting formally along with complex interrelated system and human factors, such as lack of forms, inadequate infrastructure, stakeholder issues, uncertainty about reporting responsibilities, poor interpersonal relations, perceive patient attitudes, bureaucracies, fear of wrongdoing and blame.

Conclusions – This study suggests that ADR reporting is low and often informal in the Ghanaian hospital setting but enhancing the role of pharmacists may be important in improving ADR reporting, as well as increasing HCP awareness through training – particularly for non-pharmacy staff - and logistical changes such as electronic ADR reporting.

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LIST OF ABBREVIATIONS

ADR/s	Adverse Drug Reaction/s
HCP/s	Healthcare Professional/s
ADE/s	Adverse Drug Event/s
AEv	Adverse Event
ME	Medication Error
ADEf	Adverse Drug Effect
ADRAC	Adverse Drug Advisory Committee
CEM	Cohort Event Monitoring
EMA	European Medicine Agency
FDA	Food and Drugs Authority
UMC	Uppsala Monitoring Centre
ICSR	Individual Case Safety Report
MAH	Marketing Authorization Holders
PHP	Public Health Programmes
PSUR	Periodic Safety Updates Report
PV	Pharmacovigilance
SRS	Spontaneous Reporting System
ScHARR	School of Health and Related Research
SSA	Sub-Saharan Africa
TDA	Therapeutic Drug Agency
TTH	Tamale Teaching Hospital
SDA	Seventh Day Adventist
TCH	Tamale Central Hospital
TWH	Tamale West Hospital
IDI	In-depth Interviews
FGD	Focus Group Discussion

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OUTLINE OF THESIS

This thesis presents the findings of a concurrent mixed-method empirical research study that sought to explore the perceptions and experiences of frontline healthcare professionals (HCPs) concerning adverse drug reaction (ADR) reporting in hospital settings in Ghana. The rationale for the study originates from the global importance of ADRs and associated reporting linked to adverse health outcomes, and for HCPs to recognise and appropriately communicate suspected ADRs in routine practice. Ghana was selected as the focus of the study based on the lack of current literature and evidence in this setting and the much lower than recommended ADR reporting levels in this country. The study used a combination of interviews and surveys and identified various human and system factors influencing reporting.

In relation to the thesis structure, it is organised into 6 main chapters. The **first chapter** is written in sections A and B. **Section A,** offers an introduction and overview of the focus of this research, namely ADRs and related key aspects such as their clinical consequence and more specific issues related to their reporting. Firstly, the broader concept of pharmacovigilance (PV) will be described and ADRs will be argued to be a key part of PV. Following this, definitions and classifications of ADRs and other related concepts will be provided, to further orientate the reader to understand how ADRs are distinguishable from medication errors and adverse drug events. The chapter will then go on to indicate the scale of ADRs, associated patient risk factors, factors influencing reporting and interventions to improve reporting. **Section B** then provides specific aspects of ADR reporting in Ghana and the reporting process. The **second main chapter** provides an empirical narrative literature review of the current research relating to the reporting of ADRs in Africa. The chapter concludes with a justification for this study, stating the primary and secondary research questions relating to this topic. The **third chapter** goes on to provide the methodological details and justification for a mixed-methods approach and how it best answers the research questions. The procedures are described in detail, offering transparency about the key choices of sampling, data collection and analysis strategies for both qualitative and quantitative phases of the research. The chapter concludes with a description of the quality of the research and ethical considerations, as well as methodological issues, unique to mixed methods. The findings are presented in **chapters four (qualitative findings) and five (quantitative survey),** with the final **chapter six** being an integrated discussion of findings, recommendation, reflective summary and conclusion of the thesis.

CHAPTER ONE

SECTION A

1.0 Introduction

This introductory chapter presents a review of the concept of pharmacovigilance (PV) and associated terminologies. The chapter also presents a review of the literature on epidemiology of adverse drug reactions (ADRs) and factors that potentially influence the reporting of ADRs. The methods for reporting, interventions to improve reporting and specific issues on ADR reporting in Ghana are presented here to give an overview and highlight the importance of the topic.

1.1 Pharmacovigilance and Related Concepts

The concept of PV and reporting adverse reactions was popularised by Dr William McBride, after the thalidomide disaster in the early 1960s led to the deaths of tens of thousands and caused severe congenital disabilities (Neil et al., 2015). Even though safety and prevention of potential harm from medications has been a key historical principle in medicine, the devastation caused by this disaster led health authorities to demand a more critical approach to the assessment of potential harm of medications. Therefore, in 1968, the World Health Organization (WHO) initiated the Programme for International Drug Monitoring (PIDM) in Uppsala, Sweden, intending to support countries worldwide to set up and run their vigilance systems.

The PIDM membership has increased over the years, currently reaching a membership of 166 countries (136 full members and 30 associate members) in 2019. Out of the 54 African member countries, Morocco and South Africa were the first two countries to join the PIDM in 1992, after 24 years of its existence. Since then, its African membership has also increased to 41 – comprising 34 full member countries and seven associate members (https://www.who-umc.org/). Coupled with weak infrastructure, the indifference of national governments and over-reliance on development partners, PV systems on the African continent are still basic compared to the rest of the developed world (Ampadu et al., 2018; Appiah, 2012; Dodoo and Ampadu, 2014; Pirmohamed et al., 2007). This deficiency reflects the number of Individual

Case Safety Reports (ICSR) sent to the PIDM centre from Africa. For example, Ampadu and colleagues have reported that only 0.88% of the ICSR analysed in 2015 were from Africa (Ampadu et al., 2016). Africa faces a higher risk of adverse effects because of poor pharmaceutical governance, high disease burden, and the proliferation of substandard and falsified medicinal products (WHO, 2017). Forty-two per cent of falsified products in the world are found in Africa, with antibiotics and antimalarials being commonly cited drugs. It was reported that in some African countries, up to 70% of their pharmaceuticals were substandard (Ghanem, 2019). Based on this primacy, one would expect a higher number of case safety reports from Africa due to falsified products, which is not the case. Even though effective action may not be possible in an unregulated environment, serious ADR cases may eventually be referred to regulated healthcare facilities where action may be required. Most people, particularly healthcare professionals (HCPs), are however still unfamiliar with the concept of PV and the associated benefits of ADR reporting, and this has been argued to influence their poor reporting behaviour (Terblanche et al., 2018). Pharmacovigilance represents a specific discipline of science, defined as:

> *"the science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other drug-related problem"* (WHO, 2015).

PV seeks to improve patient care and safety through the monitoring and evaluation of medicines in use by individuals and public health programmes (Harmark and van Grootheest, 2008). Safety is essential because clinical trials of medicinal products usually lack the required number of participants and the length of time to adequately detect long-term adverse effects of medicines.

Also, large patient populations, such as pregnant women and children who are not usually included in clinical trials for ethical reasons, are covered through post-marketing surveillance and wider use of a marketed product. PV, therefore, contributes to the ongoing assessment of the risks, benefits and effectiveness of medicines needed to promote understanding about the safe use of medicine (Jeetu and Anusha, 2010). ADR reporting is, therefore, a key component of PV, which helps to improve medicinal products by incorporating additional warnings or withdrawing them from the market where they cause serious harm (Onakpoya et al., 2015; Tabali et al., 2012; Vaidya et al., 2010).

1.2 Adverse Drug Reaction

The term 'adverse drug reaction' (ADR) has often been used broadly in medical literature to refer to several related but, importantly, different concepts such as side effects, adverse reaction and events, medication errors and adverse drug effects. However, defining ADR is problematic since this definition has changed over time. The traditional definition of an ADR was developed in 1973 by the WHO, and defined as:

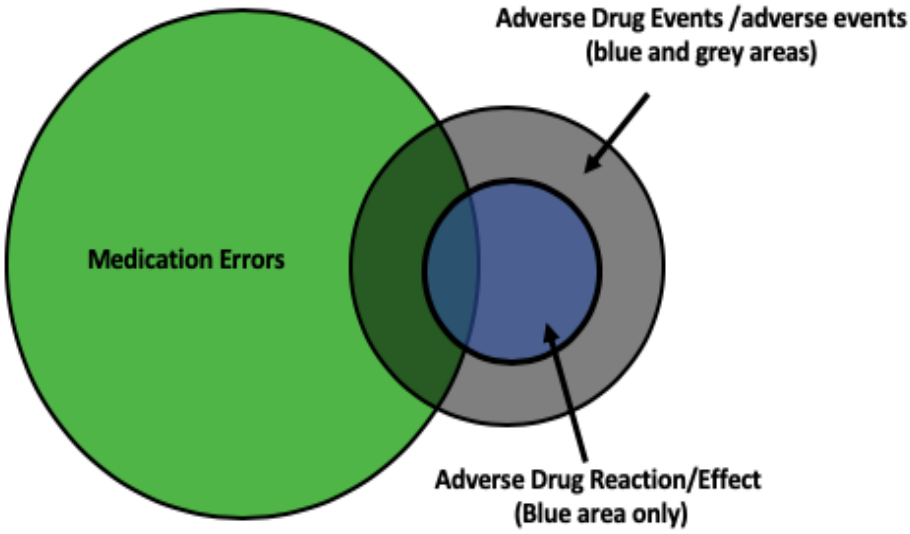
> *"Any response to a drug that is noxious and unintended and that occurs at doses normally used in humans for prophylaxis, diagnosis, or therapy of disease, or for the modification of physiological function"* (WHO, 1973).

Various authors (Bates et al., 1995; Ferner and Aronson, 1999; Laurence et al., 1998) have argued, however, that this and other definitions are old, vague, ambiguous, over-simplified and lacking specificity (Edwards and Aronson, 2000; Aronson and Ferner, 2005). Numerous definitions have therefore been proposed, with the most recent defining ADR as:

> *"An appreciably harmful or unpleasant reaction resulting from an intervention related to the use of a medicinal product; adverse effects usually predict hazard from future administration and warrant prevention, or specific treatment, or alteration of the dosage regimen, or withdrawal of the product"* Aronson and Ferner, 2005, p.855).

Notwithstanding these attempts to develop a clear, consistent and unambiguous definition for reliable ADR communication, the use of *'appreciably harmful'* in Aronson and Ferner's definition also excludes trivial adverse effects which are similar to *'noxious'* in the WHO definition. For this study, the WHO definition will be adopted since it is still widely used and accepted (Alhawassi et al., 2014). To further complicate the definitions and terminology, three closely related key terms, which appear to be used interchangeably in the literature and with a considerable degree of overlap, are medication errors, adverse drug reactions and adverse drug events (Figure 1).

Figure 1: Inter-relationship among medication-related concepts (adapted from Nebeker et al., 2004)



An ADR – which is also sometimes referred to as an ADE, using the word 'event' instead of 'reaction' – is a sub-type of the broader adverse event which is not limited to drug-related events, and it also overlaps with some types of medication error. As Table 1 illustrates, the various terms and definitions are closely related, and this arguably can be confused with ADRs. To avoid the confusion of terminologies, Aronson and Ferner (2005) therefore recommended avoiding terms such as 'side effects' in drug safety terminology. Also, caution must be taken not to interchange adverse drug reaction (ADR) and adverse drug event (ADE). All ADRs are as a result of ADEs, but not all ADEs result in ADRs, whether as a result of medication error or not (Figure 1) (Aronson and Ferner, 2005). In the literature, the term 'adverse effect' is widely used to compare synonyms such as toxic effect, side effect or unwanted effects. Even though these synonyms are generally not considered positive, there have been instances where some side effects were beneficial.

A classic example is sildenafil, which was manufactured originally for the treatment of hypertension and angina and turned out to have a beneficial side effect and was licensed for the treatment of erectile dysfunction (Guay et al., 2001). In addition, minoxidil, a blood pressure medication that had the side effect of excessive hair growth in some parts of the body, was exploited and later used to treat hair loss. Older antihistamines, such as diphenhydramine,

which had the problematic side effect of sedation, have subsequently been exploited for their use as short-term treatments for insomnia. An ADR may therefore not be reported if it is effective in supporting desirable life functions, such as helping a patient to sleep, boosting their sex drive or relieving them of other non-indicated symptoms.

Table 1: Definition of key concepts

Term	Definition	Notes
Medication Errors (ME)	"Any preventable event that may cause or lead to inappropriate medication use or patient harm, while the medication is in the control of the health care professional, patient, or consumer." (Patel et al., 2016)	ME is the most common form of patient harm which may not necessarily result in ADR or ADE (see Fig.1). Traditionally not part of PV system but has an inter-relationship.
Adverse Drug Event (ADE)	"An injury resulting from a medicinal intervention relating to a drug." (Boyle et al., 1995)	ADE includes all ADRs and sometimes may be due to preventable medication errors. They may occur during inpatient admission or outpatient observation.
Adverse Events (AEv)	"Any untoward medical occurrence in a patient or clinical investigation subject administered a pharmaceutical product and which does not necessarily have a causal relationship with the treatment." (ICH, 2009) "Any abnormal sign, symptom, laboratory test, a syndromic combination of such abnormalities, untoward or unplanned occurrence (e.g. an accident or unplanned pregnancy) or any unexpected deterioration of concurrent illness." (Aronson and Ferner, 2005)	International Conference on Harmonization (ICH) definition is typically used in clinical trial studies. All AEs are expected to be reported. AEs are sometimes generically referred to as ME, especially in Australia (Shah et al., 2013). They can be further classified as serious or not, expected or not, possible, mild, moderate, severe, life-threatening and death related. AE could involve a medicinal product or not. When they do, and the cause is attributed to a drug or medicinal product, they can be called an adverse drug event (ADE).
Adverse Drug Effect (ADEf)	"An unintended reaction to a drug administered at normal dosage." (Duan et al., 2013)	ADEf may also be used interchangeably to refer to 'side effect' or ADR. If thought to be associated with a drug, it is called a suspected ADE, but if unknown it remains an unattributed AE.
Marketing Authorization Holder (MAH)	"The company or legal entity in whose name the marketing authorisation for a product has been granted and which is responsible for all aspects of the product and compliance with the conditions of marketing authorisation." (Blake et al., 2011)	MAH usually appoints a qualified person for PV to monitor drugs and ensure all legal requirements are met.

1.3 Classification of ADRs

There are no universal standards for the classification of ADRs despite the different levels of risk associated with them. Reports have been subjective and described based on severity levels of mild, moderate, severe and lethal (Lucas and Colley, 1992). In the 1970s, ADRs were classified into two broad types: type A and type B for Augmented (dose-related) and Bizarre (non-dose-related) respectively, based on known pharmacology of a drug (Rawlins and Thompson, 1977). Type A is the most common type (80%) of ADR in hospital settings which is dose-related, has high morbidity, low mortality and can be predicted from known pharmacological action of the drug. Examples include drug toxicity dysrhythmia caused by digoxin and constipation from chronic opioid use. These are usually managed by reducing the dose, stopping the medicine or checking for associated medications interaction. Type B ADRs are referred to as:

"[…] aberrant effects that are not to be expected from the known pharmacological actions of a drug when given in normal therapeutic doses to a patient whose body handles the drug in the normal way" (Rawlins, 1981).

These types of ADR come across as idiosyncratic, unusual, not dose-related and more serious than type A, resulting in high morbidity and mortality when they occur. Examples include intolerance from small doses of aspirin causing tinnitus, and also allergies caused by penicillin-induced anaphylaxis due to immune response. Type B ADRs are managed by withholding the drug and avoiding future use.

Over time, however, this typology has evolved and others have been developed with the pharmacology of the drug, including non-dose-time (type C), delayed reactions (type D) (Smith et al., 1996), withdrawal effects (type E) (Royer, 1997), and, most recently, type F which reflects unexpected failure of therapy. These distinctions and classifications are very important for modelling automatic electronic classification systems for the detection of ADRs in the future (Sarker and Gonzalez, 2015).

1.4 The Typology Debate

Attempts have also been made to categorise ADRs based on aetiology using a pharmacological and clinical perspective. Additionally, categories of types G and H have also emerged to capture genetic/genomic and hypersensitive (allergic) reaction respectively for either immunological or non-immunological factors responsible for ADR (Riedl and Casillas, 2003).

Aronson and Ferner (2005) have also challenged the dominant typology and noted that distinguishing between dose and non-dose-related ADRs is incorrect since all ADRs are dose-related. They proposed an alternative based on three parameters, i.e. *dose-related reaction* (sub-therapeutic concentrations, collateral effects and hyper susceptibility), *time-related effects* (rapid, the first dose, early, late and delayed) and *susceptibility factors* (age, sex, disease, physiological and genetic), as a better approach to classify ADRs (Aronson and Ferner, 2003; Ferner and Aronson, 1999). These were argued to better reflect ADRs, although the new categories only reorganise the traditional typologies. For example, types A, B and F are dose-related, types C, D and E are time-related, and types G and H are susceptibility factors.

1.5 Epidemiology of Adverse Drug Reactions

Having considered the various ADR definitions and related concepts, it is important to understand the scale and extent of ADRs. Epidemiological measurement of the scale of ADRs has been inaccurate because of high levels of under-reporting by both patients and HCPs, suggesting that the actual prevalence and incidence may be higher (Hazell and Shakir, 2006b; Rehan et al., 2012; Tandon et al., 2015). Even with the lower incidence and prevalence rates, exposure of many patients, especially in public health interventions, may lead to economically or socially important events being considered. Evidence suggests that prospective studies (Lucca et al., 2016) tend to have higher incidence and prevalence rates than retrospective studies (Palappallil et al., 2016) (Table 2). Prevalence and incidence have therefore been tried in many research studies in a variety of health system settings globally which will be briefly reviewed in this section. Key outcomes and economic costs have also been assessed for ADRs and these are considered in turn in this section, further reflecting not only on related drugs and system organs associated with ADRs but also their impact on quality of life and associated mortality.

1.6 Prevalence and Incidence

Prevalence of ADR aims to assess the total population of patients affected by an ADR incident expressed as a percentage of the population, while incidence deals with the rate of occurrence or the number of new cases over a specified period. Many studies have evidenced the prevalence of reported ADRs and ADEs, but with very different findings, which make accurate reporting on the scale of ADRs difficult; prevalence has been reported as low as 0.2% to as high as 54.5% using patients being admitted to hospital as a denominator (Angamo et al., 2016). These reports have shown ADRs to be higher in specialist populations (paediatric and geriatrics) and wards (Alexopoulou et al., 2008; Hallas et al., 1992) compared to general hospital admissions (Carrasco-Garrido et al., 2010; van der Hooft et al., 2006). For example, Peter et al. 2016, found an ADR incidence of 10.45% on medical wards, which was higher than the general ADR rate of 0.86% found in a study conducted in five hospitals (Jha et al., 2007; Peter et al., 2016). Even though published studies show a considerable level of prevalence of ADRs and ADEs in patients, the majority (65%) of side effects are underestimated and unpublished (Golder et al., 2016).

Also, determining an exact figure for ADRs experienced could be a difficult task due to low reporting and quality of reports. Hazell and Shakir (2006) found under-reporting between 36% and 99% with a median of 95% after assessing 37 studies of HCPs. The bulk of the literature quantifying ADR prevalence and incidence has been based on hospital admissions and inpatients. There have been disparities in calculating both prevalence and incidence of ADRs due to the use of different methods, screening protocols, settings, patient populations, drug classes and definitions of ADEs, ADRs, Adverse Events (AEvs), Adverse Drug Effects (ADEfs) and Medication Errors (MEs) (Leendertse et al., 2010). For example, Dedefo et al. (2016) and Laatikainen et al. (2016) calculated ADR prevalence based on ADE incidence data. This type of analysis makes it difficult to find specific incidences of ADRs. Others have measured incidence based on incidence density calculated over person time (Lagnaoui et al., 2000), per 1,000 months follow-up (Gerritsen et al., 2011), based on patient admissions (Baniasadi et al., 2008; Nakamura et al., 2014) and either at department or unit level (Kiguba et al., 2017b; Lucca et al., 2016) (Table 2).

ADR data generated from prospective studies have been more accurate than retrospective studies. This can be attributed to the robust prospective process of data collection which uses

different sources and rigorous follow-up compared to retrospective studies that rely on previous data which may be incomplete. For example, while a 20-year retrospective study of 43,380 patients found 0.8% ADR-associated admissions (Burgess et al., 2005), a two-year prospective study of 18,820 patients reported 6.5%, which was higher (Pirmohamed et al., 2004). Generally, studies have shown that the prevalence rates are lower in the USA (5.6%), England (3.2%), Germany (4.8%) and Europe (4.6%) compared to global prevalence (6%) (Angamo et al., 2016; Bouvy et al., 2015). Table 2 summarises the prevalence and incidence of some selected recent studies between 2015 and 2019. It should be noted, however, that some studies reported on the broader concept of ADE, which includes ADRs and some MEs.

Table 2: Summary of prevalence and incidence of ADE/ADR reported

Study	Design/duration	Country	Sample based on admissions	Prevalence*/ Incidence**
Akhideno **et al**., 2019	Prospective cohort/9 months	Nigeria	507 patients (internal medicine wards)	10.1%*/ 6.5%**
Beauchamp **et al**., 2019	Retrospective (6 years)	USA	673 patients (ICU, emergency and general wards)	10%** (paediatric)
Kiguba **et al.,** 2017a	Prospective cohort/5 months	Uganda	762 patients (medical and gynaecological wards)	25%*
Lucca **et al.,** 2016	Prospective observational/ 24months	India	426 patients (psychiatric unit)	35.5%**
Geer **et al.,** 2016	Prospective observational/ 9 months	India	5,482 patients (internal medicine unit, and accident and emergency unit)	6.23%*
Rojas-Velandia **et al.,** 2016	Cross-sectional/4 months	Bogota	96 patients (intensive care unit)	13.8%**
Dedefo and **Mitike, 2016**	Prospective/1 month	Ethiopia	233 patients (children)	6.7%* #
Laatikainen **et al.,** 2016	Retrospective study	Finland	290 patient records (elderly geriatric emergency department)	23.1%* #
Palappallil **et al**. 2016	Retrospective/ 24 months	India	359 patients (departments of Medicine, Surgery, Paediatrics, Obstetrics and Gynaecology, Psychiatry, Dermatology, Cardiology, Orthopaedics, Neurology and Pulmonology),	12.73%*
Chan **et al.,** 2016	Prospective/3 months	Singapore	1,000 patients (general hospital wards)	12.4%*
Ivasankaran et al., 2016	Prospective/22 months	India	1,000 patients (medical unit, ICU, paediatric and surgical)	8%*
Angamo **et al.,** 2016	Systematic review of 43 studies/NS	Global (developed and developing countries)	106–668,714 adult patients (NS)	0.2%–54.5% (median 6%) *

Bouvy **et al.,** 2015	Systematic review of 22 observational studies/2 weeks to 24 months	Europe	200–18,854 patients (general hospital and departments)	0.5%–12.8% (mean 4.6%) *
Ponnusankar **et al.,** 2015	Prospective/12 months	India	6,729 patients (general hospital)	1.29**
# Data collected on ADE, Prevalence*, Incidence** NS not specified NB: Prevalence is measured based on point prevalence data for specific periods stated in the design/duration column of the table				

1.7 Hospitalisation and Length of Stay

Hospitalisation and length of stay refers to the amount of time spent in a hospital bed due to an adverse reaction. It is influenced by several factors including concomitant medication, inadequate or improper therapy, disease complication, toxicities, age, sex and genetic disposition. A prolonged hospital stay as a result of an ADR can have consequences on patients, such as increasing cost of service and pressure on the HCP workforce and on other aspects of the healthcare system.

An observational study in the UK reported that 6.5% of hospital admissions and 1.9% of bed stays were due to ADRs. Furthermore, an average bed stay of about eight days, accounting for 4% of bed capacity, was also reported (Golder, 2013; Pirmohamed et al., 2004). A study conducted in Brazil by Moura and colleagues evaluated an intensive care unit (ICU) to assess their ADEfs on the length of stay and found that each ADR presented by the patient was related to an increase of 2.38 days in the ICU (Moura et al., 2009). A similar study conducted in an Internal Medicine Department of a French hospital found a mean length of stay of about 5.8 days (range 1–26 days) (Lagnaoui et al., 2000). Apart from specific studies on ADRs, some studies have focused on the wider topic of ADEs, which also encompasses ADRs, and has been reported to be responsible for a mean hospital stay of eight days (range 5–15 days) (Hardmeier et al., 2004).

1.8 Healthcare Costs of ADRs

The economic impact of medication-related problems (MRPs) has been assessed in various settings (Field et al., 2005; Vilhelmsson, 2015) and is estimated to be a significant burden on healthcare systems. The proliferation of substandard and falsified medical products on the African continent is worrying, with studies showing up to 18.7% prevalence of essential medicines such as antimalarials and antibiotics. Also, the WHO (2017) estimates that 42% of globally detected cases of falsified medicinal products come from Africa and result in several adverse consequences:

> *"Adverse effects (including lack of efficacy) caused by substandard and falsified medical products may lead to additional spending on repeat treatment with quality-assured medicines, as well as to extra health care costs associated with adverse reactions or infections that would not have occurred had the original product been safe and effective"* (WHO, 2017).

The calculation of healthcare costs varies due to different methods used by authors to calculate cost based on population, setting, profession, drug class, system class, disease and associated factors. The major direct costs, however, have mainly been calculated based on incomes, disposable goods and drugs with an estimated cost of £640,089 (1CHF=£0.78) over a six-month period (Field et al., 2005). In England, the NHS is estimated to spend £637 million per year on hospital admissions-related ADRs (Patel et al., 2007), while it costs the US healthcare system USD30 (£24) billion annually (Sultana et al., 2013). In the UK, cost due to ADRs could go up to £2 billion per year if indirect costs, such as loss of productivity, disability, reduced quality of life, confidence in the healthcare system and social costs from outpatients are factored in (Patel et al., 2007). In the UK, specific direct annual cost as a result of ADRs is estimated at £98.5 million (Elliot et al., 2018). Similarly, the German national estimation of ADR cost based on 57,000 hospitalisations was €434 (£374) million per year, with 3.25% as serious outpatient ADRs (Rottenkolber et al., 2011). Others have estimated it to cost up to €79 (£68) billion in the European Union (Vilhelmsson, 2015). Calculating the cost of ADRs in a smaller group of inpatients in France showed that a total of 371 ADRs cost more than €11 (£9) million at €4,150 (£3,551) per ADR (Gautier et al., 2003). Although cost estimates vary because of the different parameters used in the calculation, the significance of the cost element to ADRs cannot be discounted.

However, only a limited number of studies have estimated the cost of ADRs on the African continent. The few available studies focused on specific patient populations and settings. For example, in Nigeria, the incidence and cost of ADRs on a paediatric population of 2,400 admissions in a hospital setting was estimated as USD15,466.60 (£12,450) (Oshikoya et al., 2011). ADR costs are truly variable depending on inpatient settings with more cost associated with ICUs (USD19,685) than non-ICUs (USD13,994) (Cullen et al., 1997). Costs of ADRs are therefore directly related to hospital admissions but may be variable based on setting, data collection methods and patient population.

1.9 Quality of Life

The WHO defines health as: “A state of complete physical, mental, and social well-being not merely the absence of disease”. It therefore emphasises that frequency and severity of a disease are not the only ways to evaluate healthcare, but that an estimation of well-being by measuring improvement in health-related quality of life is equally important (WHO, 2004). ADR significantly affects the health, happiness and general well-being of individuals, which disrupts their normal functions or daily activities (Felce, 1997). Studies have mainly been targeted on ADRs that are more pronounced and life-threatening physically, rather than their impact on a person’s general well-being.

Quality of life is of immense importance, and there have been concerns about poor information and lack of specific instruments put in place to measure it, especially in children and older adults who are mostly affected by ADRs (Del Pozzo-Magaña et al., 2015). For example, a study of the quality of life of tuberculosis patients experiencing ADRs in Canada was estimated as being more of a mental well-being issue than a physical one. Nevertheless, less pronounced MRPs, such as cough, depression, incontinence, dizziness, substance-induced mood disorders and minor symptoms that may not need hospitalisation, still have a long-term effect on the quality of life of a patient (Cohen et al., 2001). These subtle ADRs affect patient adherence to treatment regimen with lifelong consequences. For example, women using contraceptives may abandon treatment if they experience weight gain or disrupted menstrual cycles (Edwards et al., 2000). The distress caused by the medication could therefore affect the quality of life and daily function.

Similarly, minor ADRs in patients on antibiotic treatment may create resistance because of non-adherence, which may impact their general well-being. This was further reflected in a qualitative study assessing an overview of HCPs’ and patients’ ADR reporting, which showed that the severity of an ADR and its effect had an impact on the daily lives of patients. A patient experiencing an ADR discomfort said: “I could not keep this up anymore, I could not wear my clothes, not my underwear, it was all too much for me” (Rolfes et al., 2014).

1.10 Mortality

Apart from increasing hospital cost, decreasing quality of life and length of stay in hospital, ADRs can result in death. For example, a study conducted in the USA by Jemal and colleagues shows (from a 30-year analysis of causes of deaths in America) that ADRs are the fourth leading cause of death behind heart disease, cancers and strokes (Jemal et al., 2005). A decline in adverse event mortality has, however, been seen between 1990 and 2016, with the recent analysis of data showing an estimated 123,603 deaths in the USA (Sunshine et al., 2019). In 2000, the Institute of Medicine of the United States reported that between 44,000 and 98,000 deaths occur annually from MEs which include ADRs (Alomar, 2014). The Global Burden of Disease study analysed annual deaths in 188 countries being the high-income countries and middle to low-income countries (Haagsma et al., 2015). The study revealed that deaths from adverse effects of medical treatment rose from 94,000 in 1990 to 142,000 in 2013 and was the fourth leading cause of years of life lost (YLL) in high-income countries, while it accounted for the 14th cause in the middle to low-income countries (Haagsma et al., 2015). Serious and fatal outcomes of ADRs often result in death or disability. A worldwide characterisation of 3,013,074 ADRs saw that, overall, 16% of them were serious (Aagaard et al., 2012) with potentially fatal outcomes underscoring the importance of collecting ADRs and medication-related problems.

Specific estimations of ADR mortalities accounted for 712 deaths annually in the UK (Elliot et al., 2018). Prescription drug overdose is said to account for a 62% rise in ADRs between 1999 and 2004 and is said to have replaced cocaine and heroin as drugs commonly involved in fatal overdoses (Alomar, 2014; Paulozzi et al., 2011). This has been supported in an earlier analysis of 39 published studies carried out within the American pharmaceutical system over four decades, which found that, in 1994, 106,000 people died as a result of ADRs (Lazarou et al., 1998). The European Commission estimates that ADRs from prescription drugs cause 200,000 deaths per year (Light et al., 2013). In light of this, several studies have reported death rates of between 1.4% (8) (Fattinger et al., 2000) and 5% (1,511 deaths) (Hakkarainen et al., 2014; Mouton et al., 2015; Bouvy et al., 2015). Data on mortality rates in Africa are scant (Mekonnen et al*.,* 2018). Only a few cross-sectional studies have attempted to estimate mortality related to ADRs. In South Africa, ADRs contributed to 2.9% of medical admissions, and 16% (56/357) of those admissions resulted in deaths (Mouton et al., 2015). Similarly, a

study in Ethiopia of 1,001 patients saw 1.5% (15/1001) of deaths resulting from ADRs (Angamo et al., 2018).

1.11 The Risk Factors of ADR

Several factors make ADRs a greater risk to one population over another (De Paepe et al., 2013; Martínez-Mir et al., 1999; Routledge et al., 2003). These may be related to age, sex, genetic factors, polypharmacy or clinical setting. This sub-section elaborates on these factors to further understand the nature of ADRs.

1.11.1 Age of Patient

An important predictor of ADR has been identified as age (Aronson and Ferner, 2005). It has, however, been challenging to categorise age as an independent risk factor or confounding factor. Age becomes a risk factor when it can be used to explain the causal pathway of a reaction, but becomes a confounder when associated with other factors. Furthermore, confounders may be related to risk factors but independently of the outcome of interest. For example, a study of 9,000 patients with ADRs saw that staying on a medical ward, alcohol intake, longer hospitalisation of more than 14 days, and having more than four concomitant medical conditions were independently associated risk factors, but not age, gender, smoking and previous history of fall (Carbonin et al., 1991). Classifying age as a risk factor for ADRs, therefore, depends on the patient population and a combination of other factors. Factors such as dementia, renal failure, polypharmacy and concomitant medication have, however, been found to be associated with the high occurrence of ADRs in older adults in some studies (Nair et al., 2016; Zopf et al., 2008). This occurrence could probably be an underestimation, as Hallas (1991) found that geriatric patients experienced difficulty in remembering their ADR experiences due to poor cognitive ability (Hallas et al., 1991).

Recruiting geriatric and paediatric populations for drug trials is rare, thus, there has been growing interest in the assessment of ADRs in these populations to detect previously unidentified ADRs (Bowman et al., 1996). Children have developing immunological and body systems, while older adults have a weakening system which makes them more susceptible to ADRs compared to other populations (Alomar, 2014). Evidence from studies on ADRs in geriatric populations in Africa and elsewhere suggests that patients aged 60 and older had a much higher risk, with 82% having drug-related problems as a result of comorbidity and polypharmacy (Hailu et al., 2020; Lavan and Gallagher, 2016). Despite the lower risk in

paediatrics compared to older adults, ADRs account for a significant number of hospital admissions, of which 39% could be severe and life-threatening (Impicciatore et al., 2001). Reports on prevalence and incidence have been varied, with studies from Malaysia showing that 63.9% of ADRs reported from their national system were from children between 12 to 17 years old (Rosli et al., 2016), while studies in Germany show an incidence of 60.7% of older adults experiencing at least one ADR (Egger et al., 2003). Multi-centre studies conducted in five countries – Australia, Germany, Hong Kong, Malaysia and the UK – found 18.6% incidence in children with several underlying differences (Rashed et al., 2012).

1.11.2 Gender of Patient

Research has shown that sex is an important susceptibility factor associated with susceptibility to ADRs, and that females are at a higher risk than their male counterparts, but the reasons behind this are unclear. For example, two-thirds of drug-induced *torsade de pointes*, which is a rare but life-threatening cardiovascular ADR, are more frequent in women than men (Drici and Clement, 2001). A Spanish study of children in a hospital also indicated females were at greater risk of ADRs, with a relative risk of 1.66 (95% CI 1.03–2.52) compared to males (Martínez-Mir et al., 1999). Accordingly, some suggested reasons for this high female incidence includes the pharmacodynamics of the drug, differences in the perception of ADR and hormonal differences (Kando et al., 1995; Schwartz, 2003). Furthermore, other underlining factors such as polypharmacy, disease and other gender-specific drugs like contraceptives may influence the higher incidence rate of women than men, but require further investigation (Fattinger et al., 2000).

For example, in the study by Tran (1998), 75% of 2,367 ADRs occurred in females, and 50% of ADRs reported by women involved polypharmacy, compared with 33% of those reported by men. This was comparable to 53.1% of ADRs in adult females found in France, even though it was not statistically significant (Montastruc et al., 2002). A study by Zopf (2008), however, could not find any sex-specific differences in the pharmacokinetic and pharmacodynamic behaviour of drugs to explain why females experienced more ADRs. Another possible explanation might be centred on gender-based norms about risk perception, whereby females are more likely to report ADRs whereas males conceal them as a sign of strength or masculinity. Recent (2019) reports on analysis of the Vigibase between 1967 and 2018 showed more female ADR reports than male were submitted worldwide, with data pointing to females in their reproductive years while male reports were mostly serious and fatal ADRs. The largest

differences were observed by women in the 18–44 years age group but could not be explained after adjusting for genitourinary system and sex hormone drugs (Watson et al., 2019).

1.11.3 Genetic Characteristics of the Patient

Different individuals respond to medications differently due to hereditary factors that predispose them to ADRs. Many ADRs, which could not be predicted and were thought to be idiosyncratic or bizarre (type B) have now been explained genetically or using immunologic pathways (Kaufman, 2016). An important example of a contributor to genetically induced ADRs is the Glucose-6-Phosphate Dehydrogenase (G6PD) deficiency enzyme, which is common among African, Mediterranean and some Filipino populations (Kent, 2012). An estimated 400 million individuals are G6PD deficient worldwide with the highest prevalence in Sub-Saharan Africa (Nkhoma et al., 2009). Individuals with G6DP deficiency have increased risk of acute haemolysis and subsequent death when certain classes of drugs or foods are ingested. For example, haemolytic anaemia linked to G6PD deficiency was found in the use of intravenous artesunate for treating malaria (Mehta et al., 2007). This deficiency is mostly asymptomatic but can cause considerable harm to individuals.

Another enzyme variability in drug pharmacokinetics and response is Cytochrome P450, which can alter drug metabolism, causing ADRs (Zanger and Schwab, 2013). It is estimated that at least 8% of the UK population, 30% of the Hong Kong population and 1% of Arabs are slower metabolisers and at risk of MRPs (Kent, 2012). Central nervous system drugs and cardiovascular system drugs are more likely to be affected by this genetic deficiency, thereby causing ADRs (Royer, 1970; Ferner, 2003).

1.11.4 Polypharmacy

Polypharmacy is a recognised practice which promotes the use of two or more drugs to treat a disease condition or multiple diseases (Arnoldo et al., 2016; Davies et al., 2007). It does, however, increase the risk of ADRs occurring, especially in elderly patients (Rodrigues and Oliveira, 2016).

Most drugs are remarkably safe, but safety has become a concern because of the large number of medications consumed (Jick, 1974). In reality, assessing the interaction of two or more medications in an individual is rarely investigated through clinical trials. It is, therefore, difficult to know what might happen when two or more medications are administered concurrently to a patient. ADRs generated from drug interactions are usually captured through post-event surveillance when the drug is in normal use.

A study of polypharmacy in the Italian health system showed that 67.2% of patients were on multiple drugs and 13.5% were patients on therapy with at least 10 drugs (Arnoldo et al., 2016). The use of multiple medications puts patients at risk of ADRs and this may be significantly exacerbated if the number of medicines is further increased (Gholami and Shalviri, 1999; Moore et al., 1998; Nguyen et al., 2006; Onder et al., 2002; Routledge et al., 2003).

Even though polypharmacy may have the potential to affect patient rehabilitation negatively, it is necessary to prevent recurrence of some conditions (Kose et al., 2016). For example, elderly stroke patients may need to control their blood pressure, lipids and plasma glucose, which requires the use of multiple therapies. Notwithstanding this finding, the number of ADRs due to polypharmacy may be influenced by several other secondary factors, such as alcohol use, breastfeeding, pregnancy, age, renal function and clinical setting.

1.11.5 Department/Clinical Setting

It is expected that the occurrence of ADRs may vary depending on the type of clinical setting, hospital department or unit. HCPs work in various hospital departments and clinical settings based on job progression, the rank of professional (Junior or Senior), professional category (nurse, doctor or pharmacist) or chosen speciality. Working in a department with frequent ADR cases may influence HCP reporting behaviour positively or negatively. Even though there may be opportunities to submit more ADR reports, the workload in busy departments or clinical settings may hinder ADR reporting (Obonyo, 2014).

ADRs studied in different clinical settings/departments have shown that higher rates are recorded in specialised units, such as medical units, ICUs, psychiatric units, geriatric and paediatric units (Dedefo et al., 2016; Laatikainen et al., 2016; Lucca et al., 2017; Rojas-Velandia et al., 2016) than general care (Chan et al., 2016). This may not always be the case, since general care usually has higher patient numbers. A systematic review of 95 studies found the prevalence of ADRs to be higher (3.03%) in general hospital admissions compared to admissions from acute care (1.14%) (Leendertse et al., 2010). There may also be variations between specialised hospital departments. Research comparing the much broader picture of ADEs (which includes ADRs) from medical intensive care units (MICUs) and surgical intensive care units (SICUs) found more ADRs in MICUs (19.4%) than SICUs (10.5%) (Bates et al., 1995; Davies et al., 2007). This could have been due to the large number of medications given in MICUs and medical departments in general due to worsening medical condition, as suggested by Davies et al. (2007). Furthermore, a review showed most ADRs (12.8%) were occurring in the medical department of a university hospital in Greece, which may reflect other issues such as polypharmacy and aggravated medical conditions (Alexopoulou et al., 2008; Bouvy et al., 2015).

1.12 Methods of Monitoring and Collecting ADR Reports

Monitoring and collecting ADR reports can be undertaken in either an isolated or organised manner among HCPs. In isolated individual reporting, HCPs send reports through to a regulatory agency or Marketing Authorization Holder (MAH) spontaneously, while organised individual reporting is done by collecting reports collated by groups of practising HCPs in hospitals, or groups of hospitals in a collaborative manner. Furthermore, comprehensive monitoring (intensive hospital monitoring) uses organised specialist physician groups, especially at referral centres (e.g. teaching hospitals) to survey drug use and identify all adverse effects. Population monitoring is characterised by automatically recording drug use and patient AEvs, and finding the association between the two (WHO, 1972). Other sources of generating ADR reports are literature reviews, database searches, post-marketing studies by MAH and public health programmes.

The most commonly used method globally for monitoring and reporting ADRs is the Spontaneous Reporting System (SRS) (Pal et al., 2013). This is often complemented by other methods such as the Active Reporting System (ARS). They both involve volunteering information about adverse reactions to responsible authorities for causality assessment. These

systems traditionally relied on paper-based reporting forms, but online electronic systems have been made possible by the proliferation of technology in the last two decades (Wu et al., 2002). Monitoring ADR is essential for the identification and communication of medication safety problems. Spontaneously reporting ADRs is the most cost-effective way to collect drug ADRs routinely from HCPs, MAH and the general public through the SRS. The WHO recommends Targeted Spontaneous Reporting (TSR), which builds on the principles of SRS (Pal et al., 2013). ARS also encompasses Cohort Event Monitoring (CEM), use of observational methods and related activities to continuously create awareness for enhanced patient reporting. Other sources include data from clinical trials and health records. In the UK, all suspected ADRs to newly licensed drugs (usually labelled with an inverted black triangle (▼)) should be reported to the Medicines and Healthcare products Regulatory Agency (MHRA). For established medicines, all serious suspected ADRs from over-the-counter medications, herbal products, food supplements and off-label drugs should be reported, even if adverse effects are well recognised. If unsure whether to report, it is recommended to go ahead and report an ADR to authorities for further assessment (Mann and Andrews, 2007).

1.12.1 Spontaneous Reporting System (SRS)

This method is referred to as a passive surveillance system, where information about ADRs is volunteered by healthcare professionals, patients and the general public to the regulatory authority or the pharmaceutical company marketing the drug. As the name suggests, there is no follow-up on patients, and reporting is solely based on personal motivation. This method is considered less expensive and able to provide safety surveillance throughout the lifespan of any drug. Rare and serious drug-related problems, such as deaths related to concentrated potassium, lidocaine, cisplatin and carboplatin, have been identified through this method (Murff et al., 2003). It is, however, challenged by issues relating to quality, biases and widespread under-reporting (Hazell and Shakir, 2006a). A review of SRS in 12 countries (Hughes et al., 2002) identified a wide variation in the type of reporting system and adverse reactions that were being reported by HCPs and the general public. The review also found that whilst some schemes recommended reporting all ADRs, others were more concerned about serious ADRs and those of new medicines only.

1.12.2 Targeted Spontaneous Reporting (TSR)

This is a sub-set of SRS, which is an add-on to routine patient monitoring in a defined setting where they are receiving treatment (WHO, 2006). For example, patients switching treatments are sensitised to report medication problems they encounter. This was developed by the WHO and piloted in 2010 on patients receiving antiretroviral drugs (Pal et al., 2013). This method is simpler and less expensive compared to ARS and can focus on priority ADRs, providing some measures of rates and incidence. The challenge of this method lies in HCPs' minimal experience with the method and individuals' lack of motivation to monitor and report (Lobo et al., 2013).

1.12.3 Active Reporting System (ARS)

In an ARS, patients are given medication and followed up using methodological procedures to search for MRPs at designated sites. This ensures high quality and quantity of reports in a cost-effective manner compared to the SRS (Kang and Lee, 2009). Worldwide active reporting systems include: the combined use of multiple databases, claims records, use of pharmacy benefits or safety managers, medical records, charts, general practitioner data, interviews and questionnaires to identify MRPs (Huang et al., 2014). Oshikoya used a similar strategy by reviewing medical and pharmacy bills, medical charts and diagnostic request forms, and by interviewing the patients for ADRs incidents in Nigeria (Oshikoya et al., 2011).

1.12.4 Chart Reviews

This takes the form of a retrospective or prospective manual collection of existing data from patient records, medication charts, prescription data and lab results, to identify MRPs. This method is actually considered the 'gold standard' for identifying and reporting ADEs, and requires the use of trained assessors (HCPs or designated research assistants) (Murff et al., 2003) but can be useful in collecting ADRs too. A first and second assessor may be used to reduce bias and increase the reliability of assessment reports, for example, a nurse may take part in the case identification phase while a doctor does the case classifications (Morimoto et al., 2004).

Prospectively, chart reviews are done while patients are still in the hospital setting. This allows collection of detailed data from lab results, doctor notes, nurse notes etc. This approach usually generates more data than retrospective chart reviews (Mazer et al., 2007).

Retrospective chart reviews, on the other hand, involve following up outpatients to collect data. This is usually less data-intense than prospective chart reviews due to sporadic visits of patients who are sometimes lost to follow-up. Some studies (Forster et al., 2003) have used patient interviews to complement this method, combined with sign-out notes, discharge summaries and lab results to help construct case summaries (Murff et al., 2003). The major challenge with chart reviews, however, is the high cost of maintenance involved, high reliance on assessors, and incomplete data, especially for outpatients (Brvar et al., 2009; Leape et al., 1991).

1.12.5 Electronic/Computerised Systems

This platform creates yet another fast and reliable way for HCPs to actively report MRPs in real time, to regulatory agencies or MAH. There has been a transition by regulatory agencies and hospitals from paper-based reporting to electronic-based reporting. Electronic patient databases of medical, pharmacy, lab and administrative records have also been automated to identify triggers. Triggers occur when a connection is made between two coded terms or rules which can lead to an adverse event (Jha et al., 1998). MRPs do not need implicit physician judgement to determine causality. For example, with technology, keywords such as 'convulsion', 'allergy', 'fall', 'drug names' or 'toxic serum' levels of digoxin can be linked to form a rule that leads to a trigger (Murff et al., 2003). This is then flagged in the database for personnel to verify the abnormalities that occur.

A further example is a study by Classen where hospital information systems were monitored for generation of ADEs in which pharmacist reviewed and monitored patients' records (Classen et al., 2005). Electronic/computerised systems are less time-consuming, information can be transferred in real time, fewer personnel are involved, and they are capable of detecting more MRPs. They do, however, have an expensive initial setup cost, issues with incomplete data and may trigger false positives (Schneider, 2002). For example, ADEs identified through a hospital database review were found to be underestimated due to incomplete data (Carrasco-Garrido et al., 2010; Waller et al., 2005).

1.12.6 Cohort Event Monitoring (CEM)

This is a type of prospective observational study where trained personnel collect data of one or more medicines in a normal setting of routine clinical practice. This was adopted by the WHO in the 1970s to monitor medication safety in public health programmes, especially in resource-limited countries (Pal et al., 2013), and malaria therapy (Bassi et al., 2013; Dodoo et al., 2014; Suku et al., 2015). It is based on the same principles as the UK's Prescription Event Monitoring (PEM) (Hazell and Shakir, 2006a) or New Zealand's Intensive Medicines Monitoring Programmes (CIOMS, 2009). CEM has the advantage of being able to capture all medication-related events of interest, including MEs, ADEs, counterfeits and ADRs. It also has the ability to accurately calculate rate of occurrence and deaths. However, it is more laborious and expensive, and requires dedicated staff. Also, patient drop-out may affect cohort size and rare ADRs cannot be detected (Pal et al., 2013). For example, a CEM of artemisia-based combination therapy (ACT) for malaria in four African countries exceeded budget by 11.1%–63.2%, took longer than expected and had data management problems (Suku et al., 2015).

1.13 Under-Reporting of ADRs Globally

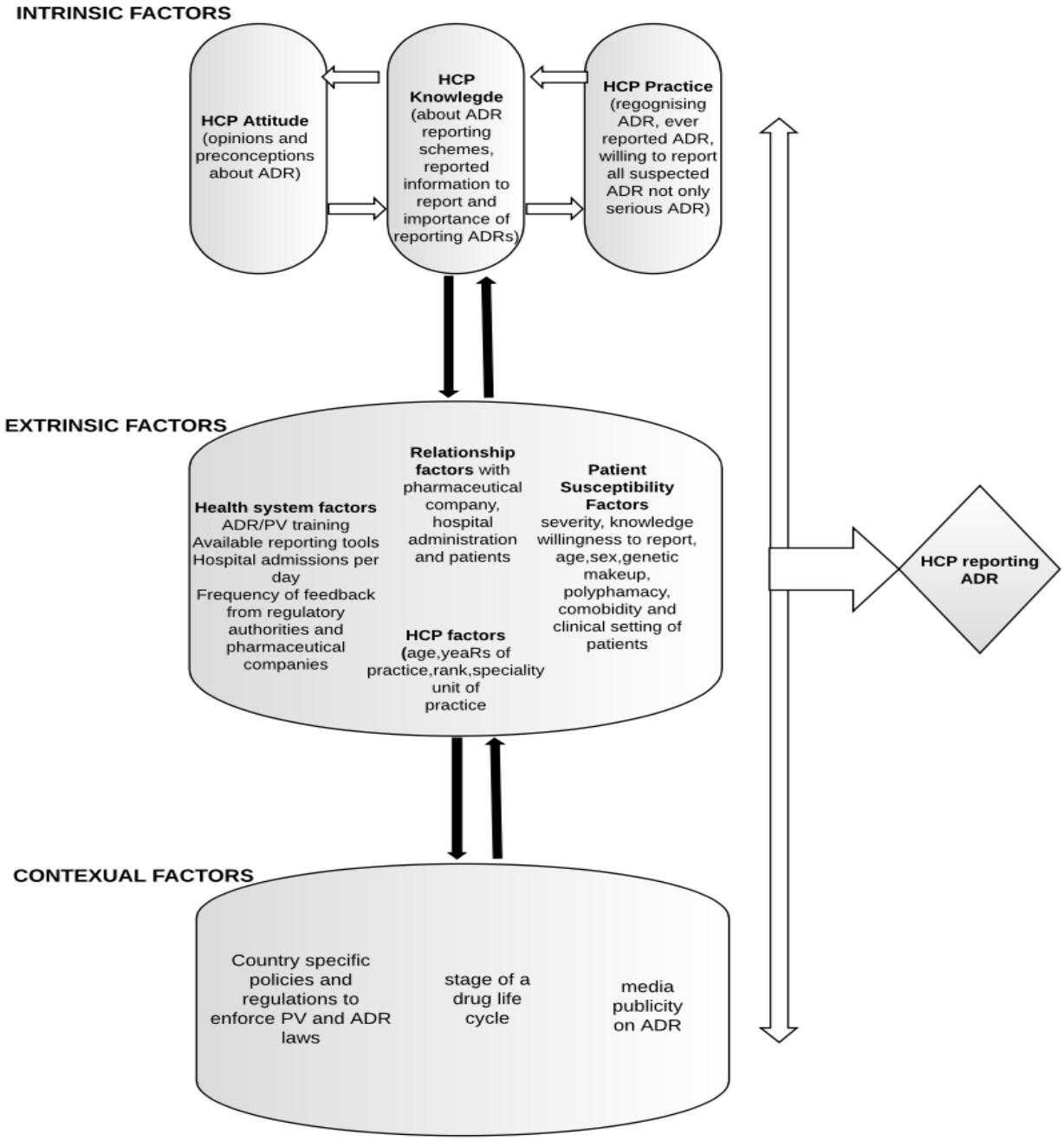
As mentioned earlier, the cheapest way of generating ADR reports is through spontaneous reporting. However, unless reporting is stimulated, it is challenged by under-reporting. Even though the WHO promotes the use of stimulated reporting, such as TSR and CEM, especially for public health programmes, the implementation of these has been challenging (Pal et al., 2013). HCPs, especially doctors, are key to the implementation of these reporting strategies, but the response has been poor. The WHO recommends a minimum of 200 ADR reports, per million population, per year, but only 10% of doctors reporting to the WHO Uppsala Monitoring Centre (UMC) meet this threshold (https://www.who-umc.org/); this could be much lower in developing countries (WHO, 2000). A systematic review suggests that 86% or more of serious ADRs leading to hospital admission go unreported (Hazell and Shakir, 2006). A more recent study reported that 70% of physicians had not reported an ADR, with the most important reason attributed to being that the ADRs were already known (41%). Several complex combinations of factors account for under-reporting. Inman (1976) suggested the '*seven deadly sins*' for under-reporting (i.e. complacency, fear, guilt, ambition, ignorance, diffidence and indifference) (Inman, 1996). These have been confirmed in several studies, including a systematic review by Lopez-Gonzales and colleagues, who suggested that the

factors identified in 45 research papers studied were more associated with Inman's typologies than with personal and professional factors, such as age, workload, educational background, training and workplace (Lopez-Gonzalez et al., 2009). Previously, only doctors were allowed to report ADRs, but recent restructuring has made it possible for patients and other healthcare professionals to send direct reports to competent authorities. Although under-reporting is still an issue, the inclusion of other calibre reporters has increased ADR reports at the UMC to more than 20 million since its inception (https://www.who-umc.org/).

1.14 Factors Influencing ADR Reporting Among HCPs

Within the subject of ADR reporting and the wider topic of how patient safety incidents are reported, several theoretical approaches and models have been developed to explain and predict particular reporting behaviours. These include broader theoretical frameworks on patients' safety, which identified 12 factors (Archer et al., 2017), as well as the use of behaviour change theories such as a theoretical domains framework (Shalviri et al., 2018). Arguably, the most influential – although somewhat outdated now – is the identification of the '*seven deadly sins*' by Inman (1976, 1996) which has been used to suggest how a multitude of factors can influence under-reporting of ADR among doctors. However, to help frame this literature review, a model that captures ADR reporting very specifically was used to draw on not only both the personal and professional (intrinsic) factors but also those external system factors of the individual which are extrinsically linked. A framework developed by Obonyo (2014) was used, which in turn drew significantly on the earlier model by Herdeiro et al. (2004) to identify a conceptual framework representing three domains affecting reporting: contextual, extrinsic and intrinsic factors. The factors tend to be inter-related and influence each other bi-directionally. For example, knowledge (intrinsic) can only be improved if the right training (extrinsic) and policies (contextual) are in place. These would be explained thematically based on available literature, and key aspects of each factor will then be elaborated on further as sub-themes explaining inter-relations and reasons for low ADR reporting based on an adapted framework from Obonyo's thesis (Figure 2).

Figure 2: Conceptual framework of factors influencing reporting of ADR by HCPs (adapted from Obonyo, 2014)



This was based on an earlier theoretical model by Herdeiro (2004) to explain this concept further, based on her mixed theoretical model (Appendix W). Herdeiro (2004) uses the theory of the acquisition of habits in health sciences – *knowledge-attitudes practices* (KAP) (Hong et al., 1995), and the *theory of satisfaction of needs* (Slotnick, 1996) to explain how intrinsic factors are influenced by other extrinsic factors towards ADR reporting, and therefore recommends combined strategies to improve reporting (Herdeiro et al., 2004). Similar factors

also emerged from an integrative review of nurses by De Angelis (2016). The authors found that extrinsic factors relating to interaction with other nurses, doctors and healthcare organisations' elements influenced nurses' reporting habits. The authors argued that reporting was influenced by nurses' intrinsic factors, which were related to their knowledge and attitudes, which was fundamental (De Angelis et al., 2016). Considering the complexity of internal, contextual and external factors, other authors have suggested exploring other possibilities for addressing the reporting culture other than just attitudinal surveys (McGettigan et al., 1997). These concepts have, therefore, been adopted to form a conceptual framework to review the literature on each classification. These are further elucidated on in the sections that follow.

1.14.1 Intrinsic Factors

Intrinsic factors refer to the core and inherent elements, which affect ADR reporting of HCPs, such as knowledge, awareness, attitude, perception and practice about PV and ADR reporting. They are considered intrinsic because they represent the innate fundamental dynamics of HCP behaviour, which determines their ability and willingness to identify, recognise and report ADRs to appropriate authorities.

A basic Google Scholar keyword search using [Knowledge AND attitude AND practice AND "adverse drug reaction" AND reporting AND "healthcare professionals"] as of January 2020, yielded 762 references. No reviews, however, summarised the literature on the factors affecting reporting in Africa. The majority of studies assessing knowledge, attitude and practice (intrinsic factors) of ADR reporting have been conducted in Europe and Asia (Alshakka, Mohamed Ibrahim and Hassali, 2013; Benkirane et al., 2015; Bhagavathula et al., 2016; De Angelis et al., 2015; Desai et al., 2011; Kamtane and Jayawardhani, 2012; Kharkar and Bowalekar, 2012; Lopez-Gonzalez et al., 2009). Under-reporting and the factors influencing reporting behaviours are therefore not adequately explored in empirical research of African studies. A review conducted in India, which shares contextual similarity to Africa as a resource-limited setting, has reported high unawareness and poor reporting attitude among HCPs. The study showed that more than half of the HCPs were unaware of the PV programme and 75% never reported an ADR (Bhagavathula et al., 2016) which may be similar in most African studies. Additionally, several reviews have shown similar trends in reporting behaviours among HCPs (Alomar, 2014; Lopez-Gonzalez, Herdeiro and Figueiras, 2009) but few have focused on Africa.

Knowledge/awareness: According to the Oxford English Dictionary (OED, 2017), knowledge is described as "facts, information, and skills acquired through experience or education; the theoretical or practical understanding of a subject" or "the awareness or familiarity gained by experience of a fact or situation". Even though knowledge and awareness are related, they may be distinct in the sense that while knowledge is based on facts through experience, education and training, awareness, on the other hand, is more about perceptions and consciousness of an individual about how things are supposed to be. For example, HCPs may be aware of the importance of the yellow card scheme but without any knowledge of the details required on the form.

Literature shows various assessments of HCPs' understanding of skills required to theoretically or practically report ADRs, but no universal tool exists to measure knowledge in PV. Most measurements, therefore, have been based on validated questions from previous studies, modified to suit research context. For example, contextually, Pulford and Malcolm's questions on knowledge were based on the meaning of the black triangle in the UK yellow card scheme, which may have only been applicable in a UK context or other jurisdiction where they have the black triangle on the label of new medicines (Pulford and Malcolm, 2010). This has resulted in different measurement scales and parameters for quantifying PV knowledge.

In the estimation of knowledge, while other studies have assessed knowledge using a few questions, others gave in-depth assessment. For example, while Almandil in her study in Saudi Arabia asked two questions to assess knowledge of HCPs, others asked 13 knowledge-based questions (Almandil, 2016; Alemu and Biru, 2019). Firstly, Almandil asked about the awareness of PV and ADRs followed by a question on types of ADRs and how to report them. She found that 62.2% were unaware of PV and 71.6% stated all types of ADR should be reported (Almandil, 2016). The majority of studies, however, have assessed the knowledge of HCPs by asking more detailed questions about the burden of ADR, where to report ADR, types of ADR to report, information to include in reports, responsible institutions, the yellow card system and PV (definition, purpose and location of WHO-IDMP) (Hajebi et al., 2010; Gupta and Udupa, 2011; Kharkar and Bowalekar, 2012; Bhagavathula et al., 2016). The designs of the questions were usually close-ended or semi-structured questions for assessing interventions or cross-sectional analysis (Avery et al., 2011; Pimpalkhute et al., 2012). The level of knowledge among key frontline healthcare staff has also been varied.

Doctors' knowledge: Physicians and doctors play a vital role in collecting ADRs because of their expertise and training in medicine and their traditional role as reporters since the inception

of the international drug monitoring programme (Jordan, Vaismoradi and Griffiths, 2016). Previously, doctors were the only HCPs allowed to report suspected ADRs, but there have been reports of low knowledge and non-reporting among them as well (Abubakar et al., 2014a; Peyman et al., 2016). The majority of studies, however, have reported moderate levels of awareness about reporting procedures even though the majority (95%) feel they are most qualified to report (Kamtane and Jayawardhani, 2012; Khan et al., 2013; Daher, Ismail and Agarwal, 2013). For example, a comparative study in Malaysia showed significant lower knowledge and awareness about PV among doctors (66.9% ± 19.86) compared to pharmacists (76.9% ± 13.87) (Abubakar, Simbak and Haque, 2014). Even though they have a good level of knowledge, reports on their level of awareness differ. For example, studies in India reported disproportionate levels of knowledge and awareness among doctors, i.e. 60% (Kharkar and Bowalekar, 2012), 52.3% (Thomas, Udaykumar and Scandashree, 2013) and 66% (Chopra, Wardhan and Rehan, 2011).

In a related review, seven studies reported high levels (90%) of knowledge and doctors knew the purpose of ADR reporting (Abubakar et al., 2014). The difference in level of awareness may therefore be due to a number of underlying factors relating to the level of doctors, age, geographical location, how data was collected and the variability in assessment tools.

Pharmacists' knowledge: Many studies have shown pharmacists to be knowledgeable and aware of the yellow card scheme and ADR reporting compared to other HCPs. In the UK they started reporting ADR independently two years before nurses, in 2000 (van Grootheest et al., 2004), and a study by Green (2001) reports that 97.7% were aware and knowledgeable about the yellow card scheme before they were allowed to report (Green et al., 2001). When assessed alone, studies have shown lack of knowledge (30%) and low ADR reporting (Afifi et al., 2014), but assessing them together with other HCPs usually shows they have better knowledge. For example, pharmacists (60.5%) and pharmacist technicians (40%) had the highest percentage of PV awareness, followed by nurses (18%) and physicians (12.1%) in a study assessing ADR reporting among HCPs (Almandil, 2016). ADRs reported by a pharmacist are said to be of better quality and quantity than other healthcare professionals because of their knowledge in pharmacotherapy (Wilbur, 2013).

Nurses' knowledge: The role of nurses has increasingly been recognised for reporting ADRs because they represent the largest cadre of HCPs in most jurisdictions (NMC, 2010; Gabe et al., 2011; De Angelis et al., 2016; Griffith, 2013). Nurses only started to report ADRs in the

UK in 2002 (Ranganathan et al., 2003) and were not part of the reporting in most parts of the world until recently. Nonetheless, reports from studies show they have improved knowledge on ADRs and how to report over time. For example, studies in Sweden showed nurses had above average (58%) knowledge (de Langen et al., 2007), similar to studies in the UAE (50%) (John, 2012), and even showed better (75%) knowledge than doctors in a tertiary hospital in India (Rehan et al., 2012). On the contrary, other studies showed that the majority of nurses (71.6%) were not aware of the reporting system and did not know how to fill in the ADR form and the reporting system, and therefore suggested poor knowledge and attitudes (De Angelis et al., 2016, 2015).

Attitudes: Attitudes deal with HCPs' feelings or emotions about ADR reporting which could be negative or positive. Even though it may be challenging to measure emotions and feelings quantitatively, researchers have widely used Inman's theoretical model of the deadly sins of reporting in surveys to assess HCP attitudes. This can be a good way to predict the knowledge of HCPs. In 1976, Inman initially presented a list of behaviours and attitudes of HCPs suspected to be causing low reporting of ADRs. He summarised the numerous and complex terms for under-reporting into seven major themes, and described them as the '*seven deadly sins*' of ADR under-reporting (Table 3). Three extra factors were added in 1996, making 10 in total (Inman, 1996). Most studies have therefore based their evaluation of attitudes of ADR under-reporting around these themes (Gent and Shigematsu, 1978; Hazell and Shakir, 2006; Kamtane and Jayawardhani, 2012; Kiguba et al., 2014; Lopez-Gonzalez et al., 2009b; Mendes Marques et al., 2016; Oshikoya and Awobusuyi, 2009; Varallo et al., 2014).

Table 3: Attitudinal factors for under-reporting of ADR (Inman, 1996)

Attitude	Definition
Complacency	Feeling content, uncritical and encouraged by the belief that only safe drugs are allowed on the market.
Fear of litigation	Anxiety of being involved in legal suits from affected individuals or investigations by the Health Departments.
Guilt	Emotionally feeling responsible for having administered a treatment which has caused appreciable harm to an individual.
Ambition	The desire to collect case series and publish for personal recognition or other rewards.
Defiance	Disobedience by the bold resistance of reporting mere suspicions without causality.
Indifference	Unimportance resulting from lack of time, interest, procrastination; by healthcare professional towards contribution to the general advancement of medical knowledge.
Ignorance	Lack of knowledge or unawareness of the process involved in submitting an ADR report.
Lethargy	A combination of procrastination, lack of time, interest and other insubstantial excuses.
Motivation (Financial Incentive)	Any monetary gain or incentive such as lottery ticket or percentage increase in salary.
Insecurity	Uncertainty about causality between a reaction and a drug.

In a systematic review of 45 studies, the most frequent attitudes affecting ADR reporting were ignorance (95%), defiance (72%) and lethargy (77%) (Lopez-Gonzalez et al., 2009a). Ignorance, which usually reflects HCPs' knowledge, has featured strongly as the most important factor for under-reporting ADRs. In a qualitative study in Ghana on ADR reporting, HCPs cited lethargy and lack of time as a result of high patient numbers in outpatients

department (OPD) as reasons for their inability to report on ADRs as shown in the following statement:

> *"… yes, it is true, some [HCPs] don't have the time to do education and I think it is OPD congestion that is causing that. Sometimes OPD will be too full with patients seeking healthcare services that you think if I should waste time doing education, I cannot finish early. I think that is the reason because all of us have been trained on counselling but we are not doing it because of pressure on us"*(health worker) (Chatio et al., 2016).

The pressure from patients gave HCPs an unfriendly attitude, keeping patients away from reporting ADRs to HCPs as expressed by the following patient:

> *"yeah at times when you go to the health facility, they would shout at you and say that it is the way the drug works...if you don't want them to shout at you, you will not go back and tell them and rather prefer to keep it (ADR)…"* (Chatio et al., 2016).

In Brazil, Varallo (2014) showed a similar trend in their study of HCPs where ignorance (82.7%), insecurity (82.7%) and indifference (79.3%) were ranked highly (Varallo et al., 2014). Many of these assessments have been explored quantitatively using structured or semi-structured interviews (Rolfes et al., 2014). Semi-structured interviews have allowed the addition and explanation of HCP attitudes. For example, a study showed qualitatively that the word 'report' was misinterpreted by nurses to mean just telling a doctor or a patient, or noting in clinical records, rather than making sure it was forwarded to the appropriate regulatory authority. The authors, therefore, added other factors for under-reporting: misinterpretation of the meaning of 'reporting', unawareness of nurses' autonomy to report ADRs and fear of consequences after ADR reporting (De Angelis et al., 2016). Several additional factors have therefore been reported based on contextual relevance. Varallo (2014) also proposed addition of 'lack of training in pharmacovigilance reporting' (Varallo et al., 2014). Attitude may, therefore, differ depending on the professional category, context and other inter-related factors. For example, doctors and nurses have similar attitudes to ADR reporting but cultural differences in roles are found to underpin their attitudes (Moumtzoglou, 2010). Nurses have been reported to have a much more positive attitude to ADR reporting than doctors (Whitaker and Ibrahim, 2016). This may be because nurses have a culture of following protocols, directives and fear of being scolded as suggested by Mirbaha and others (Mirbaha et al., 2015).

For example, in a study exploring doctors' and nurses' attitudes to reporting in Australia, a senior nurse said:

> *"our organization tell us that we need to fill out these forms, therefore we do. We have a directive..."* (Kingston et al., 2004).

This has resulted in nurses preferring to report ADRs to doctors and pharmacists rather than the appropriate authority (Hanafi et al., 2012). Even though researchers have narrowed themselves to Inman's attitudes, reasons for not reporting ADRs may still depend on complex inter-relations of personal barriers, contextual and extrinsic factors that need to be explored further.

Practice: The practice of HCPs relates to the real-world application of methods for reporting ADR. This has been tested in cross-sectional studies using theoretical questions to assess the expected method of reporting ADRs. HCPs are usually asked about where reports were submitted, number of reports submitted in the past year or month, number of times reported, training on PV, types of ADR reported, types of implicated drugs and action taken (Prakasam et al., 2012). PV training is an important aspect, which improves knowledge, attitude and practice. It helps HCPs to understand where to send reports and how to report. In Ghana, training for only higher rank doctors affected the reporting of junior doctors, thus a recommendation for more training on PV was recommended for junior doctors to increase ADR reports (Sabblah et al., 2014). Other studies, which did not put emphasis on training, noticed doctors were inclined to send ADR reports (87.7%) to pharmaceutical companies instead of to recommended government ADR centres (18.5%) (Kharkar and Bowalekar, 2012). There has been a consistent increase in the number of ADR reports submitted by nurses (Hawcutt et al., 2011). They form the largest cohort of HCPs in most jurisdictions and their contributions to ADR reporting are of immense importance (Griffith, 2013). Nurses' ADR reports have been said to be comparable in quality and quantity to doctors' (Griffith, 2013; Morrison-Griffiths et al., 2003). The success of the ADR reporting process, however, depends on the collaboration of nurses and other HCPs (Jordan et al., 2016). Nursing practice in general also has low ADR reporting rates compared to pharmacists. For example, a study showed that 91% of nurses had never reported an ADR and most (87.1%) of them preferred to report to doctors and pharmacists in hospitals' ADR centres rather than the ADR National Centre (1.8%) (Hanafi et al., 2012).

Pharmacists are noted in many studies for better quality and quantity of ADR reports than other HCPs (Wilbur, 2013) even though they are also known to have low reporting rates in practice (Green et al., 2001; Almandil, 2016). In other studies, when compared to doctors, pharmacists reported more (70.8%) ADR than doctors (51.9%) (Molokhia et al., 2016), but when evaluated alone in a different study, only 11.8% ever reported an ADR to authorities (Prakasam et al., 2012). Highly specialised professionals in pharmacology are more likely to report ADR than other professional classes. For example, other studies have shown differences within the pharmacy staff sub-specialities where clinical pharmacists were noted to be more likely to report an ADR than dispensing pharmacists (Liu et al., 2015). Most commonly associated factors affecting practice were higher professional title, training on ADR reporting and access to forms (Liu et al., 2015). Practice can be therefore influenced by rank and class of medical professional, experience and training.

1.14.2 Extrinsic Factors

Apart from intrinsic reasons affecting ADR reporting, there are also extrinsic or distal factors. Extrinsic factors are external factors which relate to health system/organisation, patient susceptibility factors (age, sex, genetic, comorbidity), confounding HCP characteristics (age, sex, rank, experience and education), administrative bottlenecks and relationship with other stakeholders, such as regulatory authorities and pharmaceutical companies which affect ADR reporting by HCPs.

HCP characteristics: Not many studies have reported the association between HCP characteristics and reporting. Older age, professional rank and longer working experience of an HCP is expected to influence the rate of ADR reporting positively. This has been demonstrated to be true in some studies (Bateman et al., 1992; Cosentino et al., 1999; Sabblah et al., 2014). For example, Sabblah's study of Ghanaian doctors reported that higher-ranked doctors were more likely to report ADR than house officers (Sabblah et al., 2014a). However, other studies have found experience and older age not to be associated with better ADR reports, because physicians and pharmacists were unable to identify potential drug-drug interactions correctly (Routledge et al., 2003). HCPs who reported ADRs were rather younger practitioners (Tubert-Bitter et al., 1998). Other studies found no significant associations between ADR reporting and sex, age, number of patients seen per day and experience (Ekman et al., 2012; Gavaza et al., 2011; Kiguba et al., 2014; Lee et al., 1994; Sabblah et al., 2014a). Association

of ADR reporting with these external factors seems to vary in many studies, suggesting the complex nature of the factors associated with reporting at the extrinsic level.

Systems and tools: Weak health systems may affect the efficiency of a reporting system. A major constraint to reporting ADR within the healthcare system is the unavailability of reporting tools (De Angelis et al., 2016; Kozamernik, 2010). In some cases, where reporting tools are available, the inefficiency in the reporting system could affect their reporting behaviour. For example, in an Iranian qualitative study, a participant stated that "*Sometimes it takes half an hour just to fax a yellow card to ADR centre*", which could have impacted his/her decision to report (Mirbaha et al., 2015a). Ability to design enabling health systems which ensures availability of reporting tools and improved systems is an important predictor of reporting and could be beneficial if developed.

Workload and type of facility: Overwhelming workload or burnout have been reported as a common factor for HCPs' inability to report ADR (Bateman et al., 1992; Belton et al., 1995; Figueiras et al., 2001; Suku et al., 2015; Sweis and Wong, 2000; Tandon et al., 2015). Several studies, however, have not found any association between workload and reporting rates (Lee et al., 1994; Bateman et al., 1992; Vallano et al., 2005; Suku et al., 2015). The type of facility can also have an impact on reporting and workload. Teaching hospitals may have more specialised cases with a high number of patients compared to a community clinic. A study in Kuwait also suggested doctors from private hospitals were more knowledgeable about PV and ADR reporting and were more likely to report than public hospitals (Alsaleh et al., 2017). Other underlying factors may be responsible for how ADRs are reported depending on the type of facility.

Patient susceptibility factors: As mentioned earlier in the chapter, ADRs occur according to different patient factors and circumstances which are multi-factorial and differ in populations. These may be patient-related, drug-related or socially related (Alomar, 2014). Examples include comorbidity, polypharmacy, age, pregnancy, intake, race, kidney disease, gender, liver function, genetic disposition and clinical setting. These may be as a result of lifestyle choices (smoking and alcohol), which could be modified, but others (genetic factors and comorbidity) cannot be controlled. Understanding the diverse effects of these factors on ADRs enables HCPs to make important reporting decisions on specific patients.

Relations with pharmaceutical companies: Healthcare professionals, especially doctors, have constant interactions with pharmaceutical companies and their representatives because the majority (92%) find it acceptable to try samples of new drugs (Morgan, 2006). Pharmaceutical companies are noted for giving HCPs gifts, continued medical education or conference and research sponsorship in order to promote their drugs. Even though doctors have denied that these incentives influence their prescriptions, rapid prescription of new drugs was found to be associated with samples tried (Wazana, 2000). As mentioned earlier, new medicines and polypharmacy may give rise to ADRs, which can lead to increased ADR reports, but the willingness of HCPs to report might affect the reporting rate (Kuo et al., 2012). On a five-point Likert scale assessing HCP reporting of ADRs, doctors (46.7%), pharmacists (41.4%) and nurses (33.3%) opposed reporting ADRs to the pharmaceutical industry (Shamim et al., 2016). A positive relationship with medical representatives, however, can be used as a means of increasing HCP knowledge about PV and increasing ADR reports submitted to regulatory authorities. For example, Indian doctors were more inclined to send ADR reports (87.7%) to pharmaceutical companies than government ADR centres (18.5%) because of a positive relationship with pharmaceutical companies (Kharkar and Bowalekar, 2012).

Feedback: A functional PV system must rely on active and timely feedback between authorities, HCPs and patients (Yadav, 2008). This involves data sharing and actions taken on the basis of submitted reports. Lack of feedback from pharmaceutical companies and regulatory authorities, however, has been observed as a demotivation factor to reporting ADRs. In Nepal, even though not a regular practice, 64% of HCPs indicated they would like to receive feedback from the national regulatory authority (Santosh et al., 2013). Patients have also considered feedback important, especially from HCPs. For example, 97% of patients in a Ghanaian study indicated they expected feedback on ADRs they reported and 61% preferred to be called directly on the telephone as opposed to receiving personalised letters (3.4%) (Sabblah et al., 2019). Feedback is therefore considered an important aspect of ADR reporting which both HCPs and patients think could be beneficial.

1.14.3 Contextual Factors

Contextual factors refer to the background, environmental or geographical setting and circumstance in which the ADR reporting could be affected. ADR reporting has been identified in the literature to be influenced by country policies, resources, regulation, law enforcement strategies, stage of a drug's life cycle, political environment to discuss ADRs and the media.

Reporting policies: Even though ADR under-reporting is a global phenomenon, the measures to improve reporting differ. Some high-income countries, such as Sweden, Spain, France and Italy, have made ADR reporting by healthcare professionals mandatory (Hazell and Shakir 2006). Such policies and laws have accounted for the high number of ADR reports generated by HCPs, and interventions often do not yield much effect compared to countries where reporting is not mandatory. For example, an educational intervention of 20–25 group sessions yielded a moderately positive effect but was not recommended for other geographical settings (Lopez Gonzales et al., 2015). Furthermore, an analysis of global reporting to the WHO database from 2000 to 2009, showed 85% of more than 3 million ADR reports generated worldwide were from the USA, UK, France, Canada, Australia and Germany (Aagaard et al., 2012), but mainly the USA (81.8%), and less than 1% from Africa (Ampadu et al., 2016). Most of the high-income countries have been members of the WHO international drug monitoring ince its inception, compared to African countries, which may have impacted on the ADR reports generated. For example, Malawi only joined in 2016, while most parts of the developed world have joined since 1968, creating a 48-year gap in legislation and regulatory framework.

Drug's life cycle: Newly introduced medication or treatment guidelines can also lead to an increased number of ADR reports, which is termed the Weber effect. The Weber effect is the phenomenon of spikes in reports the first two years after approval of a drug; the adverse event reporting increases and peaks near the end of the second year, and then reliably and rapidly diminishes with further time on the market (Berlin et al., 2008). As mentioned earlier, this effect may barely be noticed in areas where reporting is mandatory. For example, even in the USA where reporting is not mandatory, reporting trends still do not conform with what Weber described, which could be due to increased awareness about post-marketing surveillance in recent times (Hoffman et al., 2014). Nonetheless, studies have shown that an HCP will report an ADR for patient safety reasons, if the condition is serious and if the drug is new (Bäckström et al., 2007; Santosh et al., 2013).

Media publicity: ADR reporting can also be influenced by publicity. Dr William McBride's publicity about thalidomide curtailed further administration of the drug and increased reports. New changes to medicines also tend to have publicity and awareness, which can influence the rate at which ADRs are reported. For example, the Ghana FDA recorded an increase in ADR reports when a WHO new treatment guideline for antimalarial prophylaxis was introduced in children (Chatio et al., 2016). Also, media awareness about the neuropsychiatric effects of mefloquine in the UK led to a six-fold increase in reporting rates (Nevin and Croft, 2016; Schlagenhauf, 1996). Changes in the packaging of Thyrax® from a brown glass bottle to a blister in the Netherlands drew media attention which saw ADR reports increase by 85%. These media reports were carried out in newspapers and on television (Rolfes et al., 2016). A study by the New Zealand Centre for Adverse Reactions Monitoring, measuring the impact of television on adverse reports submitted after formulation change of Eltroxin (thyroxin), also saw a significant increase in ADR reporting rates (Faasse et al., 2012). Other examples include breast implants in the USA (Brown et al., 2001), paroxetine in the UK (Martin et al., 2006) and the rotavirus (Danovaro-Holliday, 2002).

1.15 Interventions to Improve Reporting of ADRs

Globally, various interventions have been used to address the problems faced by under-reporting of ADRs, targeting doctors (Abubakar et al., 2014), nurses (Hazell and Shakir, 2006a), pharmacists (Pande et al., 2013) and patients (Inch et al., 2012). Previous studies have shown that interventions can increase the number and quality of ADR reports (Gonzalez-Gonzalez et al., 2013; Molokhia et al., 2009; Pagotto et al., 2013; Ribeiro-Vaz et al., 2016). Many of these interventions have been empirical research evaluating the use of educational interventions (Pagotto et al., 2013), awareness workshops (Alraie et al., 2016; Herdeiro et al., 2012), information communication technology (Ribeiro-Vaz et al., 2016), increasing yellow card availability (Avery et al., 2011), training on ADRs (Morrison-Griffiths et al., 2003), and even a dropbox (Amit and Rataboli, 2008), as measures for improving ADR reporting. Despite the implementation of all these interventions, there is still general under-reporting of ADRs, and failure to recognise them when they occur seems to be a key area of deficiency (Carleton and Smith, 2006).

Reviewing the literature on interventions to improve reporting showed that the majority of interventions were educational, implemented passively or actively. Active educational sessions

included face-to-face lectures, workshops, training, PowerPoint presentations and meetings about PV and ADRs (Bisht et al., 2014; Figueiras et al., 2006; Jha et al., 2014; Lopez-Gonzalez et al., 2015; Mendes Marques et al., 2016; Stoynova et al., 2013). There were also passive educational interventions, which included self-study, self-study educational materials, brochures, poster displays, monthly bulletins and email reminders. Others include monitoring visits, incentives, making forms available and reporting using electronic or web-based services. The incentives included certification, a lottery ticket and percentage salary given as cash.

Overall, active educational interventions, which included regular monitoring visits, were shown to have a better outcome in increasing ADR reports by 25.5% (Gony et al., 2010), compared to less interactive approaches, such as self-study and one-off training, which resulted in a 0.6% increase in reports post-study (Stoynova et al., 2013). It was noted that the effect of the interventions, especially educational interventions, often reduced with time after implementation was stopped (Molokhia et al., 2009).

SECTION B

1.16 Pharmacovigilance (PV) and Reporting of Adverse Drug Reactions (ADRs) in Ghana

In this sub-section, the focus shifts from the broader literature and evidence relating to PV, ADRs and associated reporting globally, to the more specific issue of this topic in the Ghanaian setting of West Africa. The content of this chapter will be used to provide evidence that ADR reporting in Ghana is considerably below what is recommended, thus justifying the current research. To do this, an initial overview of current PV and ADR processes and governance in this setting is provided, and reports about reporting are reviewed.

1.17 The Ghanaian PV System

The Food and Drugs Authority (FDA) is an autonomous government agency of the Ministry of Health (MOH), which has oversight responsibility for PV activities in Ghana. A safety monitoring unit within the FDA coordinates the National Pharmacovigilance Centre (NPC). PV activities are decentralised from the national to the regional level through regional PV officers who are linked to Institutional Contact Persons (ICP) in healthcare facilities locally. The FDA has wider responsibility for the regulation and safety of food, drugs, food supplements, herbal and homoeopathic medicines, veterinary medicines, cosmetics, medical devices, household chemical substances, and tobacco and tobacco products, as mandated by the Public Health Act, 2012 (Act 851).

Ghana joined the WHO PIDM in Uppsala, Sweden (UMC) in 2001 as its 65th member and the first in a West African country, but the country still lacks the legal provision to enforce PV laws. A subsequent designation of the University of Ghana Centre for Tropical Clinical Pharmacology and Therapeutics as a WHO collaborating centre for advocacy and training in PV further enhanced the course of providing PV training and building capacity in the country and Africa at large. The FDA facilitates routine PV sensitisation and training of stakeholders to raise awareness about PV. Even though the dedicated but limited budget for PV activity is available at the national level and public health programmes, healthcare facilities may not have such budgets. A decentralised PV system is helping to improve stakeholder communication

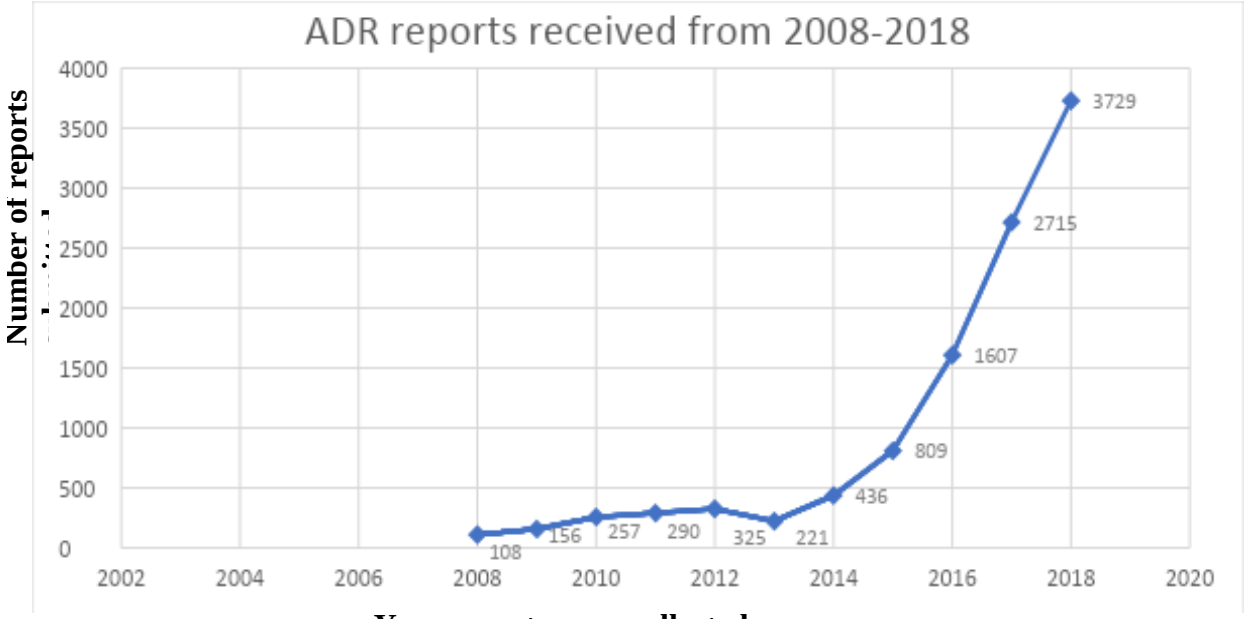
and coordination through regional FDA offices which serve as regional PV centres. They facilitate the circulation of safety newsletters, safety warnings and public awareness. The channels for receiving ADR information have been through consumers/patients, HCPs and MAH. The FDA encourages the reporting of all suspected reactions, including for herbal medicines, vaccines and over-the-counter drugs. The main tool for reporting ADRs by HCPs has been the yellow form or the ADR reporting form (Appendix I), which is used to report medication-related problems, soliciting basic information about the patient, suspected drug, reaction and reporter details. Different forms are available for patients (blue form) (Appendix J/K) and also for public health programmes, such as the Adverse Effects Following Immunisation (AEFI) (Appendix Q). All these forms can either be filled out manually or electronically from the FDA website. The HCPs' electronic platform uses the Safety Watch System (Appendix L). Through collaborative efforts, the blue form mobile application (Appendix N) was recently launched in Ghana by the FDA to facilitate ADR reporting. Details of basic requirements may differ based on needs. For example, the AEFI form (Appendix Q) requires more detail than the normal adverse reaction forms (Appendices I/J/K). Country regulations may also differ, for example, the USA requires extra patient data on height, weight and ethnic origin, whereas Denmark, Ireland and Norway do not include these on their reporting forms (WHO, 1972). Forms may be modified to suit country-specific needs, for example, Chan (2008) suggested adding details about Chinese herbal medicinal products on the Australian ADR forms.

1.18 ADR Reporting Trends in Ghana

The FDA is the primary steward of ADR reports in Ghana. ADR reporting has improved over the years compared to global trends. Reports from the FDA newsletter, *DrugLens*, were reviewed from 2008 to 2018 and showed an increase from 108 reports to 3,729. Figure 3 shows a decade of cumulative trajectory of ADR reports, with a sharp increase in reports, especially from 2014 (Figure 3). This increase could be attributed to increased awareness, government policies, mass drug administration, public health interventions and introduction to a new reporting system and tools. These reports are often reviewed and forwarded to the WHO Global ADR database: the Vigibase. A review of paediatric data on the Vigibase between 1999 and 2012 showed a corresponding increase in reports to the WHO monitoring centre, with an average reporting rate of 2.5 reports per million children per year (Cliff-Eribo et al., 2015). In

2017, the Safety Watch System, an electronic reporting system, was launched which further increased reporting of HCPs as shown in Figure 3.

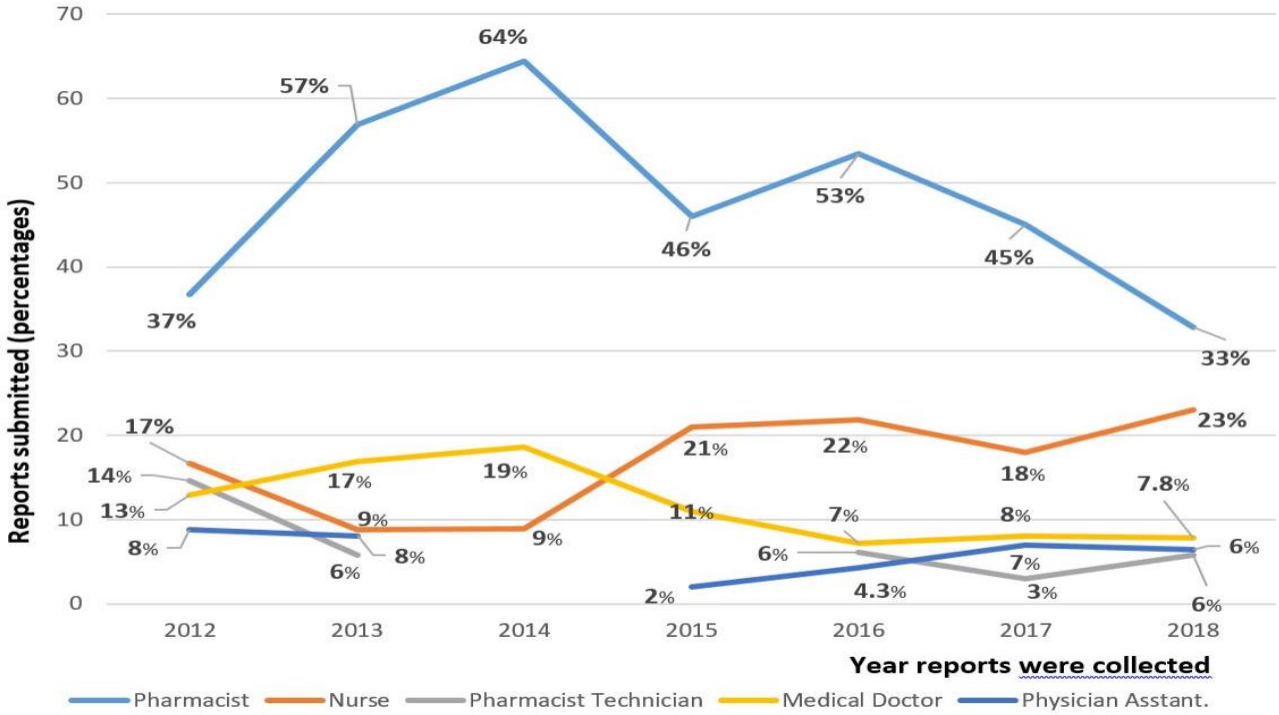
Figure 3: Graph of ADR reports received from 2008 to 2018 by the FDA in Ghana



1.19 Healthcare Professionals' Reports

The majority of ADR reports sent to the FDA have been from HCPs, followed by MAH and consumers/patients. For example, in 2015, only 0.4% (3/809) of reports were direct consumer/patient reports (*DrugLens* Issue 5, 2016). Doctors, nurses and pharmacists are often the HCPs who most commonly send ADR reports. Among HCPs, pharmacists are noted to send the most reports, peaking at 64.4% of reports in 2014 and decreasing to 32.8% in 2018 (Figure 4). A similar decline in reports is noted for doctors, who also peaked at 18.6% in 2014 but decreased to 7.8% in 2018. Nurses, however, have been increasing consistently from 8.1% in 2013 to 23% in 2018 (Figure 4). A report from Cliff-Eribo (2015) on paediatric reports between 1999 and 2012 in the Vigibase suggests that nurses submitted 50% of the reports, followed by pharmacists (23%) and physicians (15%) before 2012 (Cliff-Eribo et al., 2015). This, therefore, shows the significance and contribution of nurses to ADR reporting.

Figure 4: Graph of percentage of ADR reports sent by healthcare professionals



1.20 Patient/Consumer Reports

Direct patient or consumer reporting is infrequent in many jurisdictions. Few studies have explored consumer reporting, but consumer reports show a potential of identifying possible new ADRs that were not previously captured by HCPs and should be explored (Cox, 2009). Even though patients trust their HCPs to report, they would report themselves if they thought the HCP paid no attention to their concerns (Blenkinsopp et al., 2007). Patients may usually passively receive care, without asserting themselves to their HCPs because of power relations. Chatio (2016) identified that patients felt HCPs did not provide them with adverse effect information, were unfriendly, and coupled with long queues, this has resulted in non-reporting of adverse effects in Ghana (Chatio et al., 2016). The Ghana FDA has therefore recognised the need to capture patient/consumer reports by undertaking more education, and in 2019 introduced a mobile reporting app – the blue form app – targeting both patient and HCP reports (Appendices M/N). A study of 28 healthcare facilities in Ghana reported that only 3% of patients were aware of the FDA patient reporting system, thus the majority (68%) reported their ADR experiences to doctors (Jacobs et al., 2018). Community pharmacists have also been targeted by the FDA as stakeholders, because self-medication is widespread (Bennadi, 2014) and they have the potential to send reports on patients who visit them. The FDA has therefore increased training and distribution of yellow forms to community pharmacists as well.

1.21 MAH (Reports from Pharmaceutical Companies)

Laws govern the operations of pharmaceutical companies to ensure the safety of medicinal products in Ghana. According to the Ghana FDA, MAH are required by the FDA to report all adverse reactions through a designated Qualified Person for Pharmacovigilance (QPPV), usually an HCP who represents the pharmaceutical company. They are also legally mandated to conduct post-marketing surveillance. Surveillance activities, however, have been inadequately defined and implemented. Most MAH have relied heavily on the reports from HCPs with little efforts to facilitate reporting. Additionally, herbal medicinal product registration has also increased, creating a vigilance gap (Ghana FDA, 2016).

1.22 International Stakeholders

Similar reporting processes and regulations exist in other parts of the world, such as the UK, USA and Australia. National regulatory authorities that enable the general population to spontaneously report MRPs include the USA's MedWatch Adverse Event Reporting Programme, the UK's MHRA 'yellow card' system and Australia's Adverse Drug Reaction Advisory Committee (ADRAC) 'blue card' system (Chan et al., 2008). These schemes are used to report all suspected ADRs including incidents from fake or defective medicine, medical devices, and serious ADRs from blood and blood components.

After approval of a drug, an MAH is required to submit a Periodic Safety Update Report (PSUR), which is a PV requirement intended to provide an evaluation of the risk-benefit balance of a medicinal product at defined time points post-authorisation (Ebbers et al., 2010; Ebbers et al., 2013). This regulatory requirement differs from country to country. For example, in the USA, quarterly reports must be submitted in the first three years, followed by yearly reports. In the EU, the requirement is every six months in the first two years, annually for the next two years, and then at three-year intervals, at the time of renewal of registration. Even though operations and regulatory requirements of PV differ between countries, the basic principles are the same (Jeetu and Anusha, 2010). For example, the Australian ADRAC operates under a different name – the 'blue card' system – based on the same principles as the UK yellow card scheme (Chan, 2008).

In addition, regional agencies and blocks such as the European Medicines Agency (EMA) support MAH on applications to change a marketing authorisation, submit product data and report product defects or recalls collaboratively with other countries. For example, haemolytic

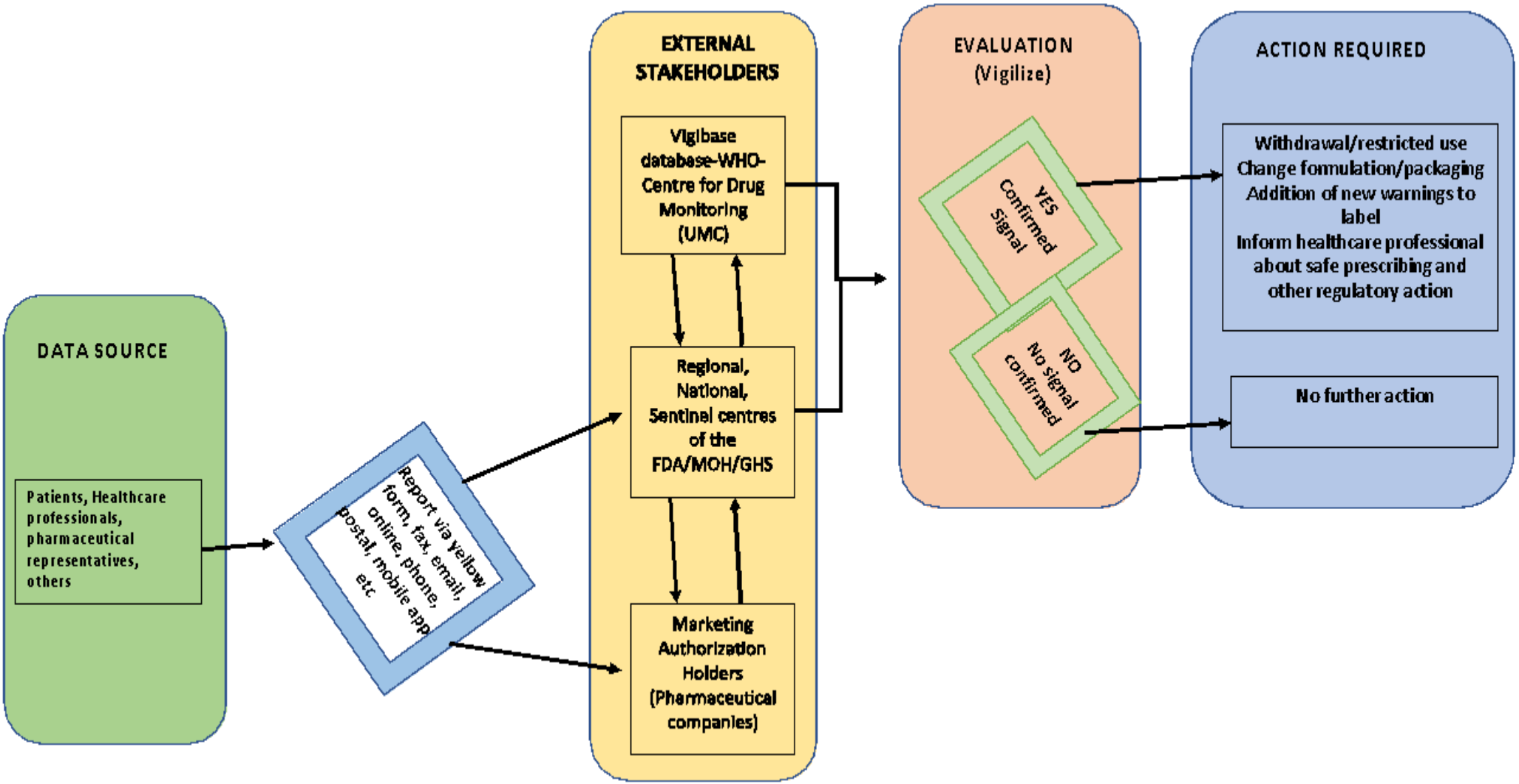
anaemia was found in using intravenous artesunate for treating malaria in Europe, which was never noted in the drug development process (Mehta et al., 2007). This information, although generated in Europe, ought to have beneficial implications for malaria treatment in Africa and signifies the need for intense surveillance in all populations (Mehta et al., 2007). There are agencies present in 150 countries globally which collaborate with the WHO-PIDM to ensure safe medicine use and patient safety. Such safety information allows regulatory authorities to make important changes, such as withdrawal or changes to labelling, dosage or mode of administration (Hajebi et al., 2010). There is, therefore, the need for international communication, collaboration and use of efficient methods in monitoring, identifying and reporting ADRs.

1.23 Reporting Process

Having clarified various definitions, terminology and related concepts, it is important to understand how ADRs are reported in Ghana, the stakeholders involved and action taken after assessment. Previously, reporting ADRs was restricted to only doctors, but now other healthcare professional cadres, pharmaceutical representatives, Public Health Programmes (PHPs) and patients can also report directly. As mentioned earlier, the primary source of ADR data in Ghana is from HCPs.

Efforts are being made to encourage consumer or patient reporting. Sending reports to a regulatory agency or MAH involves the use of multiple communication channels including electronic mail, online reporting forms, telephone, mobile applications and facsimile. All data collated from the primary stakeholders are forwarded to the external stakeholders, such as the FDA/MOH and MAH. The national regulator liaises with the WHO-International Drug Monitoring Programme (IDMP) and MAH to send the data to the international database of the WHO-IDMP, Vigibase. The reports are analysed (Vigilized) using the WHO causality assessment criteria for detecting ADR and also the Naranjo algorithm/scale, which was developed to estimate the probability of an ADR occurring based on a 10-point question criteria (Naranjo et al., 1981). This was often used in clinical trials and has also been widely adopted for routine clinical practice for the assessment of causality. Following analysis, if a signal is confirmed, regulatory actions are taken; the drug can be withdrawn, formulation changed, warnings added and HCPs informed. HCPs can report ADRs to reference centres or designated hospitals in three main ways, namely individual reporting, comprehensive monitoring and population monitoring.

Figure 5: A generic adverse reaction reporting process



In Ghana, some of these strategies have been used in an attempt to enhance reporting. They include the use of the mobile application, electronic reporting, workshops, incentives and distribution of forms, but no studies have scientifically explored the impact of these interventions on reporting.

In summary, this second section (B) of the first chapter has advanced the discussion of ADRs in relation to an overview of the factors responsible for reporting in terms of contextual issues, and extrinsic and intrinsic issues associated with reporting. It has attempted to explore important concepts of pharmacovigilance and ADRs, and also the interventions which are used to improve reporting, and also a more specific focus is given on the Ghanaian setting, and the existing PV and ADR reporting processes in this West African setting, where it will be argued that research is needed. It has been noted in the general review of the literature that studies in Africa on the topic were scant. The next chapter therefore rapidly scopes specific ADR reporting studies in Africa. This will help to provide a summary of studies and further justification for this study.

CHAPTER TWO

A NARRATIVE REVIEW OF THE FACTORS INFLUENCING ADR REPORTING IN AFRICA

2.0 Introduction

Having presented the literature more generally on ADR reporting in chapter 1, with a section on factors influencing reporting, it was noted that the literature on ADR reporting in Africa was scant. This chapter will therefore focus more on a narrative review of African-specific literature on the factors influencing ADR reporting within that context. The conceptual framework by Obonyo (2014) was adopted to organise and guide the review. The review question was, "What is the scope of literature on ADR reporting among frontline healthcare professionals in Africa?". The rationale of the study is to give an overview of the research on this topic using already identified factors in the previous review into whether they are intrinsic, extrinsic and contextual factors. There was no formal quality assessment of individual studies and the narrative lacks a comprehensive synthesis of the quantitative findings.

2.1 Sources of the Literature

Searches were conducted in PsychInfo, EMBASE, MEDLINE and Google Scholar using a combination of search terms. The searches were conducted from June 2019 and updated in January 2020, and include studies published from 1960 to date. Search terms combinations include [Doctors OR Medical Practitioners OR health professions] AND [Nurses OR Nursing Officers OR health professionals] AND [Pharmacist OR Pharmacist Officers OR health professionals] AND Hospital AND "ADR reporting" AND attitude AND practice AND knowledge OR awareness AND Africa (detailed search strategy in Appendix T).

2.2 Selection of Literature for Inclusion

Studies were included if they focused on 1) adverse drug reaction reporting; 2) population: healthcare professionals, i.e. medical (doctors/physicians), nursing (general/specialised) and pharmacy staff (pharmacists/technicians), and setting: African studies conducted in hospitals and clinics. Studies which did not meet the inclusion criteria were excluded. Using the inclusion criteria described above, the lead researcher screened all the studies retrieved from the databases, first by titles, followed by abstracts and full text articles. The process was

repeated to ensure that all relevant studies were considered. Where there was any doubt, supervisors were consulted and asked to crosscheck the selection. The aim was to ensure that the selection was carried out appropriately, and that there was no selection bias.

2.3 Data Extraction and Synthesis

Relevant data were extracted using a data extraction form. All full text articles that met the inclusion criteria were downloaded and read, and the important information needed for this review extracted onto the data extraction form. Information extracted include author, country, sample, type of healthcare professional and healthcare facility (Table 20). The data was then analysed and the findings of the factors influencing ADR reporting narratively presented into intrinsic, extrinsic and contextual factors.

2.4 Search Results

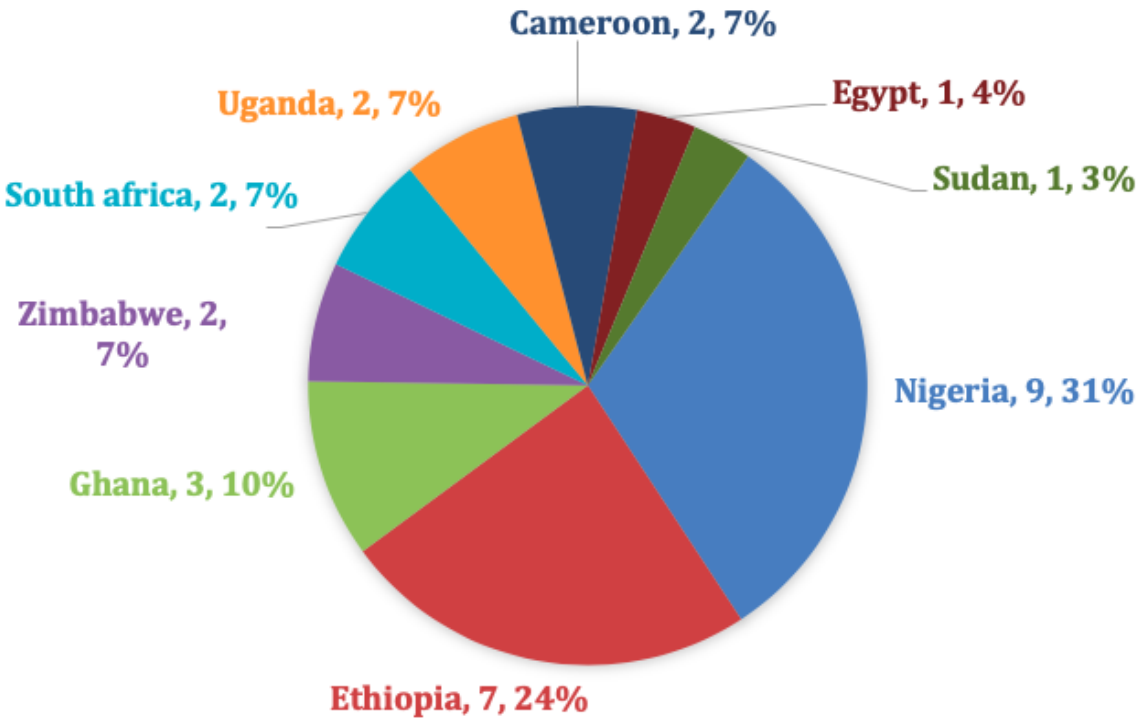
A total of 2,052 (Ovid Medline 81, Embase 268, PsychInfo 943, Google Scholar 760) African studies were retrieved following the database searches. After screening, 80 full abstracts were retained, 46 full papers were eligible for full text review, and a final 29 studies met the selection criteria and were included. The majority of the studies were excluded at title screening stage (n=1,972). At the abstract stage, because of time and resources, papers were excluded if full versions were not available online or information was only on closely related topics such as medication errors and adverse medical events. Additionally, studies were excluded if they focused on other health professionals but not specifically on doctors, pharmacists and nurses, and interventions studies not designed to address only ADR reporting problems.

2.5 Study Setting

Scope of the evidence

The studies retrieved were conducted between 2004 and 2019 in only nine African countries representing 17% (9/54) of the countries in Africa. More than half of the selected studies were undertaken in Nigeria (31%, 9) and Ethiopia (24%, 7), and the rest were in Ghana (3), Zimbabwe (2), South Africa (2), Uganda (2), Cameroon (2), Egypt (1) and Sudan (1) (Figure 6).

Figure 6: Distribution of selected studies by country of origin (n=29)



2.6 Participants

The total number of participants in the 29 studies were 6,705 healthcare professionals, of which the majority were nurses (2,995). Medical staff (2,597), pharmacy staff (680) and ancillary staff (i.e. dentists, health workers (unspecified), community health workers etc) (433) followed this. The smallest number of participants was 35 HCPs and the highest was 1,345. The average response rate was 80.3% even though nine studies did not report on this. The following table (Table 4) summarises the characteristics of the included studies. A detailed summary of papers can be found in Appendix U.

Table 4: Characteristics of included studies

AUTHOR/YEAR	COUNTRY		SAMPLE				
		TOTAL	MEDICAL STAFF	NURSING STAFF	PHARMACY STAFF	Others	FACILITY
Ezeuko et al., 2015	Nigeria	372	109	241	22	NA	NA
Nde et al., 2015	Cameroon	149	85	34	18	12	NA
Katusiime et al., 2015	Uganda	223	95	120	8	NA	1THCF
Ameade et al., 2014	Ghana	125	NA	125	NA	NA	1THCF, 2PHCF
Bello and Umar, 2011	Nigeria	61	61	NA	NA	NA	1THCF, 3PHCF
Kiguba et al., 2014	Uganda	1345	275	792	84	194	7 (THCF, PHCF, PVCF)
Sabblah et al., 2014	Ghana	259	259	NA	NA	NA	23PHCF (inclusion 6 private facilities)
***Tesfa and Wabe, 2012**	Ethiopia	82	15	49	21	NA	1THCF, 3PHCF
Awodele et al., 2011	Nigeria	251	251	NA	NA	NA	PVCF
Ohaju-Obodo and Iribhogbe, 2010)	Nigeria	330	330	NA	NA	NA	4THCF
Elnour et al., 2009	Sudan	475	175	200	100	NA	6THCF, 2PHCF
***Oshikoya and Awobusuyi, 2009)**	Nigeria	99	120	NA	NA	NA	1THCF
Okezie and Olufunmilayo, 2008)	Nigeria	192	192	NA	NA	NA	1THCF
Adedeji et al., 2013	Nigeria	35	35	NA	NA	NA	1THCF
Seid et al., 2018	Ethiopia	102	NA	61	25	16	8PHCF
Muringazuva et al., 2017	Zimbabwe	47	NA	30	NA	17	6 HCF*
Mulatu and Worku, 2014	Ethiopia	625	101	430	94	NA	9HCF
***Shanko and Abdela, 2018**	Ethiopia	297	44	230	21	NA	1THCF
Kefale et al., 2017	Ethiopia	213	5	161	27	20	1THCF
Khoza et al., 2004	Zimbabwe	144	35	74	16	19	1THCF
Gurmesa and Dedefo, 2016	Ethiopia	133	19	70	19	25	1HCF
Fadare et al., 2011a	Nigeria	65	43	20	2	NA	1THCF
Terblanche et al., 2017	South Africa	132	31	77	24	NA	1THCF
Kamal et al., 2014	Egypt	211	211	NA	NA	NA	THCF
***Charles et al., 2017**	Cameroon	188	50	122	1	13	THCF, SHCF, PHCF, CMTY PHM
***Alemu and Biru, 2019**	Ethiopia	114	26	49	17	12	SHCF and PHCF
***Amedome and Dadson, 2017)**	Ghana	145	30	110	15	NA	SHCF
Udoye et al., 2018	Nigeria	169	NA	NA	108	61	2THCF and CMTY PHM
Joubert and Naidoo, 2016	South Africa	102	NA	NA	58	44	NA
***discrepancies**		*6685	**2597**	2995	**680**	**433**	

2.7 Narrative Report of the Findings

Intrinsic factors

Knowledge was explored differently in the 29 studies. Knowledge and awareness were used synonymously to refer to the level of familiarity with information on the PV system and ADR reporting. The most common knowledge-based questions examined were on the definition of PV, ADR, the difference between ADR and side effects, and the purpose of reporting (Kamal et al., 2014; Kefale et al., 2017; Khoza et al., 2004; Muringazuva et al., 2017; Mulatu and Worku, 2014; Oshikoya and Awobusuyi, 2009; Seid et al., 2018; Shanko and Abdela, 2018), awareness about reporting locally or nationally to ADR reporting centres (Udoye et al., 2018; Oreagba et al., 2013; Nde et al., 2015; Khoza et al., 2004; Oshikoya and Awobusuyi, 2009; Katusiime et al., 2015; Terblanche et al., 2017) and also awareness about the yellow form and ADR forms in general (Adedeji et al., 2013; Ohaju-Obodo and Iribhogbe, 2010; Angamo et al., 2012; Fadare et al., 2011; Nwalwu and Harrison, 2015).

Despite the differences in the types of questions asked on knowledge, Seid (2018), Mulatu (2014) and Kefale (2017) reported an aggregated knowledge score of 52.9%, 34.2% and 33% respectively among HCPs, which indicated a moderate to low level (Kefale et al., 2017; Mulatu and Worku, 2014; Seid et al., 2018). Pharmacy staff, however, showed better knowledge and awareness of ADRs and PV in a Nigerian study by Udoye (2018), where they showed 100% awareness of PV and ADR reporting (Udoye et al., 2018). The lowest reported level of knowledge was a South African study by Terblanche (2017) where the general knowledge was only 17.5% (Terblanche et al., 2017).

Angamo et al. (2012) reported an average of 75.6% of HCPs who were unaware of the national reporting centre and the yellow card system. In Nigeria, 78% of doctors self-assessed and indicated they had adequate knowledge, but further assessment showed 47.4% were not aware of the PV process (Ohaju-Obodo and Iribhogbe, 2010). In Ghana, a small number of studies on the subject of ADR reported high levels of knowledge among doctors (88.8%), nurses (78%) and pharmacists (92.2%) when asked about PV, awareness of ADR reporting and its purpose (Amedome and Dadson, 2017). This high level of knowledge was supported by a study of doctors in Accra where more than half showed good knowledge (Sabblah et al., 2014).

High levels of knowledge among HCPs did not reflect positively on their practice; under-reporting was observed to still be high. For example, a study of doctors, nurses and pharmacy

staff reported that even though they had adequate knowledge (23.1%) and positive attitude (75%), in practice no HCP either reported (0%) or noted (0%) ADRs (Angamo et al., 2012).

Attitudinal behaviour of participants was positive in the majority of the studies. Attitudinal assessments varied between studies but were largely based on Inman's (1996) perceived attitudinal behaviours for non-reporting. Even though Inman's original research focused on doctors, the theory of the '*seven deadly sins*' of under-reporting has been widely explored and modified to suit different settings and different healthcare professionals. There was generally a positive attitude because at least eight of the studies reported that ADR reporting was necessary or part of HCPs' duty or professional obligation (Mulatu and Worku, 2014; Shanko and Abdela, 2018; Kamal et al., 2014; Terblanche et al., 2017; Kiguba et al., 2014; Oshikoya and Awobusuyi, 2009; Khoza et al., 2004). Litigation was explored in only four of the selected studies (Jarrett et al., 2013; Mulatu and Worku, 2014; Kamal et al., 2014; Ezeuko et al., 2015). Opinions about litigation varied among HCPs – while the majority agreed legal liability issues affect reporting in Ethiopia (Mulatu and Worku, 2014), only 14.3% thought litigation could affect reporting in Nigeria (Adedeji et al., 2013). Lethargy was reported in various forms among the studies which are related to fatigue, lack of time, burnout and workload.

There were contradictory reports among HCPs. Eight studies reported lack of time to report ADRs, but the majority of HCPs disagreed with this. For example, HCPs in three studies (Kiguba et al., 2014; Oshikoya et al., 2011; Joubert and Naidoo, 2016) disagreed that lack of time discouraged reporting, while fewer HCPs reported having no time to report (i.e. 16%, 37.1%, 46%). On the contrary, more than half (57%) of the HCPs in Uganda did not report because of lack of time. A closely related theme which was reported was workload, which was referred to in three studies. For example, while some HCPs suggested reporting created workload in Ethiopia (51.2%) (Angamo et al., 2012), others (62.1%) in the same country (Shanko et al., 2018) suggested otherwise. Adedeji (2013) in Nigeria reported a much lower percentage in a study of doctors where only 17% felt reporting created extra workload and only 8.6% specifically reported it was time-consuming (Adedeji et al., 2013). Ambition, complacency and guilt were not reported, but diffidence and ignorance were featured. Diffidence, which Inman (1996) referred to as hesitance of *reporting mere causality*, was observed in three studies with varied opinions and phrased as *uncertainty about causality*. The reports indicated that uncertainty about when, who and how to report was a limiting factor to reporting in seven studies (Gurmesa and Dedefo, 2016; Terblanche et al., 2017; Kamal et al., 2014; Shanko and Abdela, 2018; Necho Mulatu, 2014; Okezie and Olufunmilayo, 2008; Kefale et al., 2017). For example, Kefale (2017), in Ethiopia, reported that 77% of HCPs wanted to

establish causality before reporting an ADR, while in South Africa, the most common reasons for non-reporting were uncertainty about how, where and when to report (54.5%). Ignorance about the need to report or the reporting system, which is linked to knowledge and awareness, was reported in three studies (Fadare et al., 2011; Ezeuko et al., 2015; Charles, 2017). More than half of the participants were ignorant about reporting procedures, which affected their reporting.

Extrinsic factors

Other external factors which influenced reporting were the poor feedback, lack of feedback, and no feedback from external national reporting centres and internal stakeholders, such as the heads of departments. This was reported in seven studies where HCPs indicated that poor feedback, or the lack of it, affected their reporting. Kiguba (2014) reported that feedback to public health programmes in Uganda was much higher (60%) than from the national centre (23%) or medical superintendents (39%) (Kiguba et al., 2014). HCPs had varied responses about lack of feedback. For example, 59% in South Africa (Joubert and Naidoo, 2016) in contrast to 6.1% reported (Terblanche et al., 2017), 48% in Uganda (Katusiime et al., 2015), 62.8% in Cameroon (Charles, 2017), 55.8% in Sudan (Elnour et al., 2009), 47.1% and 58.8% in Ethiopia (Kassa Alemu and Biru, 2019; Seid et al., 2018). The majority of HCPs reported that lack of feedback affected their reporting significantly and therefore suggested improved feedback from stakeholders.

HCPs' personal and professional characteristics influenced ADR reporting. Among the studies reviewed, at least nine studies reported on the association of HCPs' background characteristics to ADR reporting. Fewer females engaged with pharmaceutical companies (Bello and Umar, 2011) or private practice (Awodele et al., 2011). There was also a lower likelihood of reporting ADRs from private health facilities compared to public ones (Kiguba et al., 2014). This was further supported in Ghana where a study showed that doctors from government and quasi-government hospitals were 1.26 to 5 times more likely to report ADRs than private hospitals (Sabblah et al., 2014). In terms of age, responses were varied: in Uganda, HCPs aged 36 to 65 years were three times more likely to report ADRs than those aged 21 to 35 years (Katusiime et al., 2015). Kiguba (2014) also reported that HCPs who were 30 years and older were less likely to report. Participants aged 40 and over were reported to have a better attitude and 20 to 29-year-olds had better knowledge in a Ghanaian study (Paul et al., 2014).

Years of experience and higher qualifications were reported to be associated with knowledge, attitude and practice. For example, HCPs with 10 years' experience and a PhD were 11.1 times more likely to have satisfactory knowledge, and those with the same number of years of experience were 1.7 times likely to have a satisfactory attitude as well (Kamal et al., 2014). Also in Uganda, HCPs with 10 years' experience were four times more likely to report ADRs than those with five years or less experience (Katusiime et al., 2015). Additionally, two studies reported that medical faculties or departments were more likely to observe and report an ADR than surgical or other departments (Okezie and Olufunmilayo, 2008; Kiguba et al., 2014).

Contextual factors

Only one study reported on policy in Sudan where the majority of participants in the facilities surveyed had reported that there was no policy in place for the detection (60%), investigation (62.1%) or reporting (50.3%) of ADRs (Elnour et al., 2009). In addition, media was only reported in one study to solicit where ADR knowledge is acquired. Only 7.2% acquired knowledge about ADRs and how to report through media. HCPs, however, suggest the media could improve reporting with varying levels of positive responses: 8.6% (Adedeji et al., 2013), 10.5% (Kiguba et al., 2014) and 62.5% (Ezeuko et al., 2015).

2.8 Conclusion

This is the first review exploring the scope of literature on ADR reporting in Africa. Only three studies were identified in the Ghanaian context and no qualitative studies were retrieved from the literature searches to the best of our knowledge. In assessing the factors influencing ADR reporting, intrinsic characteristics of knowledge, attitude and practice were common methods of assessment, but the parameters for measurements were varied. No standard scale or index for measuring any of the variables exists. The majority of studies adopted Inman's (1996) '*seven deadly sins*' modified to the local context of the research with varied responses. Some of the factors proposed by Inman, such as ambition, complacency and guilt, were not reported, probably because they were not applicable to the African setting due to the differences in the health system's culture and practice. Extrinsic and contextual factors were least explored and responses showed variation in responses with regards to these factors.

2.9 PhD Study Rationale

The literature review has justified the need for further research on ADR reporting because of continuous poor HCP practice and scant studies on the topic in Ghana. Studies undertaken elsewhere have had gaps in generalisability and variable interpretations of results. As mentioned earlier, ADRs cause significant morbidity, mortality and increased healthcare costs (Wiffen et al., 2002; Elliot et al., 2018). Several studies have shown the impact of ADRs and associated non-reporting of events on healthcare systems (Aagaard et al., 2012; Hazell and Shakir, 2006a, 2006b; Pagotto et al., 2013; Wiffen et al., 2002) with only a small number of reports from Africa. Contextually relevant data is important to understand HCP reporting behaviour. Reporting of ADRs is indeed a vital component of PV to ensure the safe use of medicines in routine care. Healthcare professionals are identified as sending the most ADRs reported to regulatory authorities. Doctors, nurses and pharmacists form the primary cohort of HCPs who are frequently involved in ADR reporting compared to patients and other stakeholders. Targeting this group is therefore important in providing multi-level perspectives about factors influencing ADR reporting. McGettigan et al. (1997) suggest exploring other avenues to understand the reporting culture rather than just attitudinal surveys. Circumstances and context may differ, thus the need to explore these factors more holistically is important for understanding ADR reporting, especially in a Ghanaian context.

Globally, and particularly in Africa, ADR reporting has been met with low interest, and ADRs are not reported due to several factors which have been identified in the literature, including lack of time, ignorance and lack of reporting tools (De Angelis et al., 2016; Griffith, 2013; Gupta and Udupa, 2011; Irujo et al., 2007; Lopez-Gonzalez et al., 2009a; Sevene et al., 2008). The majority of studies exploring these factors have, however, been skewed towards the internal or personal factors of HCPs' knowledge, attitude and perceptions, without adequately exploring other possibly related factors, such as national regulation, media, policies, health systems, patients, relationships with pharmaceutical companies and other organisational related factors.

The FDA ARS in Ghana has consistently been reporting below the WHO recommendation of 200 reports per million population (WHO-IPDM, 2000), even though reporting generally has been on the increase in recent times. Few of the studies that have explored factors affecting ADR reporting in Ghanaian hospitals have been quantitative (Chatio et al., 2016; Franklin et al., 2014; Paul et al., 2014; Sabblah et al., 2014; Amedome and Dadson, 2017). The choice of

study participants was also either narrow, e.g. exploring only doctors (Sabblah et al., 2014), or too broad, e.g. patients and public health programmes (Chatio et al., 2016; Suku et al., 2015; Yamoah et al., 2019). This study therefore seeks to focus on the key frontline HCPs (i.e. doctors, nurses and pharmacists) working in routine clinical practice in hospital settings. In the review of databases during the literature review, no qualitative studies addressing the issue of ADR reporting among Ghanaian HCPs were found. There is a need to explore specific factors affecting ADR reporting in a Ghanaian context, with more emphasis on the qualitative.

The methodological distinction between this study and other studies, which have explored similar research questions, will be the use of a mixed methods approach. The rationale for using this approach is that neither quantitative nor qualitative methods generally are sufficient to capture the trends and details of a phenomenon of interest, i.e. ADR reporting (Ivankova et al., 2006). It is therefore important to explore the topic using mixed methods where the strengths of each design can be maximised. In this way, HCP-specific factors can be identified for the development of recommendations and targeted interventions to improve ADR reporting in the Ghanaian healthcare system.

2.10 Aim and Research Questions

Based on these reviews of the ADR reporting literature, the proposed aims of this study are to explore factors associated with spontaneous ADR reporting by HCPs in Ghana. The following associated research questions are proposed:

1 What are the perceived factors associated with spontaneous ADR reporting by HCPs in Ghanaian hospitals?

In addition, the sub-aims are to understand why such factors are considered relevant, and to explore any associations between such perceived factors and HCPs' characteristics. The way in which ADR reporting is undertaken in Ghana will also be explored and, finally, this study will also seek to understand HCPs' views as to what could be done to increase ADR reporting. These are represented in the following secondary research questions:

2 Why do HCPs consider factors associated with ADR reporting to be important?

3 How is ADR reporting undertaken by HCPs in Ghana?

4 What associations are there between HCP characteristics and perceptions about ADR reporting?

5 What are HCPs' views about improving ADR reporting?

CHAPTER THREE

METHODOLOGY AND METHODS

3.0 Overview of the Chapter

This chapter provides a description of the methodology and methods selected to answer the research questions. The first section of this chapter gives the background of the epistemological underpinnings of the research methodology and builds an argument for choosing a concurrent mixed methods design. This is followed by a detailed description of the research methods used to collect and analyse data. Overall, this study used concurrent mixed methods, and each approach is described in the following sections in line with best practices for presenting mixed methods research (Meissner et al., 2011; NIH, 2019).

3.1 Epistemology and Ontology

Epistemology and ontology refer to two different philosophical ways of viewing the nature of research. Ontology refers to the nature of being or study of reality, while epistemology refers to our theory of how knowledge is created and what underpins the theoretical perspective of research (Patel, 2018). In research, ontology helps researchers to be more certain about the nature of the subject they are researching, while epistemology is concerned with all aspects and processes of acquiring, producing and transferring knowledge in a credible way (Marsh, and Stoker, 2011; Patel, 2018). It is therefore important to reflect on and be guided by this ideology of knowledge production. Epistemological debates about knowledge creation and assumptions about the natural world have resulted in different worldviews.

3.2 Worldviews

The two traditionally dominant worldviews of the construction of knowledge have been those of positivism and constructivism, which underpin quantitative and qualitative methodologies respectively (Cracknell, 1994; Walker and Baxter, 2019). Proponents of the positivist approach advocate for understanding nature through hypothesis testing, causal explanations and empiricism which is thought to form the basis of knowledge (Clark and Creswell, 2008). The nature of reality is specifically perceived and created by using valid and reliable tools.
Interpretivists/constructivists, in contrast, are proponents of the view that knowledge is based on concepts such as humanism, culture and idealism, which have been described as the best

ways of understanding human behaviour (Tashakkori and Teddlie, 2003). Interpretivism (constructivism) refers to a phenomenon where individuals create the nature of reality or groups, which can be best understood by exploring events and activities.

In addition, a third paradigm relating to realism has gained popularity in recent years, this is based on a pragmatic methodology which propounds that reality can be interpreted in light of its usefulness and what works best (Tashakkori and Teddlie, 2003; O'Cathain, 2010). This has given rise to mixed methods research, which will be considered and argued for, and represented as the most appropriate in this research. Justification of the suitability of a mixed-methods approach for this research is described further.

3.3 Mixed Methods Approach

The importance of mixed methods research has gained popularity in the last decade, redirecting the discussion about epistemological incompatibility towards appreciating the potential value of blending both qualitative and quantitative methods into a single study (O'Cathain and Nicholl, 2008). A mixed-methods design is described as a procedure of collecting, analysing and 'mixing' both quantitative and qualitative data at some stage of the research process within a single study, to understand a research problem completely (Tashakkori and Teddlie, 2006). Also, the explanation of a mixed methods research design is based on a pragmatic approach which balances the two extremes of qualitative and quantitative data to form a third paradigm (Gunasekare, 2015). It falls neither within a positivist or constructivist epistemological stance but adopts an entirely new model (Subedi, 2016). It is based on the premise that the truth is not determined once and for all but can be both objective and subjective in our search for knowledge. The immediate goal of this approach, therefore, is "to make warranted assertions and to produce pragmatic/workable solutions for valued ends" (Denzin, 2012). The style of presentation of the report of this mixed methods study followed the recommendations proposed by O'Cathain and colleagues (O'Cathain *et al.,* 2008) (Table 5).

Table 5: Good reporting of mixed methods approach

Good Reporting of a Mixed Methods Study (GRAMMS)	Where addressed in this research
Describe the justification for using a mixed methods approach to the research question	Methodological justification
Describe the design in terms of the purpose, priority and sequence of methods	General methodology (dominance and sequence)
Describe each method in terms of sampling, data collection and analysis	Methodological process: data collection, data analysis
Describe where integration has occurred, how it has occurred and who has participated in it	Integration/triangulation section
Describe any limitation of one method associated with the presence of the other method	Strengths and limitations section
Describe any insights gained from mixing or integrating methods	Discussion section

3.4 Methodological Justification

Previous studies have not sufficiently explored the trends and peculiarities of ADR reporting among HCPs in Ghana. Research on ADR reporting in Africa has predominantly been quantitative (Fadare *et al.,* 2011; Kamal *et al.,* 2014; Katusiime *et al.,* 2015; Oreagba *et al.,* 2011; Ameade *et al.,* 2014; Sabblah *et al.,* 2014; Terblanche, 2018; Bello *et al.,* 2016), with only a few writters exploring the subject either qualitatively or using mixed methods (Chatio *et al.,* 2016; Jacobs, Ampadu *et al.,*2018) and these were on patient perspectives in Ghana. A combination of both quantitative and qualitative methods would therefore produce a comprehensive account which allows a complete analysis of the research problem, maximising the strengths of each approach (Creswell, 2009; Denzin, 2012; Greene and Caracelli, 1997). No studies have explored the issue using a multi-method approach based on multi-perspectives of healthcare professionals. The few mixed methods spotted in the literature have only focused on nurse's perspective of reporting (De Angelis *et al.,* 2016; Lobo *et al.,* 2013). Creswell notes that the two most compelling reasons for using mixed methods are when researchers require multiple perspectives from participants to give a complete understanding by merging

qualitative and quantitative measures to confirm a phenomenon (Creswell, 2013). The justification is therefore to confirm or otherwise the few quantitative studies found in Ghana, while embellishing them with the qualitative approach. Furthermore, comprehensively merging the two methods increases confidence in the findings by ensuring that marginalised (especially junior staff) voices are heard (Mertens, 2003). Also, combining the two methods produces more contextually relevant knowledge than two independent research paradigms or studies would (O'Cathain *et al.,* 2007; Shneerson and Gale, 2015). This will be the first time a mixed methods study has been undertaken on the topic, to the best of our knowledge, among key healthcare professionals in Ghana. Ultimately, the outcome will provide a multilevel perspective of the problem based on contextual relevance.

3.5 Mixed Methods Design

There are several types of mixed method designs, with some authors suggesting up to forty different types of mixed methods designs in the literature (Ivankova *et al*, 2006; Palaiologou, 2016; Clark and Ivankova, 2018).

The mixed methods design commonly referred to are six which are designed based on four considerations: priority, implementation, integration and a theoretical perspective (Creswell, 2003). In this study, priority was given to the qualitative phase, which aimed to give a deeper understanding and complete picture of ADR reporting among HCPs. Priority refers to which method, either quantitative or qualitative, is given more emphasis in the study. Implementation refers to whether the quantitative and qualitative data collection and analysis comes in sequence or in chronological stages, one following another, or in parallel or concurrently. Integration also refers to the phase in the research process where the mixing or connecting of quantitative and qualitative data occurs (Creswell *et al.,* 2003). This study therefore reflects on these important aspects of mixed methods, which are incorporated in the design and implementation stages.

3.6 Concurrent versus Sequential Designs

The commonly used types are the concurrent and sequential mixed methods designs, even though there are several variants of these two forms (Cresswell, *et al.,* 2003; Terrell, 2012). These have been further differentiated into six, namely sequential explanatory, sequential exploratory, sequential transformative, concurrent triangulation, concurrent nested (embedded), and concurrent transformative (Creswell and Clark, 2011). The choice of

approach depends on the research questions, time, and resources. For the purpose of this study, a concurrent triangulation was used to complement the outcomes of the two data sources and to make judicious use of limited time and resources (Farmer *et al.,* 2006). Even though a sequential explanatory approach (i.e. analysed quantitative data informs qualitative phase) could have worked as well, this would have had an impact on time and resources, and thus was considered inappropriate.

3.7 The Concurrent Triangulation Method

The concurrent triangulation mixed methods (CTMM) design has been used widely in mixed methods (Onwuegbuzie, and Jiao, 2007; Jang *et al.,* 2008; Östlund *et al.,* 2011) where both qualitative and quantitative study designs are implemented and completed within a short timeframe independent of each other (Bryman, 2016). Several synonyms of concurrent triangulation design have been found in the literature; these include simultaneous triangulation, parallel study, and convergent parallel study (Hadi, *et al.,* 2013; Morse, 2010; Östlund *et al.,* 2011). In this study none of these synonyms are used; the term concurrent triangulation mixed method is used throughout.

CTMM is used when qualitative and quantitative methods are incorporated into a single study by a researcher and implemented at the same time, with the objective of confirming, cross-validating or corroborating findings. The strength of employing this method stems from the fact that it offsets the limitation of individual studies while building on individual strengths within a short data collection time frame (Castro, *et al.,* 2010; Östlund *et al.,* 2011). Convergence or divergence of findings can, therefore, strengthen knowledge claims and can be better explained when compared (Creswell 2004). In this research, the comparison and integration were implemented during the discussion of final findings.

In implementing a CTMM, the possibility of bias is likely to occur while collecting both qualitative and quantitative data at the same time (Collins *et al.,* 2007). This was minimised in this study by collecting data simultaneously and independently on identical samples, i.e. in each hospital, quantitative data was collected, followed by the qualitative data within the same period (Creswell and Clark, 2007).

3.8 Prioritising Dominance and Sequence

Prioritising is important in mixed methods research because it places emphasis on which method to emphasise. Dominance and sequence ascertain the primacy and order in which the research is undertaken. Dominance relates to the relative weighting of the importance of one method over another or which method is more central to the research (Creswell and Clark, 2011). Sequence, on the other hand, refers to questions of method order, the most basic being whether methods are implemented simultaneously or sequentially. The way research is designed can influence dominance (Morgan, 2013). In the implementation of a concurrent triangulation design such as this one, priority is usually the same but can favour either qualitative or quantitative dominance (Schoonenboom and Johnson, 2017; Walker and Baxter, 2019). Usually shown in literature as ***quant*** + ***QUAL***., where *capital letters* indicate the *dominant* method, lowercase represents the less dominant method, and "+" is concurrence (Hesse-Biber and Johnson, 2015).

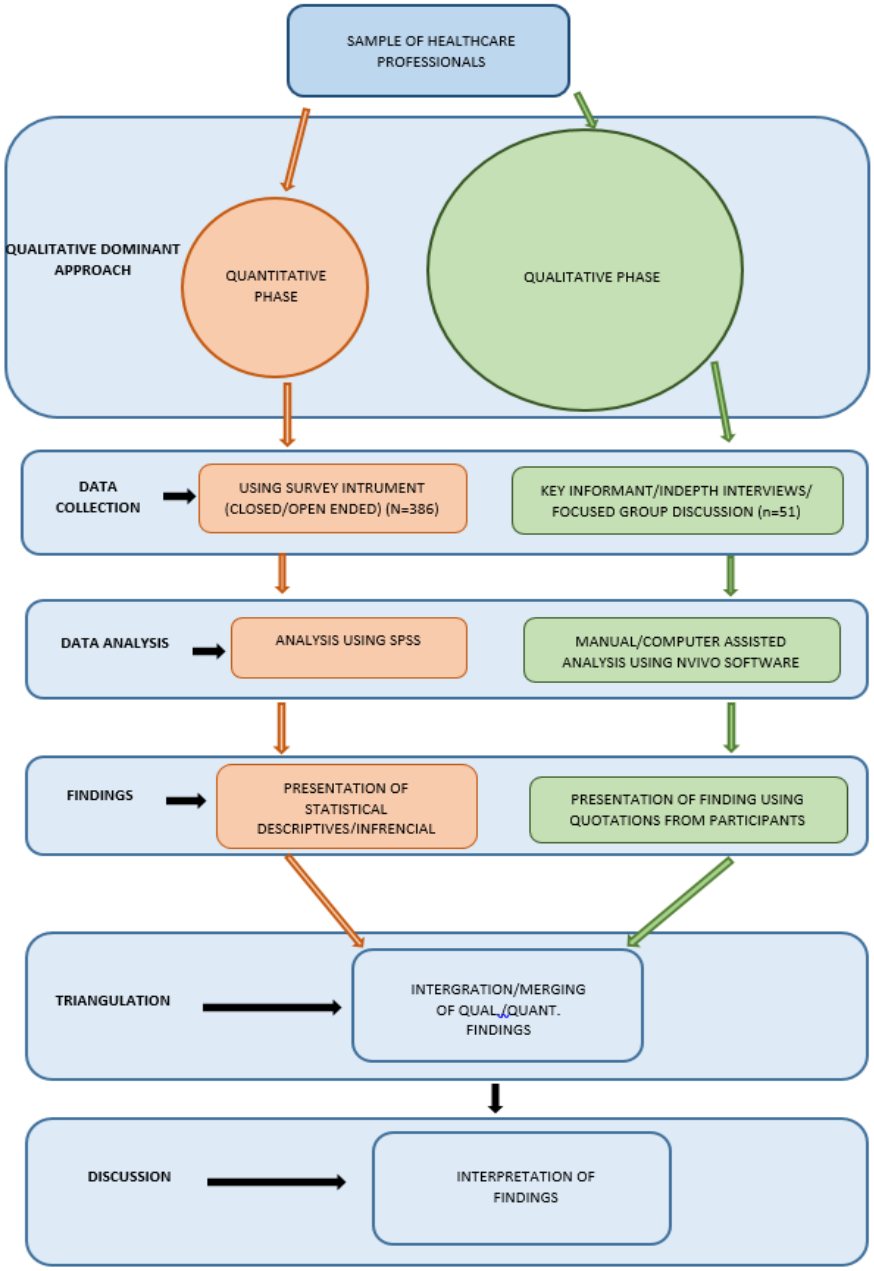
In this research, the qualitative phase was given priority (quant + QUAL) because of the saturation of quantitative studies in the literature on ADR reporting (Kharkar and Bowalekar, 2012; Abubakar, *et al.,* 2014a; Sanghavi Dhara *et al.,* 2014; De Angelis *et al.,* 2015; Marques *et al.,* 2016; Udoye, *et al.,*2018; Opadeyi *et al.,* 2019). No qualitative study has been conducted on this topic in the study context, and thus a complete understanding of ADR reporting behaviours and practices is lacking. A dominant qualitative approach would, therefore, provide complementary evidence to affirm and otherwise the quantitative results. The sequence of implementation was influenced by resource and time constraints, hence the justification for a concurrent triangulation approach where both data types were collected at the same time.

3.9 Implementation

Even though there are no generally accepted methods for implementing dominance, this study was guided by the Dominance in Mixed Methods Assessment (DIMMA) model (Walker and Baxter, 2019). In this model, three fundamental principles were used to judge dominance (i.e. sequence of qualitative and quantitative methods in each publication), whether any method dominates the paper as a whole, and how the method dominance potentially relates to method sequence. In conclusion, studies which used convergent designs had a wide variation in terms of dominance and sequence.

This research, however, initiated a dominant qualitative approach, and subsequent comparison of the respective word count in the results chapter showed 78% of results reported were based on the qualitative findings, with a sampling ratio of 386: 51 (8:1) for quantitative and qualitative research participants respectively. This represented a significant amount of qualitative data collected and therefore demonstrated a confirmation for qualitative dominance (Figure 8).

Figure 8: Methodological process of concurrent triangulation mixed methods design (author's construct)



3.10 Integration

Integration is a vital aspect of mixed methods research, which essentially brings the same participant data from two studies undertaken independently, within a project, as one to increase the overall knowledge generated. Jang (2008) describes it as "the interaction or conversation between the qualitative and quantitative components of the study" (Jang *et al.,* 2008). Researchers have proposed three integration techniques to consider in mixed methods, i.e. using a triangulation protocol (Farmer *et al.,*, 2006), following a thread (Adamson, et. al., 2009), and using mixed methods matrix-based (Wendler, 2001). O'Cathain (2010) has further suggested presenting a detailed procedural information. In this study design, a triangulation protocol (Farmer *et al.,* 2006) was used and reported in the discussion chapter (Table 25).

3.11 Triangulation Protocol

A triangulation protocol in the mixed methods approach is used to corroborate two sets of findings at the data interpretation stage, after they have been analysed to gain a complete picture of a phenomenon (O'Cathain *et al.,* 2010). During integration, researchers list findings from each component, and identify and compare where the convergence, complementarity and discrepancies are inherent (Farmer *et al.,* 2006). Denzin (2009) identified four aspects of mixed methods which could be used individually or combined at various levels (i.e. methodological, data, theoretical or investigator level) to facilitate triangulation. Methodological triangulation involves using multiple data collection methods (qualitative and quantitative), while data triangulation requires using multiple sources (HCPs) which inform the research question (Östlund *et al.,* 2011). Using a substantive theory to explain research questions refers to theoretical triangulation, while investigator triangulation entails using two or more researchers in the analysis (Farmer *et al.,* 2006; Denzin, 2012, 2009). Achieving integration, therefore, involved adopting methodological, data, and investigator triangulation techniques to explore in-depth views of HCPs on ADR reporting. This was deployed during the collection of survey data augmented by in-depth interviews (IDIs) and focus group discussions (FGDs).

3.11 Study Setting and Demographics

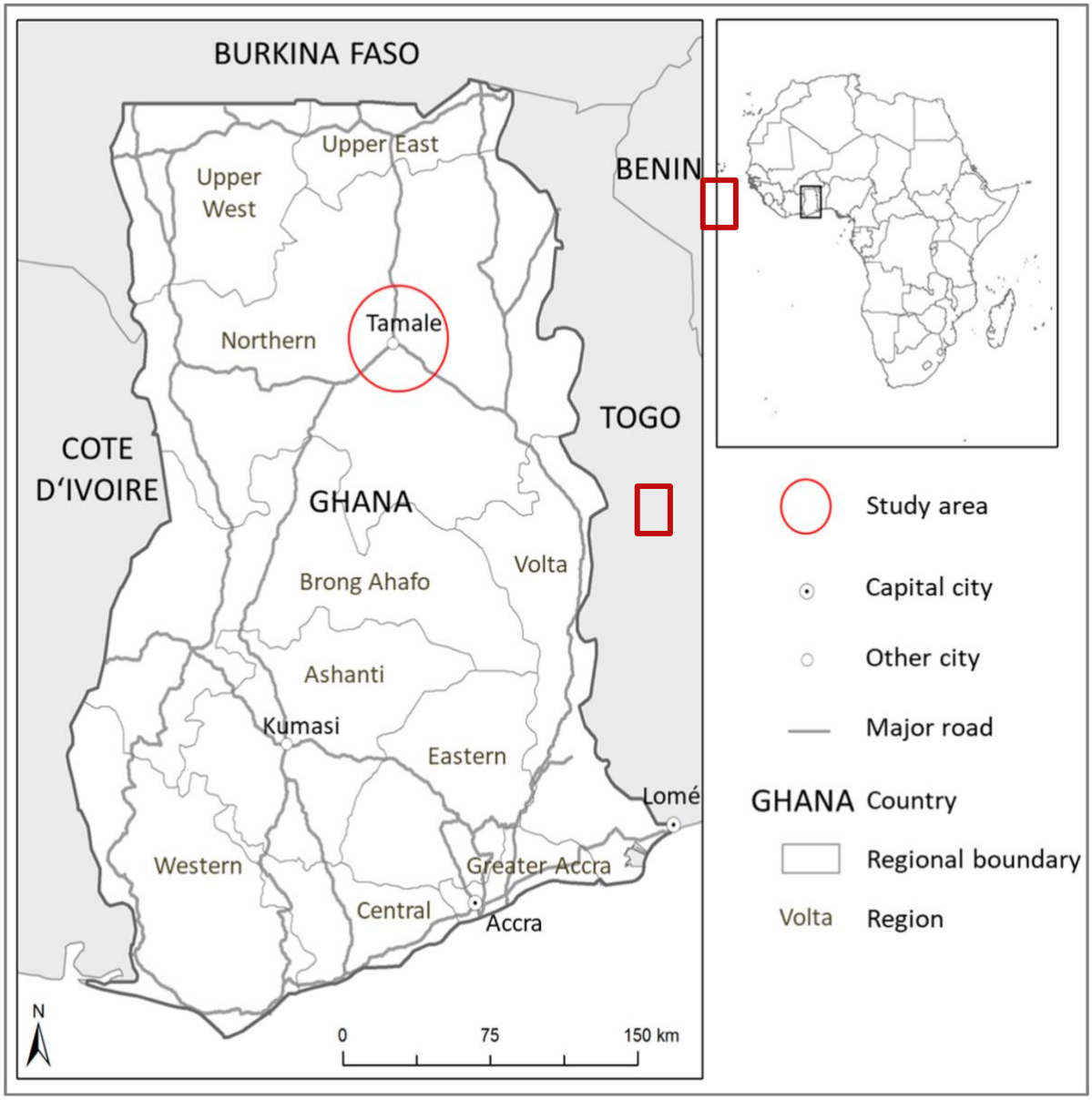
The study was conducted in Tamale, Ghana. Ghana is located off the Atlantic Ocean on the west coast of Africa (Figure 9). It has an estimated population of 29,767108 (2018) according to World Bank estimates (World Bank 2019) and a growth rate of 2.5% according to the 2010 population and housing census estimations (PHC, 2012). The country has been demarcated into 16 administrative regions. The north of the country has some of the lowest health indicators in the country (UNFPA, 2011) and has recently, geographically divided into five administrative regions i.e. Upper West Region, Upper East, Northern Region, Savannah Region and North East Region. The study location (Northern region) comprises 26 administrative districts operating at decentralised levels for efficient healthcare delivery (PHC, 2012). At the time of data collection (2017), the Northern Region and its capital city, Tamale, were the most populous in the north of Ghana, with estimated population of 2,935,622 and 269,227 respectively (GHS, 2018) (Table 6).

Table 6: Demography and vital statistics of the Northern Region (GHS, 2018).

INDICATORS		Frequency
Population with no education	Male (47.7%)	-
	Female (65.8%)	-
Critical staff	Pharmacists	36
	Pharmacist Technicians	47
	Medical officers	216
	Medical officer(consultants)	2
	Medical officer(specialists)	44
	Medical/physician assistants	131
	General nurses/Midwives	2,999
	Community health nurses	1032
	Enrolled nurses	3040
	Lab. Technicians	100
	Public Health Officers	22
HCP to patient ratio	Doctor: patient	269:11,130 (1:41)
	Nurse: patient	6,248:479 (1:13)
Hospital Beds	Christian Health Services of Ghana (CHAG)	394
	Government	1,452
Attendance *admission rate 61.3%	Outpatient	1,876,818
	Inpatient	179,351
Health infrastructure *incomplete data for private and quasi government hospitals	Community-based Health Planning and Services (CHPS)	459
	Clinics	57
	District hospitals	17
	Health centres	105
	General hospitals	16
	Maternity homes	8
	Polyclinics	5

These health facilities and human resources are sited in 26 districts (PHC, 2012). In addition, in terms of health work force training, the Tamale metropolis has one university teaching hospital, a community health nurses training school and one nursing training college, where the majority of the health human resource of the setting received their training.

Figure 9: Location map of Tamale in Northern Region, Ghana, West Africa (Karg *et al.*, 2019)



3.12 The Ghanaian Healthcare System

Structure of the health delivery system

The Ministry of Health (MOH) has oversight responsibility for the provision of quality healthcare through adequate financing of the health system, provision of logistics for health education, training, development, provision of hospitals and management of health services in general. The Ghana Health Service (GHS) has been vested with the mandate for provision of health services through promotion, curative and rehabilitative care. The MoH therefore formulates policies, while GHS sees to the autonomous implementation of government policies on health in both the public and private sectors.

MOH/GHS is a WHO development partner and has a comparatively well-developed healthcare system compared to the sub-region (Drislane *et al.,* 2014). It operates a decentralised healthcare administrative structure which functions in four tiers i.e. national, regional, district and sub-district/community level.

The primary point of contact is at the sub-district/community level, where clinics and community-based health planning and services (CHPS) are managed by nurses and physician assistants. Secondary points of care are the district and some regional health centres/hospitals, which are usually managed by specialist doctors and nurses. Tertiary care services are offered at some regional and national hospitals where specialists doctors manage advanced cases. Most of these hospitals are government/public owned and are often referred to as referral centres/hospitals and are currently located in only five of the 16 regions: Northern, Ashanti Greater Accra, Volta and Central regions.

The healthcare sector is financed largely by the government (39%) to support the National Health Insurance Scheme which finances affordable health for all (Schieber *et al.,* 2012).

The coverage of the scheme as at the end of 2017 was estimated to be about 18 million, with only 10.57 million active members (nhis.gov.gh). In-patient and outpatient visits have increased significantly since its inception, by a factor of 23 and 29 respectively (Schieber *et al.,* 2012).

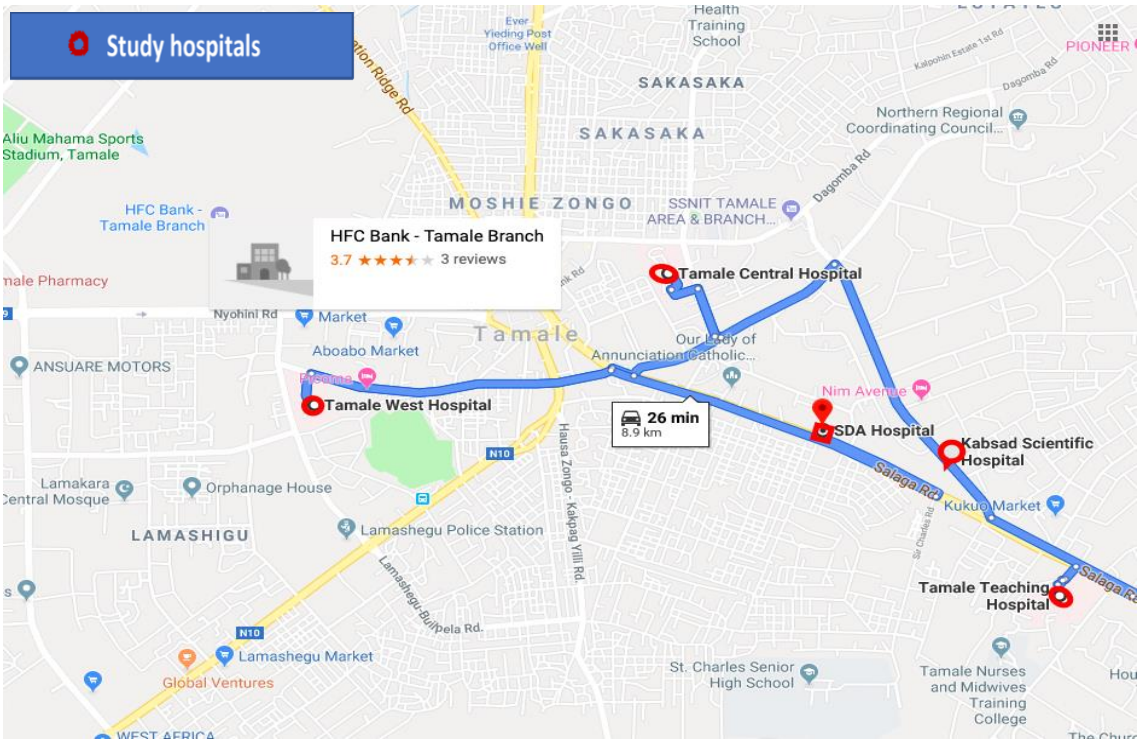
3.13 Study Sites

Hospitals: Five hospitals were selected as sites for this study: The Tamale Teaching Hospital (TTH), Tamale Central Hospital (TCH), Tamale West Hospital (TWH), Seventh Day Adventist Hospital (SDA) and Kabsad Scientific Hospital (pilot hospital). Selection of hospitals were based on the following justification:

1. The TTH is the largest tertiary referral hospital in the north of Ghana, and it serves as the teaching hospital for the University for Development Studies.
2. The TCH and TWH are the two main primary care hospitals in the metropolis, providing general primary healthcare services to the central and western parts of the metropolis while receiving referrals from sub-district clinics.
3. The SDA hospital is a mission hospital run by a faith-based organisation offering primary care services in the Tamale metropolis.
4. KABSAD is a private hospital offering secondary care and essential services to individuals who opt for private care services. Kabsad was deemed suitable for piloting the study because it shared similar characteristics to the main study sites.

The five selected healthcare facilities were the most patronised and were within a 4 to 8km radius of the metropolis (Figure 10). The Tamale meterpolis is estimated to be 646.90180sqkm with 115 communities and 223,252 inhabitants (PHC., 2010). Notwithstanding the availability of community, district and other private clinics, the selected study sites were the most pertronised and cater for the healthcare needs of majority of the population. Patients also travel form outside the metropolis to assess specialist care especially at TTH which is a referal hospital. The diversity in sample of study sites therefore offered a multi-level perspective from primary, secondary, tertiary, governmental, quasi-governmental and private healthcare settings.

Figure 10: Google map of Tamale metropolis showing the location of the selected study hospitals



QUALITATIVE STAGE

In this section, the qualitative phase of study is described. Participant recruitment, selection, data collection and analysis are described. Trustworthiness which is an important aspect of ensuring quality in qualitative research, will be discussed separately at the end of the section.

3.13.1 Participants

The target population of both phases of the research were healthcare professionals i.e. nursing, pharmacy, and medical staff, who were among the core clinical team working at the five selected hospitals in the Tamale Metropolis. A diverse group of health professionals was considered based on a report from the Food and Drugs Agency (FDA), which suggested that medical, nursing and pharmacy staff are the most frequent ADR reporters (Darko and Sabblah, 2016; FDA, 2018).

Participants included general nurses and specialities such as midwives, emergency care nurses, nurse prescribers, public health nurses, and enrolled nurses, who consented to be part of the study. Pharmacy staff included pharmacists and pharmacy technicians, while medical staff included doctors and medical officers of various specialities and seniority levels, as well as

physician assistants.Dentists, physiotherapists, laboratory and biomedical staff, radiologists, technical officers, environmental health officers, dispensing assistants, optometrists, and ward assistants were not considered for this study as they are less likely to be involved in ADR reporting.

In addition, non-clinical HCPs who were not frontline medical staff (administrators and management staff) were excluded.

3.13.2 Sample Size

The qualitative sample was selected mainly from respondents of the quantitative survey and pilot study. An open invitation was sent along with survey questionnaires for participants to indicate their interest to participate in either the FGD or in-depth interview. Out of 386 invitations, 70 expressed interest and 51 invitations were accepted (including pilot study). A total of five FGDs (19 nurses) and 32 in-depth interviews (medical, pharmacy and nursing staff) were undertaken. In FGDs, a sample of four to ten participants is usually recommended (Bryman, 2012; Barbour, 2005), so 14 participants were targeted per group in case of attrition. The pilot study had only three participants because of practical limitations. Data saturation was considered an important concept, which helps the researcher to curtail further sampling when no new information is being generated (Glaser and Strauss 1967). Identifying the required sample size for the perceived data saturation limit was based on previous studies elsewhere (Mirbaha *et al.,* 2015; Williams *et al.,* 2013; Kingston *et al.,* 2004; Nichols *et al.,* 2009), because there were no studies in the local context to base the sample on. For example, while Kingston (2004) and colleagues sampled between 4 to 11 for their FGD, Mirbaha *et al.,* (2015) sampled between 10 to 12 participants for their FDG.

3.13.3 Recruitment

Participants were approached by invitation to opt in for either an in-depth interview or a focus group discussion (Appendix B) to further understand the central phenomenon of ADR reporting in their various facilities after the survey. Information sheets about the qualitative study were also made available at various departments and units. Even though there was a high response rate from the invitation letters (Appendix E), gatekeepers recommended specific individuals, departments or units to approach in order to capture the contextual relevance of the topic. With participant permission, contact details of participants who were sent an invitation letter (Appendix E) were collected for future correspondence and appointments.

Participants who honoured the final SMS notification of invitation reminders, follow-up phone calls, and who consented, participated in the study.

3.14 Qualitative Pilot Study

The study site (Kabsad Scientific Hospital) was purposively selected because it is located in the same study area and comparable to the selected hospitals in the main study. The rationale of the pilot was to trial the study methods within the study population (HCPs) in an environment similar to the main study. Permission was sought from the hospital administration and purposive sampling techniques were used to recruit nursing and medical staff. The process was used to test interview protocols, strengthen interviewer skills and to identify the practical issues in the research beforehand (Kim, 2011). The transcripts from in-depth interviews, focus group and field notes were analysed and added to the main study. This was because qualitative interviews are progressive and continuously improve as the study progresses, thus some have argued for pilot studies to be an integral part of the main study rather than separated from it (Holloway, 1997). Throughout the interviewing process, the researcher gained confidence and insights as a novice researcher. Insights into improving interview schedules, line of questioning and introduction of the issues, were gained in the process.

The qualitative pilot phase identified a number of ethical, technical, cultural, social and professional challenges associated with the data collection. Measures were therefore put in place to limit occurrences in the main study.

1. Getting a suitable place and time for conducting interviews with those who had consented to participate in the study was challenging. For example, a scheduled interview session with a doctor in his consulting room was constantly interrupted by visitors. Some nurses who were interviewed in their staff common room were interrupted by colleagues and friends. This created a noisy environment which affected the quality of the recording. Locating a quiet environment was therefore an important measure taken in the main study, to reduce external disturbance.
2. Participants routinely excused themselves from the interviews to perform work-related tasks, which often disrupted the flow of the interview.
3. Piloted audio-recording of participants signalled poor audio quality. This indicated the need to request recordings to be conducted in a designated closed meeting area such as the staff room or consulting rooms, when no other patients or staff were present. In addition,

manipulation of the recording device was also challenging, especially in terms of positioning the device to be able to capture the best audio quality, and when the audio had to be paused and recording continued later.

4. The facility was informed, and access sought from hospital administration. A purposive sampling technique was used to sample key informants through a gatekeeper. This was a challenge however because the gatekeeper informed participants of the study but there were no direct or personal introductions. Coupled with the busy schedules and unfamiliarity with scientific research, this was a challenge. The success of the responses and data collected therefore depended on the researcher's inter-personal skills (Kim, 2011).

5. The researcher's own knowledge and expectations implicitly created a bias. It is important to block these biases and assumptions then explain the phenomenon of ADR reporting in terms of its inherent systems and meaning to the healthcare professional by maintaining the epoche process (Kim, 2011). Epoche helps the researcher maintain a position of uncertainty, suspend their judgement and refrain from any premature conclusions. On a few occasions at the initial stages of the interviews, it was noticed that leading questions were being asked, which made it difficult to maintain the epoche. This process was mastered process through practice, where reflections and self-awareness were used to better the researchers interviewing skills. The practice helped gain insight from an emic perspective while trying not to impose their own views on participants, as suggested by Seidman (2006).

6. There were instances where the researcher was asked questions by the interviewees, for example, the researcher, in trying to assess participants' knowledge, asked: "What is pharmacovigilance?" After a few seconds of silence, the participant asked the researcher the same question. This necessitated rephrasing of the interview question to include alternative phrases and terms in the main interview.

3.15 Data Collection

The data was collected between September and November 2017. The qualitative approach permitted an in-depth exploration of the rich accounts of the study participants' experiences. This was achieved using multiple strategies including key-informant interviews, in-depth interviews, focus group discussions, and analysis of open-ended questions. The process ensured data triangulation, giving a detailed and comprehensive view of the phenomenon (Sargeant, 2012) while increasing the validity and reliability of the study (Plano Clark and Creswell, 2008). The focus group discussion (FGD) in particular ensured interaction between participants, which reduced recall bias (Vaivio, 2012). Additionally, it facilitated inter and intra HCP comparisons in their natural setting where sensitive issues were discussed in a supportive environment. Participants who opted for in-depth interviews were followed up at a time and location most convenient to them for a recorded interview session.

3.15.1 Interview Guide and Procedure

A semi-structured topic guide by Kingston (2004) on incident reporting by doctors and nurses in Australia was modified, based on the current research context and questions, to facilitate the in-depth interviews and focus group discussion in this study (Kingston *et al.,* 2004). The topic guide from Kingston (2004) had the following questions:

- What comes to mind when you hear the word "incident reporting"?
- What is the current reporting process in your organisation?
- Can you think of any positive things that have occurred as a result of completing an incident report? Can you think of any negative things?
- How would you rate the current reporting system?
- If you were in charge of the incident reporting system, what changes, if any, would you make?

- How many times a year, on average, do people in your position fill out incident reports?
- Why do people decide to complete an incident report?
- How do you think people feel when they complete an incident report?
- Based on your experience, how many times a year should people in your position fill out an incident report?
- What makes people in your position decide not to complete a report?
- Does the seriousness of the situation have any bearing on whether an incident report is made, or not?
- On the sheet, I have listed some of the obstacles to reporting. Do you have any comments? Which of these do you regard as the really big issues? Are there any other obstacles?
- Would having a form with the option of not identifying the reporter make a difference?
- Is there anything else we should have discussed that we haven't touched on yet?

The questions were then modified into an introductory part, the main questions, and conclusion (Table 7). The introductory part was about the study, participant and researcher background. Some of the main questions included: what factors affected adverse reaction reporting among healthcare professionals, how adverse drug reactions were reported, and how adverse drug reaction reporting could be improved. The questioning was flexible, allowing use of several probing and follow-up questions. To conclude, the opportunity was also given at the end of each session for participants to give any additional viewpoints.

Through the qualitative data collection phase, participants were able to contribute to discussions and express their views. Through the discussion, participants learnt a lot and medication safety was also promoted. Prompts and images were used to facilitate discussion about ADR reporting. For example, pie charts and a newsletter from the Food and Drugs Authority (Darko and Sabblah, 2016) were shown to participants to facilitate discussion points. Details of the changes which were implemented are discussed in Table 7

Table 7 Modification of the interview topic guide

PILOT INTERVIEW	FINAL INTERVIEW GUIDE	SUMMARY OF CHANGES
1. **Introduction (researcher and research purpose)**	1. Introduction of researcher and research purpose. 2. Tell me about yourself and how long you have been practising. 3. Can you please tell me briefly what you know about pharmacovigilance; what is your general understanding about pharmacovigilance? 3a. What is an ADR?	The question was rephrased to allow more time during the icebreakers to introduce myself, build rapport and also hear the background of the participant. In the pilot, I only mentioned my first name and delved into the first question on pharmacovigilance (PV).
2. **What is pharmacovigilance?**		This question was rephrased to take a step back to understand whether HCPs had basic knowledge about the phenomenon. Provision was made for using alternative terms such as 'medication safety' or 'drug safety' in case the participant had never heard of the term pharmacovigilance (PV). The hypothesis was that they had at least heard about PV already before the interviews.
3. **How is the current reporting process in your facility?** 4. **Can you think of any negative or positive that has happened as a result of you completing an ADR form?**	4. Have you had some experience with adverse drug reactions from patients? If yes, tell me about your experience and how you reported it; if no, tell me why.	It was also presumed that HCPs would have encountered at least one ADR in their practice. The pilot, however, showed otherwise. Questions were therefore restructured to ask about their experience with ADRs and how they are reported incidences. It

5. **How would you rate the current reporting system?** 6. **How many times do people in your position fill out a form?**		was noticed that pilot questions 5 and 6 only generated very short responses. Asking about their reporting experience and the reporting process generated more conversation.
7. **Why do people decide to complete the ADR forms?** 8. **How do you feel when you complete a form?** 9. **Examples of your experiences – in what situation would you be compelled to report?** 10. **Roles and responsibility of providing forms.**	5. Looking at the FDA Drug Lens newsletter (show participant a copy), reporting in this region is the worst in the country – why do you think reporting is low?	Using the pilot questions 7, 8, 9 and 10 experienced short responses and moments of awkward silence. To avoid this in the main interview available data on ADR reporting from the FDA was used as a prop to facilitate discussion about why ADR reporting was low. Even though pilot questions 7, 8, 9 and 10 were merged, they were used to prompt participants if they failed to speak about them eventually.
11. **Does the seriousness of an event affect whether an ADR would be reported?**	6. How likely are you to report the following types of reactions on a scale of 1 to 5 where 1 is 'would definitely report', and 5 is 'would definitely not report'? Explain your choice of response. ● *Any adverse reaction* ● *The patient died as a result of the reaction* ● *The reaction caused the patient to be hospitalised or needing significant medical treatment* ● *The reaction included in the product information is a known adverse reaction for the drug* ● *The reaction followed a vaccination* ● *The reaction followed use of a biological product* ● *The reaction followed use of new medicine*	This question was rephrased to solicit the best response to the underlying factors which motivate HCPs to report ADR. The piloted question gave shorter responses and required further probing and prompting to solicit the required response.

12. **Suggestions for improving reporting.**	7. If you were the manager and had money to invest, what barriers do you think – if they are addressed – ADR reporting would improve, especially in your facility?	Pilot question 12 was rephrased into a preamble to get the participant involved from a point of power and to discuss what they think would work. Question 13 was asked as a follow-up question if it was not discussed.
13. **What are the most convenient ways of reporting?**		
14. **Can I have your final words to conclude?**	8. If there are any other issues, I have not raised that you would like to comment on, you are most welcome to give your final comments.	This was rephrased to present a polite conclusion, but this did not change the meaning of the question asked.
15. **Thanks for your time.**	9. Thank you for your time.	Remained the same.

3.15.2 Instruments and Interview Records

Interactions were facilitated which created a context in which the participant could relate to thereby generating data through important probing questions as suggested by Chenail (2011). As the researcher becomes the main data collection instrument in qualitative research it is important to develop the appropriate attributes (Sandelowski, 2000). Questioning and listening skills acquired were leveraged to give the participants a platform to express their opinions, as it is thought to have a therapeutic effect on participants when their views are listened to (Poggenpoel and Myburgh, 2003).

All in-depth and key informant interviews were audio-recorded and transcribed verbatim, as described in later sections. With the written consent of the research participants, an encrypted digital audio recorder was used for the data collection. All data was safely stored on the university drive. After data collection, a transcription software (Express Scribe 6.05) was used for dictation and transcription of audio files into word files. For participants who agreed to be interviewed but did not permit digital voice-recording, permission was sought for notes to be taken and crosschecked with the participant to maintain the accuracy of notes after interviews. Member checking is an important quality control measure, which allows participants to review the accuracy of their statements (Harper and Cole, 2014). All interviews were recorded at the hospital facilities, at times and places convenient to the researcher and participant and where there were minimal disruptions and apparent high sound quality.

3.15.3 Open-ended Question Analysis

An additional justification for qualitative dominance was further exploration of participant views using open-ended questions in the quantitative survey. Questions 1, 3, 5, 7 and 8 (see text box) were analysed as follow-up questions to augment questions, which preceded them. For example, question 1 followed a set of Likert-type questions about suggested methods of improving ADR reporting. This allowed scope for a deeper understanding of the discovery of diverse perspectives (Gillham, 2000). Open-ended questions were analysed by undertaking a content analysis (Erlingsson and Brysiewicz, 2017) where data extracts were condensed, coded, categorised and grouped into themes.

Text box of open questions analysed

Could you suggest other ways of improving ADR reporting in your healthcare facility?.....

Do you read the FDAs newsletter, the DrugLens? Yes/no

If yes where do you get your copy from? .....

In which department or unit do you mainly work?.....

Highest Level of education

Masters Degree [ ]

Bachelors Degree [ ]

Diploma [ ]

Certificate [ ]

Other…….. [ ] (please state)……..

How many ADRs have you reported this year **(select one option)**

0 [ ]
1-5 [ ]
6-10 [ ]
11- 20 [ ]
More than 20 [ ]

Whom did you report to?.....

Where did you record it?.....

3.16 Thematic Data Analysis

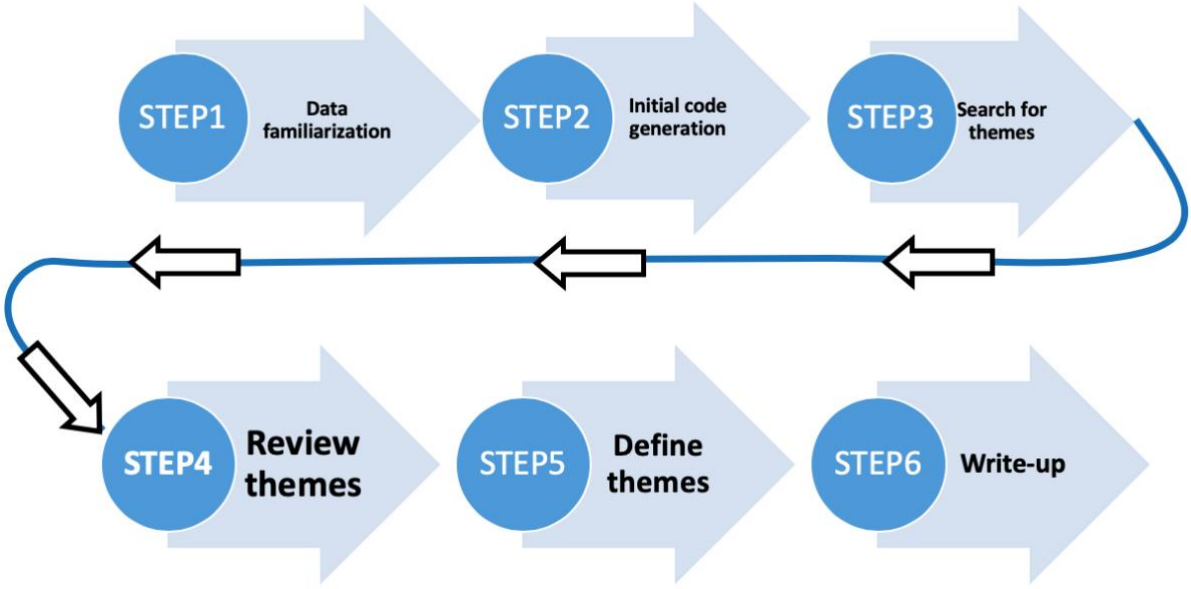
Unlike quantitative methods, qualitative data analysis is not straightforward because there are few well-established acceptable rules to guide analysis. As mentioned earlier, qualitative inquiry usually generates large amounts of data, which is often challenging to analyse, thus described by Miles (1979) as an attractive nuisance. There is often the fear of failing to carry out a true analysis due to the complexity of the data. It is therefore recommended that data collection and analysis proceed simultaneously (Merriam and Merriam, 1998). Simultaneous analysis however was not practical because of resources and time, but data analysis commenced immediately after collection, from December 2017 to September 2018.

Analysing quantitative data aims to understand the underlying patterns, trends and relationships revealed in the numerical data about a phenomenon to help draw a valid conclusion (Albers, 2017). Describing the process helps the reader to understand how the results culminated from raw data into useful information. Thematic analysis has become a popular strategy and useful strategy for analysing qualitative research, and can be adopted in different contexts of analysis, such as critical discourse (Burman and Parker, 1993) and narrative and content analysis, even though they are unique strategies in their own right. A classic thematic analysis strategy was adopted which was guided by the research questions. The decision was influenced by my stance as a pragmatic researcher, as I sought to utilise what works best based on research design and the data collected. Even though thematic analysis is criticised as not being robust and lacking sophistication (Smith and Firth, 2011), it is widely used and novice researchers find it useful in learning "core skills that will be useful for conducting many other forms of qualitative analysis" (Braun and Clarke, 2006, p.78). Through a non-linear step-by-step reiterative process, important themes were identified and used for analysis. A theme is described as a category identified by an analyst, informed by data, which relates to his/her research focus/question; codes identified in transcripts/field notes provide the researcher with the basis for theoretically understanding the data, which can make theoretical contributions to the literature relating to the research focus.

When analysing themes, it is advisable to look out for repetitions, indigenous typologies, metaphors, analogies, transitions, similarities, differences, linguistic connections, missing data and theory related to the material (Bryman, 2015). It is important to see through the "participant's eye", hence the need for abductive reasoning, which is a type of inductive reasoning that relies on explanations and understanding of the participants' world view

explained by the researcher. The FGDs and in-depth interviews were analysed deductively using the six-stage thematic analysis process described by Braun and Clarke (2012) (Figure 11). Although rarely a linear process, it systematically guides the data analysis process.

Figure 11: A six-phase thematic analysis format (Braun and Clarke, 2012)



Step 1

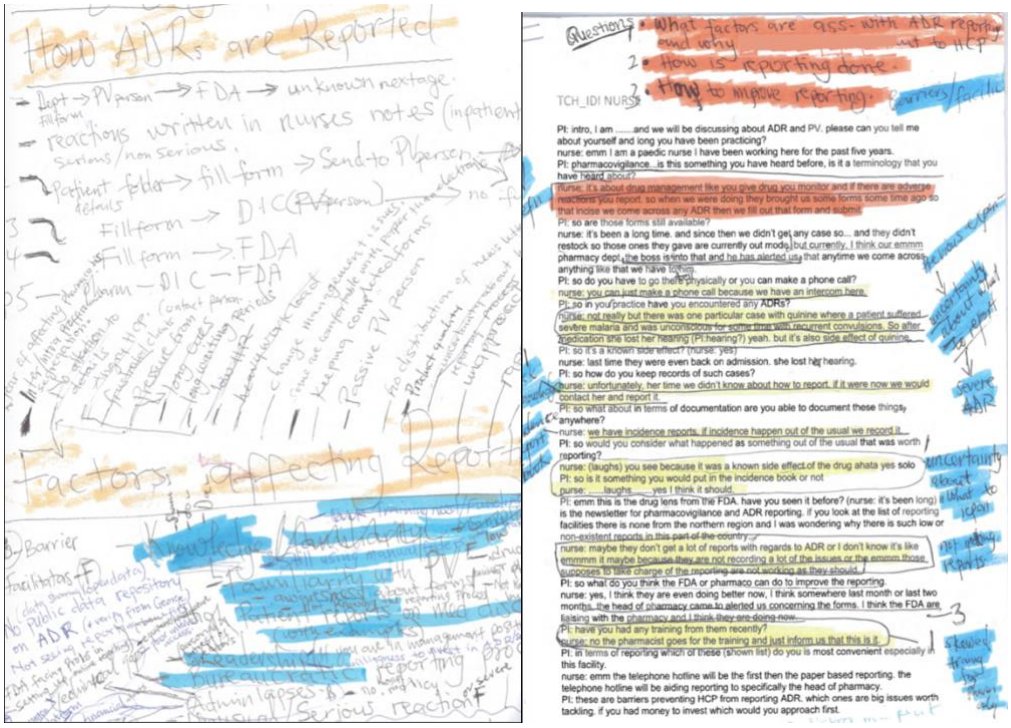
Data familiarisation: To make meaningful inductions, it is important to be familiar with the whole data corpus. Data obtained through the interviews were transcribed verbatim using the NCH transcription software, Express Scribe, and double-checked for accuracy. Field notes were typed and stored in Microsoft Word. Important emerging ideas were highlighted at this stage and noted. Even though time consuming, transcribing data, reading and re-reading the data, and noting down and highlighting initial ideas further deepened the familiarisation process, helping the researcher to become immersed, knowing the depth and breadth of the data corpus (Braun and Clarke, 2006).

Step 2

Initial code generation: It is important to code interesting features of the data in a systematic fashion across the entire data set, collating data relevant to each code. This can reduce chunks of data into manageable amounts. Initial codes were generated by the researcher in the first instance through open coding, and their appropriateness was discussed further with the supervisory team. Open coding involves reading through the data several times and creating tentative labels for chunks of the data which show interesting concepts. The open coding was

followed by axial coding, which allowed the identification of relationships between the codes. Transcribed data was coded and analysed both manually and using NVivo version 12. All files were transferred to NVivo and initial codes, generated based on ideas from familiarisation of the data and from the general literature. Manually, pen and paper were used to sketch ideas from codes and to create mind maps (Figure 12). A memo of coding was kept to document the coding process and emerging ideas. The style of coding usually depends on the research standpoint and questions. An inductive approach was used to narrow the research scope to explore a new phenomenon, rather than a deductive approach which is usually driven by a hypothesis and establishing causality.

Figure 12. Manual sketching of codes based on research questions from transcribed interviews.

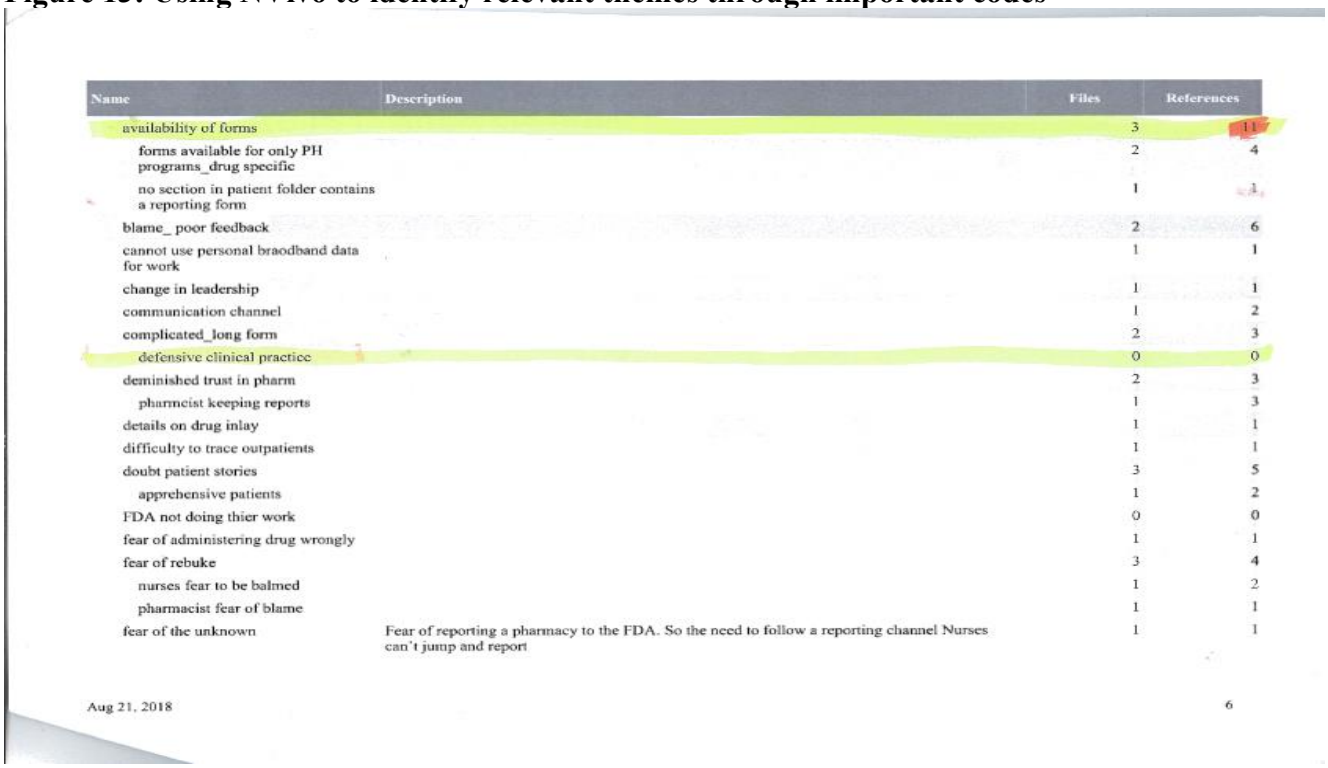


Step 3

Searching for themes: This stage involved collation and sorting of codes, and further development of the mind maps into potential themes (Figure 14). Gathering all data relevant to each potential theme was achieved by observing repeated patterns and building a visual narrative. At this stage, repetitions are an important way of identifying themes or trends in data but may not necessarily mean anything, especially if they do not relate to the research focus or questions of interest (Patton, 2002). According to Bazeley (2013), it is important to justify how

themes emerged or were identified (Bazeley, 2013). He argues that presenting themes and illustrative quotes is not sufficient in qualitative research, but that the themes need to be weighted to show the significance of one over the other. NVivo software was therefore used as a supplementary tool for coding the searching codes and identifying and prioritising themes. It helped to identify important themes based on the number of reference hits made in a file. For example, Figure 13 shows highlighted themes based on the level of importance, from transcripts of nurses' data. The code name 'availability of forms' (highlighted) shows 11 reference hits in three files. This shows the importance of the code and possible inclusion in subsequent themes. For example, 'defensive medical practice'(highlighted) shows it has not been referenced in any files among nurses, and thus is less important. Such codes were either merged or disregarded based on perceived relevance.

Figure 13: Using NVivo to identify relevant themes through important codes



Name	Description	Files	References
availability of forms		3	11
forms available for only PH programs_drug specific		2	4
no section in patient folder contains a reporting form		1	1
blame_ poor feedback		2	6
cannot use personal braodband data for work		1	1
change in leadership		1	1
communication channel		1	2
complicated_long form		2	3
defensive clinical practice		0	0
deminished trust in pharm		2	3
pharmcist keeping reports		1	3
details on drug inlay		1	1
difficulty to trace outpatients		1	1
doubt patient stories		3	5
apprehensive patients		1	2
FDA not doing thier work		0	0
fear of administering drug wrongly		1	1
fear of rebuke		3	4
nurses fear to be balmed		1	2
pharmacist fear of blame		1	1
fear of the unknown	Fear of reporting a pharmacy to the FDA. So the need to follow a reporting channel Nurses can't jump and report	1	1

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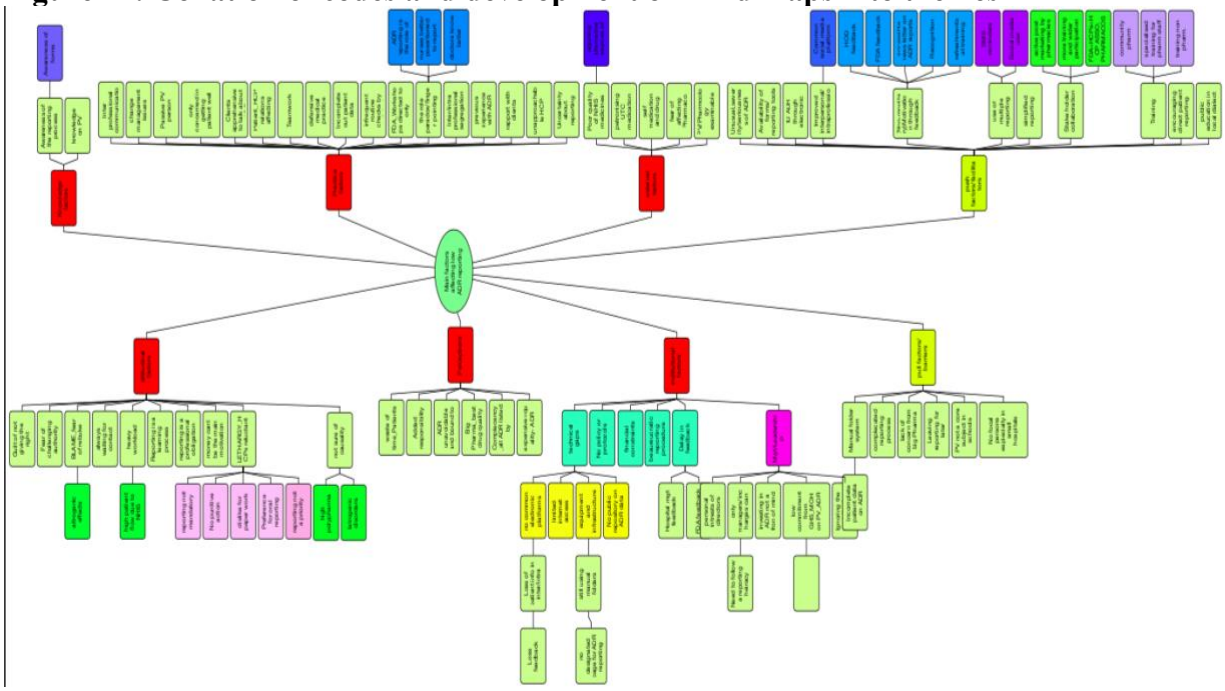
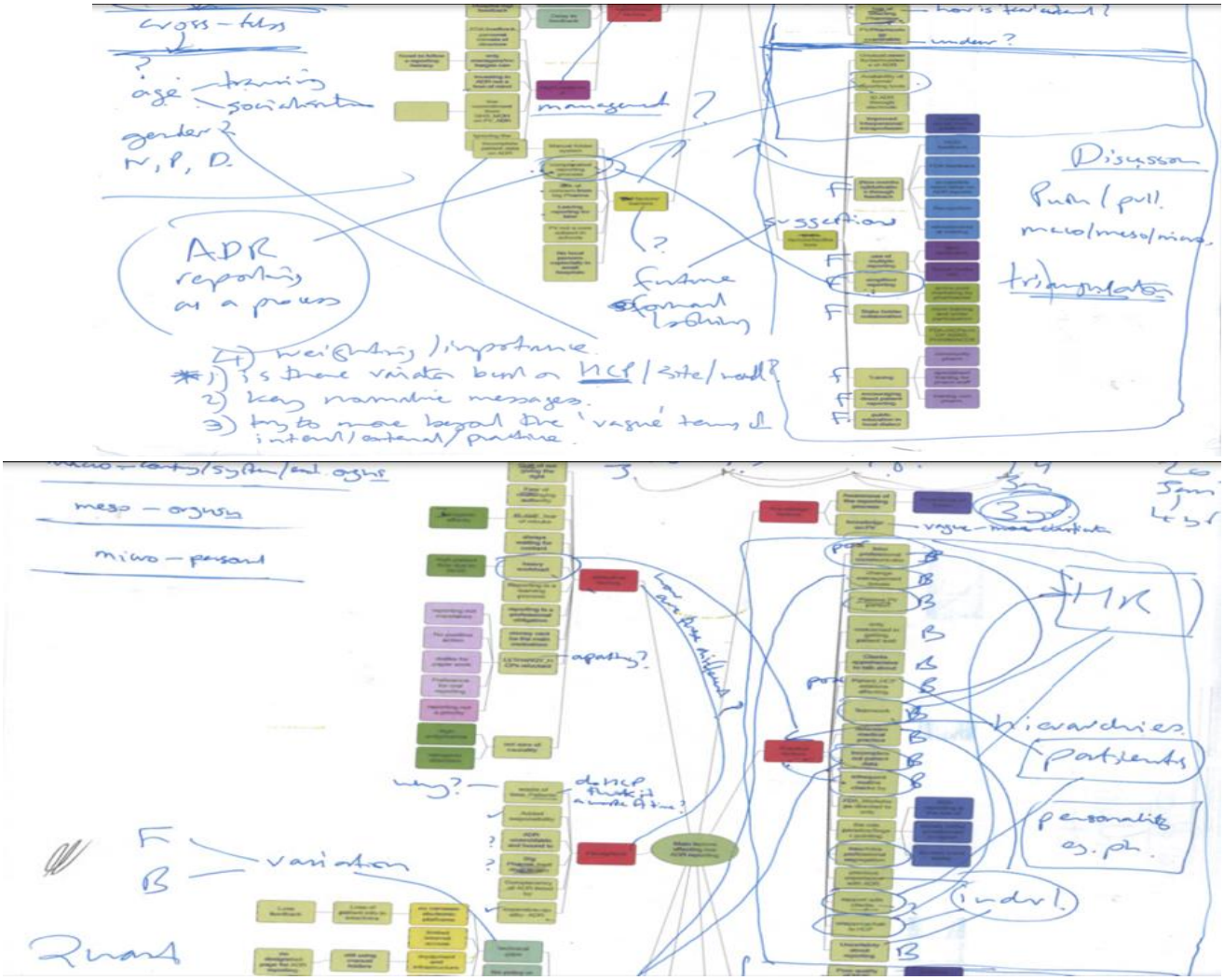
Figure 14: Collation of codes and development of mind maps into themes



Step 4

Reviewing themes: After collating codes and searching all the emerging themes, they were crosschecked to ensure they were close-fitting in relation to the coded extracts (step 1) and the entire data set (stage 2) to generate a comprehensive thematic map of the analysis. This process entailed many reiterations and discussions with the supervisory team finding the linkages between themes and codes, clarifying ambiguity and weighting importance of themes. This was prepared by printing on A3 sheets (Figure 15) where themes and codes were reviewed and revised, and occasionally by crosschecking and re-reading the transcripts to be sure of meaning.

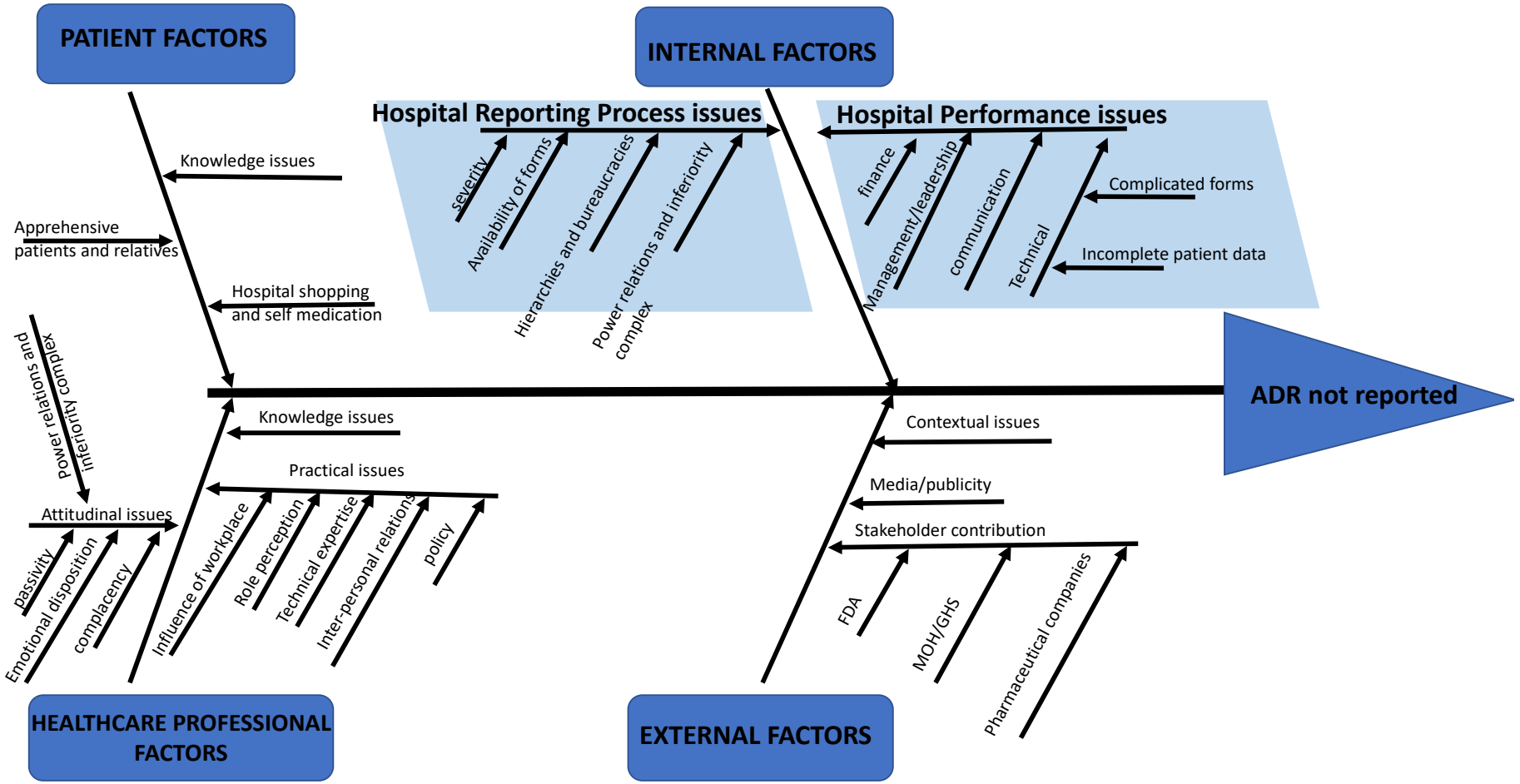
Figure 15: Picture of reiterations from supervisory team crosschecking relevance of themes in relation to codes extracted



Step 5

Defining and naming themes: There was ongoing analysis to redefine the specifics of each theme, and the overall story the analysis tells was initiated in this step. Clear definitions were generated, and refined names of each theme created. The links and interconnections between themes and subthemes were examined as proposed by Attride-Sterling (2001) and Grogran, *et al*. 2014. After weighting themes according to importance, two main themes emerged i.e. system and human factors, which resulted in internal/external factors and patient/HCP factors respectively. These were presented pictorially in a diagram (Figure 16) showing subthemes and how they interrelate.

Figure 16; Initial organisation themes



Step 6

Write-up: This step presents the final opportunity for analysis. Themes are meaningless if they are not expounded to show their inter-relatedness and how interesting they are (Bryman, 2016). The themes were linked back to the research questions and literature to draw inference and implication for the study. This process comprised selection of vivid, compelling extract examples, analysis of selected extracts and production of a scholarly report of the analysis. Continuous reiterations from the researcher and supervisory team produced succinct compelling narrative of themes and findings to address the research questions and objectives.

QUANTITATIVE STAGE

In this section, the quantitative research phase including the quantitative research design, the techniques for participant recruitment, data collection, and analysis are described. The section begins with the rationale for this component of the study design, before moving on to describe the key stages of the research process. Validity and reliability, which are important aspects of ensuring quality in quantitative research, will be discussed separately under 3.26

3.17 Study Design

The quantitative phase of the study employed a descriptive cross-sectional study design with the mixed methods study to provide snapshot evidence about ADR reporting practices among HCPs in Tamale, Ghana. As mentioned earlier, only one study utilised a quantitative approach to investigate ADR reporting among nurses in Tamale city (Ameade *et al.,* 2014). Sabblah (2014) also focused on doctors in Accra, and a third study focused on doctors, nurses and pharmacists in the Volta region. This study design therefore aimed to offer comparability and multiple perspectives of different categories of HCPs in the context of Tamale city, which is more likely to reflect inherent contextually relevant issues.

3.18 Study Participants

As in the qualitative study, the study participants were healthcare professionals: medical, nursing and pharmacy staff.

3.19 Inclusion and Exclusion Criteria

Participants were invited to take part in the study if they were directly involved in patient care and clerking. Nursing staff included enrolled nurses, midwives, general nurses, nurse practitioners (prescribers) – and other specialised categories such as eye, ear, nose and throat, paediatric care, emergency care and mental health. Medical staff comprised house officers, medical officers, medical/physician assistants, consultant physicians and specialist doctors, while pharmacy staff included all ranks of pharmacists and pharmacy technicians. Clinical staff who had additional responsibilities such as clinical, administrative support, and hospital management, were also included.

Dentists, physiotherapists, laboratory and biomedical staff, radiologists, technical officers, environmental health officers, dispensing assistants, optometrists and ward assistants were excluded from this study. In addition, non-clinical HCPs who were not front-line medical staff (administrators and management staff) were also excluded.

3.20 Participant Selection

As mentioned previously, participants were selected from five hospitals in the Tamale metropolis, i.e. Kabsad Scientific Hospital, SDA Hospital, Tamale Teaching Hospital, Tamale West Hospital and Tamale Central Hospital (Figure 17). The selection of study hospitals was purposive while selection of study participants used random stratified sampling. The stratification was based on hospital department and units. Ten main departmental units were purposively selected, and participants were selected from these units by simple random sampling. Departmental unit heads used the staff list, and participants who were selected consented and were issued the questionnaire. It was important to maintain diversity across participant characteristics representing nurses, doctors and pharmacists. Selection strategy ensured adequate representation of departments and units, and healthcare professions of interest (Palinkas *et al.,* 2015).

3.21 Sample Size

As mentioned earlier, the purpose of the quantitative phase is to provide supplementary evidence to the main qualitative findings. There is therefore no prerequisite to produce a formal statement on statistical generalisability because it only serves as a supportive element of the study, as suggested by Morgan (2013).

A sample size was, however, calculated based on a sampling frame (Table 8) of the population of 2,060 medical, nursing and pharmacy staff from the selected hospitals. The sample size was determined by using freely available online sample size calculator software (raosoft.com). The online model used was based on the following formulae using estimated sample size (n) and margin of error (E).

$$x = Z(c/100)2r(100-r)$$

$$n = N\,x/((N-1)\,E2 + x)$$

$$E = \text{Sqrt}\,[(N - n)x/n(N-1)]$$

Where

N = population size (2060)

r = fraction of response that you are interested in (50%)

Z(c/100) = critical value for the confidence level C (90%)

With an acceptable margin of error (E) of 5%, at a 90% confidence interval and a 50% response distribution, the recommended sample sizes (n) for a population of 1,716 nurses, 286 medical staff and 62 pharmacy staff in four hospitals were calculated as 234, 140 and 51 respectively. Proportions of each HCP within each hospital were estimated based on the total population of HCPs within the hospital facility. The total estimated sample size was therefore 425. Attrition of healthcare professionals was expected due to the nature of their work. Previous studies in similar settings estimated the unit non-response rate to be between 5% to 15% (Sabblah *et al.,* 2014; Fadare *et al.,* 2011; Ezeuko *et al.,* 2015). Additionally, 25 (6%) survey questionnaires were included to mitigate attrition and non-response.

Table 8: Sampling frame and selection of study participants

Hospital	Population healthcare professionals				Estimated sample size of healthcare professionals			
	Nurses /midwives (proportion)	Medical staffs (proportion)	Pharmacists /technicians (proportion)	Total	Nurses /midwives	Doctors (including physician assistants)	Pharmacists /technicians	Total
Tamale Teaching Hospital	929(54.0)	256(89.0)	41(66.13)	1226	126	125	34	285
Tamale Central Hospital	387(22.9)	10(4.3)	7(11.29)	404	54	6	6	63
Tamale West Hospital	260(15.0)	12(4.3)	4(6.45)	276	35	6	3	44
Seventh Day Adventist (SDA)	140(8.1)	4(2.40)	10(16.13)	154	19	3	8	30
Total	1,716(100)	286(100)	62(100)	2060	234	140	51	425
Total (Inc extra)								450

3.22 Data Collection

Questionnaires were handed in person to HCPs and largely self-administered and returned by participants themselves at their convenience. Some participants however requested guidance and clarification in which they were supported under the supervision of the researcher. Considering the time constraints in the study, this method was cheaper and quicker to administer. Moreover, it was a more inclusive strategy than the postal or mail system of self-administration suggested by Bryman (2016), which was not applicable in the context of this study (Bryman, 2016). The survey was administered face-to-face by the researcher only when HCPs consented to do so, because they felt would not have time to do it later. Even though responses were higher for those who consented to be guided through the questionnaire, the presence of the interviewer had a tendency to bias responses. As suggested by Tourangeau (2013), self-administered web surveys are likely to present sensitive information spontaneously if the researcher is absent (Tourangeau *et al* 2013). This was confirmed in a study comparing the trustworthiness of face-to-face and postal responses, which showed that postal responses were more likely to retrieve honest responses than face-to-face (Preisendörfer and Wolter, 2014). In both Tourangeau and Preisendorfer's cases the absence of the researcher avoided socially desirable responses. In this study, where applicable face-to-face interviews was avoided and used only when it took several reminders to retrieve some of the questionnaires, to reduce loss to follow-ups.

3.23 Data Collection Instrument

The data collection instrument for the survey was a structured, self-administered questionnaire with integrated open-ended responses described in the qualitative section (Appendix P). The instrument had a clear presentation and instructions on how to complete it. Ambiguity, long and double-barrelled questions were avoided as suggested by Bryman (20012). The items on the questionnaire were adopted and modified for a Ghanaian context from tested and validated previous studies (Bello and Umar, 2011; Ameade *et al.,* 2014; Sabblah *et al.,* 2014; Ezeuko *et al.,* 2015). The instrument was in six parts comprising 67 items. Participants were surveyed on questions related to practice (16 questions), and contextual/external issues (six questions). Additionally, five questions were aimed at establishing knowledge of healthcare professionals, which comprised five questions for which correct responses reflected participants' knowledge on ADR reporting. Part 1 omprised demographic and background characteristics of study participants; this was followed by the second phase, which considered the current practices of ADR reporting. Part 3 pecifically focused on contextual questions. Part 4 assessed ADR reporting knowledge, while Part 5 consisted of multiple-choice answers and some Likert-type questions on HCP reporting attitudes, based on Inman's typologies (Inman, 1996). Likert-type questions on suggested ways to improve ADR reporting were asked in Part 6.

3.24 Questionnaire Piloting

Similar to the quality phase of the research, the questionnaire which was adapted and modified to collect data from the research participants was administered to a small sample of participants in a small-scale pilot study. The participants were recruited from a private hospital (Kabsad Scientific Hospital) which shares similar characteristic, in terms of the population studied, with the 4 hospitals sampled for the main study. A pilot study is considered an integral part of any research process. It is described as a small-scale methodological test conducted to prepare for a main study and is intended to ensure that methods or ideas would work in practice (Kim, 2011). Hassan *et al*. (2006, p.70) described this as a: *"small study to test research protocols, data collection instrument, sample recruitment strategies and other research techniques in preparation for the main study"* (Hassan *et al.,* 2006). The pilot study helped the researcher to practise the research instruments at first hand and re-strategise. Unlike the qualitative phase, where the data from the pilot study were included in the final analysis, the data from,

quantitative pilot were excluded from the analysis, because the purpose of the pilot was to validate the adapted revised questionnaires.
Some of the challenges encountered in the pilot study, which were used to improve the final instrument, include the following:

1. Participants complained that there were too many questions, and it took several follow-ups to retrieve the questionnaires. This was addressed by reducing the number of items in the survey instrument and rewording some questions to ensure clarity.

2. Administering the questionnaires face-to-face did not work well because participants had busy schedules and preferred to complete them in their own time. A flexible approach was used in the main study, whereby participants who had time filled in the questionnaire and others returned it at their convenience before the end of the study.

3. Some questions seemed to be misunderstood and were often left blank or ticked incorrectly, especially Q29, Q31, Q37 and Q75. According to Bryman's guidelines for designing questionnaires, questions in a forced-choice format where the instructions stated, "please tick all that apply" would yield superior responses if provided with "yes" and "no" options (EXAMPLE 2) for each response rather than a single option (EXAMPLE 1) (Bryman, 2015).

EXAMPLE 1
which of the following is likely to send the most ADR reports (tick all that apply)

Doctors	☐
Nurses	☐
Pharmacist	☐
Other HCPs	☐

EXAMPLE 2
which of the following is likely to send the most ADR reports (tick all that apply)

	YES	NO
Doctors	☐	☐
Nurses	☐	☐
Pharmacist	☐	☐
Other HCPs	☐	☐

Even though this approach has been advocated by Dillman (2007) and Dillman *et al*. (2014), it was not practical to self-administer questionnaires in the context of this study; participants were often confused and left the questions blank. These types of questions were therefore rephrased in the final survey.

There was less variability in the six questions which assessed knowledge in the survey. 95% of participants selected the "don't know" option. Questions were re-structured, and one question was deleted from the final survey.

3.25 Quantitative Data Analysis

After data collection, Google forms were created to enter the data. Data were converted to Microsoft Excel spreadsheets and checked for missing data, incomplete responses and data inconsistencies. Errors which were identified were corrected, deleted or left unchanged depending on the gravity or the error, i.e. extreme or normal, as suggested by Van Den Broeck *et al*. (2005). Three participants' data was completely deleted because of incomplete data, participants who did not follow skip-patterns in the questionaire were coded as missing data, and some missing data which were not correctly coded, were corrected. After cleaning the data, the data of 386 participants were imported into IBM SPSS version 24 to perform descriptive and inferential analysis.

Preceding analysis, the data were defined in SPSS, suggesting variable names, labels and value labels, and coding for missing values. Recoding some variables was necessary to meet the SPSS formatting requirement. For example, interval data such as 20-30, 31-40 and 40+ were recorded as 1, 2 and 3 respectively. Selected variables were also regrouped and coded because of missing values or fewer responses, which made analysis problematic. For example, healthcare professionals were grouped into three main groups, i.e. nursing staff, medical staff and pharmacy staff, for analysis purposes.

In the original data, the different HCP categories required grouping midwives, mental health nurses, public health nurses and nursing specialities as nursing staff. The medical staff comprised physicians, physician/medical assistants and medical doctors (various specialities), while pharmacy staff were grouped as pharmacy technicians and pharmacists (various specialities). These were therefore grouped to aid analysis. Other variables aggregated included age, frequency of reporting and observing whether daily, weekly and monthly options recorded few or no responses (Table 9).

Table 9: Examples of aggregated data from survey.

Question from sample	Original data	Aggregated data	
Age	20-30	20-30	
	31-40	31-40	
	41-50	41+	
	51-60		
	60+		
Years of experience	0-5	≤5years	
	6-10	6-10 years	
	11-15	≥11years	
	16-20		
	20+		
Patients per day	0-10		
	11-20	≤20	
	21-30	21-40	
	31-40	≥41	
	41-50		
	51-60		
	60+		
How often do you observe ADR?	Daily	Daily/weekly/monthly	
	Weekly		
	Monthly		
	Every 3months	Every 3-6months	
	6 months		
	Once a year	Once a year	
	Never	Never	
	Can't tell	Can't tell	
How often do you report ADR?	Daily	At least once a year	
	Weekly	Never	
	Monthly	Can't tell	
	Every3 months		
	Every6 months		
	Once a year		
	Never		
	Can't tell		
How many ADRs reported in this year?	0	0	No
	1-5	1-5	Yes
	6-10	≥6	
	11-20		
	20+		

The questions were recoded into “correct” or “positive” response = 1 and “incorrect” or “negative” responses = 0 and analysed accordingly. In a similar fashion, all Likert-type responses were given assigned numerical values to support SPSS data analysis i.e. strongly disagree = 1, disagree = 2, neither = 3, strongly agree = 4, and strongly disagree = 5. Thirteen Likert type questions were addressed HCP attitudes, while twelve Likert type questions also addressed suggested methods for improving ADR reporting.

Likert-type questions have been distinguished from Likert scales by Clason and Dormody (1994). Likert-type questions have been described as a set of single questions which does not aim to combine items into a composite score scale, as opposed to an actual Likert scale in which items can be quantified into a measure for a characteristic, behaviour or trait (Boone and Boone, 2012). The Likert-type questions used were unique and unrelated and were not intended to estimate a composite score for attitude because standardised scales for measuring attitudes to reporting ADR are unavailable in the literature.

There has also been debate about analysing Likert scales using parametric or non-parametric methods and whether they can be treated as interval rather than ordinal data to support parametric tests, which has more statistical power (Maydeu-Olivares, 2005). Data was therefore analysed using non-parametric analysis where mode and median were used as measures of central tendency, and frequencies were used to measure variability. Using a non-parametric method for analysis was justified because the data were largely categorical, ordinal (‘Likert-type’ responses, ADR reporting rates, etc), and nominal (sex, grade, department, HCP category etc), and was required to meet fewer statistical assumptions.

3.26 QUALITY OF RESEARCH

This section describes the theoretical underpinnings of undertaking a research project of high quality, with practical examples of steps which were taken to ensure this. This therefore encompasses what strategies were used in terms of the qualitative (trustworthiness), quantitative (validity and reliability), and mixed methods (legitimization) in undertaking this research.

3.26.1 Trustworthiness in Qualitative Research

Lincoln and Guba (1994) suggested that the primary methods of assessment in qualitative research should focus on *trustworthiness* and *authenticity* of a study. As mentioned earlier, the quantitative terms of reliability and validity in qualitative research rather focuses on the aspects of trustworthiness and authenticity. This study was guided by Lincoln and Guba's constructs of *credibility, transferability, dependability and confirmability,* which confirms, the trustworthiness of the research (Guba and Lincoln, 1994).

Credibility and *transferability* are synonymous with the quantitative criteria of internal and external validity (generalisability) respectively. Credibility refers to emphasis on multiple accounts to establish social reality, while transferability refers to the production of rich and detailed accounts of a culture (Geertz, 1973). Mixed methods equivalents such as multiple validity, insider-outside and political approaches were considered as ways to legitimise the research to emphasise multiple accounts and rich detailed accounts. Participants therefore gave accounts from different categories of healthcare professionals (i.e. medical, nursing and pharmacy perspective) and also different health facilities, including a teaching hospital, private hospital, primary and secondary care hospitals. The findings can therefore be credible and transferable in the context of the research.

Dependability and *confirmability* parallel the quantitative equivalent of reliability and objectivity respectively. Dependability refers to keeping a complete audit trail of all phases of the research process, while confirmability suggests not allowing personal values to influence the conduct of the research. To draw credible inference from the mixed methods, weakness minimisation, sequence, sample integration, commensurability and conversion were issues which were reflected on by the researcher. The researcher influences and bias were

acknowledged through personal reflections, and every step of the research process was documented by keeping a field notebook and comprehensively reporting the process details to justify the methods used.

In addition to the criteria proposed by Lincoln and Guba, an additional issue of authenticity explores the wider political impact, which is similar to the legitimation issues of multiple validity and political impact to ensure credibility of a mixed methods research (Onwuegbuzie, Johnson and Collins, 2011). The wider political impact of this study was seen as a form of awareness creation about the topic of ADR, in which participants suggested they learnt something new which generated discussion among colleagues. *Authenticity* further seeks to infer how educative the concepts are in the sense of helping to understand different perspectives of other members of the society (educative authenticity), how change in circumstances can be enforced (catalytic authenticity), and empowering members to take action (tactical authenticity). Even though taught, provoking the implementation of authenticity in practice has been said to be controversial (Bryman, 2016, p.386). The potential wider political impact and authenticity of this research would help start conversations about ADR and possibly develop appropriate training and future actions.

To validate the findings and determine the credibility of the information and whether it matches reality (Merriam, 1988), four primary forms were used in qualitative, phase of the study: (1) triangulation – converging different sources of information (interviews, documents, pictures) and making meaning; (2) member checking – getting feedback from the participants on the accuracy of the identified categories and themes; (3) providing rich, thick description to convey the findings; and (4) external audit – asking a person outside the project to conduct a thorough review of the study and report back (Creswell, 2003; Creswell and Miller, 2002). This was undertaken by cross-checking with participants and getting feedback from colleagues through external audits.

3.26.2 Validity and Reliability

Reliability and validity are traditionally quantitative ideas of measuring the quality of a piece of research, as mentioned earlier. Pilot testing a survey data collection instrument is therefore considered essential and, widely advocated of enhancing both the validity and reliability of a questionnaire (Bowling, 2014; Bryman, 2016; Creswell, 2013; Denzin and Lincoln (1994); Oppenheim, 1992).

Reliability issues include *stability, internal and inter-rater reliability* (Bryman, 2016). A measure can be tested for *stability* by the *test-retest method*, i.e. administering a test to the same sample twice on different occasions. This study relied on questions which were already tested and had been used in previous studies (Adedeji *et al.,* 2013; Ezeuko *et al.,* 2015; Nde *et al.,* 2015; Oshikoya *et al.,* 2011; Sabblah *et al.,* 2014; Angamo *et al.,* 2012).

Using multiple indicator measures, such as Likert-type responses, required checking for the *internal reliability* of the instrument. The internal reliability refers to whether the indicators which make up the scale or index are consistent and can result in the same findings if reanalysed by an independent researcher (Burns, 1999, p.21). The review of literature showed no existing reliable scales for measuring parameters of interest such as knowledge, attitude and perceptions of healthcare professionals. To guard against threats of internal reliability, the study was implemented using peer examination (utilising other researchers' findings), mechanically recorded data (keeping a detailed account of the data), multiple researchers (involving my supervisory team) and low inference descriptors (ideas that can be easily quantified), as suggested by LeCompte and Goetz (1982).

The Likert-type responses used in this study were modified and used as an index to assess HCP attitudes and also to explore suggested ways of improving ADR reporting. The internal reliability was retested by measuring the indices used, using SPSS Cronbach's alpha test for reliability. As a rule of thumb, the acceptable alpha level is set at 0.80, but some studies have accepted a much lower figure. For example, Berthoud (2000, p.169) writes that a minimum alpha level of 0.60 is 'good'. After modification of Likert-type items from previous studies, an alpha of 0.62 for 14 items on attitude was achieved, while 0.82 was found for 13 items on suggested methods of improving ADR reporting.

Several other methods of exploring validity have also been reported in literature, including face validity, concurrent validity, predictive validity, construct validity, and convergent validity. In the context of this study, only face validity was explored. Face validity is considered an essential intuitive process where a researcher tries to establish that the measure of interest is actually reflected in the content. Local experts were contacted for expert judgement of the survey instrument, and the final instrument was reworded to reflect the language, which was understood by participants. Additionally, the supervisory team provided guidance and reiterations until the final survey instrument was ready.

While validity and reliability may be of importance, and a common discussion in quantitative research, it is less pronounced in qualitative research, where the primary focus is to capture real-life experiences of participants.

3.26.3 Mixed Methods (Legitimation)

To measure the strength and quality of a mixed methods study, the most recommended term used instead of validity is *legitimation* which uses a bilingual nomenclature and can be adopted by both qualitative and quantitative studies (Onwuegbuzie, Johnson, and Collins, 2011). Other authors prefer to use *quality inference* to refer to issues of reliability, trustworthiness and validity in mixed methods (Subedi, 2016).

Legitimation is where the researcher draws inferences that are credible, trustworthy, dependable, transferable and confirmable in a mixed methods study. Nine types of legitimation discussed in literature include: (1) sample integration – yielding quality meta-inference; (2) inside-outside – accurate and appropriate utilisation of insider (group member) and observer view (researcher) in explaining or describing ADR reporting; (3) weakness minimisation – balancing the strengths and weaknesses of each approach; (4) sequential – minimising the effect on meta-inference by not trying to reverse the quantitative and qualitative sequence; (5) conversion – the extent to which data conversion techniques can lead to interpretable and high-quality inference data; (6) paradigmatic mixing – the extent to which different researchers' paradigms, epistemological and ontological underpinnings blend and combine; (7) multiple validity – the extent to which quantitative and qualitative research strategies are utilised for high yielding meta-inference; (8) commensurability – ensuring meta-inferences reflect a mixed worldview based on the cognitive process of Gestalt switching and integration; and (9) political – and extent to which and audience or consumers of mixed methods research value the meta-inference from both quantitative and qualitative components (Clark and Creswell, 2008).

The study took into account these important underpinnings to ensure that the research process was trustworthy, reliable, valid and legitimate in understanding ADR reporting among healthcare professionals.

3.27 ETHICAL CONSIDERATIONS

3.27.1 General Considerations

Consideration of ethical principles and how robustly the related procedures are undertaken is an important aspect of any research involving human participants (Bryman, 2016). This section will examine how the study adhered to ethical guidelines during recruitment, data collection, data storage and analysis. The standard theoretical framework from which to analyse ethical situations in medical research generally stems from Beauchamp and Childress's literature on the ethics of biomedical literature (Beauchamp and Childress, 2019). They provide basic universal guidelines for the conduct of human research internationally, ensuring the core principles of autonomy, justice, beneficence and non-maleficence, confirming that harm does not occur or is minimised for participants. These have however been modified to country-specific recommendations based on these principles. It is important to ensure that research is transparent, and procedures acknowledged to authorities and participants alike. The significance of adhering to honesty, rigour, respect and scientific integrity in the whole research process are widely discussed in literature (Brinkmann and Kvale, 2008; de Vaus, 2002; Iphofen and Tolich, 2019).

As a researcher at the University of Sheffield (UoS), the university policy guidance requires researchers to undertake recommended training on ethics and submit research proposals for ethical review approval before any research can be undertaken. The researcher therefore undertook the required module on Research Ethics and Integrity (FCS6100) to ensure that the rights of research participants in the study were protected.

In addition, the University's ethics policy governing research involving human participants, personal data and human tissue required submission of the research proposal to the University Research Ethics Committee (UREC) for ethical approval. The research was however undertaken in Ghana, and The University of Sheffield Research and Innovation Services (RIS) recognises the ethical review process of the Ghana Health Service (GHS) Ethics Review committee (ERC). The Ghana Health Service is on the list of "organisations overseas that are recognised by the University of Sheffield's Research Ethics Committee as having in place sufficiently robust ethics review procedures." It was therefore passed as a recognised Alternative Ethics Review Procedure by Univeristy of Sheffield. As such, this means that a separate application to an internal University of Sheffield departmental research ethics review was not required.

A study protocol was therefore submitted for ethical approval to the Ghana Health Service Ethics Review Committee. Recommendation for conditional approval was given, subject to the requested modifications incorporated into the main protocol (ID NO: GHSERC001/07/17). After addressing queries on the main protocol, elaborating on ethical considerations, informed consent and seeking a local supervisor for the research project, a final approval decision was granted to commence the study from 31st August 2017 to 30th August 2018 (Appendix O).

Literature suggests that engaging effectively with the research setting and being sensitive to the organisational hierarchy and structure, particularly getting clearance from gatekeepers, is critical for success of the study (Ritchie *et al.,* 2014; Snape and Spencer, 2003). After ethical approval at the national level, written permission to assess study sites was therefore also requested locally from the Northern Regional Health Directorate of the GHS (Appendix D). After approval (Appendix H), an additional certificate of authorisation (Appendix R) was requested and received from Tamale Teaching Hospital's administration to have access to units and departments, because of its autonomous administrative nature compared to other GHS facilities.

3.27.2 Specific Considerations

Specific features and how they were addressed have been elaborated in table 10. Because this study was a mixed methods study, the procedures differed even though they were based on the same ethical principles, and additional comments have been provided.

Table 10: How the basic ethical principles were addressed

ETHICAL ISSUE	HOW IT WAS ADDRESSED		
	Qualitative Phase	**Quantitative Phase**	**Additional Comments**
Research should be worthwhile and should not make unreasonable demands	Participating in in-depth interviews, key informant interviews and focus group discussion required demands on HCPs time. Participants chose a time and a place which was convenient for discussions, which were kept brief and concise with minimal disruptions. They could also choose to either be part of a focus group discussion or an in-depth interview. After interviews, invited participants were acknowledged via SMS for their time, while drinks and snacks were provided, especially for those who participated in focus group discussions.	The number of items on the survey questionnaire was reduced to decrease the time spent on a questionnaire, considering the busy schedules of HCPs. They were also offered the opportunity to self-administer the survey questions at their own convenience and for completed questionnaire to be collected later at a time and place convenient to them. Participants were also given University of Sheffield labelled pens as souvenirs to show appreciation for their time after the survey.	Firstly, it was established earlier during the upgrade of the PhD that the study was worthwhile and would not make unreasonable demands on participants. This was justified by passing the upgrade review. Secondly, ethical approval from GHS-ERC further confirmed the research was within scope and did not undermine research participants. As a mixed methods research, it was likely the research placed a higher burden and time constraints on those who participated in both qualitative and quantitative phases. This was addressed by appreciating their time and providing snacks and drinks during focus group discussions. Using both (Qual./Quant.) approaches was worthwhile as it provided greater research benefits, and this was reiterated to participants.

ETHICAL ISSUE	**HOW IT WAS ADDRESSED**		
	Qualitative Phase	**Quantitative Phase**	**Additional comments**
Participation in research should be based on informed consent (Appendix A).	Informed consent is an important basic principle and best practices were adopted for this study (Bryman, 2016; Ritchie *et al.,* 2014). Participants who responded to the study's invitation to participate in either an in-depth interview (IDI) or focus group discussion (FGD) were presented with an informed consent. They read the information sheet specific to IDI or FGD and asked questions (Appendix B). The informed consent also contained summary of the study (Appendix A) including; contact information of researcher, affiliated institution, research aims and purpose, potential risk and benefits, anonymity, confidentiality of data including personal information, required data to be collected, autonomy and ability to withdraw from the research at any time. Participants were also given details about approximate duration of interviews. They were given the opportunity to ask questions and seek further clarification and participated in the study based on an informed choice.	Verbally accepting to be part of the study was the first stage of consent. The second stage involved presentation of a detailed participant information sheet for the survey (Appendix V) similar to the qualitative phase to make an informed choice to proceed with the survey or not. Once willingness to participate was confirmed, a consent form was signed and dated (Appendix A). Some participants declined to be part of the qualitative phase after the survey.	The study information was presented to HCPs at staff meetings to advertise the research, indicating who the researcher is, why the research is being carried out, what the researcher will be doing and who will be involved. A two-stage informed consent process was employed. HCPs who agreed to participate in the research were first to consent for the survey (Appendix V), invited to the qualitative phase (Appendix E) and if they agreed to be contacted, they consent again for either a focus group discussion or in-depth interview (Appendix B).

ETHICAL ISSUE	**HOW IT WAS ADDRESSED**		
	Qualitative Phase	**Quantitative Phase**	**Additional comments**
Participation should be voluntary and free from coercion or pressure.	Participants were well informed during the consent process to exercise their autonomy. They were also given the opportunity to withdraw at any point, since the consent process is a dynamic and evolving process (Pope and Mays, 2006). Even though drinks and snacks were provided during the qualitative phase, this was an act of good will, which was offered to participants as a gesture of appreciation for their time after the sessions rather than before, to avoid any impressions of coercion.	As mentioned in the qualitative phase, the quantitative phase provided explicit information in the informed consent. Even though both parties signed it, the researcher respected the participant's decision to participate in the study and provided gentle reminders to participants who self-administered the survey questionnaire. There was no pressure on participants to participate. Participants were lost to follow-up if they failed to return the questionnaire before the close of study. University labelled pens were given to participants as a gesture of good will and not to coerce them.	Recruiting participants through gatekeepers who were heads of departments or units may have threatened their voluntariness but having a face-to-face information session reaffirmed their authonomy in the study.

ETHICAL ISSUE	**HOW IT WAS ADDRESSED**		
	Qualitative Phase	**Quantitative Phase**	**Additional comments**
Adverse consequences of participation should be avoided, and risks of harm known	Non-favourable or derogatory responses by participants about ADR procedures in a facility could lead to rebuke from superiors especially during focus group discussion and in-depth interviews. Recall of traumatising personal events in hospital was also considered a potential psychological risk to participants. Also, risks of confidentiality in focus group discussions were of concern. Personal data were therefore anonymised and delinked from interviews, and focus groups were homogenous (i.e. same cadre and same rank of staff), to manage and ensure appropriate protection and well-being of the participants. Participants were informed and reassured about the purpose of the study, which was not to audit their practice but to understand their perceptions of the problems of ADRs reporting and ways to improve the current system. An information sheet included contact information of researcher, affiliated institution, research aims and purpose, potential risk and benefits, anonymity, confidentiality of data including	In order to avoid the risk of work-related queries from superiors, the researcher avoided administering the survey to HCPs during working times. The stress of completing the questionnaire was also considered. Participants were given ample time to respond to the survey, in order to avoid psychological trauma and burnout already compounded by work related stress.	Generally anticipated harm for both methods was perceived as minimal (if any). Potential harm to research participants can be queries from superiors and dismissal if appropriate organisation guidelines were not followed. Permission was therefore sought from the management of the facility to ensure research procedures and protocols were in line with the organisation's policy so that the job of study participants was not put at risk.

	personal information, required data to be collected, autonomy, and ability to withdraw from the research at any time.		
ETHICAL ISSUE	**HOW IT WAS ADDRESSED**		
	Qualitative Phase	**Quantitative Phase**	**Additional comments**
Confidentiality and anonymity should be respected	As mentioned before, there was risk of participants not respecting the confidentiality of what was discussed or of disagreement issues during the focus group discussions, which are challenging to control (Ritchie *et al.,* 2014). Then participants were informed about data confidentiality in the participant information sheet (Appendix B). This was further addressed by effective moderation of the session. Even though interviews were face-to-face, participants' transcribed data were anonymised, and any reference directly linked to any personal identification were removed from results presented or for future publications. Personal data such as phone numbers, which were collected to arrange interviews, member check and send appreciative messages, were collected for the purpose of the research only and would not be shared with any third party. All data would be stored safely and destroyed two years after the	Survey questionnaires were anonymised without any reference or trace linking to personal data (person or hospital name, department, location etc.). Contact details of participants who opted to be part of the qualitative study were collected after the survey and retained for further correspondence purpose only. Electronic data (files and folders) were stored on an encrypted pass worded electronic storage device for reuse indefinitely. Further details about data management were stipulated on the participant information sheet (Appendix V). Hard copies of survey materials were stored in a secured cabinet under lock and key to be destroyed two years after study closure.	Some types of integration in mixed methods research allow the researcher to trace back to participants' data to identify where the discrepancies may lie (O'Cathain *et al.,* 2010). The analysis strategy of this concurrent mixed method was at the analysis stage and did not require tracing back to particular research participants. Participant details in both phases of the study were therefore confidential and not traceable. Access to the data was restricted to the research team only. The University of Sheffield's 'Udrive' was used as backup storage for both survey data and audio files.

	end of study. Anonymised data would however be stored safely indefinitely and perhaps used for future research.		

3.28 Positionality

Positionaility refers to “the stance or positioning of the researcher in relation to the social and political context of the study, the community, the organisation or the participant group” they plan to understudy (Coghlan and Brydon-Miller 2014). As the researcher becomes the data collection tool in qualitative research, it is important to discuss how the researcher’s relationship with his research environment influenced the research outcome. This ensures quality control and a realistic presentation of data that is thrustworthy. It is therefore essential for the researcher to understand the effect of their personal circumstances in the study. Furthermore, being self-critical and aware of oneself in the research is paramount in ensuring that our backgrounds or positionality does not bias our findings.

I come from the northern part of Ghana and my educational background originally is a bachelor’s in Applied Biology following which I worked briefly in a biomedical laboratory. I went ahead to study for a master’s degree in Clinical Trials, with the aim of enhancing my laboratory career, but my faith changed. I worked as a social development officer instead in poor rural setting of northern Ghana. It was during this time I developed an interest in exploring people’s experiences, perspectives and beliefs about life.

Even though I enjoyed working as a social development officer, my duties became routine, and I wanted something more challenging. It brought me to the realisation that I needed to undertake a PhD. The choice of interest in my topic was based on earlier interest from my MSc. course in clinical trials at the University of Ghana. It was during this time I became intrested in Phase IV trials and post authorisation studies, which are the final stage of the drug development process, usually focused on the safe use of the medicines. Even though I wanted to undertake research on that topic for my masters’ level dessertation, I was disappointed about the lack of data on safety monitoring in routine clinical practice. I became interested in pharmacovigilance and wanted to understand challenges in this crucial aspect of health. Having enjoyed my time exploring people's views in my earlier work, I envisaged part of my study would be a qualitative study. This background therefore influenced my choice of the study site, research participants and study design. On going awareness of my perpective helped to ensure that the data was analysed and interpreted more objectively.

CHAPTER FOUR

QUALITATIVE FINDINGS

4.0 Introduction

This chapter presents details of findings from the qualitative stage of the study, which as noted in chapter three represented the dominant methodology in this exploratory descriptive study (Walker and Baxter, 2019). There are no gold standards or guidelines on how to present a qualitative-dominant mixed methods study. This thesis therefore firstly presents the findings from the qualitative phase, followed by presentation of quantitative findings in the next chapter. The chapter begins with the description of participant demographics and later presentation of emerging themes from focus group discussions and in-depth interviews of healthcare professionals. As described in the earlier chapter, these were data collected from a sample of five healthcare facilities in the Tamale metropolitan area of Ghana. The participants were medical staff (doctors and physician assistants), pharmacy staff (pharmacists and pharmacy technicians) and nursing staff (general nurses and specialised nurses). Data from the surveys will be reported in the next chapter both descriptively and using inferential statistical analysis to explore associations between responses and a variety of factors relating to ADR reporting. The open-ended questions on suggestions to improve ADR reporting is presented as part of the qualitative findings in the chapter. The overall research aim was to investigate the factors influencing adverse drug reaction reporting among healthcare professionals in Ghana. As a reminder, the qualitative phase sought to explore the main questions of what the perceived factors influencing ADR reporting are but specifically focusing on the following questions:

1) What are the factors associated with ADR reporting, and why do HCPs consider them important?
2) How is ADR reporting undertaken by HCPs in Ghana?
3) What are HCPs' views about improving ADR reporting?

4.1 Participant Demographics

Data was collected from a total of 51 healthcare professionals (28 females and 23 males) who were interviewed from 5 healthcare facilities (the pilot study sample was added to the main study). Additionally, findings were based on data from discussions and personal reflections of individuals who did not wish to be voice recorded but were knowledgeable about the reporting process and were willing to contribute. The healthcare facilities comprised one tertiary care facility, two primary care facilities, one non-governmental primary healthcare facility, and one non-governmental secondary care facility. Thirty-two healthcare professionals participated in the in-depth interviews (IDI) and 19 participated in the focus group discussions (FGD). The justification for combining both IDIs and FGDs was to enhance data richness. Among the in-depth interview participants 12 were nursing staff, 9 were medical staff and 11 were pharmacy staff (Table 11). There were also four FGDs comprising only nurses; six in group 1, five in group 2, three in group 4 and four in group 5 as shown in table 12. The interview process, notes taking, and voice recording was moderated by the investigator.

Table 11- Individual participant characteristics of in-depth interviews (qualitative phase)

Participant Number	Healthcare Professional	Facility	Sex	Department	Years of Practice
Nursing Staff					
1.	Nurse practitioner	PCF	Female	OPD	8
2.	Nurse	TCF	Female	ICU	6
3.	Nurse practitioner	PCF*	Female	OPD	10
4.	Nurse	PCF	Female	Paediatric	5
5.	Nurse	PCF	Female	Psychiatry	11
6.	Nurse practitioner	PCF	Female	Psychiatry	6
7.	Nurse	PCF	Female	Medical	20
8.	Nurse	PCF	Female	Paediatric	16
9.	Nurse	PCF	Male	Paediatric	7
10.	Nurse practitioner	PCF*	Female	OPD	8
11.	Nurse Manager	PCF	Female	Administration	33
12.	Nurse Manager	PCF*	Male	Administration	9
Medical Staff					
1.	Doctor	PCF	Male	General	22
2.	Doctor	PCF	Male	Surgery	10
3.	Doctor	PCF	Male	General	9
4.	Doctor	PCF	Male	General	5
5.	Doctor	SCF*	Male	General	7
6.	Doctor	SCF*	Male	General	5
7.	Doctor	PCF	Male	Administration (Med. Director)	20
8.	Physician Assistant	PCF*	Female	General	20
9.	Physician Assistant	PCF	Male	General	20

Pharmacy Staff					
1.	Pharmacist	TCF	Male	OPD	6
2.	Pharmacy technician	TCF	Male	Paediatric	6
3.	Pharmacy technician	TCF	Male	Ear, Nose and Throat	4
4.	Pharmacist	PCF	Male	Administration (HOD)	15
5.	Pharmacist	PCF*	Male	General	7
6.	Pharmacist	TCF	Male	Obstetric and gyaenacology	6
7.	Pharmacist	TCF	Male	OPD	4
8.	Pharmacist	TCF	Female	ICU	8
9.	Pharmacy Technician	PCF	Female	Paediatric Unit	2
10.	Pharmacist	PCF	Male	Administration (HOD)	21
11.	Pharmacy Technician	PCF	Female	General	13

Abbreviations
Non-Governmental Facility, PCF_ Primary Care Facility, SCF_ Secondary Care Facility, TCF_ Tertiary Care Facility, OandG_Obsterics And Gyaenacology, OPD_Outpatient Department, ICU_Intensive Care Unit and HOD_Head of Department.

Table 12. Individual participant characteristics of Focus Group Discussion (qualitative phase)

Participant Number	Healthcare Professional	Sex	Department	Approximate of Practice
NON-GOVERNMENTAL PRIMARY CARE FACILITY (PCF*)_GROUP1				
1	Nurse	Male	Paediatric	1
2	Nurse	Male	Emergency	0.5
3	Nurse	Female	Antenatal	0.5
4	Nurse	Female	Male Medical	5
5	Nurse	Male	Emergency	1
6	Nurse	female	Paediatric	0.5
NON-GOVERNMENTAL SECONDARY CARE FACILITY (PSF*)_GROUP2				
7	Nurse	Female	OPD	3
8	Nurse	Female	OPD	2
9	Nurse	Female	OPD	4
GOVERNMENTAL PRIMARY CARE FACILITY (GPCF)_GROUP 3				
10	Nurse	Female	OPD	10
11	Nurse	Female	Surgical	6
12	Nurse	Female	Surgical	15
13	Nurse	Female	OPD	13
14	Nurse	Female	Psychiatry	10
GOVERNMENTAL PRIMARY CARE FACILITY (GPCF)_GROUP 4				
15	Nurse	Female	Theatre	9
16	Nurse	Male	Male medical	1
17	Nurse	Female	Theatre	14
18	Nurse	Female	Theatre	3
19	Nurse	male	Emergency	2

4.2 Overview of Emerging Themes.

As summarised in figure 17, the qualitative data analysis revealed two central themes; system factors and human factors. These were considered in light of other sub-themes which emerged; the system factors comprised of both internal and external aspects, which in turn were represented by specific factors identified to influence these sub-themes. Similarly, the human factors could be distinguished in terms of healthcare professional perceptions about themselves as HCPs and patients. As Figure 17 illustrates, the interviews revealed considerable complexity and depth to the perceived issues relevant to ADR reporting in Ghanaian hospitals. These factors are now considered in more detail terms, with quotations used to illustrate and support the various themes. It is also noteworthy that these themes emerged from the initial organisation of themes in Figure 16 and evolved still showing significant connections between the two Figures.

SYSTEM FACTORS

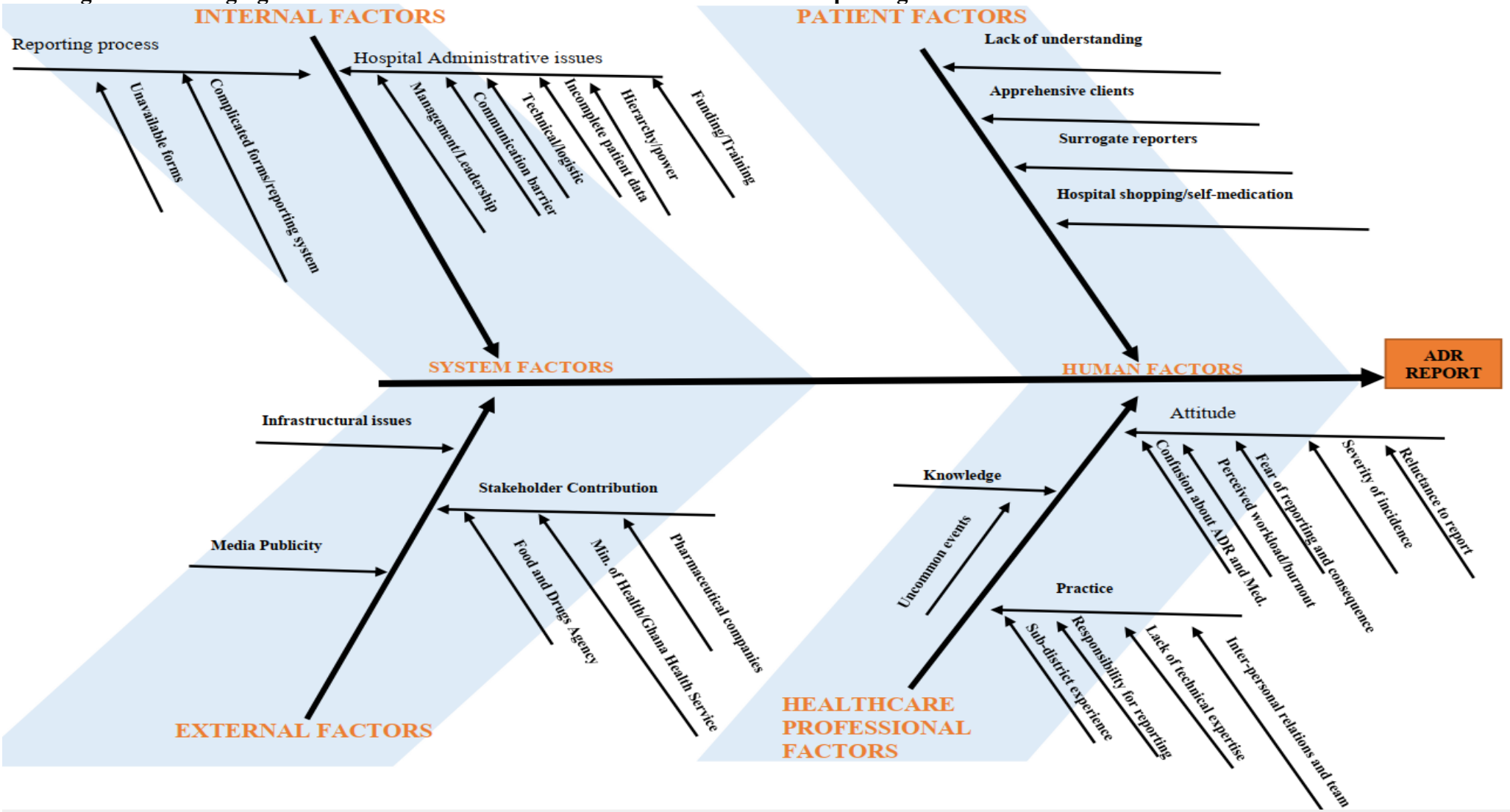
System factors are divided into internal and external system factors based on what HCPs considered as important factors influencing their reporting behaviour.

Previously studies have reported on human factors such as knowledge, attitudes and practice of ADR reporting. In this section, the themes reported show that the majority of emerging themes related to system factors which refered to various internal and external systems, whether this was within the hospital itself or beyond, and these are now considered in more detail as follows.

4.3 Internal Factors

Analysis of interviews revealed various internal factors, which could also be understood in terms of organisational level factors. These were often attributed to the administration of healthcare facilities, which were affected by either the official reporting process or institutional performance of the hospital. The instituted reporting process was affected by availability of forms, severity, hierarchy and power relations, while the performance of the hospital was affected by finance, management and leadership, communication, and technical issues. The reporting process and submission of completed forms to relevant authorities such as the FDA was perceived to be affected by three main internal system factors: availability of forms, severity of incidence and bureaucracies.

Figure 17- Emerging themes and subthemes identified to influence of ADR reporting.

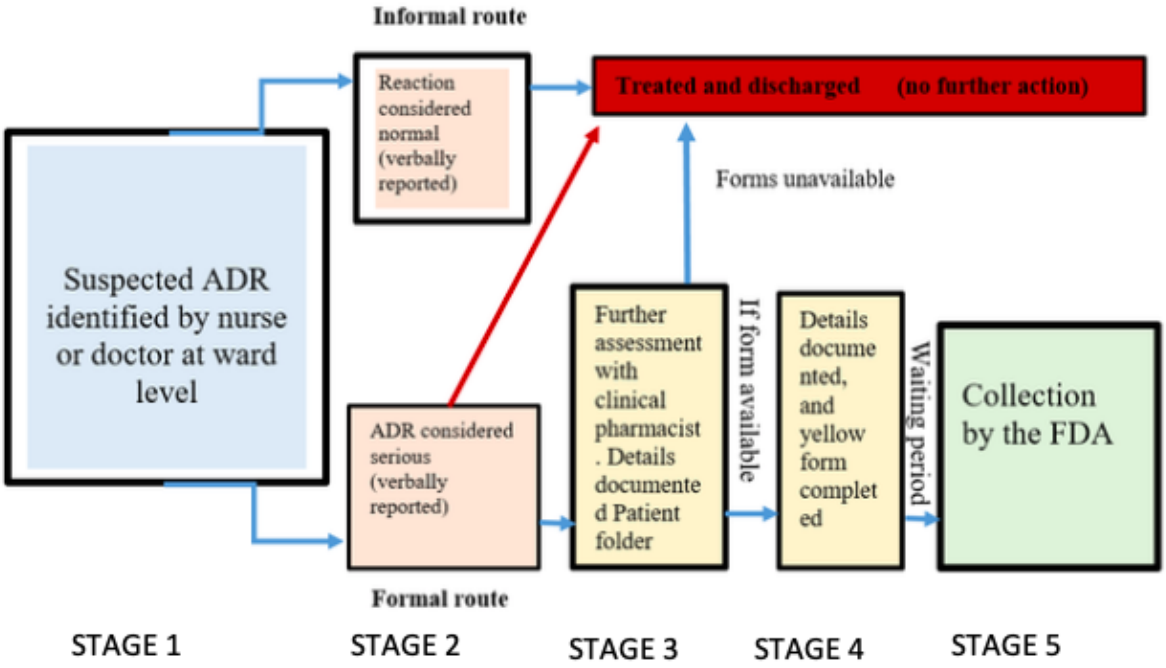


4.3.1 Reporting Process

In all the study hospitals (Tamale Teaching Hospital (TTH), Tamale West Hospital (TWH), Tamale Central Hospital (TCH), Seventh Day Adventist Hospital (SDA) and Kabsad Scientific Hospital (KSH), only one facility (TTH) had a drug information centre/pharmacovigilance unit led by a pharmacist. The reporting process differed between hospitals and appeared to be influenced primarily by the availability of pharmacy staff. TTH was the largest hospital and had more staff, with at least one clinical pharmacist in each department. In contrast, TWH, TCH, KSH and SDA were smaller facilities, which sometimes had one pharmacist responsible for the whole facility. As will be shown in subsequent sections, pharmacy staff were the lead persons identified by participants as being responsible for coordinating the ADR reporting process and assisting in medication-related problems in all facilities. Complaints and reports from other HCPs in various wards and units were channelled to the pharmacist, who then completed the ADR forms.

Figure 18 summarises the five-stage reporting process in the healthcare facilities sampled. **Stage 1:** ADRs were initially identified at ward level, usually by medical or nursing staff. **Stage 2:** The report would then take either a formal or an informal route depending on severity of the incident. If the incident was considered a normal reaction, the informal route was used, which involved a verbal report of the incident to officers in charge, treating the patient and discharging with no further action. In this case, reports were lost because of improper documentation. In instances where doctors and nurses were able to manage the reaction at the ward level without the need of a pharmacist, a patient could be treated and discharged without any further action. On the other hand, a formal route would be activated if a serious ADR required the assessment of a pharmacist.

Figure 18: ADR reporting process at the hospital facility level



Stage 3: Through the formal route, a clinical pharmacist may be involved to assess and document the reaction. Further documentation may be detailed in the patient folder or nurses' notes. If forms are unavailable, the patient is treated and discharged without further action. **Stage 4:** If a form is available, the reaction is documented by completing the yellow form. **Stage 5:** Forms from the various departments, units and wards are compiled by the pharmacist for collection by the FDA.

The FDA was responsible for the distribution and collection of completed forms, and the primary points of contact with the FDA were the hospital pharmacy units; the decision to distribute them to various units and wards or to keep them at the pharmacy were at the pharmacist's prerogative.

4.3.2 Familiarity with the Reporting Process

A drug information centre/pharmacovigilance unit was already established in one of the study hospitals. The reporting process therefore was to report ADRs to the designated contact person (pharmacist). They collated reports and were responsible for informing the FDA about a subsequent collection. A pharmacist describes the process as follows:

> *"…well we have forms from the FDA that we are supposed to document. So, what we usually do is that we may ask the patient to stop the medication and recall whatever medication has been given. So, in the form we have to write the name of the patient, the drug that the patient took, the dose and then the harmful effect that occurred or the ADR that occurred you document that one. And you the person filling the form should sign. And usually what we do is that we keep it for a couple of days and we inform the FDA to come and pick it up[...]"* ***Pharmacist 1***

Some pharmacists and medical officers were, however, not aware of the reporting process in their places of work. This was a key theme that will be considered in the next section on human factors and HCP knowledge. A doctor shared his lack of awareness about instituted reporting channels n in the following quote:

> *"… I am not aware of any official communication channel. For instance, should a patient react we would probably see (treat) them but I am not aware of any official reporting channels…"* ***Doctor 5***

Although TTH had a drug information unit where all pharmacy staff were supposed to send completed ADR reports, most HCPs were not aware of this arrangement. This lack of awareness was common among the different HCP staff. There was the tendency for HCPs to be reliant on the pharmacist for information about ADR reporting. Some pharmacists, however, were not well informed about the process. At a different unit of work in the same hospital, a pharmacist shared his uncertainty about who to send the reports to:

> *"… according to one of my colleagues, there is someone who is suppose to collate (ADR forms) but I don't know of this arrangement. Actually, myself, I don't know of it, so the form I filled is even still with me…"* ***Pharmacist 6***

Some medical staff were equally not certain about the reporting process in their hospital although they felt verbally reporting to the pharmacist to take further action was appropriate.

> *"I do not know if at the pharmacist they will have something in place to key in the complaints. But if you're going to report, going directly to the person reporting verbally if you have to sign that…or if the pharmacist will enter something that is needed in the report [...] but having to write a report like written report and presenting it I think would not be very convenient. People will end up not reporting…"* ***Doctor 7***

HCPs therefore viewed reporting as not only completing the required form but also relaying the information to the officer or supervisor in charge.

4.3.3 Verbal Reporting

Analysis revealed that the preferred mode of reporting ADR was verbal. 'Reporting' was largely understood as merely telling a person in charge rather than completing the required form. So, when asked about the ADR reporting process in facilities where HCPs worked, most participants – depending on rank of officer – said they informed their supervisor about the ADR or referred to ADR reporting as the work of the pharmacist. Cases of ADRs encountered at the ward level were usually managed by telling the immediate supervisor and changing the medication while drawing it to the attention of a supervisor. Any changes to medications were

recorded in the patient folder but not in designated ADR forms, which were usually kept with the pharmacist.

> *"…the channel actually […] here we don't have anything like a pharmacovigilance […] something like a unit or maybe some forms to report. We don't have anything like that so when it comes, when we get cases like that, we either change the medication for them then we draw the pharmacist attention […] but we don't have anything like a unit we report to. Usually that's what happens [...]"* ***Nurse 1***

Most pharmacy staff also agreed reporting was their primary role and responsibility, which unconsciously encouraged verbal reporting. The following quotation illustrates their role in the reporting process.

> *"…the nurses administer the medication for patients. So, when they administer the medication and there is any suspected ADR, they report to me […] as I said the form is here at the pharmacy and I am in charge of the filling. But what happens is that…you know because mostly it's the nurses who administer the medications, the reports usually emanate from the nurses…"* ***Pharmacist 7***

4.3.4 Documentation Fatigue

Unlike medical staff, nurses – by virtue of their role in the clinical team – were often in a position to observe at first-hand medication-related harm, including ADRs. Cases were, however, often not reported because of the procedure of completing a form. Most nurses perceived the official reporting procedure as complicated. They preferred to report their observation verbally to their immediate supervisor or the pharmacist, without having to complete a form. The following nurse describes one of the barriers to reporting saying;

> *"…because it entails filling a form, that is why people don't … sometimes if you observe, you will see that things that you report verbally, people prefer doing that. But anything that entails…they say 'go and write' people try to shy away from it …yes and I think that that is one of the barriers in addition to what I have already said…"* ***Nurse 5***

Their perception of filling in additional documentation made them distance themselves from having to complete an ADR form, thereby relegating it to be the duty of a pharmacist. Nurses viewed officially reporting an ADR or medication-related cases as not part of their core mandate, as captured in the following quote. They viewed their role as one of observation or being vigilant to spot and draw attention to further action to be taken by either a doctor or a pharmacist. The following nurse was surprised when she saw a chart showing the Northern region with the lowest ADR reporting rates nationally, because she had reported (verbally) incidences in the past:

> *"...I think as nurses, ours is to report to the [pharmacist] because in this facility, it is the pharmacist... our duty is to report to them, and it is their duty to also forward to whoever. As you are saying I am also surprised, because I know we have reported such incidents in the past to the pharmacies[...]"* ***Nurse 12***

Overall, the reporting process as described by participants showed verbal reporting to be the common practice preferred by many, because of the challenges in reporting officially to a competent authority using the required forms. Their motivation to report depended on their level of awareness about PV and ADR reporting, and on other prevailing factors such as availability of forms.

4.3.5 Unavailability of Forms

Issues relating to the availability of ADR forms were considered a major impediment to the ADR reporting process. Though forms were distributed in some units, most HCPs could not locate the forms when asked about them. Unavailability of forms at unit level resulted in delays and non-reporting. Forms were often not readily available even at the pharmacy unit where HCPs trusted they could find some. Even though the following pharmacist indicated forms were available, they could not find a sample form to show when asked about the availability of the form:

> *"*[…] *we have the forms; the forms are available [...] right now I do not have a sample here but normally they are available. So that if you suspect you just go there you pick a form and you just fill it. But however, at times they do give samples. They do give samples at some various departments [...]"* ***Pharmacist 4***

Unavailability of forms further complicated the reporting process, deterring HCPs from reporting. The following doctor points out that the unavailability of the form coupled with workload prevented him from reporting:

> *"…In fact, there is a lot that we don't get to report [...]. Because erm like I said the forms may not be readily available and the workload may not allow you to want to go back and want to fill a form and the pharmacist does the necessary things on the form…"* ***Doctor 3***

The standard practice, however, was to keep forms at the pharmacy unit even though they occasionally distributed them to other units or consulting rooms. Most nurses were not familiar with the reporting of ADRs using the required forms when asked.

> *"[…] the form I have never seen one before. Me, I have never seen anything like that. But I know sometimes they (ADR reporting) are just oral communications… (****Investigator:*** *have you ever reported to the Food and Drugs Authority; have you seen the ADR form before?****)*** *[…] no, we haven't crossed that limit yet, just within just within…no, I think the facility should provide these things [ADR forms]?"* ***Nurse 7***

Even though there was basic training and education from nursing school about pharmacovigilance and the importance of ADR reporting, availability of forms seemed to be a barrier to reporting. The quotation that follows is from a nurse who expounds the disconnect between theory and practice:

> *"[...] I think the first and last time I saw one was when I was in school. FDA had a forum with us in school, on pharmacovigilance [...] they came with some forms and said since we are about to go out into the job market…we were in our final year… these are some of the issues we will be faced with. People will take medication and come with adverse side effects. So in case we encounter such, these are the forms. We should fill and submit to them but since we started working, we have not seen these forms…"* ***Nurse 4***

4.3.6 Policy Issues

The lack of policy guidance on ADR reporting made HCPs pay critical attention only in situations where incidences were life-threatening. Most healthcare facilities lacked protocols for reporting ADR. High patient numbers in consulting rooms made prescribers pay attention to only serious incidents, as quoted by the nurse practitioner as follows:

> *"...So when you get the situation and it is not something that is so disastrous to life you just try to handle it and carry on. That's what often times we do but there is [...] like erm a laid down[...]what do I say [...]protocol[...] in the facility that when you get a drug reaction this is the channel this is the protocol do this do that, report to this person, draw the attention of so and so. There is no such laid down rules…ahaa… so we are practising as individuals though collectively our interest is a patient should not suffer the consequences of or otherwise…of any of the medical prescribers…"* ***Nurse 10***

In the delivery of healthcare by HCPs, SOPs and internal guidelines for reporting ADRs were absent in facilities and this affected the practice.

> *"...probably that will make us bring them out. Maybe some see and they don't mind because it is not[...] like they are not even aware of it because it is not a policy in the hospital as part of our practice that when you see an ADR, document it or report it. So maybe that one could have helped…"* ***Nurse 8***

HCPs were unaware of any policy guidelines and of the recommended protocols instituted by management to ensure reporting of ADRs or medication related incidents.

> *"...I don't know of any policy at the hospital level where there is a framework for reporting. Even if it's in the books it is not made known to us. I don't remember it being mentioned when I was employed and oriented…"* ***Pharmacist 10***

Lack of enforcement by the Ministry of Health (MOH)/GHS caused reporting not to be of priority or importance to participants. Even though HCPs felt it was important to report, there was no policy requiring them to do so.

"… it is not happening, why because it is not mandatory. Are you getting it? And as I said if you leave human beings to do what they like certainly you won't get results… here you know we want to do something but we do not have… you see human beings naturally will not just do something unless there is a little pressure. Unless there must be a force. That will compel you whether you like it or not to do…" ***Pharmacist 4***

4.3.7 Hospital Administrative Issues

Key indicators to effective functioning and optimal performance of healthcare facilities were identified as being linked to the problem of reporting. Fundamental among them were management and leadership, communication barriers, technical issues, incomplete patient data, funding, and training, which were identified as important factors affecting ADR reporting.

4.3.8 Management and leadership

HCPs were concerned with the way ADR issues were managed administratively. MOH or GHS annual review meetings seldom featured the pharmacist and ADR issues. Pharmacy staff criticised the way invitation letters to such meetings and workshops were often addressed requesting either the pharmacist or the matron, instead of inviting both to attend.

"… here in the region in particular, it's pathetic. I will give you a classical example…their [Ghana Health Service] annual review meetings for example. They will send out information and say med. sup, administrator, matron or pharmacist…it means we are not getting it right. Are you saying the matron can go and handle pharmaceutical issues like the way the pharmacist runs [...] no no no. Are you saying the pharmacist can go and handle the issues about nursing? [...] and you don't understand it…and these things keep happening and I will be asking 'aah what is wrong with us'…so some people [hospital management] sit somewhere, do not think it's [ADR reporting] important…[...]once you have one of these people [nurse or pharmacist] that it's ok [laughing] [...] yeah so structurally we have fundamental issues and those people at leadership positions are not seeing too [...] I mean not getting it right. And these things are compounding the problem…" ***Pharmacist 4***

From personal reflections and interviews, it was observed that the FDA's invitations to HCPs to attend training on some occasions were often received and attended by administrators instead

of selected clinicians. HCPs were of the view that administrators who went for these training sessions or orientation on ADR reporting often came back without cascading the training.

> *"[…] I think the FDA should give training directly to HCPs rather than administrators. Most of these trainings administrators go for them, come back to sit with the knowledge […]"* ***Nurse 11 (FGD)***

Despite better understanding and training opportunities, senior level staff – especially nurses – were less likely to directly observe an ADR in inpatient departments at first-hand; they were often involved in administrative duties. They relied on junior officers who were at the bedside of patients but were less likely to be knowledgeable about the reporting processes.

In addition, high staff turnover created human resource constraints, which affected reporting. Hospital management were challenged by staff shortages due to attrition of HCPs for further education and retirement of HCPs, exacerbated by high patient attendance. The following nurse describes how reporting declined when a person responsible for the coordination of reports was moved;

> *"…ahhh, because our place the drug [...] immediately anything happens, small thing and they are sending it. Ahaa and that guy makes sure that they have focal persons in the wards. But I think he has joined some NGO [...] it's like he has left. At least he should be for two years [...] but at least he has prepared the grounds before leaving…"* ***Nurse 1***

4.3.9 Bureaucracies

An important factor influencing the reporting process was the perceived need of participants to conform to an established hierarchy. They often required a second opinion and further assessment to establish some sort of causality before reporting an ADR. After assessment, and if deemed worthy of reporting, all HCPs expected the pharmacist to contact the regulatory agency or pharmaceutical company to report the case officially. Bureaucratic reporting processes influenced the reporting process, as described earlier. The informal hierarchy in place was for nurses to report to doctors and doctors to pharmacists. Within each professional category the reports would first go to the person 'in charge' (the 'boss') first.

HCPs could also complete a form and directly report to the FDA if they felt confident to do so. This was, however, a rare occurrence. Conversely, if an ADR was considered not serious by the HCP it was reported to the next in charge and managed within the core clinical team (nurses and doctors). No action or further reports were sent to external stakeholders (pharmaceutical company or the FDA) for ADRs considered non-serious.

As mentioned earlier, verbal reporting was considered convenient for nurses and junior officers because of fear of blame and the bureaucracy of the process. According to participants, only doctors were allowed to write in patient folders, while nurses were not permited. This arrangement therefore created a barrier to reporting, and instead of nurses documenting an incident when they observed it, they had to wait and verbally report to the doctor. The doctor then decided to either note it in the patient folder or consider it as non-serious. Even though nurses sometimes observed cases, it was impossible to document them in the patient folder for fear of being blamed or reprimanded.

Nurses within their professional category preferred to verbally report to their in-charge, the in-charge to the matron, and the matron may report to the doctor. The doctor may then involve the pharmacist to further assess the case and take notes. Reporting ADR to the authorities was often left in the care of the pharmacist, and pharmacy staff also preferred to send these reports through their superiors before they went out to the authorities. For example, a pharmacy technician may inform his/her supervisor (clinical pharmacist) before a completed form is submitted to the authorities. The pharmacist quoted in the following passage has eight years' experience and was asked if he had ever sent a report directly to the authorities; he responded in the negative, citing bureaucracies and hierarchies inherent at his place of work as factors affecting reporting.

> *"[...] have not sent a report but erm when we get the [...] erm when we come across some of those cases the in-charges (senior pharmacist) take it up. And from there I don't know what happens. You see if you are working with someone [...]a senior colleague. You understand. If there is something you have to channel it through him. So those are some of the things. You can't go behind your boss and do anything. When it happens that way (ADR incident) he takes it up and you don't see anything or any move again…"* ***Pharmacist 2***

It was also common for junior officers to expect senior officers to take action on reporting ADR, which was done to respect hierarchy and avoid blame. The following pharmacist was asked about an occasion when he observed an ADR and what action he took. He indicated in the following quotation that he had to wait for his superior to come and do the documentation and after the documentation, he received no feedback.

> *"[…] He is my boss erm he did most of the questioning and filling of those things and trying to find out other details. So that was what we did we followed up filling these details and submitting it to the erm the one in charge… from there I don't know what happens. You see if you are working with someone … a senior colleague. You understand. If there is something you have to channel it through him. So those are some of the things. You can't go behind your boss and do anything. When it happens that way, he can take it up […]"* ***Pharmacist 27***

Nurses did not feel confident about reporting ADRs directly; they often wanted validation from a pharmacist, doctor or a senior colleague before reporting. This was seen as respecting protocol and not wanting to over-step responsibility, because they were unsure about the recommended procedure.

> *"… it is not our duty as nurses to go straight and report to FDA, it should pass through a channel. Yes! And the highest channel should report it to the FDA [...]"* ***Nurse 3***

> *"…the reporting channel should be through the in-charge to the pharmacist and he will now forward the report to the FDA. But if there is a way to send it directly too would be better[...]"* ***Nurse 9***

Even though some nurses felt they could report directly, it was often not the practice and they relied on multiple opinions before sending a report.

> *"…I think you can go straight to report or if there's a doctor on ward rounds at that particular time you tell the doctor that, this is what I have observed, then he can also bring in his (expertise)… maybe go to this person or go to that person…"* ***Nurse 7***

Organisational hierarchies and inherent power relations between HCP categories as well as within cadres influenced bureaucracies related to ADR reporting.

4.3.10 Hierarchies and Power

HCPs felt incompetent because superiors influence on their reporting. Senior staff made it unlikely for subordinate HCPs to report ADRs. Power relations within professional categories and between HCP cadres played a major role in getting ADRs reported.

It was perceived that the hierarchy and power between HCPs made it a challenge to discuss clinical issues together. Superiors often seemed to dominate, listening less to the opinion of junior officers. This imbalance created a communication gap between junior officers and senior officers. It was less likely for junior officers to report ADRs and medication safety concerns, as suggested by the nurse in the following quotation:

> *"… But sometimes the superior [senior officers] always sit down and think that yes they are above and we the rest we [junior officers] are below, so whatever you [junior officers] say will be pushed aside. So how then do I report such issues to such a person. Because look as we were just saying now if […] they [authorities] come and say 'oo how come the child's condition has deteriorated'… how do I report it?[...] I will never do it…"* ***Nurse 7 (FGD)***

From personal reflections and opinion of nurses, there were hierarchy and power dynamics among the core clinical staff. A hierarchy was evident, with nurses being considered the lowest in terms of authority and power, followed by pharmacy staff, with doctors being considered to be most senior and influential. Junior nurses felt they were not confident enough to challenge the clinical decisions of doctors or prescribers due to an inferiority complex. For example, sometimes nurses felt antibiotics were overprescribed for children by doctors but could not challenge or assert themselves. It was therefore often difficult to complete a form in such a situation and also to identify which antibiotic was causing the reaction, as this quote illustrates:

> *"These are all antibiotics[...]overloading the system but if you go to tell the prescriber, this is what is happening, they will say 'ooh you don't know anything'…that it's their work…can't even do anything so how do you even fill the form?"* ***Nurse 10 (FGD)***

There was also perceived fear of consequencies from colleagues or superiors for exposing wrongdoing. HCPs did not want to be seen in their teams as 'bad people' for reporting a safety issue which has resulted in an ADR. This could be linked to fear of ADR reporting and consequences of reporting, as captured earlier. The following quote illustrates this factor better:

> *"[…] We will be looked down upon and if anything at all comes they will quickly ask you, so when you went to her and this and that happened who did you report to? There is nothing. We are sitting down here we don't have a medical sup. So if an MA [medical assistant] does something wrong, the next person you should have reported to should have been the medical superintendent. Here we don't have a medical sup. And I can't report an MA to my matron. You see the problem? So sometimes you the nurse you also have the fear that you will bring this thing forward and people will tag you as a bad person. You see the problem…so this hospital, inferiority complex. I know what I am doing but because I am a junior, I can't say it. I fear to approach. You understand […]"* ***Nurse 5 (FGD)***

4.3.11 Inferiority Complex

Within professional categories, it was common to observe junior officers feeling inadequate and, likely to be reprimanded by senior staff. An imbalance of power and the manner in which senior staff members managed this relationship made junior officers feel inferior.
The following nurse describes situations in which they find it challenging to report issues to their supervisors because of the power imbalance and fear of consequences.

> *"…sometimes the superiors always look down on the lower ranks[...]so you see sometimes that's what we are just saying, so if it was her (superior) that I am supposed to report to her, now she is the one who has prescribed it, I have gone to you, you are even prescribing it […] If the side effects come, how do I report to you? You see what we are saying. So basic thing that we know, as we have learnt, you might have your Master's, I might have a certificate, but I know what you don't know. You see, so it should be a teamwork…"* ***Nurse 18 (FGD)***

Between HCP cadres, it was observed that nurses were more likely to feel an inferiority complex than other HCPs. These affected inter-personal relations, resulting in inter-professional conflict and distrust.

4.3.12 Communication Barriers

Ineffective communication contributed negatively to ADR reporting to a large extent. As noted earlier, internal communication channels at various health facilities were complicated, and HCPs were often not aware of the channels of communication. Also, when issues were raised, feedback was delayed and was often not received by reporters. FDA communications with healthcare facilities were usually only directed or communicated to pharmacy staff or contact persons. The FDA established cordial relationships with individual clinical pharmacy staff and contacted them directly with medication safety-related issues. They often bypassed administrative bureaucracies which created communication challenges among hospital administrators, medical superintendents and pharmacy staff.

> *"…erm I still think that the FDA should be more proactive than they are. I think they should interact with us [administrators/hospital managers] more often…and me if they continue with that am sure we will turn around. I tend to hear their meetings after the meetings have passed, because they tend to communicate with the pharmacist directly. Instead of getting through to[...]at least as a manager I should know when… if you are going to hold a meeting of such things maybe I would want to add some of my clinicians to go and listen to it… but if you call pharmacist alone to go and sit down, expecting that they will also come and bring it out. This newsletter you talked about, I came and saw it lying on my desk I don't know who brought it… yes, so it should involve more of managers and clinicians not just pharmacy staff…"* ***Doctor 7***

Internal communication between healthcare professionals was also weak. Pharmacy staff found it difficult to get feedback from their superiors and from nurses who were at the frontline of healthcare delivery to patients.

> *"…this hospital our channel of communication is very poor…when you first started I told you that our communication system is very poor…at times you can even send a problem to the bosses but at the end you will never get the feedback. That's our problem*

*here, communication is very bad, it's very very poor. (**Investigator:** "So I was just wondering what could be some of the problems")… you see those at the wards, the nurses at the wards, they will have been the best people to be giving us the [...] those informations (sic) but we never hear anything from them…*" ***Pharmacist 10***

4.3.13 Technical and Logistic

Logistic and technical challenges were also perceived to obstruct the efforts of the FDA in the distribution of forms and creation of an electronic platform. It was noted that internet connectivity at all healthcare facilities was unstable. The FDA made efforts to set up an electronic system and train HCPs, but they were unable to use the system due to technical challenges.

"[...] the last meeting we had at one of the venues in Tamale here they talked about having a platform. That is web-based platform where we were supposed to be signed on and such that when the case comes you can just log in and deliver it directly[...]yes[...]but you know how our internet system is[...] unfortunately, even before we left the meeting [...] they (FDA) couldn't set us up there because of challenges…" ***Pharmacist 4***

The basic infrastructure was in place in the various hospitals, but HCPs were challenged by broken equipment, poor Wi-Fi connection, lack of a common software platform and management of information systems, making digitalisation problematic.

*"…now naturally in Tamale here, the internet is not perfect but as a regional hospital, the Metro hospitals within the Metro and even some of the district hospitals all have internet access. They can all be hooked on. So, if as a nation we are cautious about these things[...] yes, the CHIPS [*Community Health Improvement Services*] compounds, the health centres if it is not possible let's leave those ones now. But the teaching the teacher in the secondary to primary levels that can be put onto this system should have a common platform…"* ***Pharmacist 4***

"Here we have HAMS [Hospital Administration and Management Systems Software] the HAMS we have we are not even [...] exploring it fully. We still use manual folders

[laughing][...]But it can be folder-less… So that is where the problem is you see and this hospital is using HAMS (software), another person is using this, another person is using that, another person is using that, at the end of the day everybody is doing different things…and some as at now are not even using any software… they are not interested in going folder-less because is demanding people have to sit down and type in the only thing that you see is that drugs and diagnosis[...]" ***Pharmacist 4***

Patient record-keeping was based on a manual folder system even though efforts were being made in hospitals and the National Health Insurance Scheme to create electronic patient records. The objective of keeping electronic patient records was, however, for the purpose of managing insurance claims electronically, rather than for medication safety purposes. Some management information systems' software had the ability to compile ADRs from electronic patient records, but this was underutilised. Among HCPs, it was observed that only pharmacy staff could access these electronic interfaces for health insurance claims-related purposes. HCPs lamented the lack of a common electronic platform to coordinate or harmonise the activities of ADR reporting.

"…Well you know one of the biggest challenges we have here in this country is that we haven't really done due diligence with regards to harmonising the way we work. Till date health insurance has come to stay, we have to manage our claims. Every facility has to struggle on its own and acquire any software that they come across that they think it's good and all these software's have their deficiencies they might not be compatible like talking about data because we as Ghana Health Service knowing what we want or as a country, we have to fashion out these software's [...]" ***Pharmacist 4***

4.3.14 Sociotechnical Constraints

HCPs were also concerned that the FDA electronic reporting system was not user-friendly. The high workload, coupled with technical difficulties faced by HCPs in using the system, discouraged them from completing ADR forms, especially using the electronic system. They perceived the process of reporting an ADR electronically to be a long process which required logging onto a website before submitting a form. Older staff were also perceived to be more challenged with computer assited reporting. This process made HCPs passive about reporting.

> *"[...] now there's a problem (ADR) or even if I have internet, I have to go to your (FDA) own website go and search for it and now sit down and begin to type a whole lot of things in there. You think somebody has that time to do it? [...]"* ***Pharmacist 6***

4.3.15 Incomplete Patient Data

Incomplete patient information was a major concern for HCPs, especially pharmacists who were often tasked with reporting incidences of ADR or medication-related issues.

> *"…but the patient maybe is discharged, and it's gone…so how do you complete a form… then always you find out that is always half half (incomplete) you are unable to gather the data…"* ***Pharmacist 5***

Cases were also lost because some HCPs usually insisted on waiting for the clinical pharmacist to collect patient details, because they considered ADR reporting as not part of their core duty. Pharmacy staff also blamed the issue of incomplete data on the inability of nurses, doctors and prescribers to document detailed enough patient information to complete an ADR report form. By the time the pharmacist is available to collect the details it is often challenging to complete patient information.

> *"…so quite recently there was a case, was it a few months ago, I wasn't around. They only came to tell me later and that the patient is even gone so we couldn't document it. The other day I gave the form, there for them to document… I don't know if I can trace the leaflet. They brought the thing [making faces] [...] It's like …I don't know…"* ***Pharmacist 10***

> *"…That's the bottom line is not in existence look a patient will even suffers ADR he will pick the folder and will know that much from the folder. They are not going to make any conscious effort to chronicle the event in there… 'ooo he reacted to this maybe it's done'. Or maybe withdrawn or stopped the treatment. So, you even pick the folder and its useless[...]now the patient too is gone so …these are the real issues, so you see when you are asking the people to provide the data…from where? Where are they picking it from? Do we have one? I doubt it we don't…yes let's be fair[...]I am telling you these are the facts on the ground, we don't. So, when it happened and the person who is to document it is not there, there and then and approach the case then it becomes a difficult one. You will hear about it, but the folder will not be able to help you to do the*

capture and write up the details, because they will not find any details like that in the folder. You may just find one or two sentences that talk about it, but they might not even bother much to even I mean chronicle the event…" ***Pharmacist 4***

4.3.16 Complicated Form and Reporting System

Despite efforts by the FDA to keep the form to two pages and make it as simple as possible, HCPs – especially nurses – still found it complicated. They were not acquainted with the reporting system.

"…and the constraints too sometimes complicated administrative or reporting procedure, sometimes the booklets for reporting is so cumbersome you open here right now the questions so many things like you are in class…you have to go through a whole lot of …they should make it simple, a simplified something…" ***Nurse 8***

They were often not aware of where to report ADRs and who specifically to report to.

"…even the channel of reporting is actually difficult we don't even know where to report it and who to report to. So what we do is that once the doctor comes around we just tell the doctor your observation, what you noticed and if there is the need for the person (doctor) to change the drug then the person will change the drug. But we don't usually go further to see what really happened…" ***Nurse 4***

4.3.17 Funding and Training

External factors such as the stakeholders, i.e. FDA, MOH, and pharmaceutical companies, provided limited budgetary allocation for promoting ADR reporting. Similarly, internal elements such as hospital administration, management and leadership provided no internal budgetary allocation. Financial administrative decisions taken by the internal management and leadership were dependent on finance from stakeholders. Limited funding therefore affected the education, training and sensitisation on ADR. It was perceived that lack of funding affected training, and there was advocacy for financing and training through internal elements.

"[...] if you want people to do a job you have to make sure they are well trained, and they understand what exactly you want them to do. So they will do it but you see these things sadly, here is when we say that we are supposed to come and cascade the training but you know it's a system […] you take one or two people you send them you train them and they come and they are in the system [...] but no money no money syndrome and things like that[...] people are not prepared to organise trainings, you see in Ghana here one of our biggest challenge is that, everything you want somebody to come and sponsor. Oo that's so so and so erm global fund has given some money to do what…[...] so why can't we ourselves make money and make it regional thing[...]" ***Pharmacist 10***

"…I think FDA should continue to do the sensitisation, especially adverts in local dialect. That one is very necessary. But they will tell you they don't have money because when they do the adverts they have to pay. So, the sensitisation should be there to patients and caregivers. That if you take any medications and you have any issues report to FDA[...]" ***Pharmacist 2***

4.4 External Factors

External factors were described as factors which were distal, and beyond the immediate control of the HCPs. These elements were identified to be influenced by the social, economic, political and environmental activities, which were distal, and beyond the hospital setting directly but were still considered to have an effect on ADR reporting. The three external factors identified were infrastructural issues, media publicity, and stakeholder contribution.

4.4.1 Infrastructural Issues

These were factors participants described as socio-political and physical geographical barriers, which hindered efficient and effective collation of ADR reports. Poor road network, communication network and lack of social amenities in remote communities hindered reporting. The perceived inability of leadership to release resources meant barriers to work in these communities was further compounded due to political reasons. Even though nurses were willing to report as part of their duty, resources needed to work in these remote locations were lacking.

"... You see sometimes there are certain things you are not supposed to say. But like everything in Ghana or Northern region in particular, it's politicised in the sense that maybe somebody was paid to do that job. The fellow doesn't belong to this [...] so you are not allowed to do that [...] ('they will side-line you...' ***Nurse 4)*** *[...]. You are willing to do it but there are no resources for you to do it. Imagine you are to leave here and have to go to somewhere Santani [...] overseas community (remote community) [...] you have to use your motorbike, pick a boat and cross. So, like, you are risking your own life. Meanwhile the money has been sent to somebody's account. To release it to do that work yet is not there [...]"* ***Nurse 5 (FGD)***

Getting core HCPs to these remote locations was a disincentive due to a lack of basic social amenities in these locations. HCPs therefore often refused postings in the past, which has had a ripple effect on the current reporting situation in the region.

"[...] these are the facts on the ground[...] There are still districts without pharmacist[...] not even a technician [...] a pharmacy technician [...]" ***Pharmacist 3***

4.4.2 Media Publicity

Dissemination of relevant health-related topics, especially in local dialects, had a positive impact on reporting medication-related problems. Lack of funds for adverts on TV, radio and print negatively affected this initiative. Environmental factors affected media publicity. The dispersed geography of communities limited their access to some types of information. The most popular were TV and radio. Previous radio announcements resulted in patients visiting healthcare facilities to report medication safety-related issues to healthcare professionals.

"[...] one day I was sitting here, and somebody came and said he heard some announcement on radio that they said if you have a mental problem you should come to the hospital. That announcement was actually meant for Upper East, but he had it and he came. And we attended to him and give him medication and he went [...]" ***Nurse 7***

In public health interventions, the involvement of media increased consumer awareness about medication-related harm and therefore increased reports.

"[...] I remember some time back when they started taking SP (Sulphurdoxine Peramitamin) and people were dying and the media came in [...] erm a lot of education was done to increase awareness, you remember SP? [...]" ***Pharmacist 1***

4.4.3 Stakeholder Contribution

Major stakeholders, such as the FDA, pharmaceutical companies and the MOH, were often cited as not doing enough even though some interventions have been put in place.

4.4.4 Food and Drugs Agency

The FDA is the central agency responsible for drug regulation and safety of medication. Some interventions were in place to increase reporting, but most healthcare professionals were not aware of them. HCPs who had a positive feedback experience were personally motivated to send more reports, while those with negative experiences felt reluctant. Change of leadership within the FDA administration also affected ADR reporting. Participants commended the efforts of the current FDA leadership:

"...am glad to say that the current boss (FDA) that came, he has taken it upon himself to do a lot of sensitisation, training and letting people be aware that any time they see an ADR they should report. But formally there was no trainings like that but since this guy (FDA director) came, he has been doing well [...]" ***Pharmacist 2***

It was observed that the motivation for renewed efforts from the FDA administration stemmed from the background of the head of administration as a pharmacist, unlike his predecessor who was a food microbiologist. The director noted that the FDA had several indicators to fulfil and ADR reporting was just one of them. Generation of reports and awareness creation therefore depended on the direction or focus of the FDA administration at any point in time.

4.4.5 Ministry of Health/Ghana Health Services (MOH/GHS)

There were no specific policies, by-laws or protocols for reporting ADRs at the health facilities investigated. This affected HCP attitudes because they were inclined to pay more attention to memos from MOH/GHS-driven policies than to those from other stakeholders. Also, MOH

nursing schools did not have pharmacology as a core or examinable subject, so nurses therefore did not attach importance to that aspect of their practice.

> *"…I don't know of any policy at the hospital level where there is a framework for reporting. Even if it's in the books it is not made known to us. I don't remember it being mentioned when I was employed and oriented…"* ***Pharmacist 7***

> *"…all these things about pharmacovigilance the Ministry of Health itself haven't done anything about this thing (ADR reporting). They are not so much interested whenever you see the brochure is coming from FDA or coming from pharmaceutical company. But the Ministries side is indifferent. So, if you are indifferent about it why should the nurse be so interested. Even I believe that in the training of these people pharmacovigilance should become a core subject. Because we use medicines almost every day it should be a core subject people should take it and understand why monitoring is important…"* ***Pharmacist 4***

MOH/GHS had no medication safety and monitoring unit at the regional level. The regional pharmacy unit had oversight responsibility over all medication safety issues, but no dedicated unit was available.

4.4.6 Pharmaceutical Companies

Pharmaceutical companies were less involved in pharmacovigilance and medication safety at the health facility level. The only interaction HCPs had with pharmaceutical companies was during clinical meetings or in consulting rooms when they came to market their products. Marketing executives were more concerned with promoting their products than discussing the ADR-related issues. The following is the reaction of a pharmacist when asked about the contributing role of pharmaceutical companies in reporting ADRs:

> *"[…] they (pharmaceutical companies) come, they just talk about the few side effects associated with the products. Sometimes they are too silent unless question time when people ask what the side effects of this product is and all that. They are always gentle (quiet) about it but as I said they put into their leaflet that if you have any ADR or side effect you see your HCP…"* ***Pharmacist 1***

Some pharmacists indicated that they were not aware of any pharmaceutical company actively engaging HCPs in ensuring that their medicines were safely used, and ADR reported.

> *"[...] never!! I have never seen that […] seriously the only relationship or the only people that you see around are reps, reps would not even want to dive into that area (ADR reporting) [laughing] (**INVESTIGATOR:** because they are marketing?) [...] exactly!!…theirs is to come and market their product, package it nicely and make sure they push it. For them whatever comes […] that is not their business they will not even want to talk about it […]"* ***Pharmacist 8***

There was a perception among some HCPs that reporting ADR may affect the marketing and sales of a pharmaceutical product. HCPs therefore feared the risk of being targeted by pharmaceutical companies for reporting the negative consequences of a drug. HCPs were confident to report if they felt protected by authorities.

> *"…sometimes too intimidation…from pharmaceutical companies and then drug producers. Somebody (a company) produces a drug, it is prescribed… then the patient takes the drug and does not do well (reacts), if you come out to say this drug did not do well (reacted) with the patient, then it becomes like you are against a company or you are sabotaging the product. You know and then… they may be legally fighting you or seeking to cause you harm. Yeah uhuh so and then also erm maybe the ability of the authority to protect people who will report on these reactions …uhuh. So, I think these are some of the key issues…"* ***Nurse 10***.

Coupled with the fear of being negatively targeted by powerful pharmaceutical companies, incentives and rewards from pharmaceutical companies served as a motivation to prescribe particular drugs. Some HCPs were of the view that doctors were under pressure from pharmaceutical companies to impose brands on patients. Receiving souvenirs and incentives from pharmaceutical companies often made it difficult to report ADRs that occur in practice.

HUMAN FACTORS

The central and most important factor was knowledge of HCPs about ADR reporting. Knowledge affected their attitude, practice, and willingness to report. Even though system factors affected ADR reporting, human factors were central to improving the overall reporting system. Human factors referred to how HCPs' and patients' actions were variously perceived by participants to influence ADR reporting.

4.5 Personal HCP Factors

Interviews revealed three HCP-related factors, relating to **knowledge, attitude and practice**: knowledge related to HCP awareness about pharmacovigilance and ADR reporting issues learned over time and also the importance of reporting; attitudinal factors related to the views and opinions held by the different HCPs about ADR reporting and finally, practice factors identified in the interviews related to the application of knowledge and attitudes to the routine daily practice of HCPs. ADR reporting was often affected by a combination of these factors and was also related to key issues such as medication quality, inter-personal relationships, influence of drug promotion activities, and clinician burnout.

4.5.1 Knowledge

Knowledge was explored based on responses to questions about pharmacovigilance, its importance, ADRs and the reporting process. HCP knowledge about what and where to report ADR affected the whole reporting process. HCPs were firstly asked if they were aware of the term pharmacovigilance and were then asked to describe their understanding of the term. Pharmacy staff and medical staff seemed more knowledgeable than nurses did; they offered more detailed descriptions and appeared to have a better understanding of the importance of pharmacovigilance and the ADR reporting process in their hospital. The following doctor was asked about their knowledge on pharmacovigilance and ADRs:

> *"[…] every drug after manufacturing is tested before approval is given, however where it was tested is just a small fraction of the whole population. So there is anticipation that using this medication anybody may react to it differently, […] so there are some (reactions) that are noted already by the manufacturer. There are some that are not captured. They are expected by the manufacturer himself, so when these things happen*

and we report it [...] it informs us and the manufacturer to modify or if possible, do something about it. This is how we keep the entire health delivery system in terms of medications safe for the general population…" ***Doctor 3***

In contrast, nurses appeared less sure of terms such as pharmacovigilance and overall ADR reporting. Some admitted to having never heard the term pharmacovigilance for example. Some made informed guesses about terms such as pharmacovigilance, by separately describing the words 'pharmaco' and 'vigilance' and, for example, using the term 'cautious' in relation to the latter. Some were able to describe this as relating to medicines and being watchful for side effects of drugs (Nurse 3). Most nurses were also not well-informed about the formal reporting process. The following quotations reflect the responses of some nurses about pharmacovigilance and ADR reporting in focus group discussion:

"… about pharmacovigilance, it's more or less like English [...] to be vigilant, trying to be very cautious about drugs, trying to be very careful with the way and manner of issuing prescribed drugs, when we give drugs to patients, if I want to put it…" ***Nurse 2(FGD)***

"...yeah… I have head of it, though it's not a very [...] erm if you like…it's not a very…[...]popular term which is of much concern to us, it's something I have heard of it's more about being vigilant on… you know… erm the issues of drugs and the side effects of the drugs…" ***Nurse 3 (FGD)***

Nurses who were senior-level staff were more likely to have had experience and training on pharmacovigilance, which appeared to give them a better understanding of pharmacovigilance as shown in the following quote:

"[...]Pharmacovigilance I think we even had a workshop about it. We even had about two workshops on it. Umm let's even take just the word vigilant, you need to be very cautious of the drugs that you give to people and their side effects; we have normal ones and we have the adverse[...]the adverse drug reaction, they are reactions sometimes we don't anticipate but it occurs and as we are giving the drug we should also monitor to see the reaction or the outcome of that; either it will be within the normal ranges or it will be beyond that may also cause another problem." ***Nurse 11***

Of note in the above quote was that the nurse manager explicitly referred to the distinction between side effects and adverse drug reactions, which was unlike most nurses, who referred to side effects and adverse drug reaction inter-changeably during interviews.

4.5.2 Ignorance

Perceived patient ignorance was influenced by other interrelated factors such as forgetfulness, low socioeconomic background of patients, and misunderstanding about reactions. Patients often could not remember the medications and misunderstood ADR as normal and an indication that the drug is working. For example, "*[…] some patients when they see ADRs they say yes!! the drug is potent and working […]" Pharmacist.* HCPs were of the opinion that patient misconceptions about their medications and forgetfulness often led to them not reporting important ADRs experienced as reported in the following quotation;

> *"[…] I have seen one [ADR] from the ward level at the accident and emergency unit where a patient according to her took some drugs she had a reaction could not recall the drugs[...]"* ***Pharmacist 1***

Some patients and relatives were perceived not to be knowledgeable enough to identify ADRs and take prompt action to report them. They were only able to report if they could attribute the reaction to the medicines they received from their HCP's and this was often felt to not be the case. Low literacy and educational attainment were also perceived to affect patient understanding of medication instructions. This made it difficult for HCPs to obtain information about consumed medications from clients who often mixed their medications or consumed them incorrectly. A doctor relates the following scenario:

> *"[...] here are others that go home and don't know, and they go, and they mix up the drugs. They pick this, and after they don't know which package for which is. That's in the case of polypharmacy then afterwards they mix. And next time they are taking they take this one more and this one less. And when you ask them (patients) and they tell you how they took it you know they didn't take it right. So those ones sometimes you don't know whether to report those cases as ADR or you should just take them as side effects*

due to an overdose. So that is usually the thing. The knowledge on these issues is a problem really[...]" ***Doctor 5***

Lack of knowledge about indications and contraindication of medications was also identified as a challenge for patients receiving treatment. HCPs were of the view that reactions experienced by some patients were seen as a normal indication of the drug and thus not reported:

"… they expect to feel a certain way when they are taking medication for them to feel that it is working so when they start experiencing some of those things some of them think it is a normal thing… some of them feel that it is a normal part of taking the medication and if they take the medication and for instance they are sweating which is not normal with the drug, they will not report it, they will say 'ooh this thing is due to the medication' and they will not report it…" ***Pharmacist 8***

4.5.3 Recognising the ADR

HCPs seem to lack knowledge about how to identify an ADR and what to report. For some HCPs, there was a belief that authorised medicines and ADRs were considered uncommon and therefore infrequently observed. Even though some HCPs had practised for longer periods in health facilities, they indicated that they had never encountered an ADR and that they were a rare occurrence.

"[…] in fact, all the drugs on the essential medicine list, experts meet to decide that in Ghana we are using this. So as much as possible we procure within that list. And all those drugs are drugs that have been used in Ghana before and we know most of the basic side effects; though some people react to them it's not much…" ***Pharmacist 11***

"[…] like I said they don't come significantly enough for us to be reporting. So if they are not [...] erm if the reactions are not much… I mean we will not, we will not report […]" ***Nurse 6***

"…umm yeah but in practice I think it is rather uncommon. I think in all my practice, the only two cases I can think of were in 37 military hospital, but that was way back in

the 90s, late 90s, where they were cases of umm two cases of Stevens-Johnson syndrome. Since then I don't think I have actually seen any…" ***Doctor 5***

"[…] to be honest I wouldn't know. But if I make any guess, it's just that either we don't see it, therefore we are not sensitised enough to report to anybody because we don't see it. Because if I don't see the drug reaction, what am I going to tell the pharmacist? But if I see it definitely, I will let him know. So, for the whole two years or eight years that I have been here I have not seen it. Definitely I haven't seen it…" ***Doctor 7***

ATTITUDE

Overall HCPs considered reporting as important and thought of reporting as beneficial, but other negative behaviours were identified to influence HCPs' ADR reporting behaviour: reluctance to report, uncertainty, fear of reporting, and product misconception.

4.5.4 Reluctance to Report

Some HCPs felt reluctant in reporting an ADR and for some, it was considered a waste of time. They paid less attention to ADR issues and were sometimes forgetful about reporting, blaming high workload. Doubts about symptoms related to the drug, reporting not deemed important, and possible forgetfulness affected reporting. An interaction between these factors triggered passivity among HCPs, as expressed by the following doctor who said clinicians do identify ADR but are too lazy to report it:

"…what I believe, as I said [...] it's not that we are not getting the reactions, but we are not documenting it …yes that is the major problem. I mean it is not also lack of training because we have had [...] FDA has done several trainings on these things. I just think as I said it's laziness on the part of, we the clinician…" ***Doctor 1***

Some HCPs attributed their reluctance to report as lapses caused by high patient numbers and reactions not being serious enough to be reported. This coupled with the technical challenges of the reporting system made HCPs feel reluctant to report.

"…the workload is so much with health insurance and the number of patients that come into the hospital. So sometimes, it can be an oversight. Once you handle it and it's gone, it might not occur to you to report…" ***Physician Assistant 9***

The main reason, however, for the reluctance of HCPs to report ADRs was the lack of knowledge, which translated into poor reporting attitudes. The following quotations highlight the above concerns when HCPs were asked why ADR reporting in their hospital is among the lowest in the country:

"…yes, this is an issue. In fact, the FDA pharmacist once told us this 'that in Northern Region our reporting system is very bad'. It isn't that we don't get cases, the cases are there, but it looks as if the people are feeling reluctant or they don't know in fact[...]…the HCPs[...]. So those who work with the patients you understand that…they feel reluctant and I believe it's not umm as if they are reluctant, but they don't know that[...] this thing they are seeing they are supposed to report. If not, we have been getting a lot of them we do…" ***Pharmacist 6***

"…you see I have come to realise that majority of us really have certain tendencies. The youth of today[...]the average Ghanaian worker, you know in terms of diligence [...]the attention of making sure that the right thing is done. Dealing with people with that right attitude…there are some people [diligent HCPs] …But the majority don't take things so seriously, they don't take things serious…" ***Pharmacist 10***

4.5.5 Severity of Incidence

A further influence on ADR reporting was the perceived severity of the ADR. It was apparent that HCPs were not keen on minor medication incidents and thus were less likely to consider reporting them. This was the case for all HCPs, including pharmacy staff who were viewed to be well informed on matters relating to ADR reporting. They equally appeared to be concerned with only serious reports and were unsure about reporting minor events.

"…If there is anything and there is a serious reaction, then they will come and tell us (pharmacist) but I don't know about whether those minor or less serious reactions that come up and they don't let us know… Recently we had some cases about anti snake

venom. That some of the patients were reacting to it. That one there was a report and they took it to the FDA. Yes, they took samples and they also came and looked at it. They filled the forms and took it to them. They brought in people…" ***Pharmacist 8***

However, HCPs completed ADR forms if they considered the case serious or life-threatening enough to report. The quote that follows is in response to a follow-up question asking a physician assistant if she remembered the last time she reported an ADR; cases which were considered not severe were often managed and discharged, as the quote below suggests:

"… well it depends on the severity of the reaction. But I can't remember the last time we even filled a form and reporting it officially. We just manage it when they come. Either you stop the medication or you give something to contract (stop) the reaction. But this hospital[...]no we do not report[...]" ***Physician Assistant 8***

Severe incidences of ADR, however, influence HCPs to complete an ADR form, as suggested by the nurse in the following quote:

"…well one was about a child, but I don't remember the particular drug, but it was an antibiotic suspension or so and she had swollen face as a result. Yes, so she reported back and we had to fill the form…" ***Nurse 2***

In situations where HCPs were uncertain about severity and if an ADR needed to be reported, nurses who were often perceived to be of the lowest ranking, exercised restraint and wanted a confirmation from a senior colleague, doctor or pharmacist before reporting.

"… the nurse will see it and say… 'this one I don't think it is so serious' and maybe will write it in their notebook that 'oo this has happened'. Then they will alert the pharmacist or the any other person around to come and report [...]" ***Nurse 10***

4.5.6 Uncertainty between ADR and ME

There were also misunderstandings emanating from HCPs' confusion between ADR and medication errors (ME). The FDA encourages HCPs to report ADRs even when they are not sure it resulted from a medication administered. HCPs, especially nurses, feared that reactions

from wrong administration of a medication could cause them to be questioned and to have undesirable professional consequences. The following discussion in one of the focus group elaborates on this attitude. A nurse describes an incident that was encountered in the paediatric unit in the FGD as follows:

> *"...somebody was to give IM [intramuscular] quinine he went and gave IV [intravenous][...]instead of diluting it[...] if the patient is reacting how do you report"* ***Nurse 3 (FGD)***

HCPs therefore feared that incorrect administration of a drug and reporting reactions may have negative repercussions on the individual. The competence of the HCP may be brought into question because they may be exposing themselves.

> *"...so my question is[...]how did you administer and you tell the person that he chewed…now it's like you didn't do your work well. So that fear will be there[...]in reporting… yes and knowing everything about the drug before you administer…in filling the form aren't you exposing your ignorance? When a doctor writes and you know it's not good you shouldn't give. Now you have to fill a form. So it comes with legal issues…"* ***Nurse 5 (FGD)***

4.5.7 Fear of ADR Reporting and Consequences

A number of issues arose in relation to concerns about the ADR reporting process, and more specifically whether ADR reporting posed any consequences to staff. A number of emotional aspects were linked to this, including the fear of being blamed and guilt of being involved in unprofessional conduct. The fear of blame from either a supervisor or a colleague made HCPs, especially junior ranking officers, reluctant to report ADRs. They feared that an action could also be taken against a fellow colleague and they could not bear the emotional guilt of being responsible for it. HCPs implied that junior staff generally feared such criticism and therefore concealed ADRs observed at the ward level. This was linked to hierarchy and rank as factors, which stimulated fear among HCPs.

> *"... sometimes the patient is genuinely reacting to a drug but because of lack of trust among colleagues… I[nurse] observe and report to a superior who doesn't take time*

to actually look at the things and start to criticise that, if you had done this or if you had done that…because of such criticisms, sometimes they would rather not tell especially if the superior is not there to see it right there they conceal it and it ends there… they manage their thing and they keep it there they don't want it to go out and they will say 'oo you should have done this, if you had done this you could have prevented that'. So I believe that is a factor that the junior staff would rather conceal it than report so that somebody would criticise them…" ***Nurse 8***

HCPs also felt that reporting an ADR may implicate or challenge the competency of a colleague in relation to their work. To avoid embarrassment of a colleague, many HCPs ignored ADR reporting.

"…because our system is like…it is some way as if we are trying to report somebody or you as trying to undermine the capability of another person…that he doesn't know what she or he is doing, that's why the person is getting the drug reaction[...]. You know these things[...]" ***Nurse 2***

4.5.8 Product Misconception

Some HCPs, especially pharmacy staff, were of the view that pharmaceutical products which were more expensive and from recognised pharmaceutical companies were less likely to cause ADRs. They believed that patients taking medications from renowned pharmaceutical companies were likely to get a better therapeutic effect and fewer side effects compared to patients who bought other less expensive generic products or bought from unregistered local shops.

"[…] see this drug it's expensive [showing medicine packages with recognised brand names] compared to this other one (a cheaper generic) … So you see the differences? There is no way you will give this drug (expensive brand name) to a patient and he will react …It's of high quality. Are you getting me? So, the drug is a contributing factor. The source of the drug, the company that is manufacturing. For example, Sanofi producing a drug when you give it to a patient, you will get the yielded result that you are looking for […]" ***Pharmacist 3***

Product misconception was therefore seen as a notion whereby HCPs overly trusted a product because of its brand name or cost, which could impact their judgement and perceptions of what to report.

PRACTICE

The study identified several real-world issues affecting ADR reporting practices among HCPs. Key among them were *sub-district experience, responsibility of reporting, lack of technical expertise, inter-personal relations, and teamwork.*

4.5.9 Sub-district Experience

Decentralised sub-district community health centres are managed by the GHS. These sub-districts are usually supervised by trained nurses or a small team of specialised HCPs (between two to five). Working at the sub-district level appeared to have exposed them to more ADR issues than working in a larger hospital facility.

> *"…in this facility it is really rare. It was only when I was in the sub-district in Bole, that in fact it was very common especially when we were giving elephantiasis disease drugs. And sometimes people taking procaine and sometimes quinine injection[...]. They sometime get these reactions but here it is very rare…"* ***Physician Assistant 8***

HCPs who worked at a sub-district level before were more likely to have sent some reports or attended training compared to when they moved to a secondary or tertiary care facility.

> *"… like I told you when I was in the sub-district…you know as a nurse but same time you were more or less like a doctor where we were not having a lab system as practised but we do almost everything…anytime they sort of um[...]um [...][...]workshop for those things for pharmacovigilance at the region we do organise at the district and go… yeah you know like I told you in the village, you prescribe*[...]*"* ***Nurse 1***

> *"…yeah at the district level or sub-district level you know because I was once responsible for the whole issue (pharmacovigilance) so that at any time there is that kind of adverse drug reaction you have to contact me. So as for the district level I have a lot of experience…"* ***Nurse 12***

4.5.10 Responsibility for Reporting

Clear views about the responsibility of reporting ADRs emerged and for doctors and nurses, it was not considered by them to be their responsibility. Instead, they felt it was the duty of a pharmacist rather than theirs:

> *"[...] the pharmacist should be the one. Personally, I will hold the pharmacist responsible because he is the link person and he should be doing the reporting. Unfortunately, this facility I have issues with him because he is not reporting as he should report…"* ***Doctor 3***

Nurses considered their role to be one of reporting their observations to the pharmacist only, and this was often verbal and required contacting the pharmacist about any events observed.

> *"...I think as nurses, ours is to report to them ... because in the facility, it is the pharmacist… our duty is to report to them, and it is their duty to also forward to whoever[...]"* ***Nurse 8***

Nurses assumed this perception because they considered the pharmacist as more knowledgeable on drug-related cases and were likely to be more knowledgeable about the reporting process.

> *"...I believe maybe the pharmacist should have been doing that because they have the knowledge[...]it will be easier them to identify some of these things because they are more technical with drugs, more than we the nurses. It's not all the categories of nurse that have much knowledge on drugs so if they do that it would be much better…"* ***Nurse 7***

In contrast, pharmacy staff felt that ADR reporting should be a collective responsibility requiring other HCPs to give them the necessary information or draw their attention to incidences of ADRs. Other HCPs however (i.e. nursing and medical staff), felt it was the responsibility of the pharmacists to go to the wards to collect and report ADRs.

"… it becomes a bit difficult, the pharmacist is not in the ward often[...]goes to the ward few hours in a day and you are not there so if information doesn't come from the people who are with the patient most of the time it becomes difficult. So we keep thinking that someone has to do it. This person thinks this person has to do it[...]and so nobody ends up doing it…" ***Pharmacist 9***

Pharmacy staff were aware of the assumptions made by other HCPs about their role and the perceived responsibility for ADR reporting:

"[...] generally I think there's that perception 'Oh it's not my work is not my work' that is bottom…healthcare workers[...]. I think healthcare workers we keep shifting the posts…mostly people think it is the duty of the pharmacist to do this if the patient has an adverse drug reaction in the ward[...]" ***Pharmacist 7***

4.5.11 Perceived Workload and Burnout

There was a perception of workload as a hindrance to reporting among HCPs. Reporting was considered a waste of time. They were therefore concerned with treating patients and solving their reaction problems rather than reporting.

"…we are overworked. We are always overwhelmed so they would rather, like I said earlier, on concentrate on solving the problem than reporting…you go to the ward and one nurse is taking care of about ten people…" ***Nurse 10***

Perceived workload led to HCPs passively reporting ADR verbally and mainly leaving the documentation process as the sole responsibility of the pharmacist. Participants were asked about the ADR reporting process in their hospital, and the quotes that follow report a common description by most HCPs:

"[…] the pharmacist on duty is on the ward, so we have a pharmacy in our ward so if something happens you just move, and you tell them. You just tell them you have given this drug to the patient and you observed that this is what happening [...]" ***Doctor 7***

"…because they think the workload already is too much and based on these things, they [HCPs] think it is an added-on responsibility. I think at times we all feel [...]…we are a part of that, we all feel like that. So, at times we are under pressure and then you need to take other time off to attend to these things. It's only maybe when you are less under pressure that is the time you can comfortably interact with the patient who comes with this…" ***Pharmacist 11***

4.5.12 Lack of Technical Expertise

Pharmacy staff are often the technical experts on medication-related issues. HCPs regularly required some level of support from a clinical pharmacist in identification and reporting of ADRs. HCPs reported that a major drawback affecting reporting, however, was the availability of a clinical pharmacist. Discussions with the director of pharmacy showed that there was a critical staff shortage among the pharmacy staff category in the study area, with the few available staff concentrated in regional hospitals.

Nurses expressed dissatisfaction that the lack of clinical pharmacists to augment a comprehensive health delivery was a challenge. It was perceived that the presence of a clinical pharmacist could help identify medication safety issues in patients and spot ADRs more accurately:

"…the pharmacist will be with you and some of the things… like the complaints the patient will be giving, the clinical pharmacist will draw your attention, that could be an adverse effect then they pick it on from there…but you go on rounds there is no clinical pharmacist the patients will be giving the complaints you will think…it's another symptom yes." ***Nurse 4***

4.5.13 Inter-personal Relations and Teamwork

The level of interaction, communication and association with fellow healthcare professionals was considered to affect the reporting. From observation and personal reflection, some HCPs reported that teams did not have congenial relationships, which affected their practice and performance. The following quote highlights a poor working relationship with the hospital

pharmacists, which makes nurses feel too uncomfortable to approach them with medication-related issues.

> *"[...] having a chat with him [pharmacist] like maybe a client will come, the medications you discuss with him [pharmacist] maybe you tell the patient to come after maybe seeing maybe some adverse effects and all that, to report back to you […] I have realised that that thing* (congenial relationship) *is no more […] I have realised that that is not there and that is something I complain every time. But you know when you are like the only person complaining, your other colleagues don't see it that way, it will be like [...]why are you alone complaining? [...]"* ***Nurse 5***

Linked to the previous point, improper change management within the healthcare facilities was reported to affect inter-personal relationships. Medical and pharmacy staff were frequently transferred due to staff shortages. This high turnover affected rapport and often required the staff to adjust to potentially different personalities and approaches of new pharmacists and doctors. Furthermore, it was perceived that this situation often resulted in communication barriers and inter-personal/professional conflicts as expressed in the following statement:

> *"[…] with the new pharmacist I cannot have any discussion with him. I cannot have any discussion with him because he is always acting defensive [...] I believe that you [the pharmacist] have gone to specialise in pharmacy, I have not, I have not done pharmacology […] I have to call a pharmacist outside to have a discussion with and what is my pharmacist doing?[...]"* ***Nurse 6***

Inter-professional conflict as a result of a poor inter-personal relationship was considered to cause two further problems: firstly, it impacted negatively on the role of the pharmacist in ensuring that updates or new information on ADR or medication safety-related issues were circulated; secondly, other HCPs felt less comfortable in approaching the pharmacist on medication safety issues such as ADRs.

Creation of a congenial work atmosphere in which HCPs could easily interact and discuss issues was observed as a determining factor for reporting ADRs. Some HCPs would only approach their fellow staff if they felt comfortable and welcomed. The demeanour of fellow HCPs therefore determined the level of interaction and possibly the amount of information that

could be retrieved in relation to ADR or other patient safety issues. Pharmacy staff explain the situation in the following quote:

> *"[...] it looks like there is that kind of segregation among even the same professionals [...] so if that team thing is there and somebody feels comfortable that 'oo I can easily walk to this professional to inquire about this' [...] 'this is what this patient is experiencing what do you think?' It looks like people all think that they should be in their corner and they shouldn't even let somebody know that, they even require an explanation about something[...]"* ***Pharmacist 7***

Poor interaction between HCPs therefore affected teamwork. Staff who therefore needed education or explanation of a procedure from a colleague often lost that opportunity due to poor inter-personal relationships. Communication barriers among inter/intra-professional categories was a limiting factor in reporting. Pharmacy staff were of the view that approaching fellow HCPs in a friendly way, having a contact person in charge of ADR, and continuous learning about ADR could develop a positive reporting culture.

4.5.14 Patient-related Factors

So far in this chapter, individual factors relating to the reporting of ADRs have been presented from the perspective of the different HCPs and key differences in terms of their knowledge, attitudes and practices in relation to ADR reporting. However, analysis further revealed a group of individuals of relevance to ADR reporting were patients. HCPs attributed the low reporting of ADRs to patients not volunteering reports to them, which was related to several key factors. A predominant feature recounted was a perception among HCPs that patients lacked understanding and awareness about what they experienced as a possible ADR. Linked to this was patients' perceived inability to remember sufficient details to be reported. This made it difficult to capture patient experiences in patient folders or ADR reports. Patients were also considered to be apprehensive about reporting ADR issues to HCPs. They were also often involved in self-medication and visited different hospitals refered to as "hospital shopping" (hospital hopping) for the same medical condition because dissatisfactory experience with one healthcare service. These factors were observed to be inter-related and dependent on each other. For example, apprehensive clients usually had low levels of knowledge and were likely to go hospital "shopping" because they were dissatisfied with the service received. The over-riding

concern was that unless an ADR was identified and reported at the bedside of a patient, patients themselves would typically not volunteer information to the HCP about a possible ADR:

> *"[…] unless the thing is happening in the hospital, in the ward, under the watch of the healthcare professional[...]that is the only time we report but we do advise the patients too[...] but hardly will a patient come and report any ADR…and it is only the one the healthcare providers see with their eyes[...]that is the one[in-patient] [...] but what they[patients] feel they will never say it ..."* ***Pharmacist 6***

Some participants went further and argued that responsibility actually lay primarily with the patient, and that it was for them to report the ADR:

> *"[…] I think if there will be a problem then…it should come from the patient first and foremost. It is the person who was taken the drug who is going to feel something…and if he attributes it to the drug, he will come and tell you the doctor that I took this drug and something happened. But if the patient feels those things are not attributed to the drug, he will not come to you; so far as you are concerned there's no drug reaction[...]"* ***Doctor 2***

4.5.15 Apprehensive Patients and Relatives

Patients and relatives were considered apprehensive about reporting in both Out-Patient Departments (OPDs) and In-Patient Departments (IPDs). They were hesitant about forwarding medication safety-related complaints, including ADRs, to be assessed and reported by HCPs. Reasons were found to be related to patients' inability to communicate their concerns, fears, long waiting times, poor inter-personal relationships and previous experience.

The official language for clerking patients was English and may require interpretation if clients did not understand, which was often the case according to the participants. This created a communication barrier, making patients uneasy and less confident. Patients' inability to communicate in English was as a result of poor educational outcomes, which affected their ability to communicate with the HCPs, resulting in apprehension. HCPs were also of the view that uneducated clients found difficulty in reading and understanding drug information sheets, and thus lacked knowledge of what to be cautious about.

> *"… the majority of our people [patients and relatives] are not educated so things happen to them and they don't know what to do. But if it is in the local language that, if you have any issues you should report back to the pharmacist who gave you the medication or if it is a pharmaceutical shop [community pharmacy] in the local dialect so that they understand…"* ***Pharmacist 7***

Submitting ADR reports through the HCP was recognised as being a significant challenge for patients. Some patients ended up not reporting because they were either hesitant to talk to an HCP or were unaware of how to directly report to the FDA. Only educated patients were confident and aware of how to contact the FDA directly.

> *"[...] you know usually if the information comes to the pharmacist first before it goes, sometimes there can be under-reporting but if there is a line that patients can report directly. And I think patients do, especially the educated ones, those that are not really educated they hardly do but the educated ones when they take medications and they have any issues they sometimes call FDA directly[...]"* ***Nurse 12 (FGD)***

Patients were also more assertive if they could read or understand their medication information. HCPs, however, suggested that patients may be afraid of reporting ADRs for fear of exposing the harm of pharmaceutical companies, which might put them at risk.

> *"…what I mean is that like you have gone to buy something [medication] and it is now giving him/her problems. She thinks that reporting it will have a negative effect from the source [pharmaceutical company]. As if he is going to do harm to the source [pharmaceutical company] …"* (***Investigator:*** *"…so they are protecting?") …yes they think that they will be endangering[...]the source [pharmaceutical company] …"* ***Pharmacist 3***

As noted above, low socioeconomic and educational attainment were felt by participants to affect their communication with HCPs and their ability to be assertive. Coupled with unfriendly HCP attitude, patients and relatives rarely discussed ADR issues with HCPs, especially prescribers. A pharmacist describes the situation in the following quote:

> *"[...] at times it's difficult for them [patients] to approach some health professionals. So, they might even come, you ask them a question, something that they should have even told the prescriber, they couldn't. It is something that has been happening. You ask them and it looks like they fear talking to them [prescribers] so maybe at times they will just sit, get their prescriptions written for them, then they bring the folder to you [pharmacist] at the pharmacy…"* ***Pharmacist 1***

Patients only opened up to HCPs with whom they felt comfortable discussing their conditions. Pharmacists who were able to develop an inter-personal relationship with patients also took time to analyse their prescriptions and gave them more attention, making sure their prescriptions were not giving them any problems. According to HCPs, patients open up when they are approached in a friendly manner without feeling rushed.

One scenario in which participants felt that patients and relatives were assertive or inclined to report medication-related issues was if they had previous experience of a different healthcare system where they reported, and action was taken. It was also challenging to retrieve information from patients' relatives where the actual patient was incapacitated and therefore unable to talk or describe their own condition. This was understandably more common in

paediatrics where mothers often had to describe reactions experienced by children to clinicians. Inability to communicate these events clearly often made carers apprehensive.

4.5.16 Surrogate/Carer Reporters

HCPs highlighted the challenging nature of reporting ADR from children, older adults and emergency cases. This group of patients may not be able to give information about their reaction other than through their carer. Furthermore, emergency situations often required information about any reactions to be requested from the carers, and these were often incomplete or lost. Some patients were also sometimes uncomfortable discussing their reactions in the presence of their carer.

> *"…when we get reactions…the majority of them (patients) when they come they are not the people talking […] it is their relatives who bring them so if you don't ask the relative to go out you want to talk to the clients yourself, some of these things (ADR) you're not be able to pick them up if they don't say…So I need time, we will prefer talking to the patient [...] if the person cannot communicate then it's understandable…"* ***Nurse 5***

Nurses expected mothers and carers to be able to identify ADRs and report to them. ADR information, however, was often lost due to the carer's inability to recognise that the cry of a child may be due to an ADR.

> *"[…] like quinine reactions and all that [...] for that one it takes time before you get to know if the mother doesn't tell you… because if they don't sleep overnight it's the mother who will be able to let you know…and you know some mothers, they are not very observant, they child may be doing that and the person will think that the child is just crying. so, they will not be able to tell they are due to drug reactions…"* ***Nurse 6***

Potential reports from carers were therefore often lost due to lack of vigilance and their inability to identify reactions to be reported to the HCP.

4.5.17 Hospital Hopping and Self-medication

Patient apprehension was also cited as being likely to contribute to what was termed 'hospital shopping', which also influenced ADR reporting negatively according to participants. Hospital shopping was described as the tendency for patients to move from one hospital to another in search of better medical care. Access to free healthcare through the national health insurance also facilitated hospital hopping and self-medication, because clients were able to get access to extra medicines by subverting the healthcare system. Poor healthcare system infrastructure made it challenging to identify patients who were receiving care or medicines from multiple facilities for the same condition at the same time. The following quotation capture why it is challenging to report ADRs from patients;

> *"Here actually because of the health insurance we have a lot of hospital shopping [...] patients move from hospital to hospital. So, you may take a drug here get a reaction but will not go back to that same hospital for them to activate the process. They feel the doctor didn't treat him or her well, so they move to a different hospital. And they may see it as part of the disease. So that could be another reason."* ***Doctor 2***

This behaviour also involved the use of herbal medicines at local pharmacy shops. HCPs cited this patient behaviour as an important barrier affecting ADR reporting, as it created uncertainties about how and what to report.

> *"[...] if you look at the way our clients take medications, apart from what we prescribe most of them have taken other drugs and others have taken local concoctions (herbal medicines), before they get here. So how sure are you that what you have given is what is causing the reaction and not the interaction between the two medications [...]"* ***Doctor 2***

Exacerbation of the issues was caused by lack of electronic records which made tracing patient details difficult as well. Self-medication was also recognised as a common practice among the general population, including in patients during a hospital admission. On admission, patients often brought along their medication without disclosing it to the HCPs. For fear of being told

off, patients also concealed all extra unprescribed medications from HCPs. Nurses blamed this practice on patients taking medical advice from family and friends.

> *"[...] Even sometimes as we are talking about those things [ADRs] it will even be surprising you see some patients they will come and lay on their bed and have their own medications[…] but because we have no right to search the fellow's bag, the fellow takes the drug while myself and my sister (colleague nurse) here we are running round, he or she (patient) will take the medicine again and take [self-medicate][…]yes the last time such things happened, we went round only for us to come back and the fellow is unstable. Not knowing that day she was having a particular drug […]"* ***Nurse 5***

In summary, HCP participants identified issues that could be related to them as individuals as well as to their other healthcare colleagues and also to patients. Many of these represented negatives and were viewed as factors that were present that tended to make ADR reporting less likely. In the next section, the focus shifts away from aspects of the individual, whether HCP or patient, and to more system- and process-related aspects.

4.6 IMPROVING ADR REPORTING

Introduction

This section summarises a further key theme related to the suggested ways HCPs thought ADR reporting could be improved. Key aspects related to HCPs views about proposed reforms in governance and policy, and motivation from stakeholders for improving reporting. With reference to motivation, internal and external strategies were identified, including educational training for both HCPs and patients, which was seen as key. Further analysis from FGD and IDI highlighted important aspects of these findings, where it was widely held that education and empowering the pharmacy staff to report or monitor ADRs could improve reporting. Several subthemes emerged as a result of the analysis, of which the key findings will be expounded on here.

4.6.1 Education and Training Governance

Governance and policy on training involving major stakeholders was suggested by HCPs as strategic to improving HCPs. It was also proposed that pharmacovigilance and drug related issues should feature in annual reviews at the district, regional and national levels. Furthermore, the idea of engaging professional bodies such as the Nursing and Midwifery Council or Medical and Dental Council, to develop policies, which accept continuous professional development points (CDP) from attendance at medication safety workshops, could improve reporting. One doctor used the analogy of compulsory ethics training required of doctors each year to argue that a similar training on pharmacovigilance and ADR reporting should be instituted:

> *"[..] So the FDA can collaborate with other regulatory agencies like the Nursing and Midwifery Council or Medical and Dental Council to make it a compulsory training need, so that every year healthcare professionals will be required to update their knowledge in this area. If they do it more it will encourage people to report [...]"* ***Doctor 4***

As noted earlier in the chapter, ADR reports were often lost to undocumented incidents. To improve the reporting and documentation, it was proposed that verbal reporting by hospitals be encouraged in addition to written reports. As one participant notes, this also needed to be

embedded in practice and there was a suggestion to *"make ADR reporting part of the nursing care plan"* **Nurse 11**. Furthermore, another nurse noted that this would be analogous to the already existing verbal reporting for communicable diseases:

> *".....Ok so I think if we institute oral reporting or verbal reporting....so that the one you are reporting to just like how we do disease [...]Communicable disease reporting....you just call the disease control officer and say I think I have a case....so the person comes to do the assessment and do his or her documentation....so you are the one reporting but normally you don't document anything....so it increases their reporting rates...."* ***Nurse 12***

Unavailability of forms at the ward level was classified as a governance issue because of the external power play in ensuring that the forms were constantly available. The pharmacy units were the most likely places to find ADR forms. They could also be found sometimes in doctors' and prescribers' consulting rooms. It was observed that some HCPs, when asked to show a sample of the reporting form, often took a considerable amount to time to find one in the above places. Some nurses therefore advocated that management should make forms available, or to make it part of the patient folder system. For example, *"[...] there should be forms attached to the patient's folder."* ***Nurse 1 (FGD)***. These suggestions however required a change in policy and governance from either external agencies or internal hospital structures. Suggestions such as the following would be easier to implement internally by modifying hospital governance and protocols.

> *"[...] they should be in the ward; the wards too should have them. The forms should be common just like anytime you want it you can find it [...] so if they give the forms to the hospitals actually, they will share it to the wards. So that should in case of anything you just report [...]"* ***Nurse 5 (FGD)***.

Attaching forms to patient folders, training, and accepting CPD points however would require an external policy change and would usually take time to implement, contingent on resources.

4.6.2 Monitoring

At the time of the research, no hospital had an ADR or incidence committee in place for monitoring and investigation of medication safety related cases. The majority of healthcare facilities also lacked a designated or contact person for ADR reporting. Only one facility had a drug safety unit and a contact person. All other facilities relied on the pharmacist as a default contact person for monitoring ADR. Monitoring was however low due to lack of interest, the absence of a clinical pharmacist, or lack of contact persons at localised units and departments. Some nurses were of the opinion that regular monitoring of prescriptions at the department and wards level by a pharmacist could be of benefit in improving reporting.

> *"[…] you know umm pertaining to my facility (hospital), we especially lack a clinical pharmacist […] yeah I think erm we mostly have interactions (ADR) with drugs mostly from the in-patients […] I think some time ago they started something (monitoring), they used to come around and check on medications and even dosages…because sometimes if you overdose that's when all these things come to play. So, I think if they come round also like the doctors […]"* ***Nurse 11***

4.6.3 Motivation

Unmet expectation of reward to an HCP as a result of reporting an ADR influenced their action negatively. Compensation from stakeholders was proposed as a way of improving reporting. Open-ended analysis showed HCPs were in favour of general motivation, reward and compensations. The enthusiasm with which HCPs approached ADR reporting and related issues was usually inspired by self-motivation, external motivation (FDA or MOH) or financial motivation.

4.6.4 Self-motivation

At the internal level, individual HCPs were self-motivated by their love of patient safety and were happy to report for non-monetary or financial gains. For example, the following pharmacist thinks it is the duty of HCPs to ensure patient safety.

> *"[…] so for me I think that once you are a healthcare professional, you should help the system to ensure that there is quality….so the motivation should be that you are helping the system to ensure that there is quality of care as a caregiver 'cause your duty is to ensure that the patient is safe, so the motivation is for you to push and ensure that systems are better […]"* ***Pharmacist 4***

Some self-motivated HCPs felt it was unprofessional to take any money for reporting an ADR. They felt it was their duty to report if the necessary resources were made available, as captured in the following:

> *"[…] like they're saying here I don't need to be paid….at the end of the day if they say that okay this is the money for reporting adverse drug reaction then I shouldn't have administered drug as well….so if things are available, I don't think the nurses are lazy. they will definitely do the work….."* ***Nurse6 (FGD)***

Some participants were self-motivated because they saw reporting as a learning process, and they participated in reporting because they felt they could learn from feedback as expressed by a pharmacist:

> *"…so, when you do it in fact it's even [...]you learn more. Because there may be something new that you do not know. It's something that one should all the time do. Not for reward or anything. Yeah… we should even do it the more you do it the more you know. You understand you learn new things….so don't sit down and say 'oo if they don't pay me'…."* ***Pharmacist 1***

4.6.5 Financial Motivation

It was common for participants to be motivated by non-monetary gains. Among the few who wanted financial rewards for reporting ADR, it was noted that most of them were nurses. Excerpts from FGD of nurses articulates a nurse's view as follows:

> *"…listen to this one [...]that she wants motivation (teasing)(Investigator: What kind of motivation?), [...] if possible financial….they should give you an envelope (money) after you have reported something and maybe congratulate you maybe a plaque…."* ***Nurse 3***

The choice of financial motivation was re-emphasised by a few nurses, as for example in the following extract:

> *"…So if it is agreed that the number of forms you fill per the month or year, maybe something should be done, some small allowance [monetary] should be given to such group of people, people[HCPs] they will get interested in and report ADRs[...]* ***Nurse 1***

When probed further to enquire how much they would expect as financial compensation for ADR reports submitted, another nurse commented that;

> *"…as a token for whether you have reported one or three you should be given at least 50 cedi [£8] maybe first quarter, this number of people were able to report on ADR, it will be in me [motivated] that I want to track drug reactions…."* ***Nurse 3 (FGD)***

4.6.6 External Motivation

Healthcare professionals were also motivated to report if they had a supportive external working environment which encouraged reporting. Some nurses were of the view that presentation to a reporter by FDA or MOH with a recognition plaque was a good incentive to keep HCPs reporting. This view was as a result of a similar gesture by the FDA, as quoted in the following statement:

"[…] like how they (FDA) did …. that guy (HCP) was going around the wards with his this thing [referring to a nurse who was acknowledged by FDA for reporting] you understand …the motivation is there […]" ***Nurse 2***

At the external level, motivation was derived from workshops organised by stakeholders such as the FDA and MOH which train HCPs and acknowledge them for reporting. This resulted in a positive attitude, as captured in the concluding remarks of this interview:

"…At least opportunities to attend workshops is something we need. It can motivate us for example if you want an upgrade or further study, some of these little things when you add them to your CV makes it rich. At least they should have certain things like that to make us happy…." ***Nurse 2***

This was confirmed by other pharmacy staff and medical staff, and the following doctor suggested the need for citations;

"… I think it's good, if they can even add a citation to the person and something for the facility it's good…." ***Doctor 7***

Overall, even though HCPs were generally self-motivated, some nurses were in favour of the introduction of financial or monetary incentives as a source of motivation.

4.6.7 Reminders and Feedback

Correspondences with the FDA after submitting ADR reports, served as reminders and motivation for HCPs to report more. Feedback from FDA or pharmaceutical companies to individuals and hospitals was suggested to positively impact reporting behaviour.

Previous experience of the absence of feedback after sending reports affected HCP attitude. An effective feedback system was therefore seen as necessary for improving ADR reporting. Some participants had positive feedback from the FDA coupled with favourable internal organisational elements and this led to submission of reports.

> *"…I think it is the time. The time in which you get feedback from my experience is motivational. I got into it because of just that. I have ever reported a case and the way they (FDA) called me and when they called, they told me they were in the process of investigating and gave me feedback when they finished…. I think that was just enough motivation for me to want to do it, but forms were always running out and I was out of town (remote healthcare facility) so once a while they will send it or I come to town for them. Yeah so lack of feedback can be an issue[...]I don't know now but it used to be very prompt…."* ***Doctor 5***

Feedback from the FDA was used to educate HCPs, using an experiential or problem-based learning approach where incidence of safety was used as feedback to train HCPs.

> *"…Yes, what he is saying is actually true, because when they (FDA) came for the training the kind of feedback that they brought. They brought the feedback from different facilities. They brought the feedback to us, so they told us that Lisinopril was given to somebody and a person appeared like a person who had burns. So that is what they were telling us. So, they were telling us that if you couldn't report by filling the form, and submitting it to them they will also report to a different facility. Though they will bring us the feedback they will also give evidence to other facilities…"* ***Nurse 19 (FGD)***

Poor feedback experience however deterred some HCPs from reporting ADRs to relevant authorities.

> *"…. I think lack of feedback will be this thing[...] because I never had any feedback. and the responsibility factor…. at least if I should report and you tell me that 'oooo you are doing well' [...]are you getting me? [...]. Keep on bringing them. I will be happy but when I report [...] but after reporting, that ends it. Yeah I know I am working for it, I am earning my salary but at least just that[...] pat my back and 'say ooo you are doing well oo' so next time I will, I will do it more, so motivation [...]. Lack of feedback is important and lack of motivation yes but that is what I said motivation is just about[...]. It's not necessarily financial motivation (Investigator: the feedback will[...]) the feedback will do. 'We have taken note of your report and we will act on it' [….]"* ***Nurse 9***

HCP therefore suggested that general motivation and feedback had the potential to improve ADR reporting considerably.

4.6.8 Education and Training

The FDA was the main provider of education and training for HCPs. The FDA however tailored most of their training to pharmacists. In-service training which was cross-disciplinary often invited senior staffs and administrators to the neglect of junior staff who were most likely to encounter ADRs. HCPs therefore requested more training for all staff to increase their knowledge.

> *"[...]so if they are properly trained or educated on ….that look it's not only for pharmacist that can report on this then they will build on lack of knowledge…I always keep on saying if you really want the people (other HCPs) to do the job, then they need to know because if they say report on this, how do I report on it if I don't know it. So everything it's about [...] let the people know what it is the importance of adverse drug reactions [...]"* ***Pharmacist 9***

HCPs were also of the view that the FDA was seen as an external organisation and their training should be integrated with existing MOH/GHS training.

> *"...so if there should be a proper education erm I would recommend that if truly the Ministry of Health or Ghana Health Service is really serious about this thing there should be proper training on this particular thing in this hospital. I think we have to do it every month. If we do it every month... awareness, we should create the awareness about ADR..."* ***Pharmacist 3***

4.6.9 Patient Education

Even though the FDA was campaigning in healthcare facilities for patients to report ADR, especially via text messaging, uptake was very low. Education of the public on the importance of reporting especially in local dialect was therefore suggested by some HCPs.

> *"...I think FDA should continue to do the sensitization, especially adverts in local dialect…. that one is very necessary. But they will tell you they don't have money 'cause when they do the adverts, they have to pay…. so, the sensitization should be there to patients and caregivers; that if you take any medications and you have any issues report to FDA…. so, there should be a constant reminder, because that is key for the success of pharmacovigilance in our healthcare system…"* ***Pharmacist 2***

The low education levels and poor socioeconomic status affected patient reading and writing skills. Radio broadcasts in the local language was therefore suggested as an important way of improving reporting.

> *[...] In fact there should be umm like radio broadcast, programmes they will be educating the people small small [...] I think continuously sensitising the public will help. Because if it doesn't help the patient himself or herself, it's going to help the public. because we will finally get to know either this drug is dangerous or it's not potent so that we avoid it or improve on it[...]* ***Physician Assistant 8***

4.6.10 Summary of Qualitative Findings

Overall, these findings showed that HCPs recognised ADR reporting as an important activity for patient safety in clinical practice. There were significant variations in experiences and beliefs about ADR and associated reporting based on professional roles with varying knowledge, power and responsibility aspects emerging. The role of the pharmacist was viewed as significant in the ADR reporting process, but current practice and beliefs appeared to limit the degree to which these could comprehensively enhance ADR reporting. Negative attitudes to reporting as a result of multiple threats from internal, external, patient and HCP related factors appeared to strongly affect reporting. HCPs suggested three key areas to improve reporting through changes in governance and policy, monitoring and motivation. Interventions targeted at improving reporting may be required for each of the cardinal factors identified that influence reporting.

In terms of strategies for improving reporting, the concluding section of the chapter shows what HCPs considered imperative ways to improve ADR reporting. Motivation was a key determinant for improving reporting, and HCPs were either self-motivated or depended on external initiatives such has financial rewards, reminders, education and training. HCPs also suggested improvements in governance, policy, reminders, and regulations on education. The next chapter (quantitative) will explore further suggestions for improving reporting, alongside other factors influencing reporting such as knowledge, attitude and practice of reporting ADRs.

CHAPTER FIVE

QUANTITATIVE SURVEY RESULTS

5.0 Introduction

This second chapter of findings reports the emerging data based on analysis of the surveys of HCPs at four hospital sites. The first sections report descriptively the survey responses based on the background characteristics of the sampled population. Frequencies and percentages are used to summarise the characteristics of the sample in tables. The subsequent sections of this chapter will firstly focus on responses relating to factors affecting ADR reporting, such as knowledge, reporting practices and attitudes. Finally, suggested opinions for improving ADR reporting will be reported on. Pearson Chi Square tests were run to test difference between categorical variables to show how likely the results were due to chance. Some variable cells were aggregated in order not to invalidate the Chi Square test because of low cell counts. Cells which were invalidated by low sample size were excluded from Chi Square analysis. The main research questions explored were:

1) What self-reported factors are related to ADR reporting among Ghanaian HCPs?
   - Are HCPs aware and knowledgeable about reporting ADRs?
   - What are the attitudes of HCPs towards reporting?
   - What are the practices and perception of HCPs' role in reporting ADR?

2) What is the association between the factors affecting ADR reporting and HCPs?
   - Were their knowledge, attitudes and practices influenced by any background characteristics, such as training, internet access, department, hospital, HCP category, number of patients seen per day, level of experience or education?

3) What methods can be suggested to improve ADR reporting?

5.1 Sociodemographic Characteristics

Out of 450 survey questionnaires distributed, 386 were completed, representing a response rate of 86%. Of these, 70% (n=295) were nursing staff, 13% (n=48) were medical staff and 9% (n=34) pharmacy staff (Table 13). Even though pharmacy staff made up the smallest number of staff in the sample, they represented more than half of the pharmacy staff population in the selected hospitals. For example, out of the population of 62 pharmacy staff in the four study hospitals, the response received represents half (55%, n=34) of the overall sample of pharmacy staff compared to the total representation of doctors (21%, n=286) and nurses (17%, n=1,716). Just over half were aged between 20 to 30 years and fewer than half (48%) were female. The majority (43%, n=164) of participants had a diploma level qualification and at least (62%, n=235) five years' experience. Also, 63% (n=232) of HCPs reported attending to no more than 20 patients a day, and the most commonly reported department was surgery with 24% (n=89), followed by general medicine (15%, n=59), and obstetrics and gynaecology (13%, n=48). In terms of the hospital facilities investigated, Tamale Teaching Hospital (TTH) was the largest representation (61%, n=236) and Seventh Day Adventist Hospital (SDA) the smallest (8%, n=29). Tamale Central Hospital (TCH) and Tamale West Hospital (TWH) had similar proportions, representing 15.9% and 14.3% of HCPs respectively. Comparative representation of nurses within each healthcare facility showed more nurses in the SDA sample (88%) and the least from TTH (73%). There was, however, more representation of medical and pharmacy staff in TTH than the rest of the hospitals (Table 13).

Table 13: Sociodemographic characteristics of the sample (n=386)

Main group	Category	n (%)	Total
Age (years)	20-30	201 (53)	381
	31-40	148 (39)	
	41+	32 (8)	
Gender	Male	199 (52)	386
	Female	187 (48)	
Healthcare professional category	Nursing staff	295 (78)	377
	Medical staff	48 (13)	
	Pharmacy staff	34 (9)	
Level of education	Postgraduate	22 (6)	385
	Bachelors	120 (31)	
	Diploma	164 (43)	
	Certificate	44 (11)	
	MBChB	35 (9)	
Years of experience	≤5years	235 (62)	370
	6-10 years	100 (26)	
	≥11years	44 (12)	
Patients per day	≤20	232 (63)	367
	21-40	102 (28)	
	≥41	33 (9)	
Hospital	Tamale Central Hospital (TCH)	63 (16)	386
	Tamale West Hospital (TWH)	58 (15)	
	Seventh Day Adventist Hospital (SDAH)	29 (8)	
	Tamale Teaching Hospital	236 (61)	
Department	Psychiatry	11 (3)	370
	General medicine	59 (16)	
	Surgery	89 (24)	
	Obstetrics and gynaecology	48 (13)	
	Out-patient Department	39 (10)	
	Paediatrics	47 (12)	
	Accident and Emergency	22 (6)	
	Public health	14 (4)	
	Pharmacy	31 (8)	
	Intensive Care Unit	10 (3)	

5.2 Knowledge of ADR Reporting

Knowledge of HCPs was assessed based on five questions, which were designed to determine the level of knowledge and awareness about the ADR reporting process in their healthcare system. Firstly, their general awareness was ascertained, followed by specific knowledge-based questions to support their first response. Participants were required to select the correct or expected response from a multiple-choice question on ADR.

The results show that HCP knowledge was generally low across all the five questions asked, with an average awareness of 19% slightly skewed in favour of pharmacy staff (35.4%) who showed better knowledge compared to nursing (16%) and medical staff (21%). Facts about reporting showed that more than a quarter (32%) of HCPs' responses showed they were aware of the national PV centre. Comparative levels of knowledge showed that a majority of 74% of pharmacy staff were more likely to be aware of the national PV system than medical (48%, n=23) and nursing staff (24%, n=71) categories ($P<0.05$) (Table 14). PV awareness was statistically significant for HCPs between 31–40 years of age (X_2=18.332, P=0.000), males (X_2=4.691, P=0.030) and HCPs who saw at least 20 patients per day (X_2=26.395, P=0.000) (Appendix S).

Only 5% percent reported they knew the short code (4015) to send an ADR report via a mobile phone Short Messaging System (SMS) to the FDA when they were asked about this. Most correct responses about this were from pharmacy staff (26.5%, n=9), compared to medical (4%, n=2) and nursing staff (2.7%, n=8) categories (X_2=35.554, P=0.000). This was a statistically significant difference for HCPs who saw at least 20 patients per day (X_2=8.722, P=0.013) (Table 14).

Table 14: Comparative level of knowledge among HCPs on selected ADR topics

KNOWLEDGE QUESTIONS		Nursing staff (%)	Medical staff (%)	Pharmacy staff (%)	Total (%)	Pearson Chi χ^2
Aware of national PV centre?	Aware	71 (19)	23 (6)	25 (7)	119 (32)	X_2=40.831 df=2 P=0.000
	Not aware	222 (59)	25 (7)	9 (2)	256 (68)	
SMS short code for reporting ADR	Correct response	8 (2.1)	2 (0.5)	9 (2.4)	19 (5)	X_2=35.554 df=2 P=0.000
	Incorrect response	284 (76)	45 (12)	25 (7)	354 (95)	
What basic info is required on ADR forms	Correct response	86 (54)	18 (5.0)	22 (6)	126 (35)	X_2=15.833 df=2 P=0.000
	Incorrect response	195 (24)	29 (8.0)	12 (3)	236 (65)	
All ADRs should be reported within how many days?	Correct response	2 (1)	0 (0.0)	0 (0.0)	2 (1)	NA
	Incorrect response	286 (78)	48 (13)	33 (9)	367 (99)	
Serious ADRs should be reported within how many days?	Correct response	50 (14)	13 (4)	11 (3)	74 (20)	X_2= 2.648 df=2 P=0.266
	Incorrect response	239 (65)	35 (10)	22 (6)	296 (80)	
Average correct responses within professional category (%)		217 (16)	56 (21)	67 (35)	340 (19)	

Thirty-five per cent (n=126) of respondents demonstrated good knowledge on what basic information was required on the ADR form (i.e. patient details, suspected drug, suspected reaction and reporter details) by selecting the right response from three others. Nearly two thirds (65%, n=22) of pharmacy staff demonstrated correct responses compared to responses from medical staff (38%, n=18) and nursing staff (31%, n=86) (X_2=15.833, P=0.000). Basic demographics showed statistical significance difference for years of practice, where more than half of those who correctly responded that had practised for at least five years (X_2=10.224, P=0.037) (Appendix Q).

The knowledge domain that HCPs were least aware of was the recommended 28 working days to report any type of ADR observed to authorities, as required by the FDA. Additionally, the regulation on submitting a serious ADR report within seven working days following an

encounter was known by only 20% of HCPs (P<0.05). Within professional staff categories, only 13.5% (n=50) of nurses indicated correct responses compared to pharmacy (33%, n=11) and medical staff (27%, n=13), and the difference was statistically significant. There was a statistical significance when comparing demographic variables such as age, patients seen per day and years of practice. This was statistically significant for HCPs between 31–40 years (X_2=14.732, P=0.001), seeing between 21 to 40 patients per day (X_2=15.320, P=0.000) and who had practised for at least five years (X_2=24.181, P=0.000) (Appendix S).

In summary, levels of awareness on key aspects of ADR reporting were low and varied from an almost complete lack of knowledge (of the time limit to report an ADR) to just over one third knowing the basic information to report and also being aware of a national PV centre. Pharmacy staff were more likely to be aware than the other two HCP groups, and nurses were less likely to be knowledgeable about ADR reporting.

5.3 ADR Reporting Practices

As well as exploring knowledge of ADR reporting, a key aim was to understand the scale of ADRs observed and associated reporting, as reported by HCPs in their clinical practice. Three key aspects were explored in the survey: self-reported frequency of observing an ADR, frequency of subsequently reporting an ADR, and the frequency of using an ADR reporting form. These are now considered in turn and are summarised in Figure 18, and, as will be shown, revealed wide variation in the self-reported incidence overall and also between HCPs.

5.4 Observing ADRs

It was common that HCPs had not witnessed an ADR in practice. Overall, aggregated data showed that fewer than half (43%, n=158) of participants had observed an ADR at least once. Nineteen per cent indicated that they had never observed an ADR, and 38% could not recall observing one (Table 15). There was a statistically significant difference comparing HCPs who observed ADRs and worked in a general medicine department (P<0.05) and those who saw at most 20 patients per day (P<0.05). HCPs who reported having observed an ADR indicated they reported it once a year (13.2%, n=49), which was the most frequently reported period (Table 15). Daily observations (10%, n=38) and weekly (2%, n=9) observations were infrequent, especially among medical and pharmacy staff. Aggregating the data, HCPs were more likely to have observed an ADR at least monthly (19%, n=70), compared to those who witnessed an

ADR at least every six months (11%, n=39) or once a year (13%). Fifty-four HCPs (14%) who observed ADRs indicated that they had also reported an ADR, and 34 (9%) of them completed an ADR form. Only 5% (18) of HCPs stated that they had observed, reported and completed a form at the same time.

There were more pharmacy staff (56%) observing ADRs than nursing (41%) and medical (43%) staff. Within professional categories, the majority of medical (15%) and nursing (14%) staff were more likely to observe an ADR once a year than during any other time period. The most frequent period ADRs were observed by pharmacy staff was every three months (18%). There were more pharmacy staff who observed ADRs every three months than nursing (5%) and medical (11%) staff. Furthermore, nursing (11.7%) and pharmacy (12%) staff were more inclined to observe ADRs daily compared to medical staff (0%). Further aggregation showed a greater percentage of pharmacy staff (n=9, 27%) had observed ADRs within a three- to six-month period compared to medical (n=6, 13%) and nursing staff (n=24, 8%).

Table 15: Observation of ADRs among HCPs

Paraphrased Questions (See Appendix N for full version)		**Number of respondents**			**TOTAL**
		Nursing staff N (%)	**Medical staff N (%)**	**Pharmacy staff N (%)**	**Total within HCP N (%)**
Ever observed an ADR?	Yes	119 (41)	20 (43)	19(56)	158(43)
	No	51 (18)	15 (32)	6 (18)	72 (19)
	Not sure	120 (41)	12 (26)	9 (27)	141 (38)
How often do you observe ADR?	Daily	34(12)	0(0)	4(12)	38 (10)
	Weekly	8(3)	1(2)	0(0)	9(2)
	Monthly	13(5)	6(13)	4(12)	23(6)
	Every 3 months	15(5)	5(11)	6(18)	26 (7)
	Every 6 months	9(3)	1(2)	3(4)	13(4)
	once a year	40(14)	7(15)	2(6)	49(13)
	Never	51(18)	15(32)	6(18)	72(19)
	Not sure	120(41)	12(26)	9(26)	**141(38)**

5.5 Reporting and Documentation

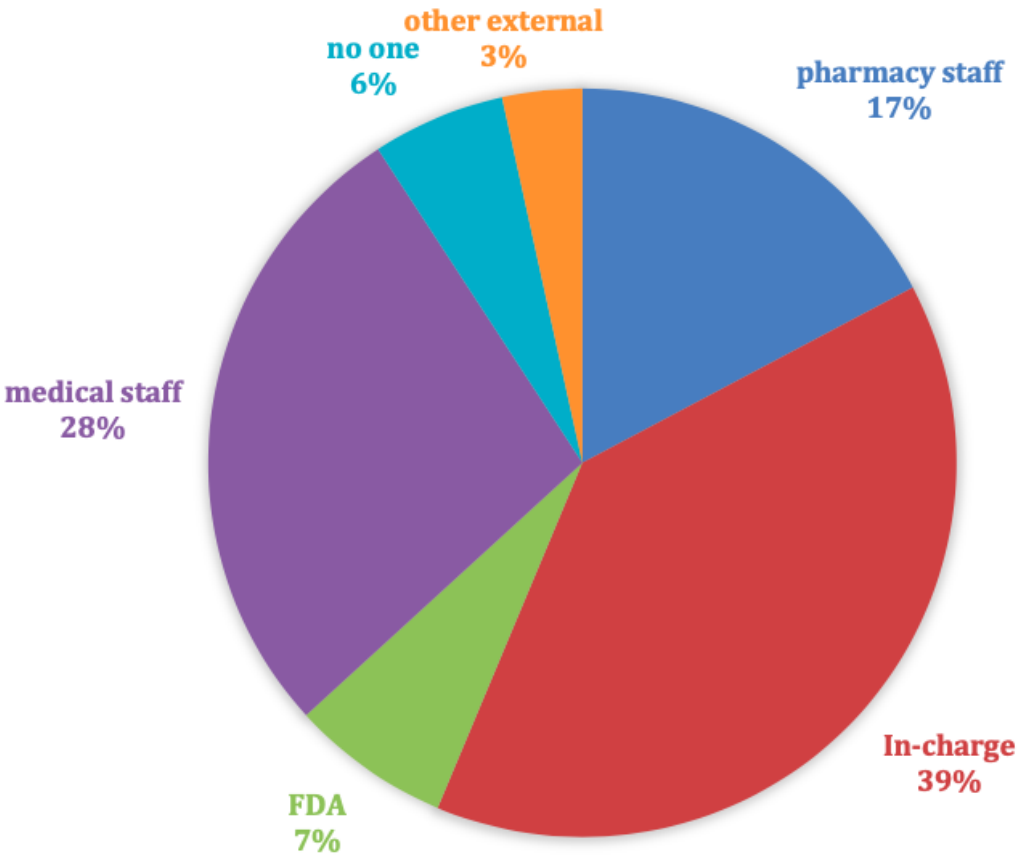
Even though 43% (162/379) of participants indicated to have observed an ADR, only a quarter (24.6%) of HCPs reported (61/250), and only 14% (38/265) completed a form for it (Figure 18). In practice, among HCPs who indicated to have ever reported, medical staff were least (9%) likely to have ever reported an ADR, compared to nursing (24%, n=47) and pharmacy staff (52%, n=11) (X_2=14.090, P=0.000). The most common frequency with which HCPs sent

reports was every six months (5%). Aggregating the frequency of reporting ADRs, 38% of HCPs indicated that they reported ADRs at least once a year. Further analysis within HCP categories showed pharmacy staff reported ADRs regularly compared to other HCPs (Table 16). A statistically significant result showed that more than half (55%) of pharmacy staff were more likely to report at least once a year compared to nursing (38%) and medical staff (22%) ($p>0.005$). Open-ended responses concerning to whom HCPs reported an ADR, indicated that the 'in-charge' or the supervisor (39%) on duty was the person HCPs commonly reported incidents to first hand, followed by medical staff (28%) and pharmacy staff (17%) (Figure 19). Some of the 'in-charges' at the departmental level were medical staff, but mostly nurses.

Table 16: Reporting and documentation practices among HCPs

Paraphrased Questions (See Appendix N for full version)		**Number of respondents**			**TOTAL**
		Nursing staff N (%)	**Medical staff N (%)**	**Pharmacy staff N (%)**	**Total within HCP N (%)**
Have you ever reported an ADR?	Yes	46 (23)	2 (9)	12 (55)	60 (25)
	No	154 (77)	21 (91)	10 (46)	**185 (76)**
How often do you report ADR?	Daily	29 (12)	0 (0.0)	3 (10)	32 (10)
	Weekly	11 (5)	1 (3)	1 (3)	13 (4)
	Monthly	8 (3)	2 (5)	3 (10)	13 (4)
	Every 3 months	9 (4)	1 (3)	2 (7)	12 (4)
	Every 6 months	7 (3)	2 (5)	7 (24)	16 (5)
	Once a year	29 (12)	3 (8)	0 (0)	32 (10)
	Never	51 (21)	20 (50)	7 (24)	78 (25)
	Not sure	103 (42)	11 (28)	6 (21)	**120 (38)**
How many ADRs reported in this year?	0	154 (77)	21 (91)	10 (46)	**185 (76)**
	1-5	32 (16)	2 (9)	11 (50)	45 (18)
	≥6	14 (7)	0 (0)	1 (5)	15 (6)
Did you complete a form?	Yes	24 (11)	2 (8)	10 (44)	36 (14)
	No	158 (75)	20 (77)	8 (4)	**186 (72)**

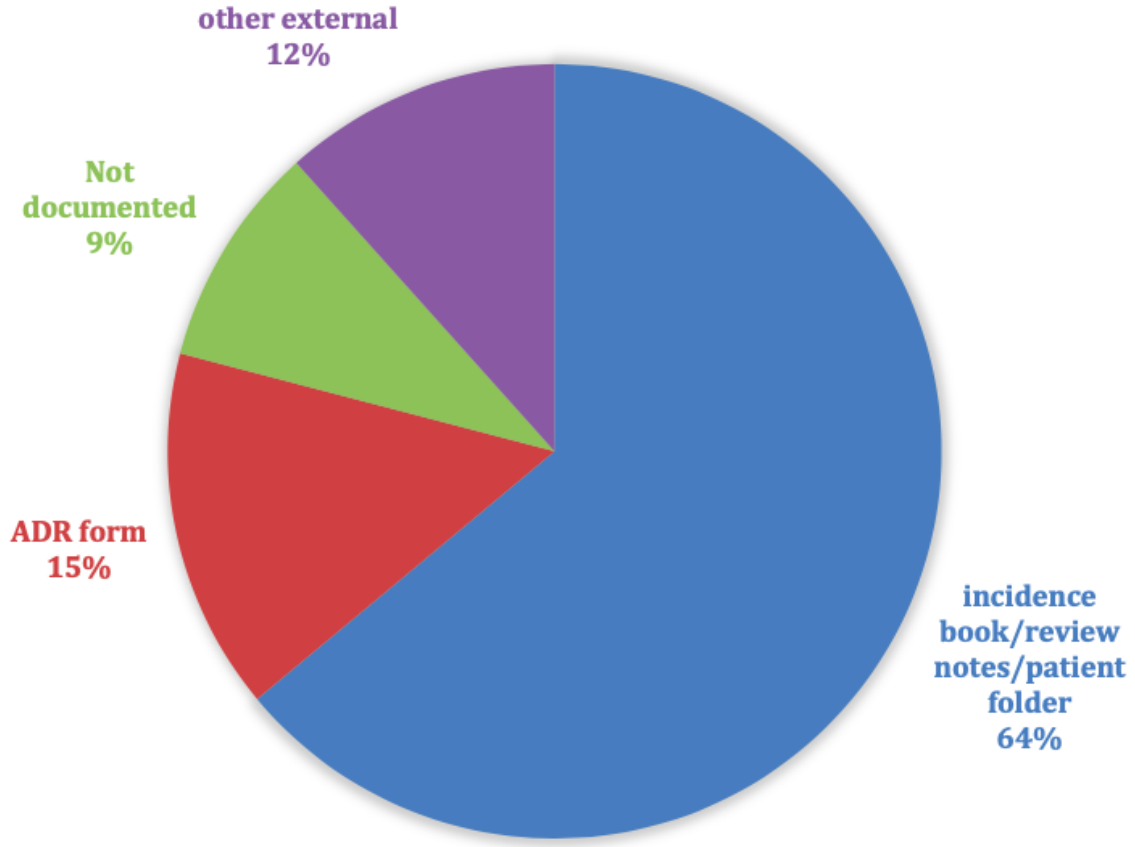
Figure 19: Recipients of ADR reports



5.6 Completing a Form

HCPs who completed ADR forms were mainly pharmacy staff (43%, n=10), followed by nursing (11%, n=24) and medical staff (7%, n=2). In addition to using the required ADR (yellow) forms, documentation of ADR information through alternative channels, such as incidence books, review notes and patient folders, was common as was indicated by 64% of HCPs (Figure 20).

Figure 20: Where ADRs were documented



Sixty-nine per cent of nurses and 67% of medical staff used different reporting channels compared to pharmacy staff (14%) (X_2=12.921, P=0.044). Patients form an important source of information – approximately half (50.3%) of HCPs responded affirmatively that patients always reported ADRs, and more than half of medical (51.1%) and 53% of nursing staff responses were affirmative of this, compared to pharmacy staff (27%) (p>0.005). The majority of HCPs (62% n=229) specified that patient education was part of their clinical practice, but there was no statistically significant difference in HCP responses.

Self-reported responses on number of ADRs reported in the year showed that 18.4% (n=45) recounted between one to five ADR reports, while the majority (76%) submitted no report to an authority. Only a small fraction of HCPs (6.1%, n=15) reported six or more ADRs, of which the majority were nurses (93%, n=14). Among those who reported, only 13.9% (n=36) completed an ADR form. It was noted that 11% of HCPs who indicated they reported did this

by notifying their in-charge (superior) (40%), pharmacy staff (17%) or medical staff (27%). Pharmacy staff were more likely to report an ADR to the FDA (46%), nursing staff were more likely to report to an in-charge (33%) or a member of medical staff (44%), and medical staff were also most likely to report to pharmacy staff. A minority group of nurses (6%) were more likely not to report ADRs and took no further action (p>0.005).

5.7 Contact Person and Availability of Forms

ADR reporting forms were generally unavailable. Only 95 (28%) HCPs indicated the forms were available in their departments or units. Within HCP categories, 77% of pharmacy staff were more likely to indicate that the forms were available, compared to medical (16%) and nursing staff (24%) [x_2=45.415, df=4, p=0.000] (Table 17). Among the four healthcare facilities investigated, only one healthcare facility (TTH) had a designated department and contact person for PV and medication safety. At other facilities, pharmacy staff took on the responsibility for ADR reporting activities. The overall majority (81%, n=305) of HCPs indicated they were either not sure or did not have an institutional contact person at their place of work. Among the 19% who indicated that they had a contact person, nearly half of the pharmacy staff (48%) were more likely to be aware of this compared to nursing (16%) and medical staff (13%) [X_2=24.612, df=4, P=0.0000]. Even though TTH had an institutional contact person and a department ensuring the distribution of forms and coordination of ADR-related activities, only 37 (14%) respondents from that facility indicated they had one. Within HCP categories, medical staff (6%) were least likely to be aware of the presence of a contact person in TTH compared to nursing (10%) and pharmacy staff (X_2=31.650, df=4, P=0.0000).

Table 17: Reporting personnel and form availability in healthcare facility

Paraphrased Questions (See Appendix N for full version)		**Number of respondents**			**TOTAL**	Pearson Chi Value (*99%CI*)
		Nursing staff N (%)	**Medical staff N (%)**	**Pharmacy staff N (%)**	**Total within HCP N (%)**	
Do you have an institutional contact person?	Yes	47 (16)	6 (13)	17 (50)	70 (19)	*X^2=24.612* df=4 P=0.0000* (0.000-0.000)
	No	93 (32)	15 (31)	6 (18)	114 (30)	
	Don't know	153 (52)	27 (56)	11 (32)	**191 (51)**	
Are forms available in your facility?	Yes	65 (24)	7 (16)	23 (77)	95 (28)	*X^2*=45.415 df=4 P=0.000* (0.000-0.000)
	No	140 (52)	19 (43)	5 (17)	**164 (48)**	
	Not sure	66 (24)	18 (41)	2 (7)	86 (25)	

5.8 Training and Feedback

Training on PV and ADR reporting is a routine practice by the FDA and stakeholders to update HCPs' knowledge base on medication safety practices. Participants were therefore questioned about training and feedback from stakeholders.

Only 23% of HCPs recalled having training on PV and ADR reporting. Pharmacy staff were more likely (65%, n=22) to have received training compared to nursing (16%, n=47) and medical staff (31%, n=15) (P<0.005) (Table 18). Even though other HCPs perceived pharmacy staff as knowledgeable and given reporting dominance, levels of training were low. Pharmacy staff were, however, more likely to have had recent training, e.g. three months ago, compared to medical and nursing staff, who indicated they had training up to six months ago. More than half of participants could not remember the last training they had on PV and ADR reporting. Sixty-nine per cent of HCPs, however, felt they were more likely to report after the training, while the rest either indicated '*no'* or were '*not sure'.* Although HCPs occasionally received information from the FDA, especially during training, feedback was low and only 12% (n=34) of HCPs received feedback from the FDA after submitting ADR reports, while 14% (n=51) specified they read the FDA newsletter *DrugLens*. Again, pharmacy staff were most likely (30%, n=10) to have read the FDA newsletter on medication safety compared to medical (4%, n=4) and nursing staff (13%) (P<0.005). Thirty four per cent of HCPs received products from pharmaceutical companies. Of these, medical staff (58%) were more likely to be presented with products more frequently (i.e. every month) compared to nursing (10%) and pharmacy staff (38%). Further enquiry about awareness of posters and adverts on ADR reporting in their facilities showed 27% (n=96) had noticed this (Table 18).

Table 18: Training and feedback practices among healthcare professionals

Paraphrased Questions (See Appendix N for full version)		Number of respondents			TOTAL	Pearson Chi Value (*99%CI*)
		Nursing staff N (%)	Medical staff N (%)	Pharmacy staff N (%)	Total within HCP N (%)	
Do you receive feedback from FDA?	Yes	27 (12)	3 (8.8)	4 (17)	34 (12)	*X^2=4.346* df=4 P=0.361 *(0.357-0.381)*
	No	82 (36)	14 (41)	4 (17)	100 (35)	
	Not sure*	121 (53)	17 (50)	16 (67)	154 (54)	
Recall having PV training?	Yes	47 (16)	15 (34)	22 (65)	84 (23)	*X^2=44.657* df=4 P=0.000* *(0.000-0.000)*
	No	217 (76)	28 (64)	10 (29)	**255 (70)**	
	Not sure	22 (8)	1 (2)	2 (6)	25 (7)	
Do you read the FDA newsletter?	Yes	37 (13)	4 (8)	10 (30)	51 (14)	*X^2=13.769* df=4 P=0.008 *(0.007-0.12)*
	No	214 (74)	42 (88)	18 (55)	**274 (74)**	
	Don't know	39 (13)	2 (4)	5 (15)	46 (12)	
Aware of ADR reporting adverts in your facility?	Yes	73 (26)	7 (15)	16 (47)	96 (27)	*X^2=15.316* df=4 P=0.004* *(0.002-0.005)*
	No	112 (40)	14 (30)	10 (29)	**136 (38)**	
	Don't know	96 (34)	25 (54)	8 (24)	129 (36)	
Approached by pharmaceutical companies with products?	Every month	32 (11)	28 (60)	13 (39)	73 (20)	*X^2=115.677* df=8 P=0.000* (0.000-0.000)
	Every 3 months	12 (4)	12(26)	4(12)	28 (8)	
	Every 6 months	18(6)	3(6)	1(3)	22(6)	

5.9 Reporting Methods and Responsibility

HCPs preferred reporting ADR to medical staff (39%, n=138) as they considered it convenient. Nursing staff (45%) were more likely to report to medical staff, compared to medical staff themselves (25%) and pharmacy staff (6%) (P<0.005). Reporting electronically was the most preferred option for pharmacy staff, while doctors preferred using the paper forms. Sixty per cent (n=213) of HCPs in general preferred to report to either the pharmacy staff or medical staff (Table 19).

When asked about which HCP category had the potential to send the most reports, more than half (57%, n=215) expressed the view that nursing staff had the potential to send the most reports compared to other HCP categories (P<0.005). However, whilst the majority of medical and nursing staff held this belief, most pharmacy staff respondents thought that all HCPs had the potential to send the most reports. Overall, more than half (51%, n=191) were of the opinion that all HCPs were ultimately responsible for reporting ADRs. Within HCP categories, the majority (77%, n=26) of pharmacy staff felt more strongly that reporting was a responsibility for all in contrast to nursing staff of which less than half (48%, n=140) (P<0.005) were of the same opinion. Considering what HCPs thought of themselves, 32% of nurses felt nursing staff had the ultimate responsibility, 17.6% of pharmacy staff felt it was their responsibility and 38% of medical staff felt it was their responsibility. Pharmacy staff therefore were observed to be less keen on having the ultimate responsibility of reporting as perceived by other HCPs (Table 19).

Table 19: ADR reporting responsibilities in practice

Paraphrased Questions (See Appendix N for full version)		Number of respondents			TOTAL	Pearson Chi Value (*99%CI*)
		Nursing staff N (%)	**Medical staff N (%)**	**Pharmacy staff N (%)**	**Total within HCP N (%)**	
Do patients report ADR?	Yes	155 (53)	24 (51)	9 (27)	**188 (50)**	*X^2=9.824* df=4 P=0.044 *(0.035-0.045)*
	No	30 (10)	3 (6)	4 (12)	37 (10)	
	Sometimes	108 (37)	20 (43)	21 (62)	149 (40)	
Does HCP do patient education during working hours?	Yes	184 (63)	24 (51)	21 (62)	**229 (67)**	*X^2=2.974* df=4 P=0.562 *(0.559-0.584)*
	No	13 (5)	2 (4)	2 (6)	17 (5)	
	Sometimes	94 (32)	21 (45)	11 (32)	126 (34)	
Most convenient method for ADR reporting	Paper forms	53 (19)	12 (25)	10 (30)	75 (21)	*X^2=27.604* df=8 P=0.002* *(0.001-0.0036)*
	electronic	38 (14)	13 (27)	9 (27)	60 (17)	
	To Pharmacist	53 (19)	10 (21)	12 (36)	75 (21)	
	To Doctor/medical assistant	124 (45)	12 (25)	2 (6)	**138 (39)**	
	Other	5 (2)	1 (2)	0 (0)	6 (2)	
Who has the potential to send the most reports?	Nursing staff	190 (64)	19 (40)	6 (18)	215 (57)	*X^2*=92.436 df=8 P=0.000* (0.000-0.000)
	Medical staff	6 (2)	12 (25)	2 (6)	20 (5)	
	Pharmacy staff	14 (5)	2 (4)	11 (32)	27 (7)	
	All	82 (28)	15 (31)	15 (44)	112 (30)	
	other	3 (1)	0 (0)	0 (0)	3 (1)	
Who has the ultimate responsibility to report ADRs?	Nursing staff	93 (32)	0 (0)	2 (6)	95 (25)	*X^2=85.765* df=6 P=0.000* (0.000-0.000)
	Medical staff	13 (4)	18 (38)	0 (8)	31 (8)	
	Pharmacy staff	48 (16)	5 (10)	6 (18)	59 (16)	
	All	140 (37)	25 (52)	26 (77)	191 (51)	

5.10 Attitudes and Opinions on ADR Reporting

Attitudinal data was acquired using a five-point Likert-type scale which sought to explore HCP perspectives on ADR reporting by modifying Inman's theoretical model of the '*deadly sins*' of under-reporting (Inman, 1996). Additionally, seven questions further soliciting their opinions on ADR reporting were explored. In total, 14 questions were reworded as presented (Table 20). These attitudinal questions were a combination of negative and positive statements to explore HCPs' inclination towards these statements. Further assessment of the difference in response between HCPs was completed by recoding the five-point Likert scale to a three-point one, to satisfy Chi Square assumptions.

Table 20: Likert statements of attitude

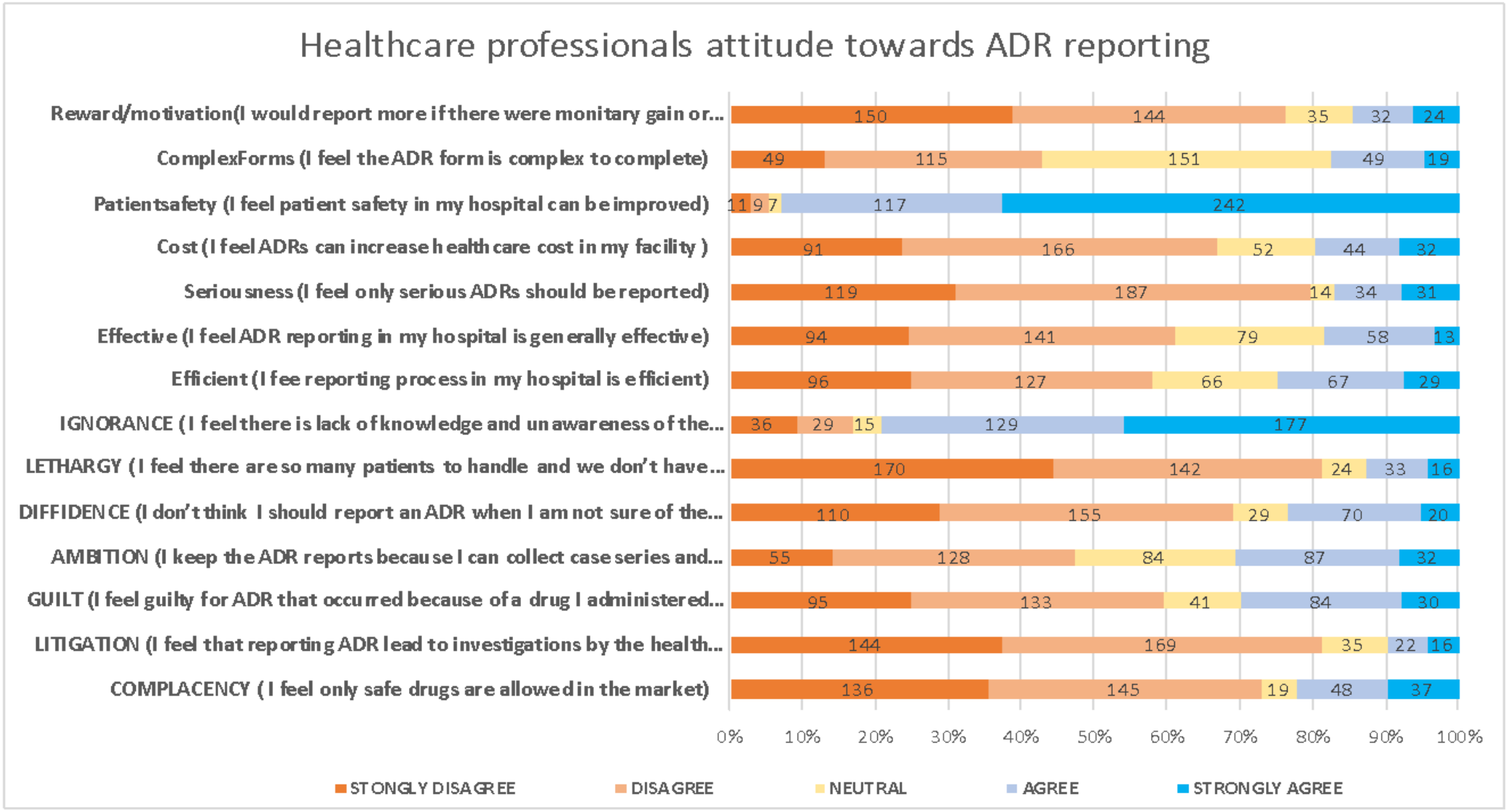
Abbreviation	Full statement
Reward/Motivation	I would report more if there were monetary gain or percentage increase in salary
Complex Forms	I feel the ADR form is complex to complete
Patient Safety	I feel patient safety in my hospital can be improved
Seriousness	I feel only serious ADRs should be reported
Cost	I feel ADRs can increase healthcare cost in my facility
Effective	I feel ADR reporting in my hospital is generally effective
Efficient	I feel reporting process in my hospital is efficient
Ignorance (Inman)	I feel there is lack of knowledge and awareness of the reporting process involved in submitting an ADR report
Lethargy (Inman)	I feel there are so many patients to handle and we don't have time, so ADRs become unimportant
Diffidence (Inman)	I don't think I should report an ADR when I am not sure of the causality between the reaction and the drug
Ambition (Inman)	I keep the ADR reports because I can collect case series and publish to better my career.
Guilt (Inman)	I feel guilty for ADR that occurred because of a drug I administered or prescribed
Litigation (Inman)	I feel that reporting ADR can lead to investigations by the health department which can affect my job
Complacency (Inman)	I feel only safe drugs are allowed in the market

Overall, the line of response of HCPs showed a positive attitude towards ADR reporting. The majority of HCPs agreed or strongly agreed with statements which encouraged reporting but disagreed or strongly disagreed with statements which discouraged reporting or were usually negatively worded. For example, HCPs' response to "I don't think I should report an ADR when I am not sure of the causality between the reaction and the drug" showed a 70% disagreement/strong disagreement with this statement, indicating a positive attitude.

Most HCPs were not in support of financial motivation. Seventy-six per cent of HCPs strongly disagreed (39%) or disagreed (37%) with reporting for monetary gain or percentage increase in salary. There was, however, a statistically significant difference where pharmacists (21%) were more likely to agree or strongly agree with this statement than medical (13%) and nursing staff (14%) ($P<0.005$) (Table 15). There were a large number of neutral responses (i.e. 39.4% neither agreed nor disagreed) when HCPs were asked for their opinion about the complexity of the ADR forms. Only 5% strongly agreed that the ADR forms were complex. The majority (93%) of HCPs agreed (30%) and strongly agreed (63%) that patient safety in their hospitals could improve through ADR reporting. There was a general disagreement (79%) about reporting only serious ADRs – 31% of HCPs strongly disagreed and an additional 48% disagreed. HCPs had a negative attitude to cost, effectiveness and efficiency of the reporting systems. In terms of cost, they either strongly disagreed (24%) or disagreed (43%) that ADRs could increase their healthcare costs. HCPs also felt that the reporting process in their facilities was not efficient (i.e. 24% strongly disagreed and 37% disagreed). They also doubted (i.e. strongly disagreed (25%) and disagreed (33%)) the effectiveness of the ADR reporting in their hospitals.

In relation to Inman's typology, only '*ignorance*' was agreed or strongly agreed with. HCPs' responses showed that the majority (79%) either strongly agreed (46%) or agreed (33%) that there was a lack of knowledge and awareness about reporting. HCPs either disagreed or strongly disagreed with the other attitudes proposed by Inman (lethargy, diffidence, ambition, guilt, litigation and complacency) thereby reflecting a positive attitude towards reporting. The majority (81%) strongly disagreed (44%) or disagreed (36%) with the statement "*I feel there are many patients to handle and we don't have time, so ADRs become unimportant*". More than half (69%) of the participants either strongly disagreed (29%) or disagreed (40%) that HCPs must establish causality before reporting an ADR. The ambition to keep ADRs for publication and career progression was a disagreeable attitude for 47% of HCPs. Fifty-nine per cent of HCPs felt no guilt (i.e. strongly disagreed (25%) and disagreed (34%)) for an ADR which occurred as a result of a drug they administered. Eighty-one per cent of HCPs strongly disagreed (37%) or disagreed (44%) that investigations could affect their job because of reporting an ADR. There was also a large (73%) disagreement that only safe drugs were marketed (i.e. strongly disagreed (35%) and disagreed (38%)) (Figure 21).

Figure 21: Responses to questions on attitude to reporting ADRs



Responses were recoded into agree, neutral or disagree to enable inferential analysis and comparison of attitudinal responses with key independent variables. Comparing attitudinal responses between the HCPs interviewed, reward/motivation, complex forms and cost were found to be statistically significant (P<0.005). In terms of financial reward and motivation, medical staff were more likely to disagree (83%) compared to nursing (79%) and pharmacy staff (50%). Pharmacy staff were most likely to agree to rewards and incentives for reporting compared to nurses and doctors (X_2=22.296, df=4,, P=0.000). Only 19% (n=72) of HCPs agreed ADRs could increase healthcare costs. Within staff categories, 79% of pharmacy staff were more likely to disagree with this statement than medical staff (50%) or nursing staff (69%).

In terms of ambition, when HCPs were asked to assess a statement about keeping case reports for the purpose of compiling case series for publication to better their careers, 48% disagreed with this. Within HCP categories, more than half (58%) of medical staff disagreed with this compared to nursing staff (47%, n=139) and pharmacy staff (21%, n=7).

Although not statistically significant, the majority of HCPs agreed reporting ADRs could improve patient safety. This was especially so for nurses, with 93% (n=275) agreeing to this statement. Also, a large number of respondents (81%, n=306) disagreed with the statement "*I feel there are so many patients to handle and we don't have time, so ADRs become unimportant*". Most medical staff (88%, n=42), disagreed with this statement compared to other HCPs. In terms of reporting an ADR, pharmacy staff were the majority (85%, n=29) who were most likely to disagree about litigation issues based on the statement that "*I feel that reporting ADR can lead to investigations by the health department which can affect my job*" when compared to other HCPs (Table 21).

Table 21: Difference between HCP attitudinal responses

Abbreviated statements (see Table 16)	Likert Response	Nursing Staff (% within staff)	Medical Staff (% within staff)	Pharmacy staff (% within staff)	Total	Pearson Chi χ^2
Reward/motivation	Disagree	231(79)	40(83)	17(50)	288 (77)	
	Neutral	22 (8)	2 (4)	10 (29)	34 (10)	*X^2=22.296*
	Agree	41 (14)	6 (13)	7 (21)	54 (15)	df=4 P=**0.000***
Complex forms	Disagree	127 (43)	14 (30)	21 (62)	162 (43)	
	Neutral	117 (40)	28 (60)	3 (9)	148 (41)	*X^2=21.725*
	Agree	49 (17)	5 (11)	10 (29)	64 (17)	df=4 P=**0.000***
Patient safety	Disagree	14 (5)	3 (6)	3 (9)	20 (6)	
	Neutral	6 (2)	1 (2)	0 (0)	7 (2)	*X^2=1.764*
	Agree	275 (93)	44 (92)	3 (91)	322 (92)	df=14 P=0.779
Cost	Disagree	204 (20)	24 (50)	27 (79)	255 (67)	
	Neutral	32 (11)	15 (31)	2 (6)	50 (13)	*X^2=18.032*
	Agree	58 (69.4)	9 (19)	5 (15)	72 (19)	df=4 P=**0.001***
Seriousness	Disagree	228 (78)	45 (94)	26 (77)	299 (79)	
	Neutral	11 (4)	1 (3)	1 (3)	13 (3)	*X^2=7.167*
	Agree	55 (19)	7 (21)	7 (21)	69 (18)	df=4 P=0.127
Effective	Disagree	178 (61)	33 (69)	21 (62)	232 (62)	
	Neutral	58 (20)	10 (21)	7 (21)	75 (20)	*X^2=2.443*
	Agree	58 (20)	5 (10)	6 (18)	69 (18)	df=4 P=0.655
Efficient	Disagree	166 (57)	33 (69)	19 (56)	218 (58)	
	Neutral	48 (16)	9 (19)	7 (21)	64 (17)	*X^2=5.129*
	Agree	80 (27)	6 (13)	8 (24)	94 (25)	df=4 P=0.274
Ignorance (Inman)	Disagree	52 (18)	4 (8)	9 (27)	65 (17)	
	Neutral	11 (4)	2 (4)	2 (6)	15 (4)	*X^2=5.274*
	Agree	232 (79)	42 (88)	23 (68)	297 (79)	df=4 P=0.260
Liturgy (Inman)	Disagree	236 (80)	42 (88)	28 (82)	306 (81)	
	Neutral	21 (7)	2 (4)	1 (3)	24 (6)	*X^2=2.332*
	Agree	37 (13)	4 (8)	5 (15)	46 (12)	df=4 P=0.675
Diffidence (Inman)	Disagree	200 (68)	37 (79)	24 (71)	261 (70)	
	Neutral	20 (7)	6 (13)	2 (6)	28 (7)	*X^2=7.637*
	Agree	74 (25)	4 (9)	8 (24)	86 (23)	df=4 P=0.106
Ambition (Inman)	Disagree	139 (47)	28 (58)	13 (38)	180 (48)	
	Neutral	58 (19)	15 (31)	7 (21)	80 (21)	*X^2=12.571*
	Agree	98 (33)	5 (10)	14 (41)	117 (31)	df=4 P=**0.014**
Guilt (Inman)	Disagree	175 (60)	29 (62)	20 (59)	224 (60)	
	Neutral	26 (9)	9 (19)	6 (18)	41 (11)	*X^2=7.949*
	Agree	92 (31)	9 (19)	8 (24)	109 (29)	df=4 P=0.093
Litigation (Inman)	Disagree	239 (81)	40 (83)	29 (85)	308 (82)	
	Neutral	27 (9)	5 (10)	2 (6)	34 (9)	*X^2=1.146*
	Agree	29 (10)	3 (6)	3 (9)	35 (9)	df=4 P=0.887
Complacency (Inman)	Disagree	209 (71)	42 (89)	23 (68)	274 (74)	
	Neutral	16 (5)	0 (0.0)	3 (8)	19 (5)	*X^2=8.642*
	Agree	70 (24)	5 (11)	8 (24)	83 (22)	df=4 P=0.071

5.11 Attitude on Completing a Form

Cross-tabulation of ADR form completion as a dependent variable against HCPs' attitudes showed that reward/motivation (P<0.05) and complex forms (P<0.05) were statistically significant, when comparing those who completed ADR forms with those who did not and those who were not sure. HCPs who felt ADR reporting in their hospital was generally effective, and those who were hesitant to report because they were unsure about causality, were statistically significant.

Among HCPs who disagreed with reward and motivation, the majority (71%, n=140) did not report ADRs or were not sure (14%, n=28) if they reported. There was a statistically significant difference between those who agreed that the form was complicated and those who did not complete an ADR form (P<0.05). Of those who disagreed that the form was complicated, only 21% (n=24) completed a form for an ADR they had observed, which may be attributed to other reasons associated with form completion.

The majority of HCPs disagreed that ADR reporting in their hospitals was either effective (62%, n=164) or efficient (58%, n=218), although this was not significant (X_2=2.443, P=0.655). There was marginal significant difference between those who disagreed (50%, n=38) that reporting was effective (X_2=9.407, P=0.052) and those who reported an ADR (Table 22). HCPs who disagreed that it was either effective or efficient were more likely to be medical staff than nursing or pharmacy staff.

The only Inman factor which was statistically significant (P<0.05) was 'diffidence', which stated that "*I don't think I should report an ADR when I am not sure of the causality between the reaction and the drug*". Diffidence referred to the belief that HCPs would only report an ADR if sure that it was related to the use of a particular drug and not based on mere suspicion. The majority of HCPs disagreed (65%, n=172) with the statement on diffidence. Seventy-three per cent (n=125) of those who disagreed either did not complete a form or were not sure (12%, n=20) whether they did. Only 12% (n=9) agreed they would report only if they were sure of causality between a drug and a reaction, and also completed an ADR form (Table 22).

Table 22: Association between HCP attitude and completion of an ADR report form

Abbreviated statements (see Table 20)	Likert Response	COMPELETED ADR FORM				**Pearson Chi χ^2**
		YES	**NO**	**NOT SURE**	**TOTAL**	
Reward/motivation	Disagree	30 (79)	140 (75)	28 (72)	198 (75)	*X_2=9.096* df=4 P=0.059
	Neutral	7 (19)	14 (7)	4 (10)	25 (9)	
	Agree	1 (3)	34 (18)	7 (18)	42 (16)	
Complex forms	Disagree	24 (63)	79 (42)	14 (36)	117 (44)	*X_2=13.700* df=4 P=0.008
	Neutral	4 (11)	76 (41)	17 (44)	97 (37)	
	Agree	10 (26)	32(17)	8 (21)	50 (19)	
Patient safety	Disagree	4 (11)	8(4)	1 (3)	13 (5)	*X_2=5.394* df=4 P=0.249
	Neutral	0 (0)	4(2)	2 (5)	6 (2)	
	Agree	34 (90)	176 (94)	36 (92)	246 (93)	
Cost	Disagree	24 (65)	122(65)	25(64)	171 (65)	*X_2=3.409* df=4 P=0.492
	Neutral	2(5)	28 (15)	5 (13)	35 (13)	
	Agree	11(30)	38 (20)	9(23)	58 (22)	
Seriousness	Disagree	30 (79)	145 (78)	26 (67)	201 (76)	*X_2=4.654* df=4 P=0.325
	Neutral	2 (5)	6 (3)	4 (10)	12 (5)	
	Agree	6 (16)	36 (19)	9 (23)	51 (19)	
Effective	Disagree	19 (50)	126 (67)	19 (49)	164 (62)	*X_2=9.407* df=4 P=0.052
	Neutral	10 (26)	25 (13)	11 (28)	46 (17)	
	Agree	9 (24)	36 (19)	9 (23)	54 (20)	
Efficient	Disagree	19 (50)	110 (59)	19 (49)	148 (56)	*X_2=2.185* df=4 P=0.702
	Neutral	7 (18)	28 (15)	6 (15)	41 (16)	
	Agree	12 (32)	50 (27)	14 (36)	76 (29)	
Ignorance (Inman)	Disagree	8 (21)	29 (15)	11 (28)	48 (18)	*X_2=3.844* df=4
	Neutral	2 (5)	10 (5)	2 (5)	14 (5)	
	Agree	28 (74)	149 (79)	26 (67)	203 (77)	

						P=0.428
Lethargy (Inman)	Disagree	30 (79)	155 (83)	26 (67)	211 (80)	X_2=5.443 df=4 P=0.245
	Neutral	2 (5)	10 (5)	4 (10)	16 (6)	
	Agree	6 (16)	22 (12)	9 (23)	37 (14)	
Diffidence (Inman)	Disagree	27 (71)	125 (67)	20 (51)	172 (65)	X_2=11.836 df=4 P=0.019
	Neutral	2 (5)	10 (5)	8 (21)	20 (8)	
	Agree	9 (24)	53 (28)	11 (28)	73 (28)	
Ambition (Inman)	Disagree	20 (53)	90 (48)	14 (36)	124 (47)	X_2=2.696 df=4 P=0.610
	Neutral	8 (21)	44 (23)	10 (26)	62 (23)	
	Agree	10 (26)	54 (29)	15 (39)	79 (30)	
Guilt (Inman)	Disagree	24 (65)	107 (57)	22 (56)	153 (58)	X_2=3.126 df=4 P=0.537
	Neutral	5 (14)	18 (10)	61 (15)	29 (11)	
	Agree	8 (22)	63 (34)	11 (28)	82 (31)	
Litigation (Inman)	Disagree	33 (87)	151 (80)	29 (74)	213 (80)	X_2=4.232 df=4 P=0.375
	Neutral	2 (5)	20 (11)	3 (8)	25 (9)	
	Agree	3 (8)	17 (9)	7 (18)	27 (10)	
Complacency (Inman)	Disagree	27 (71)	138 (73)	25 (64)	190 (72)	X_2=2.268 df=4 P=0.687
	Neutral	1 (3)	10 (5)	2 (5)	13 (5)	
	Agree	10 (26)	40 (21)	12 (31)	62 (23)	
*P<0.005						

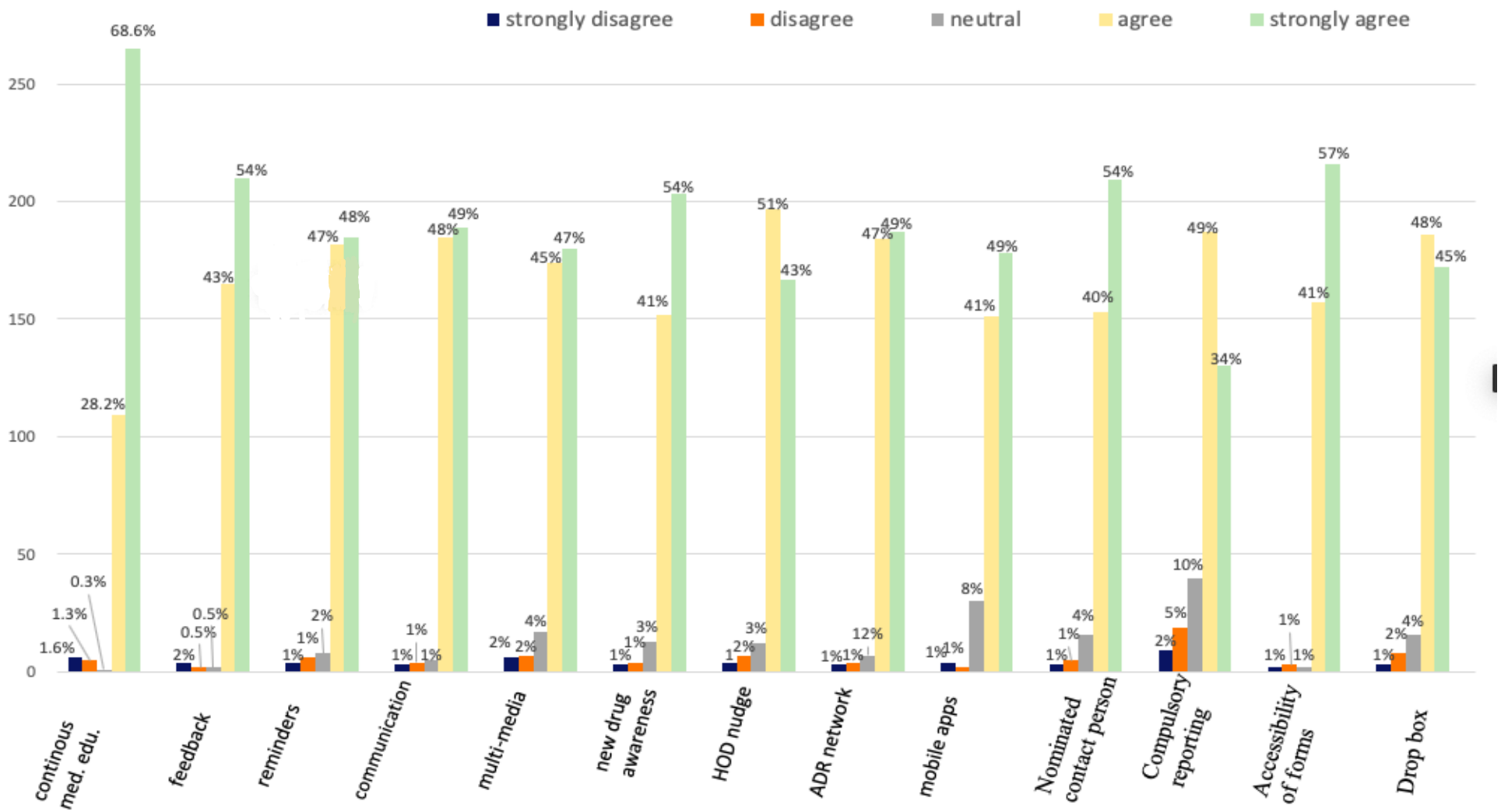
5.12 Improving ADR Reporting

Additional data was collected in the quantitative phase about improving ADR reporting to embellish the qualitative phase, which explore that same question. Questions about improving ADR reporting were posed to HCPs in 13 Likert-type questions with a five-grade response (strongly agree, agree, neither, disagree, strongly disagree) (Table 23) and a final open response qualitative question. The option most strongly agreed with was continuous medical education (68%, n=265). The option least strongly agreed with of the suggested ways of improving ADR reporting was making ADR reporting compulsory. Compulsory reporting reported the largest (10.4%, n=40) number of neutral opinions compared to the rest, especially continuous medical education where only one person was neutral. Furthermore, even though a small percentage (5%) disagreed with compulsory reporting, it was the opinion which HCPs disagreed with the most. HCPs agreed strongly with four out of the thirteen suggestions, i.e. feedback (54%, n=210), increasing awareness about new drugs (54%, n=203), nominated contact person (51%, n=209) and accessibility to forms (57%, n=216) (Figure 22).

Table 23: Suggested opinions to improve ADR reporting

Abbreviated statement	Full statement
Continuous med. Education	Organizing continuous medical education, training and refresher courses for staff on ADR reporting.
Feedback	Encouraging feedback among patients, prescribers and dispensers of medicines.
Reminders	Regular reminder visits from a qualified person for pharmacovigilance (QPPV).
Communication	Increased communication among different healthcare professional cadres
Multimedia	Increased multi-media publicity about the reporting scheme at various healthcare facilities.
New drug awareness	Increasing awareness about new drugs in health facilities.
HOD nudge	Encouragement from heads of departments.
ADR network	Forming an ADR reporting network
Mobile app	Introduction of mobile phone application for online reporting. Having an ADR focal person in every unit/department
Compulsory reporting	Make ADR reporting a compulsory obligation for all healthcare professionals
Accessibility of forms	Making ADR forms available and accessible in every department/unit
Drop box	Providing an ADR drop box in all units/departments.

Figure 22: Responses to suggested ways of improving ADR reporting (n=386)



5.13 Comparing HCPs' Responses to Improving ADR Reporting

Overall, HCPs were positive and agreed with all the methods for improving ADR reporting, although there were differences in the level of agreement between HCPs. The opinion about making ADR a compulsory obligation was the only statistically significant variable (p=0.006). Eighty-three per cent agreed that making ADR reporting compulsory would improve reporting. The highest level of agreement was among nursing staff (85%, n=252), compared with medical (79%, n=38) and pharmacy staff (61.8%, n=21).

Medical staff were in total agreement (100%) with three statements on *creating awareness on new drugs*, *support from heads of departments* and *forming an ADR network.* Similarly, pharmacy staff were in total agreement (100%) with six suggested ways of improving ADR: *continuous medical education, feedback, using mobile phone applications, accessibility of forms, reminders* and *communication*. Nursing staff, however, were not in total agreement about any of the suggested ways of improving reporting (Table 24).

Table 24: Association between HCPs and suggested opinions to improve ADR reporting

Opinions (abbreviated see Table 20)	Likert Response	Nursing Staff (% within **cadre**)	Medical Staff (% within **cadre**)	Pharmacy Staff (% within **cadre**)	T**otal** % within HCP
Continuous Med. Education	Disagree	9 (3.1)	1 (2.1)	0 (0.0)	10 (2.7)
	Neutral	1 (0.3)	0 (0.0)	0 (0.0)	1 (0.3)
	Agree	285 (96.6)	47 (97.9)	34 (100)	366 (97)
Feedback	Disagree	4 (1.4)	1 (2.1)	0 (0.0)	5 (1.3)
	Neutral	2 (0.7)	0 (0.0)	0 (0.0)	2 (0.5)
	Agree	286 (97.9)	47 (97.9)	34 (100)	367 (98.1)
Multimedia	Disagree	12 (4.1)	0 (0.0)	1 (2.9)	13 (3.5)
	Neutral	13 (4.4)	2 (4.3)	1 (2.9)	16 (4.3)
	Agree	269 (91.5)	45 (95.7)	32 (94.1)	346 (92.3)
New drug awareness	Disagree	7 (2.4)	0 (0.0)	0 (0.0)	7 (1.9)
	Neutral	11 (3.8)	0 (0.0)	1 (3)	12 (3.3)
	Agree	270 (93.8)	46 (100)	33 (97.0)	349 (94.8)
HOD nudging	Disagree	6 (2.1)	0 (0.0)	0 (0.0)	6 (1.6)
	Neutral	10 (3.4)	0 (0.0)	1 (2.9)	11 (2.9)

	Agree	276 (94.5)	48 (100)	33 (97.1)	357 (95.5)
ADR network	Disagree	6 (2.0)	0 (0.0)	1 (2.9)	7 (1.9)
	Neutral	6 (2.0)	0 (0.0)	1 (2.9)	7 (1.9)
	Agree	282 (95.9)	48 (100)	32 (94.1)	362 (96.3)
Mobile App	Disagree	24 (8.1)	1 (2.1)	0 (0.0)	25 (6.7)
	Neutral	25 (8.5)	3 (6.4)	0 (0.0)	28 (7.5)
	Agree	246 (83.4)	43 (91.5)	33 (100)	322 (85.9)
Focal Person	Disagree	7 (2.4)	1 (2.1)	0 (0.0)	8 (2.1)
	Neutral	14 (4.7)	1 (2.1)	1 (2.9)	16 (4.2)
	Agree	274 (92.9)	46 (95.8)	33 (97.1)	353 (93.6)
Compulsory reporting	Disagree	20 (6.8)	3 (6.3)	4 (11.8)	27 (7.2)
	Neutral	23 (7.8)	7 (14.6)	9 (26.5)	39 (10.3)
	Agree	252 (85.4)	38 (79.2)	21 (61.8)	311 (82.5)
Accessibility to forms	Disagree	4 (1.4)	0 (0.0)	0 (0.0)	4 (1.1)
	Neutral	1 (0.3)	1 (2.1)	0 (0.0)	2 (0.5)
	Agree	285 (98.3)	47 (97.9)	34 (100)	366 (98.4)
Dropbox	Disagree	10 (3.4)	1 (2.1)	0 (0.0)	11 (2.9)
	Neutral	13 (4.4)	1 (2.1)	1 (2.9)	15 (4)
	Agree	272 (92.2)	46 (95.8)	33 (97.1)	351 (93.1)
Reminders	Disagree	8 (2.7)	1 (2.1)	0 (0.0)	9 (2.4)
	Neutral	7 (2.4)	1 (2.1)	0 (0.0)	8 (2.1)
	Agree	279 (94.9)	46 (95.8)	34 (100)	359 (95.5)
Communication	Disagree	6 (2.0)	1 (2.1)	0 (0.0)	7 (1.9)
	Neutral	4 (1.4)	1 (2.1)	0 (0.0)	5 (1.3)
	Agree	285 (96.6)	46 (95.8)	34 (100)	365 (96.8)

5.14 Summary of Quantitative Results

These findings show a complex set of factors affecting PV and ADR reporting among HCPs. Variations in self-reported attitudes, practices and knowledge show apparent variation between medical, nursing and pharmacy staff.

Firstly, HCPs showed low levels of knowledge, demonstrated by the high percentage of incorrect responses from questions on knowledge. Pharmacy staff, however, were comparatively more knowledgeable than medical and nursing staff on PV and ADR issues. On the other hand, nursing staff were likely to be less knowledgeable on ADR issues compared to pharmacy and medical staff.

Secondly, a generally positive attitude to reporting ADR was observed among HCPs. For example, the majority of HCPs disagreed with statements which had unfavourably worded statements and agreed with optimistically worded attitudes. HCPs disagreed about financial motivation, complex forms, litigation, guilt, diffidence, cost implications and complacency as factors affecting reporting. They agreed, however, that patient safety could improve with reporting and that HCPs' ignorance about the reporting system mired ADR reporting.

Thirdly, in practice, reporting ADRs was presumed to be the responsibility of the pharmacy staff. Although 43% observed an ADR at least once a year, with 19% observing daily, weekly or monthly, it did not translate into reporting. Forms were generally unavailable, and a large proportion of HCPs were unsure of whom their institutional contact person for ADR was. There were more pharmacy staff observing ADRs than medical and nursing staff. Only a few had ever sent a report, and a large proportion had never completed a form. In addition, even though pharmacy staff were more likely to receive training, feedback from the FDA to HCPs in general was low. Overall, half of HCPs acknowledged that reporting ADRs was the responsibility of all HCPs. More than half of HCPs specified that nursing staff had the potential to send the most reports, as affirmed by half of the nursing staff.

Overall, HCPs supported the suggested approaches for improving ADR reporting; although levels of agreement varied, continuous medical education was the most favourably considered. There was, however, a significant number of HCPs who were uncertain about suggestions to make ADR reporting compulsory. The majority, however, agreed with this, and there were more nursing staff than pharmacy and medical staff in favour of it.

CHAPTER SIX

DISCUSSION AND INTEGRATION OF FINDINGS

6.0 Introduction

This concluding chapter provides an in-depth discussion of the findings from both phases of the study and considers how these have answered the research questions set out in chapter 2. It begins by offering an overview of the main findings before going on to present an integrated discussion of findings; this offers additional context on critical aspects, as well as considering how the findings from this study relate to the existing literature and theory presented in chapters 1 and 2. The study's strengths and limitations will be considered, before moving on to consider various recommendations and implications of the findings; this section will describe how the emerging data could inform different aspects of policy and practice, particularly in the context of the Ghanaian healthcare system. Opportunities for further research will be suggested before a final reflective section on the overall doctoral research process. The chapter and thesis conclude with a further summary statement of the main aims and findings.

6.1 Key Findings

This study sought to explore the perceived factors influencing ADR reporting among Ghanaian HCPs, and ways of improving reporting in routine hospital practice. Specifically, the research aimed to understand the self-reported knowledge, attitude, perceptions and practices of ADR reporting from the perspective of key HCPs, primarily including doctors, nurses and pharmacists. Furthermore, the research sought to describe the reporting process more generally, together with associated contextual issues and suggestions for improving the reporting process. HCPs identified several underlying and sometimes inter-related factors influencing reporting in both phases of the study, reflecting both system and human factors.

System factors were often perceived as distal and not in the immediate control of HCPs and were either internal or external. Key internal factors related to *hospital administrative issues* and a challenging *reporting process*, whilst key external system issues were viewed as being contingent on *infrastructure*, *media publicity* and *the contribution of stakeholders*.

In contrast, human factors involved opinions about personal and professional aspects of HCPs and beliefs about how patients influenced reporting. This study suggests that knowledge of the ADR reporting process was low among HCPs, although pharmacy staff were more likely to be knowledgeable and were perceived to have a more significant role in reporting than medical and nursing staff. Pharmacy staff were also the main HCPs engaged in reporting, as identified in the survey and interviews. The data suggest that they considered reporting as part of their duty, and their supervisors encouraged them to report. This contributed to a greater proportion of pharmacy staff reporting ADR compared to other HCPs, based on self-report responses in the survey in particular. Pharmacy staff, however, did not perceive themselves as having the ultimate responsibility to report ADRs even though they played such a significant role. Self-reported evidence suggests that less than half of HCPs (43%) had ever observed an ADR and only around a quarter (25%) had ever reported an ADR, with 14% of those reported to having done so using a form. These results show a lower ADR observation compared to studies in Nigeria which stated between 70% to 93% observations. The rates of ADR reporting, however, were varied, ranging between 3% to 43% among HCPs. These variations may be due to variations in methodologies and samples (Ohaju-Obodo and Iribhogbe, 2010; Okezie and Olufunmilayo, 2008; Adedeji et al., 2013; Fadare et al., 2011).

In terms of measurement of participant attitudes, in this study, HCPs were generally positive. The majority (92%) strongly believed that patient safety could be improved if they reported ADRs. Only one of Inman's '*seven deadly sins*' (Inman, 1996) – relating to *ignorance of the reporting system* – was viewed as influencing their ADR reporting and was considered a significant reason for non-reporting. All the other attitudes proposed by Inman were either disagreed with or strongly disagreed with by a majority of HCPs, indicating a positive attitude. Using concurrent triangulation design was suitable for cross-validation and confirmation of findings from both phases of the study into a single study. The design, however, was limited in that some discrepancies were difficult to explain. For example, even though HCPs disagreed with six of Inman's typologies, i.e. *ambition, lethargy, diffidence, guilt, litigation* and *complacency* in the survey, they highlighted some of them in the qualitative interviews as essential factors influencing reporting, in addition to several other factors. While HCPs disagreed that fear of litigation affected reporting in the survey, it was raised as an external factor relating to engaging with pharmaceutical companies; a nurse said she would report if she trusted the "*ability of the authority to protect people who will report on these reactions*" because she feared the risk of litigation or harm. Protection was considered as the establishment of a law or policy to safeguard reporters. A sequential explanatory design would have been

beneficial in generating data and guided by a theoretical perspective which would have been easy to implement. Challenges in time and resources made it difficult to use this alternative approach. In the sections that follow, the findings from this study are considered in relation to the main research questions explored using a concurrent design and compared to existing research to understand the level of evidence which was considered important in this study.

6.2 Factors Influencing ADR Reporting

Moving on from the overall key findings, attention is now focused on what emerged significantly as factors influencing ADR reporting. These would be considered in light of existing evidence and literature, and it is argued that this research established several related but unique experiences of HCPs identified to influence ADR reporting in a Ghanaian context. Key examples relate to the human (patient or healthcare professional) and system (internal or external) factors where HCPs had positive attitudes and were willing to report, but poor knowledge, working relations, availability of reporting tools and other administrative bottlenecks became a challenge.

As already noted, the findings of this study suggest that ADR reporting was low and intentions to report were influenced by four factors: internal systems, external systems, healthcare professional and patient-related factors. HCPs identified more system factors than human factors. A key emerging finding was that HCPs appeared to have broadly positive attitudes towards reporting (as observed from responses to questions and the operationalisation of Inman's '*seven deadly sins*'). However, a contrast existed in relation to this positivity about intentions and actual self-reported incidences: poor practice affected by lack of knowledge, low reporting and availability of ADR reporting tools being more typical. Several of these issues are now considered in more detail, with particular emphasis on inadequate knowledge of HCPs, perceived patient attitude, positive HCP attitudes, roles and responsibilities of HCPs, and the reporting process.

6.2.1 Inadequate Knowledge and Information

One of the most important factors influencing ADR reporting was associated knowledge of ADRs, specifically how to report, and crucially the relative lack of such knowledge among HCP participants. Both phases of this study showed a general lack of knowledge among participants which has been reported widely in the literature. Ignorance and lack of awareness

about PV, poor definition of ADR, the inability to differentiate between ADR and side effects have been identified in the literature as examples of poor HCP knowledge on PV and ADRs, especially in Africa (Ezeuko et al., 2015; Lopez-Gonzalez et al., 2009a; De Angelis et al., 2016; Fadare et al., 2011; Daher et al., 2013; Okezie and Olufunmilayo, 2008). In this study, only an average of 18.5% of participants remembered key information used to assess HCPs' knowledge on ADR reporting, such as awareness of the national PV centre, SMS short code to send a report and details needed on the reporting form. This was found in similar studies reported elsewhere which found generally inadequate knowledge among HCPs as well (Necho Mulatu and Worku, 2014; Shanko and Abdela, 2018; Kefale et al., 2017; Khoza et al., 2004; Gurmesa and Dedefo, 2016). The majority of participants in these studies were not familiar with the terms 'PV' or 'ADR', or with the reporting system in general.

The majority of nurses had inadequate knowledge compared to medical and pharmacy staff. Pharmacy staff in contrast showed comparatively better understanding. For example, even though only 32% of staff were aware of the national PV centre, 74% of pharmacists knew about this. In the qualitative phase, pharmacy staff showed greater familiarity with PV and the significance of reporting compared to other HCPs. This may be attributable to their training as drug specialists or the additional workshops and training that they receive as part of their continuous professional development (CPD). Other studies (Hailu et al., 2014; Alraie et al., 2016; Granas et al., 2007) have also found pharmacists to be more knowledgeable in ADR reporting and that their reports were of higher quality. Such a finding in this and previous research is arguably not unsurprising, given that pharmacists have a key role in healthcare systems for the safe use of medicine (Thamby and Subramani, 2014). HCPs were of the view that the FDA was channelling more training to pharmacists than to other HCPs, which was further enhancing their knowledge and capacity, and demanded a rather general approach to training and workshops on ADRs. Both phases of the study mutually underscored the general lack of knowledge and the importance of the role of the pharmacist in pharmaceutical care. A triangulation protocol (Table 25) (Farmer et al., 2006) shows how the mixed methods were used to mutually enforce the findings in terms of the level of knowledge which was assessed among HCPs.

6.2.2 Positive Attitude to Reporting

There was a positive attitude to reporting ADRs if HCPs had the tools and an enabling environment that supports reporting. HCPs agreed or strongly agreed with statements which were worded to suggest optimism in the reporting system. For example, "*I feel patient safety in my hospital can be improved*". In contrast, they either disagreed or strongly disagreed with statements which suggested falsehood or misrepresentation of a functional reporting system. For example, "*I feel the ADR form is complex to complete*" or "*I feel only serious ADRs should be reported*" were either disagreed or strongly disagreed with, which was interpreted as a positive attitude. Although this study did not attempt to produce a composite score based on reporting attitude, comparisons can be made with other studies. Several of these estimated composite scores for attitude, and although results did vary somewhat, they presented a positive attitude among HCPs in Africa. For example, in Ghana, Ameade et al. (2014) undertook an assessment of nurses in the Tamale region (where the present research was undertaken) and found attitudes to reporting to be generally positive (59%). Similarly, a regional study of the Volta region of Ghana found a much higher attitudinal score of 74%, with pharmacists being more likely to have a higher (84%) attitudinal score than doctors and nurses, even though they scored the lowest attitude scores for the assertion that reporting was their professional obligation (Amedome and Dadson et al., 2017).

A further sign of a positive attitude was HCPs saying that reporting increased patient safety. Other studies in Africa have shown positive attitudes as well, for example in Uganda, HCPs disagreeing (73%) that reporting took up their time or put their careers at risk (76%), which showed a positive attitude towards reporting (Kiguba et al., 2014). Other studies from Nigeria, Sudan and Ethiopia (Oshikoya and Awobusuyi, 2009; Angamo et al., 2012; Awodele et al., 2011) have used different questions and methods in the assessment of attitudes. These studies reported that most HCPs, however, perceived reporting and monitoring to be important and part of their professional obligation, which was interpreted as a positive attitude similar to this study. This positive attitude is reassuring, although as noted previously it was not matched by similar self-reported behaviours in relation to ADR reporting. Nonetheless, such positivity could be capitalised on, and shows that HCPs may be receptive to interventions aimed at improving reporting because of their recognition of the importance of reporting. Of note, again,

is that these themes were clear in both phases of the study and underscore the difference in levels of attitude and positivity among HCPs.

6.2.3 Negative Patient Influences

Compared to other studies on ADRs, HCPs had a different perception of factors affecting their reporting behaviour, which was linked to patient attitudes, which has not been previously explored. They identified several patient attributes, and particularly behaviours, which made it difficult to retrieve information on ADRs from patients and exerted a negative influence on whether an ADR was reported. This study is unique in identifying HCP perceptions about patients in relation to ADR reporting. HCPs seem to suggest that, in this study, patients were apprehensive, involved in hospital hopping, self-medication of serious illness and poor awareness about reporting. These patient attitudes may have influenced HCP reporting negatively. As noted in chapter 2, Obonyo (2014) briefly described the role of patients in 'healthcare provider factors' that influence ADR reporting and recognised the importance of this relationship. However, the majority of previous studies have tended to focus more exclusively on patient reporting, of which some have reported on patients' perceptions of HCPs as being unfriendly and uncommunicative about ADR reporting.

Similar reasons for non-reporting of ADRs among HCPs identified in this study have been reported among patients as well, such as lack of feedback, poor awareness and not being sure who to report to (Dweik et al., 2017; Dweik et al., 2016). Even though this study did not receive any direct patient responses, other patient studies in Ghana have reported specific factors, such as unfriendly HCP attitude and inadequate patient education on medication effects as factors affecting patient reporting (Chatio et al., 2016). Patients' attitudes to reporting can be influenced by the consequences of reporting and HCP assertiveness (Jacobs et al., 2018; Sabblah et al., 2019), where positive patient reporting attitudes could be as a result of positive HCP attitude and vice versa. There is evidence to suggest that knowledge about health information can influence attitudes and subsequently could result in positive health practices (Abubakar et al., 2014a). In the theory of the acquisition of habits in health sciences (Hong et al., 1995), elements of the theory of KAP were identified as predictors to behavioural change and could explain the factors influencing HCPs' reporting behaviour.

HCP factors for non-reporting were closely linked and inter-related with patient factors in this study and are worth mentioning even though this is not a patient-centred study. When asked if HCPs educated patients about ADRs, 62% of survey respondents answered in the affirmative

and 50% suggested patients reported their ADRs directly to them. This corresponds with other patient-centred studies where 67% of patients also indicated they reported the ADRs they experienced (Jacobs et al., 2018). In this study, however, HCPs felt some patients were apprehensive and did not report to them because they were engaged in unapproved practices such as hospital hopping and self-medication of serious illnesses. For fear of being admonished, patients who were perceived to be involved in these practices often did not feel confident in reporting any ADRs experienced.

Also, weak healthcare system infrastructure made it more challenging to identify if a patient had received care from a different healthcare facility due to lack of electronic patient records and a robust health informatics system. Additionally, this attitude of patients could be associated with the unfriendly nature of HCPs as identified by Chatio (2016). Most patients were seen as passive receivers of care. HCPs noted that patients were more open to discuss their ADR and health issues if they felt confident the HCP would be friendly to them, but high in-patient numbers and busy schedules often made HCPs come across as unfriendly. The only way ADR reports could be increased is if HCPs encourage patients to report. The relationship between HCP and patient remains a key one however, and it has been argued that there are competing responsibilities for both patients and HCPs:

> *Spontaneous reporting of ADRs […] 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 (Pharmacy and Poisons Board) 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 [sic] 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"* (Obonya, 2014, p.42).

A further challenge relates to surrogate reporting, which made it even more problematic for HCPs to retrieve and document ADR information from children or critically ill patients who could not communicate or explain their conditions. Even though patient reporting confers advantages on the reporting of novel information and ADR experiences by providing detailed

descriptions of events (Inácio et al*.,* 2017), surrogate reporting made this more challenging. In paediatric units, children often reported ADRs through their parent or guardian, and it took extra vigilance by parents to identify and report them to HCPs, which often resulted in incomplete patient data. This was often challenging, even with serious ADRs, and those which HCPs would usually report often went unreported. HCPs believed that these patient attitudes were because of lack of awareness of reporting procedure and of what is expected of them.

6.2.4 Defined ADR Reporting Roles and Responsibilities

It was observed that clear roles and responsibilities about what and how to report, and understanding of the obligations, was lacking. The majority of HCPs were of the view that it was the pharmacists' responsibility to report ADRs. Lack of clear roles and responsibilities has been observed as an important and common reason for under-reporting in many studies (Nde et al., 2015; Gurmesa and Dedefo, 2016; Kiguba et al., 2014; De Angelis et al., 2016). Even though pharmacy staff had positive attitudes and acknowledged reporting as important for patient safety, they felt reporting ADRs was not their sole responsibility. Over-reliance on the pharmacists for ADR reporting initiatives may explain the general low reporting among HCPs. The quantitative phase showed that half (191/377) of the respondents perceived reporting as the responsibility of all, while only 29.7% (112/377) felt all HCPs had the potential to send the most reports. Uncertainty about roles and responsibilities led to HCPs thinking that ADR reporting was the responsibility of the pharmacist, which was very apparent in the qualitative interviews. This was seen in the pre-data-collection stage, where most nursing and medical staff, upon hearing about the study, suggested it was the type of study for pharmacists and not them. Pharmacy staff only partly accepted this view. The majority of them accepted reporting as part of their routine work but felt that other HCPs were also responsible, and that ADR reporting was a collective responsibility for all HCPs. For example, when asked who had the potential to send the most reports and who had the ultimate responsibility for reporting ADRs, pharmacy staff saw nursing and medical staff as having the potential and ultimate responsibility. This contrasted with medical and nursing staff who saw themselves as having the potential and ultimate responsibility. Even though this could be linked to a positive attitude to reporting, it contrasted with what was being practised. Similar research has been reported in a Pakistani study of pharmacists (Hussain et al., 2018). Nursing and medical staff have shown less commitment to actual reporting responsibilities, such as filling in a form for an ADR. The findings are similar to the literature, which suggests burnout, workload, lethargy, blame,

bureaucratic procedures, lack of incentives and availability of forms as common reasons for non-reporting (Aljadhey et al., 2015). Most HCPs, especially nurses, resort to verbal reporting because they find it more convenient and less time-consuming to tell their immediate superior about an ADR rather than completing a form, especially when forms are not available at the ward level. Another plausible reason for verbal reporting, especially among nurses, was fear of blame and merely following organisational bureaucracies. The nurses' traditional role of taking instructions made them susceptible to fear and the blame of wrongdoing or malpractice, thus they preferred not to be at the forefront and often needed to check with doctors before reporting ADRs. As part of a functional PV system it is required that a committee be set up to oversee and take responsibility for reporting. This, however, was lacking in all study sites, even though one study site had a PV centre. Pharmacy staff were solely responsible for reporting ADRs in other facilities. Also, based on the data, there critical staff shortages within the pharmacy staff category leading to few clinical pharmacists at healthcare facilities. Reporting ADRs therefore became an additional responsibility. It would be useful to have nominated persons from each HCP cohort, unit or department as contact persons and facilitators of reporting among HCPs. Lack of roles and responsibilities created gaps and reporting challenges among HCPs. Academic detailing has been argued to be relevant; this involves a form of educational outreach and:

> *"[…] structured visits by trained personnel to health care practices for the purpose of delivering tailored training and technical assistance to health care providers to help them use best practices"* (Soumerai and Avorn, 1990, p.24).

This has been shown to improve knowledge, attitude and practice among HCPs in prescription behaviours and other public health interventions (Izham et al., 2018; Markey and Schattner, 2001), which could help to improve reporting systems and support reporting responsibilities, especially through clinical pharmacists.

6.2.5 The Reporting Process and Verbal Reporting

The way in which ADRs were reported and the factors responsible for that were important in predicting whether a form would be completed, or a designated responsible authority would be contacted. Lack of awareness of the ADR reporting processes has been identified in many

studies as a barrier to reporting ADRs (Bhagavathula et al., 2016; Wilbur, 2013; Ezeuko et al., 2015; Gupta and Udupa, 2011).

The reporting processes in the study hospitals were similar. Apart from TTH, which had a PV unit and a designated officer-in-charge, the facilities channelled their reports through a clinical pharmacist. Despite the provision in TTH, 86% of staff were unaware there was an officer-in-charge of PV, which resulted in high levels of under-reporting. Generally, identification and reporting of ADRs were carried out either formally or informally. Formal reporting was influenced by two factors, i.e. severity and availability of reporting forms. This suggests that if an HCP perceived an incident as serious, felt capable and forms were available, they would formally report it by completing a form and reporting appropriately. The system was often challenged by the unavailability of forms. In the quantitative phase, only 28% of HCPs indicated that ADR forms were available in their facility, with 64.1% of TTH staff indicating no availability of ADR forms. Lack of availability of forms has been a significant factor for under-reporting in several studies (Dweik et al., 2017; Gupta and Udupa, 2011; Aljadhey et al., 2015; Amin et al., 2016; Amedome and Dadson, 2017).

The unavailability of forms and reporting tools, coupled with other human factors, resulted in informal reporting which was often verbal. Informal verbal reporting was common among HCPs where superiors were often informed about cases which were sometimes either noted in nurses' notes or patients' folders. This suggests that ADR reports were being lost through informal routes despite a large number of ADRs being observed. Documenting in patients' folders was, however, problematic because it was unauthorised for junior staff, especially nurses, to write on patient folders.

There was also inter-staff conflict where some pharmacists felt challenged by doctors for writing in patients' folders. This perceived and actual medical dominance was observed between doctors and nurses as well as doctors and pharmacists. Medical dominance is described as:

> *"the medical profession's control over the content, terms and conditions of its own work (autonomy), control over other health occupations and the health division of labour (authority), control over clients and control over the broader context of health care (sovereignty)"* (Freidson, 1970, p.30).

This has been explored in many studies, with a recent finding showing how pharmacists felt frustrated and undervalued when doctors evaded scrutiny and demeaned their expertise

(Luetsch and Scuderi, 2019). Recent approaches to healthcare and prescription practices in Ghana have decentralised patient care and some medication prescriptions to medical assistants, nurse practitioners and pharmacists. Medical dominance has not declined as a result of the decentralisation but has rather created some degree of conflicting interactions between HCPs about who can write in patient folders and responsibilities about whom to report to. Pharmacists and nurses in this study felt challenged when they wanted to document in patients' folders and the ability for HCPs to satisfactorily support in ADR reporting process and PV activities effectively was therefore compromised. This was partly linked to internal hospital hierarchy and power, and the need to follow bureaucratic procedures. Nurses, in particular, felt less confident and capable of sending reports directly without approval from a doctor, pharmacist or in-charge. This created disruptions and delays in reporting. Electronic reporting, which has been reported in many studies as a way of improving the reporting system or process, was not in place at the time of the study even though a new electronic reporting system has recently been launched for patients and HCPs to report through mobile applications. The ADR reporting system was challenged by technical problems, which incapacitated HCPs in their reporting duties. A combination of electronic patient records and recent ADR reporting applications could improve the reporting process and medication safety practices. Even though theoretically HCPs knew patient care involved teamwork, the reporting process was often challenged by interprofessional interactions as a result of medical dominance. Notwithstanding this, the patients' folders and nurses' notes may serve as a repository for ADR cases often not officially reported through the yellow form.

6.2.6 External Factors

This research identified negative factors influencing HCP ADR reporting, both within and outside the settings in which they occurred, as previous research and typologies of ADR reporting factors have also shown (Oboyo, 2014). In terms of external system factors, HCPs identified concerns with stakeholder activities, coupled with infrastructural challenges and inefficient use of multi-media to enhance reporting. The main external stakeholders were patients, the FDA, MOH, the media and pharmaceutical companies. Even though the FDA was advocating training and creating awareness about reporting, some HCPs were of the view that these pieces of training were only channelled to pharmacy staff. This assertion may be true because pharmacists were seen as gatekeepers of adverse reaction reporting, and most interactions by the regulatory authorities were directly with them. HCPs were also concerned

that the few pieces of training meant for clinicians were sometimes attended by administrators who returned without cascading the training to clinicians. HCPs noted this behaviour was as a result of financial benefits and allowances participants received by attending these workshops. The links between FDA/MOH and also pharmaceutical companies/healthcare professionals or facilities on adverse reaction and safety reporting was weak. Even though healthcare professionals/facilities and pharmaceutical companies had a strong link in terms of product marketing, aspects of ADRs and PV were non-existent. HCPs were of the view that MOH-led training and protocols were often taken more seriously than external organisations, such as the FDA or pharmaceutical companies. HCPs appeared to pay attention only to MOH directives rather than to other stakeholders. In the survey, 20% of HCPs, especially pharmacy and medical staff, indicated they had contact from pharmaceutical companies at least every month. According to the Ghana FDA, MAH are required to have a QPPV representing manufacturing companies or distributors, which was not the case. Most of the QPPV were based in the capital city (Accra) with no representatives at the regional and district levels.

6.2.7 Administrative Issues

Healthcare facilities in this study were confronted with several administrative challenges. Hospital management and leadership did not prioritise PV and ADR reporting. The study showed that these administrative lapses also led to HCPs not treating ADR reporting issues seriously. From the data, HCPs pointed out that the MOH rarely featured these issues in their annual review meetings, there seemed to be limited budget and funding, and there was over-reliance on external donor support. It was also observed from how the reporting system operated that the FDA was the only stakeholder actively facilitating pieces of training and education on ADR reporting and PV; reporting activities were not adequately integrated into MOH plans. This, therefore, created a gap in vigilance, which affected HCP engagement and reporting rates. Even though there was necessary technical infrastructure, such as an electronic platform for the management of patient records (Hospital Administration and Management Systems Software), this was often challenged by technical glitches. Furthermore, reporting forms were often also unavailable, especially at the ward level, further complicating documentation challenges. These challenges made HCPs resort to verbal reporting, and pharmacy staff, who were often the gatekeepers, were challenged by incomplete patient data.

6.2.8 Infrastructural Concerns

Inadequate infrastructure, such as telecommunication network, poor road network and access to information, was a challenge, particularly for rural communities. Rural community health centres were challenged with transportation and communication issues (Kiguba et al., 2014). This made it difficult to send or receive ADR reports and other important safety reports in real time, especially during public health programmes, which involve mass administration of medicines in rural areas. Media publicity through radio has therefore been useful in disseminating medication safety issues to rural communities. Previous broadcasts saw an increase in reports, which could be explained as a facilitator, especially in rural areas. Also, recent introduction of mobile applications for reporting can bridge the gap between rural and urban centres, but a study of implementation of similar reporting systems in Kenya has raised concerns about the challenges of internet connectivity and other technical glitches which may need consideration and re-evaluation based on feedback as time goes on (Agoro et al., 2018).
In summary, several key factors have been argued to influence HCPs' perceptions of ADR reporting in the hospital setting in Ghana. Many of these reflect existing themes and evidence in the literature, both in Africa and elsewhere, suggesting that there are common issues within healthcare systems and hospitals more specifically that are of concern and could be the focus of improvements; these are considered more specifically in the next section.

6.3 Improving Reporting

This sub-section sees a shift from exploring the situation of ADR reporting from 'what it is' to 'what should be', considering HCPs' suggestions of improving reporting. As well as considering attempts to address issues identified in the previous section, this study also sought specific responses from the three professional groups of HCPs about how they felt ADR reporting could be improved. Two main themes emerged from participants' views, relating to education and also motivation for HCPs.

Education and training were the most important interventions HCPs found which could improve ADR reporting in both phases of the study (Table 21). In the quantitative phase, out of 12 suggestions, HCPs were mostly in favour of "*organizing continuous medical education, training and refresher courses for staff on ADR reporting*" (97%, n=374), "*encouraging feedback between patients' prescribers and dispensers*" (98%, n=375) and "*encouragement from heads of department*" (95%, n=364). As mentioned earlier, several empirical studies have

shown the beneficial effect of educational interventions (Pagotto et al., 2013), awareness workshops (Alraie et al., 2016; Herdeiro et al., 2012), information communication technology (Ribeiro-Vaz et al., 2016), increasing yellow card availability (Avery et al., 2011), training on ADRs (Morrison-Griffiths et al., 2003) and a dropbox (Amit and Rataboli, 2008) as measures for improving ADR reporting. Common among these studies, however, is that only sustainable interventions yielded the desired effect. Organising continuous medical education would therefore be more beneficial than one-off activities or interventions. The evidence shows that active multi-faceted educational strategies appear to be more beneficial and sustainable. The most effective intervention used three multi-faceted strategies involving weekly educational outreach, reminder cards and distribution of reporting forms. In Ghana, efforts have been made to incorporate PV subjects in the training of HCPs, especially in nursing training. The FDA's *DrugLens* also reported that 40 pharmacists were awarded CPD points for taking online courses on PV and reporting medication safety issues to the FDA in 2018. These strategies, although they are passive, have a positive impact on reporting, and similar arrangements for nurses and medical practitioners would therefore also be beneficial to reporting.

Three types of motivation were identified as facilitators to improving reporting: self-motivation, financial motivation and external motivation. HCPs were self-motivated to report because of personal reasons, such as patient safety and feeling that reporting is a professional obligation. These strategies have been reported in similar studies as facilitators of ADR reporting. Some HCPs, especially nurses, were of the view that financial incentives would be a motivational factor for reporting. External motivation such as awards, feedback, recognition or public acknowledgements for reporting efforts was seen as an important motivation which the FDA was already doing – the FDA acknowledges and gives feedback for HCP reports albeit not efficiently. HCPs therefore advocated improved feedback and reminders for reporting.
The least favoured opinions about improving reporting were using a dropbox and making ADR reporting compulsory. A suggestion about making ADR reporting compulsory was not an idea welcomed by most HCPs. They believed that it was important to first establish the knowledge base through education and training before approaching the issue of compulsory reporting. As mentioned earlier, developed countries such as Sweden, France and Italy have made reporting compulsory, which has accounted for the high number of ADR reports generated by HCPs. Interventions for improving reporting in such countries, therefore, often show no difference in reporting rates (Hazell and Shakir, 2006). Even though using a dropbox has been shown to increase reporting among doctors in other low- and middle-income countries, such as India,

where ADR reports increased from 14 to 32 in three months (Amit and Rataboli, 2008), it was a less popular option for HCPs in this study.

6.4 Triangulation Protocol

As mentioned earlier in the methods and methodology chapter, triangulation is an important component of mixed methods research which ensures that both qualitative and quantitative methods are integrated. The triangulation protocol proposed by Farmer (2006) has been used widely and is explored to identify where the convergence, complementarity and discrepancies in the data are inherent. These are based on the research questions and findings from both the qualitative and quantitative phases of this research (Table 25).

Table 25: Triangulation protocol (Farmer et al., 2006)			
QUESTIONS	QUANTITATIVE PHASE	QUALITATIVE PHASE	SUMMARY
What knowledge do HCPs have of ADR reporting?	HCPs showed a low level of awareness by their response to five general knowledge-based questions on ADR reporting. Even though more than a quarter (31.7%) were aware of the existence of a national pharmacovigilance centre, the majority (94.9%) were unaware of the SMS short code for reporting an ADR, basic information required on an ADR form (65.2%), required number of days to submit any type of ADR (99.5%) or serious reaction (80.0%).	Further exploration of HCP knowledge was based on a personal account of the reporting process and awareness of pharmacovigilance. It emerged that pharmacy and medical staff were more aware of the term 'pharmacovigilance' than nursing staff. Nursing staff reflections were characterised by long pauses, and they often guessed the meaning of the word 'pharmacovigilance'. There was uncertainty about the reporting process and what to report, especially by nursing staff.	Both phases of the study mutually enforced each other, showing a general lack of awareness about ADRs and how to report them. Pharmacy staff were, however, much more knowledgeable and aware of the reporting process compared to other HCPs.
What are the attitudes of HCPs towards reporting?	Among the 14 attitudinal parameters explored on a five-point Likert-type scale, 92.3% either strongly agreed or agreed that patient safety could be improved by reporting. On the other hand, 81.2% strongly disagreed or disagreed that HCPs were lethargic. They felt their busy work schedules were not a hindrance to reporting. Among the 7 Inman attitudes tested, ignorance of the reporting process was considered a cardinal factor; 78.8% either agreed or strongly agreed about it.	A key theme from the findings was centred on human and system factors. The majority of HCPs' accounts were human attitudes which were influenced by system factors. HCP attitudes identified were linked to their perceived patient attitudes including reluctance to report, the severity of incidence, confusion between ADR and medication error (ME), fear of consequence and product misconception.	Both phases of the research revealed different perspectives of HCP attitudes. Even though there were similarities in attitudinal parameters measured, the qualitative aspect provided an in-depth view. For example, the theme reluctance to report was similar to lethargy in the quantitative aspect, where 81.4% either disagreed or strongly disagreed that there were so many patients and ADR became unimportant. The qualitative aspect, however, showed that HCPs considered it is important, citing forgetfulness, workload and uncertainty about what to report as an explanation for their reluctance to report ADR. Additionally, perceived patient attitudes were identified, which HCPs felt were responsible for patients not reporting ADRs to them.

What are the ADR reporting practices and HCPs' role?	HCPs reported about practical organisational and personal factors affecting reporting. Organisationally, only 11.8% and 23% received feedback and training from the FDA, respectively. 28% reported that forms were available in their facilities. A combination of personal factors resulted in an annual reporting rate of 25% with 18.4% reporting at least 5 ADRs. 14% reported to have completed a form for it. 75% of HCPs had never reported an ADR in practice. The majority (39%) of HCPs preferred to report ADR to the medical staff. Half (50%) of HCPs felt ADR reporting was the ultimate responsibility of all, while a quarter felt it was nurses' responsibility. In terms of relations with patients, 50% of HCPs confirmed that patients reported ADRs and 62% indicated that they were able to educate their clients during working hours.	HCPs confirmed they observed more ADR than they reported. Emerging themes included sub-district experience, taking responsibility, perceived workload/burnout, lack of technical expertise and interpersonal relations among HCPs. HCPs also identified perceived practices of patients which affected reporting, including ignorance, apprehensive clients, hospital hopping/self-medication and surrogate reporting. Other broader system practices which influenced reporting were verbal reporting predominance, form availability, policy issues, funding, management and leadership, sociotechnical issues and stakeholder influence (i.e. FDA, MOH and pharmaceutical companies).	The quantitative phase highlighted why 75% of HCPs had never reported an ADR. The more extensive system practice of verbal reporting affected reporting. Most (39%) HCPs preferred to report to the doctor. This type of reporting was, however, seen as verbal as most HCPs said: "[…] *having to write a report like a written report and presenting it, I think I would not be very convenient. People will end up not reporting […]"* (Doctor 19). There was an agreement between data that the form was complex. Discord about the responsibility of reporting. While the majority wanted to report to medical staff and half agreed reporting was the responsibility of all, the qualitative phase showed that pharmacists were identified as the principal staff members who should be reporting ADRs. Stakeholder influence, management and leadership, and funding were not considered in the quantitative phase.
How do they understand the importance of reporting?	The importance of reporting was captured in some attitudinal questions on patient safety and lethargy. In these, HCPs strongly agreed patient safety could be improved, and disagreed strongly that patients were many and they did	The majority understood pharmacovigilance and the importance of reporting. A few nursing staff, however, were not aware of the term 'PV'. Concluding remarks from interviews showed that HCPs considered reporting important, for example both medical and pharmacy staff considered reporting as an essential aspect of practice.	Of those who knew what pharmacovigilance was, they equally knew the significance of reporting. The importance of ADR reporting was highlighted in both phases of the study, but it was more explicit in the quantitative phase than the qualitative phase. Attitudinal questions and questions on the responsibility of reporting showed how HCPs perceived the importance of reporting. Concluding

	not have time, so ADRs became unimportant.		remarks of the qualitative interviews also highlighted the importance and how HCPs wished they could report if only they had an enabling environment.
How is ADR reporting undertaken?	Open-ended questions – to whom did you report to and where did you report? – were a precursor to the process of reporting among HCPs. Most reports were verbal, and junior HCPs preferred to report to a doctor, pharmacist or in-charge.	The reporting process was characterised by 5 stages, namely identification, judging severity of reaction, assessment by a clinical pharmacist, documentation of details and collection by the FDA.	Challenges of prevalent verbal reporting, knowledge about the reporting process, complicated forms and unavailable forms affected the reporting process.
What is the association between the factors affecting ADR reporting and healthcare professionals?	There was significant difference between some background characteristics and knowledge, attitude, practice and suggested ways of reporting ADRs. Statistically significant variables were age, sex, number of patients seen per day, educational qualification and years of practice.	NA	Awareness of PV was significantly affected by age, sex and number of patients seen per day. Most HCPs who were aware of PV were in the 31–40 age bracket which was similar to a study in Nigeria (Okezie and Olufunmilayo, 2008).
What are the suggested ways of improving ADR reporting in the hospital setting?	HCPs concurred to all 13 suggested methods for improving ADRs. There were, however, variations in the levels of agreement. The majority were in favour of continuous medical education (97%), while compulsory reporting (83%) was the least favourite. Additionally, there was a higher level of neutral responses for mobile apps (8%) and compulsory reporting (10%) compared to the other methods.	Key suggestions among HCPs were on governance and policy changes, monitoring and motivation. Among the governance and policy issues HCPs wanted changes to nursing care plans, supply of forms, an improved patient folder system and CPD points for HCPs who report. HCPs suggested getting a responsible person monitoring units and departments. Motivation included sustaining self-motivation, financial motivation, reminders and education.	There was agreement about continuous medical education, feedback, reminders, HOD support, focal person/contact person for ADR, access to forms and multi-media use. This allowed in-depth understanding. There was, however, silence in the qualitative phase on communication, drug awareness, ADR network, compulsory reporting and a dropbox. Issues of governance and policy on CPD points, nursing care plan and improving the patient folder system were not captured in the quantitative phase either.

6.5 Strengths and Limitations

Strengths

This study is the first to explore ADR reporting among HCPs in the northern region of Ghana using a mixed methods approach. Using mixed methods research helped to triangulate the findings, draw on the strengths and minimise the weaknesses of undertaking this research as individual methodologies. The study used multiple approaches, including a random sample of 386 with a high response rate (86%), and a variable group of HCPs and hospital facilities, which enhanced the generalisability of the study. Previous studies on this subject have mainly focused on nurses (Bäckström et al., 2007; De Angelis et al., 2015; Paul et al., 2014), pharmacists only (Wilbur, 2013; Jarernsiripornkul et al., 2009; Terblanche et al., 2018; Granas et al., 2007) or doctors only (Sabblah et al., 2014; Khan et al., 2013; Adedeji et al., 2013; Okezie and Olufunmilayo, 2008; Oshikoya and Awobusuyi, 2009). A varied combination of HCPs therefore enhanced the validity, reliability and trustworthiness of the findings. Additionally, the qualitative phase, which also used both focus groups and in-depth interviews, further generated rich data, which added depth to the study and which has not been undertaken in the study area before. The different healthcare facilities sampled gave multiple perspectives of primary, secondary, tertiary and private healthcare.

The study used a combination of deductive and inductive theoretical approaches to answer the research questions, including the exploration of Inman's theoretical '*seven deadly sins*', and Herdeiro and Obonyo's works (Herdeiro et al., 2006; Inman, 1996; Obonyo, 2014).
Being a Ghanaian from the study location also became a strength because it helped to build rapport quickly with participants and gatekeepers. This resulted in a high response rate and the large number of interviews undertaken. Additionally, the report reflects the in-depth feedback from the supervision team and also experience of the study setting, which gives authority to the interpretation of the findings while reflecting on my own bias as researcher. Additionally, feedback from HCPs indicated they learnt a lot from participating in this study, which in itself served as PV promotion, raising awareness among HCPs.

The reporting of findings was guided by recommended, recognised guidelines and frameworks such as the Good Reporting of a Mixed Methods Study (GRAMMS) (O'Cathain et al., 2008) and the Triangulation Protocol (Farmer et al., 2006). This enhanced the validity and reliability of the research findings. The literature review was also based on systematic approaches, ensuring current relevant literature was retrieved.

Limitations

Nurses formed the majority of the study participants in both phases of the study. Randomisation did not account for an equal number of participants in the different professional categories of the study. Despite the significance of focus group discussions (FGD) where recall bias is reduced, enhancing inter/intra HCP comparison (Vaivio, 2012), doctors and pharmacists were unable to participate in the FGD for practical reasons; only nurses participated in the FGD. Medical and pharmacy staff, however, participated in an in-depth face-to-face interview to share their perspectives on ADR reporting.

Even though sampled hospitals gave multi-perspectives of different levels of health service delivery, i.e. primary, secondary and tertiary, the study focused on only metropolitan hospitals, excluding patients, rural and community clinics, and pharmacies. Perspectives of community pharmacists, patients and rural clinics about ADR reporting were given in the viewpoint of the HCP. Even though accounts from these other stakeholders may be useful for the implementation of HCP intervention approaches, they were not directly from patients, community pharmacists and rural healthcare providers, and thus further work may be required on their perspective about ADR reporting.

The limited number of earlier studies was a major challenge; only three studies were found in Ghana. This therefore affected the scope and depth of discussion of the findings in the local context. For example, only one study was found in Tamale and it focused only on nurses.

Even though it was reflected upon and the response rate was high, the survey of 67 items on the questionnaire could have introduced respondent fatigue (Lavrakas, 2013), where the latter end of the survey, which were Likert items, could have been given less thoughtful responses. Also, the design of the survey items resulted in many categorical variables which resulted in limited in-depth inferential statistics.

This study is not claiming generalisability of findings but shows important insights into reporting practices, enhanced by the qualitative findings and a mixed methods approach.

6.6 Recommendations

This section presents recommendations for public health policy, practice and future research. They may require further feasibility and acceptability testing with stakeholders responsible for the implementation. Based on the findings the following are recommended:

EXTERNAL ACTORS

- As a major stakeholder, the MOH should be more active and visible in relation to ADR monitoring. The FDA and MOH should jointly develop policies and protocols for routine hospital monitoring and reporting. The MOH should be visible in taking the lead in implementation of some of the strategies because HCPs were not taking reporting seriously because they came from the FDA rather than the MOH. There is a need for efficient internal systems of healthcare governance on PV and ADR reporting.

- HCPs valued recognition and feedback as motivations for reporting ADR. The FDA, MOH and pharmaceutical companies should develop innovative feedback and souvenirs for reporters to encourage reporting.

- Also, the general lack of knowledge of PV and ADR reporting among HCPs suggests the need for continuous education and training of HCPs. Where funds are limited, priority should be given to nurses and lower ranking frontline HCPs, because they have the greatest lack of awareness. The need for tailored education focusing on a non-blame culture, patient safety culture, and differentiation between error and malpractice is important. Education should also be patient-centred and focused on encouraging and engaging in patient discussions, since patients were seen as apprehensive and ignorant about medication safety.

- The FDA has CPD points and eLearning programmes on PV for pharmacy staff. This is, however, lacking for doctors and nurses. As part of collaborative efforts with stakeholders, the FDA should liaise with the Nurses and Midwives Council, and also the Medical and Dental Council to accept PV eLearning courses as CPD points for their members. This was suggested by medical and nursing staff for improved interest in PV and ADR reporting.

- Furthermore, it was apparent in this study that combined strategies may be useful for improving reporting. For example, TTH is a University Teaching Hospital and can therefore be an effective strategic and collaborative partner in the provision of PV-driven academic research and training support for HCPs.

- HCPs in this study were concerned about the lack of direct involvement of pharmaceutical companies in PV activities. Pharmaceutical companies relied on HCPs for ADR reports (O'Callaghan et al., 2018), but the lack of involvement was worrying. The FDA already requires that all companies must have a qualified person for pharmacovigilance (QPPV) but these were lacking in study hospitals. It is therefore recommended that the FDA should nudge MAH to get involved in general PV, general awareness and training, and not only marketing of their products but safety as well. PV should be part of their corporate social responsibility on patient safety, thus thinking of PV as part of production cost rather than profits.

INTERNAL FACTORS

- There were also power, bureaucratic and hierarchical issues identified in this study. This may cause delays to access to essential reporting tools or create communication barriers. The use of reporting tools should therefore be accessible to appropriate staff and reporting should be without blame and bureaucracy.

- There were organisational challenges and lack of critical frontline staffing. Pharmacy staff experienced high shortages in study locations. Reporting of ADRs may not require expert guidance or causality assessment before reporting. Where there are shortages of clinical pharmacists, it would be beneficial to have departmental contact persons and unit representatives to facilitate reporting. These individuals can work in close partnership with pharmacy staff to collate reports and educate other HCPs on PV. The role of the pharmacist was considered important. Reporting was often perceived as the duty of the pharmacist, but they rarely went on ward rounds. An academic detailing strategy could be beneficial by mentoring other HCPs on PV and ADR reporting.

- This study also showed low levels of knowledge, shortage of clinical pharmacists and how clear roles and responsibilities about reporting were lacking. Soumerai and Avorn (1990)

have shown academic detailing to be beneficial in educating and changing attitudes and behaviours of HCPs. Hospital management can therefore form incidence committees for individual hospitals to have oversight responsibility for academic detailing on ADR reporting and other patient safety issues since this is a characteristic of an effective and functional PV system.

- The reporting process was challenged by administrative and infrastructural issues. For example, Wi-Fi was limited, there are no institutional websites with content about the health centres and no institutional email addresses for HCPs. Adopting an efficient IT communication system within hospitals could facilitate the efficient circulation of information and enhance ADR reporting.

6.7 Further Research

- Based on the factors identified in this study, further research could explore patient-related factors affecting ADR reporting. In this research patients' attitudes were reported as a key factor that was influencing non-reporting of ADR in Ghana. From the literature review, very few studies have focused on exploring patient-related factors. This is an area that needs to be considered for future research.

- Further research using a universally acceptable approach to assessing knowledge, attitude and practice of PV and ADR is also needed. Even though this study used validated questions from previous studies, the adopted studies had varied questions and assessment criteria. Further research to design a standardised scale or algorithm for the assessment of knowledge and attitude would therefore provide an acceptable approach measuring these important aspects of PV. Additionally, practical aspects, such as assessing specific type of drugs and reactions based on system classifications, can help identify and focus on specific ADR issues.

- The study showed that 86% of HCPs used smartphones and the majority of HCPs were in favour of the introduction of mobile applications. With the introduction of reporting apps (Med Safety) by the Ghanaian FDA, further studies on the potential of mobile apps, electronic reporting, use of electronic patient records and other interventional approaches in Ghana would be beneficial to measure impact and sustainability of these interventions.

- Further research on the role of other stakeholder pharmaceutical companies, the MOH and academia would be useful.

- Understanding ADR reporting in population-specific studies, such as paediatric, geriatric population and public health programmes, would be important in understanding reporting in high-risk populations which this study was unable to explore.

6.8 Reflective Insights

This section follows on from a consideration of the study strengths and limitations and represents a summary of reflections and insights gained on both specific aspects unique to this study as well as wider learning from the research process. It is written based on the premise that reflective practice fosters experiential learning, thus the need to record and present our experiences transparently. Reflective writing within research is a key component of reflective practice, which is an important aspect of self-directed, experiential learning and can ultimately change one's attitude and practice (Jasper, 2005). Bulman (2013) describes it as:

"when an individual thinks critically about an event in order to understand how it made them feel, why they behaved the way they did, what other factors influenced the event, and what they might have done differently" (p.33).

My experiences over the past four years of undertaking this research have had a significant (and positive) impact on me, both personally and professionally, and in this section I want to explore in particular the cultural changes that shaped both myself and the research, as well as logistical aspects and latter recognition of specific learning needs. In doing so, it is hoped that this will provide insights that may be of relevance to future researchers working in such settings.

Moving from Ghana to study in the UK as an international student, being in a different culture and educational environment had its own challenges. The University, however, created a supportive environment where I was able to adapt and quickly settle down for studies. I started the programme not having any foundation in qualitative research, even though it was an integral part of my proposed research. My previous experience in quantitative methods and information retrieval were barely utilised in my previous job, thus the need for a refresher course as well. Being out of education for a while, I undertook courses provided by the University in qualitative research methods, systematic reviews and introductory statistics. It was an exciting time to learn new skills and develop existing ones. These gave me the required foundation in review of literature and preparation for my confirmation review and subsequently data collection.

As part of my training, my goal was to develop as many transferable skills as possible through internal and external activities. I therefore participated in competitions, consultancies, conferences, seminars, online courses, workshops, departmental and PGR-led activities to improve my knowledge, communication, networking, teamwork, organisation and presentation skills. In addition, I also supported teaching and learning activities and gained recognition as an Associate Fellow of the Higher Education Academy, UK, which has enhanced my CV.

Going into the field as a novice researcher and collecting primary data for the first time, made me nervous. Moreover, collecting data and being supervised remotely was also problematic. Frequent power outages, internet glitches and administrative bureaucracies further delayed the process, but the advice, support and guidance of my supervisory team helped me to overcome them. During interviews, I was also sometimes faced with participants' misconceptions about ADRs. I had to take the information as it was and discuss it further after the interviews. For example, a pharmacist suggested drugs manufactured by renowned pharmaceutical companies were less likely to have adverse effects. Through these further discussions about ADRs, HCPs suggested they learnt a lot from participating in the study. Researchers collecting data from similar settings must take into account the possibility of some of these challenges and make adequate preparation and backup plans.

Reflecting in particular on the intense data collection period, I believe I experienced a reverse cultural shock when I returned to collect data in Ghana. This is a recognised phenomenon (Gaw, 2000) which occurs when individuals, such as overseas students for example, return to their home countries following often extended periods away in another location where the culture and other practices may be different. Of note were the inefficient manual processes and bureaucracies I had to go through to get permits for my study. This sharply contrasted the structured and almost seamless processes I became accustomed to in the UK. As it is with many lower- and middle-income countries, the ethics application process involved submission of a lot of hard copy forms which resulted in printing more than 300 pages of hard copies. In addition, I had to travel more than 10 hours from the primary study site in Tamale to the capital city Accra in order to facilitate the application process. This was both physically and mentally exhausting. Even though the application was initially submitted in May for a June start, the project officially began in September. Administrative bureaucracies and delays affected the main study design which was eventually modified from a sequential to a concurrent mixed method because of limited time and resources. Lack of electronic infrastructure (e.g.

institutional email) and inefficient physical infrastructure (home postal address system) at the study site (Tamale) made it difficult to utilise a postal or online survey. Questionnaires were either self-administered or face-to-face with several call backs to retrieve completed questionnaires. Being familiar with the study setting and organisational culture, however, helped me to recruit a high number of study participants in the short time I had.

These logistical issues impacted on planned aspects of the research design and delivery, and in particular on the proposed use of an explanatory sequential approach. As noted previously in the methods chapter, the aim had been to deploy the surveys first, and collect data and analyse them fully before undertaking the qualitative stage. Using a concurrent mixed method eventually answered the research questions but an explanatory sequential approach could have helped in the design of specific qualitative questions after analysing the quantitative data. For example, I asked participants about ways to improve ADR reporting, both in the qualitative and quantitative phases, and the suggested responses were similar. If I had analysed the quantitative first, the most prominent suggestion, which was '*education and training'*, could have been explored specifically in depth in the qualitative phase for a deeper understanding of that theme. I learnt that advanced preparation and familiarisation with local guidelines could have minimised some of the challenges encountered.

After I returned from data collection, transcribing the data was time-consuming, but it gave me first-hand experience of the data and allowed me to familiarise myself with the data as suggested by Braun and Clark. While the standard for transcribing an hour of audio is estimated at about four hours, I was taking between five to six hours depending on audio quality, which was time-consuming, but a great way to learn. Analysis of the data and report writing was also challenging because of my underlying specific learning difficulties. Additional reiterations and support from Mathematics and Statistics Help (MASH), Disability and Dyslexia Support Service (DDSS), colleagues and the supervisory team helped me to overcome and improve my writing skills. However, in hindsight, I recognise that if these challenges had been identified earlier it could have ensured a more efficient utilisation of time and improved the quality of the work further.

6.9 Conclusion

In conclusion, this research found that Ghanaian HCPs do recognise the importance of reporting ADRs in their work. Even though HCPs recognised ADR reporting as important for patient safety in routine clinical practice, there were several challenges, particularly poor self-reported practices and knowledge related to ADR reporting which were of more concern. Greater opportunities for the role of pharmacists were identified, but also many other factors both within and beyond the hospital setting and involving human factors, relating to patients and also HCPs, affected reporting. Patient-related barriers identified further challenged HCP practice resulting in low/poor ADR reporting. To adequately estimate and reduce ADR-related morbidity and mortality, policymakers may need to focus on re-evaluation of current strategies and introduction of innovative interventions, such as academic detailing by designated staff, especially pharmacists, to improve ADR reporting. Key opportunities exist to enhance education and training for HCPs and the public, and enhance the role of pharmacists, particularly in relation to collaborative efforts.

6.10 References

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6.11 Appendices

Appendix A: Participant Consent Form

The University Of Sheffield.

Version 1 22/05/17

Participant Consent Form

Title of Research Project:
Factors Affecting Spontaneous Adverse Drug Reaction Reporting Among Healthcare Professionals in Northern Ghana

Name of Researcher: **Walter-Rodney Nagumo**

Participant Identification Number for this project: **Please initial box**

1. I confirm that I have read and understand the information sheet dated [ ] explaining the above research project and I have had the opportunity to ask questions about the project. ☐
2. I understand that my participation is voluntary and that I am free to withdraw at any time without giving any reason and without there being any negative consequences. In addition, should I not wish to answer any particular question or questions, I am free to decline. Contact +233208390330 /+447826186489. ☐
3. I understand that my responses will be kept strictly confidential (only if true). I give permission for members of the research team to have access to my anonymised responses. I understand that my name will not be linked with the final research materials, and I will not be identified or identifiable in the report or reports that result from the research. ☐
4. I agree for the data collected from me to be used in future research ☐
5. I agree to take part in the above research project. ☐

Name of Participant *(or legal representative)*	Date	Signature
Name of person taking consent *(if different from lead researcher)*	Date	Signature
NAGUMO WALTER-RODNEY		
Lead Researcher	Date	Signature

To be signed and dated in presence of the participant
Copies:

Once this has been signed by all parties the participant should receive a copy of the signed and dated participant consent form, the letter/pre-written script/information sheet and any other written information provided to the participants. A copy of the signed and dated consent form should be placed in the project's main record (e.g. a site file), which must be kept in a secure location.

Appendix B: Participant Information Sheet (focus group/indepth interview)

Appendix C : External Supervisor Support Letter

Version 1 12/06/17

14th June, 2017

The Adminstrator,
Ghana Health Service Ethics Review Committee.
Research & Development Division,
Ghana Health Service,
P. O. Box MB 190, Accra.
Email: ghserc@gmail.com

Dear Madam,

COMMITMENT AND SUPPORT LETTER

This is to confirm that I Prof. Alex Dodoo of the University of Ghana Medical School and Director of the WHO Collaborating Centre for Advocacy and Training in Pharmacovigilance at the University of Ghana School of Medicine and Dentistry has agreed to be the local supervisor for Mr. Nagumo Walter-Rodney. The title of his research is "Investigating Factors affecting Spontaneous Adverse Drug Reaction Reporting among Healthcare Professionals in Northern Ghana."

I will provide technical support during the research.

Do not hesitate to contact me if you require further clarification or information.

I look forward to your usual cooperation.

Thank you.

Yours faithfully,

Prof. Alex Dodoo

Director

Visiting Address: ONE Medspina PLACE, Mango Tree Avenue, Asylum Down, Accra, Ghana.
Postal Address: P. O. Box LT 282, Accra, Ghana
Tel: 0302 268 746 | **Cell:** 0289 014 000 | **Fax:** 0302 268 746
Email: info@who-pvafrica.org | **Website:** www.who-pvafrica.org

Appendix D : Access Request Letter

Version 1: 20.09.16

The University Of Sheffield.

University of Sheffield
ScHARR
Public Health Section
S1 4DA, UK
wnagumo1@sheffield.ac.uk
8th August, 2017.

The Regional Director

Ghana Health Service

Northern Region

Tamale

Dear Sir/Madam,

PERMISSION FOR ACCESS

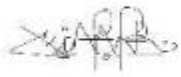
I am a PhD student at the University of Sheffield and I would like to request for assess to selected hospitals in the Tamale metropolis. The proposed hospitals are the Tamale Teaching Hospital, Tamale Central Hospital, Tamale West Hospital and the SDA hospital. The research is titled**: Investigating Factors affecting Spontaneous Adverse Drug Reaction Reporting among Healthcare Professionals in Northern Ghana.**

It is supervised by Dr. Richard Cooper and Dr. Robert Akparibo both from the University of Sheffield. Professor Alex Dodoo of the WHO Collaborating Centre for Advocacy and Training in Pharmacovigilance, University of Ghana Medical School will be the local supervisor in Ghana.

Ethical approval will be from the Ghana Health Service Ethics Review Comittee.

It is my hope that my submission will meet your standards for consideration and clearance.

Yours faithfully,



Nagumo Walter-Rodney

Appendix E : Participant Invitation letter

The University Of Sheffield.

Department of Public Health
ScHARR
University of Sheffield
S1 4DA

INVITATION LETTER

Study Title: Investigating Factors Affecting Spontaneous Adverse Drug Reaction Reporting Among Healthcare Professionals in Northern Ghana

We would also like to invite you to participate in a focus group discussion to further explore your experiences of reporting adverse drug reactions. If you are interested in doing so, please fill in your details below and we will send you further details.

I would be willing to be contacted by a researcher about taking part in an interview for the above named study.

Name.....

Address.....

.....

.....

Signed.....

Date.....

Phone number.....

Email address.....

A good time to contact me is.....

Please indicate preference by ticking the boxes below (CHOOSE ONLY ONE)

Focused Group Discussion ☐ ANY ☐

In-depth Interview ☐

Appendix F : Statement to Comply with Ethical Principles

The University Of Sheffield.

STATEMENT TO COMPLY WITH ETHICAL PRINCIPLES

As the principal investigator (PI) of this study, I write on behalf of my supervisors and research team to uphold the fundamental ethical principles of respect for autonomy, beneficence, nonmaleficence and justice towards research participants.

I will therefore ensure that there is safe keeping of all research instruments and digitised data. Recorded survey questionnaires will be stored under lock and key in a plastic storage container. Digital recordings will be transferred on an encrypted and pass worded personal computer. Only the PI will have access to the to the data.

We shall strictly adhere to all ethical principles and guidelines throughout this study. The supervisors are also committed to ensure the successful completion of the study.

Data collected for this study will not be used for any other purpose than for the PhD dissertation.

Thank you

.....

Walter-Rodney Nagumo

School of Health and Related Research (ScHARR)

University of Sheffield, UK

.....

Dr. Robert Akparibo

School of Health and Related Research (ScHARR)

University of Sheffield, UK

.....

Dr. Richard Cooper

School of Health and Related Research (ScHARR)

University of Sheffield, UK

.....

Prof. Alex Dodoo

University of Ghana Medical School

Legon

Appendix G : Supervisor Support Letter

Appendix H: Access Approval Letter

The University Of Sheffield.

School Of Health And Related Research.

Dr Richard Cooper Senior Lecturer

Section of Public Health
School of Health and Related Research
Regent Court
30 Regent Street
Sheffield S1 4DA

Telephone: +44 (0) 114 222 0683
Fax: +44 (0) 114 272 4095
Email: Richard.Cooper@sheffield.ac.uk

7th August 2017

Ref: ID NO:GHSERC001/07/17

To whom it may concern,
I would like to confirm in this letter as the lead supervisor of Walter-Rodney Nagumo for his doctoral research that it has been confirmed with the University of Sheffield Research and Innovation Services (RIS) that it recognises the ethical review process of the Ghana Health Service Ethics Review committee. This is covered as part of what is termed the Alternative Ethics Review Procedure and the Ghana Health Service is on the list of "*organisations overseas that are recognised by the University of Sheffield's Research Ethics Committee as having in place sufficiently robust ethics review procedures.*" As such, this means that a separate application to an internal University of Sheffield departmental research ethics review is **not** needed.

I hope this information is sufficient to allow you to finalise Walter-Rodney Nagumo's application

Yours sincerely

Dr Richard Cooper PGCHE, BSc, LLB, MA, PhD, FHEA, MRPharmS

The University Of Sheffield.

GHANA HEALTH SERVICE
REG. HEALTH DIRECTORATE
NORTHERN REGION
05 SEP 2017
RECEIVED

University of Sheffield
ScHARR
Public Health Section
S1 4DA. UK
wnagumo1@sheffield.ac.uk
13th July. 2017.

The Director

Ghana Health Service

Tamale N/R

Dear Sir.

REQUEST FOR PERMISSION

I am a PhD student at the University of Sheffield and I would like to request for permission to investigate factors affecting spontaneous adverse drug reaction reporting among doctors, nurses and pharmacists in four healthcare facilities in the metropolis.

The process will involve administration of a survey questionnaire which will be followed by in-depth interviews and focus group discussions. The study will be conducted at times that do not interfere with their normal working hours.

The project is expected to last five months and will be conducted in four selected hospitals (Tamale Teaching Hospital, SDA hospital, Tamale Central Hospital and Tamale West Hospital) all in the Tamale Metropolis.

It is my hope that my request will meet your kind consideration.

Thank you.

Yours faithfully.

Walter-Rodney Nagumo

(3) Please for your approval 05/09/17

(4) Action taken 08/09/2017

DDSH 6/9/17

Appendix I : Adverse Reaction Reporting forms

FDA/SMC/SMD/GL-RAR/2013/01

APPENDIX I- Adverse Reaction Reporting Form

Age/Date of Birth (dd/mm/yyyy): / / Gender: M ( ) F ( ) Wt: .....kg
Name/Folder Number .....Telephone No:.....
Hospital/Treatment Centre.....

(B) DETAILS OF ADVERSE REACTION AND ANY TREATMENT GIVEN (Attach a separate sheet when necessary)

Date reaction started (dd/mm/yyyy) : / / Date reaction stopped (dd/mm/yyyy): / /

(C) OUTCOME OF ADVERSE REACTION:

Recovered ( ) Not yet recovered ( ) Unknown ( )
Did the adverse reaction result in any untoward medical condition? Yes ( ) No ( ) If yes, specify.....
SERIOUSNESS: Death ( ) Life threatening ( ) Disability ( ) (specify)..... Hospitalization ( )
Others (specify).....

(D) SUSPECTED PRODUCT(S) (Attach sample or product label if available)

Brand name	**Generic name**	**Batch no.**	**Expiry date**	**Manufacturer**
Reasons for use (Indication)	Daily dose:	Route of Administration:		
Date started: (dd/mm/yyyy)	Date stopped: (dd/mm/yyyy)			
Did the adverse reaction subside when the drug was stopped (de-challenge)? Yes ( ) No ( )				
Was the product prescribed? Yes ☐ No ☐	**Source of Drug:**			

Was product re-used after detection of adverse reaction (re-challenge)? Yes ( ) No ( )
Did adverse **reaction** re-appear upon re-use? Yes ( ) No ( )

(E) CONCOMITANT DRUGS INCLUDING HERBAL MEDICINES TAKEN PRIOR TO THE ADVERSE REACTION

(Attach a separate sheet when necessary)

Name of Drug	**Daily dose**	**Date started**	**Date stopped**	**Reason(s) for use**

Attach all relevant laboratory tests/data

(F) DETAILS OF REPORTER

Name of Reporter: .....Profession.....
Address:.....
Signature: ..... Tel: ..... E-mail:.....
Date (dd/mm/yyyy) : / /

Appendix J : Consumer/Patient reporting form, page 1

APPENDIX II-Patient Reporting Form

1. The person who had the Side Effect

Give details of the medicine you suspect of causing the side effect.

* Name of the medicine _____

☐ Prescription ☐ bought in pharmacy name of pharmacy _____

☐ bought elsewhere please specify _____

☐ bought on the internet

Dosage (for example, one 250 mg tablet, twice a day) _____

What was it taken for? _____

Start date: dd / mm / yyyy End date: dd / mm / yyyy

Give details if you (or the person you're reporting for) were taking any other medicine at the same time or two weeks earlier

Name of other medicine/herbal medicine _____ ☐ Prescribed by doctor ☐ Bought in pharmacy

Dosage(for example, one 250 mg tablet, twice a day) _____ ☐ Bought elsewhere (please, state)_____

What was the medicine/herbal remedy taken for _____

Start date: dd / mm / yyyy End date: dd / mm / yyyy

Did you stop because of the side effect? ☐ Yes ☐ No

Attach a sample or product label or relevant laboratory tests/data if available.

2. The person who had the Side Effect

We need contact details- please supply a full postal address, even if you prefer not to give a phone number or email address

* Title Dr. / Prof. / Mr. / Mrs. / Miss / Rev. First name _____ Family Name _____

* Address _____

_____

Telephone number _____ Email address _____

Please sign and date this form: ☐ I agree that the Food and Drugs Authority (FDA) can contact me to discuss the suspected side effect, and to ask for more information that might help in understanding the case.

* Signed: _____ Date dd/mm/yyyy _____ / _____ / _____

Appendix K : Consumer/Patient reporting form, page 2

Complete all lines marked with * and give as much other information as you can

4. The person who had the Side Effect

* **Who had the side effect?**
  ☐ You ☐ Your child ☐ Someone else
* **Information about the person:** Supply as much information as you can, even if you prefer not to give a name.
  First name or initials _____ Family name _____ ☐ Male ☐ Female
  Age _____ Weight _____ (kg) Height _____ (meters) _____
  Any other relevant information? For example, does the person have any medical conditions or allergies?
  _____
  _____
  _____

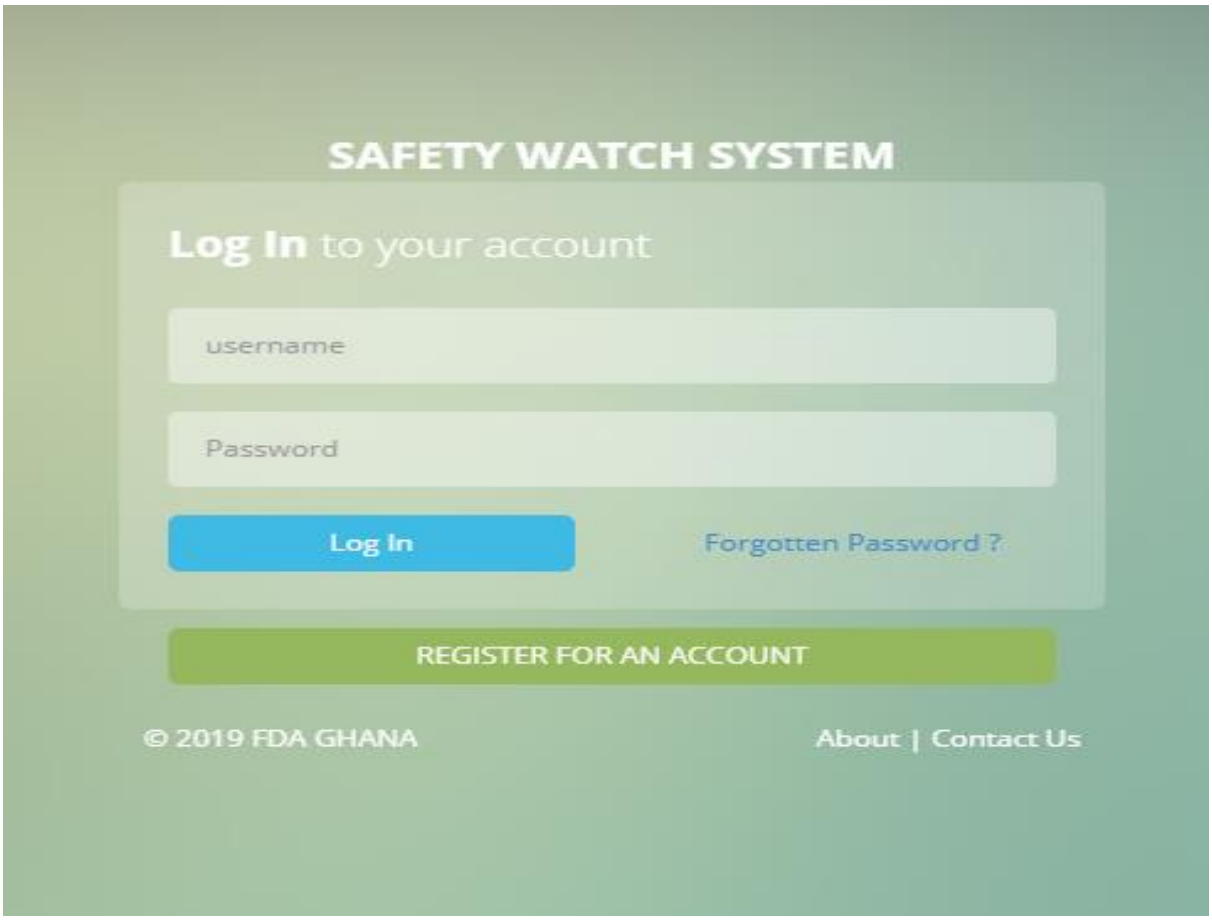
3. The Side Effect

* **What were the symptoms of the side effect, and how did it happen?** (If there isn't enough space here, attach an extra sheet of paper).
  _____
  _____
  _____
  _____
* **How bad was the side effect?** Tick the box that best describes how bad the symptoms were.
  ☐ Mild ☐ Unpleasant, but did not affect everyday activities ☐ Bad enough to affect everyday activities ☐ Bad enough to see doctor
  ☐ Bad enough to be admitted to hospital ☐ Caused permanent disability ☐ Caused death ☐ Other _____
* **When did the side effect start?** dd / mm / yyyy _____
* **How is the person feeling now?** Tick the box that best describes whether the person still has symptoms of the suspected side effect.
  ☐ Better (no more symptoms) ☐ Getting better ☐ Still has symptoms ☐ More seriously ill ☐ Died ☐ Other
* **Can you give any more details?** For example, did the person take or receive any other treatment for the symptoms? Did they stop taking the medicine as a result of the side effect?
  _____
  _____
  _____
  _____

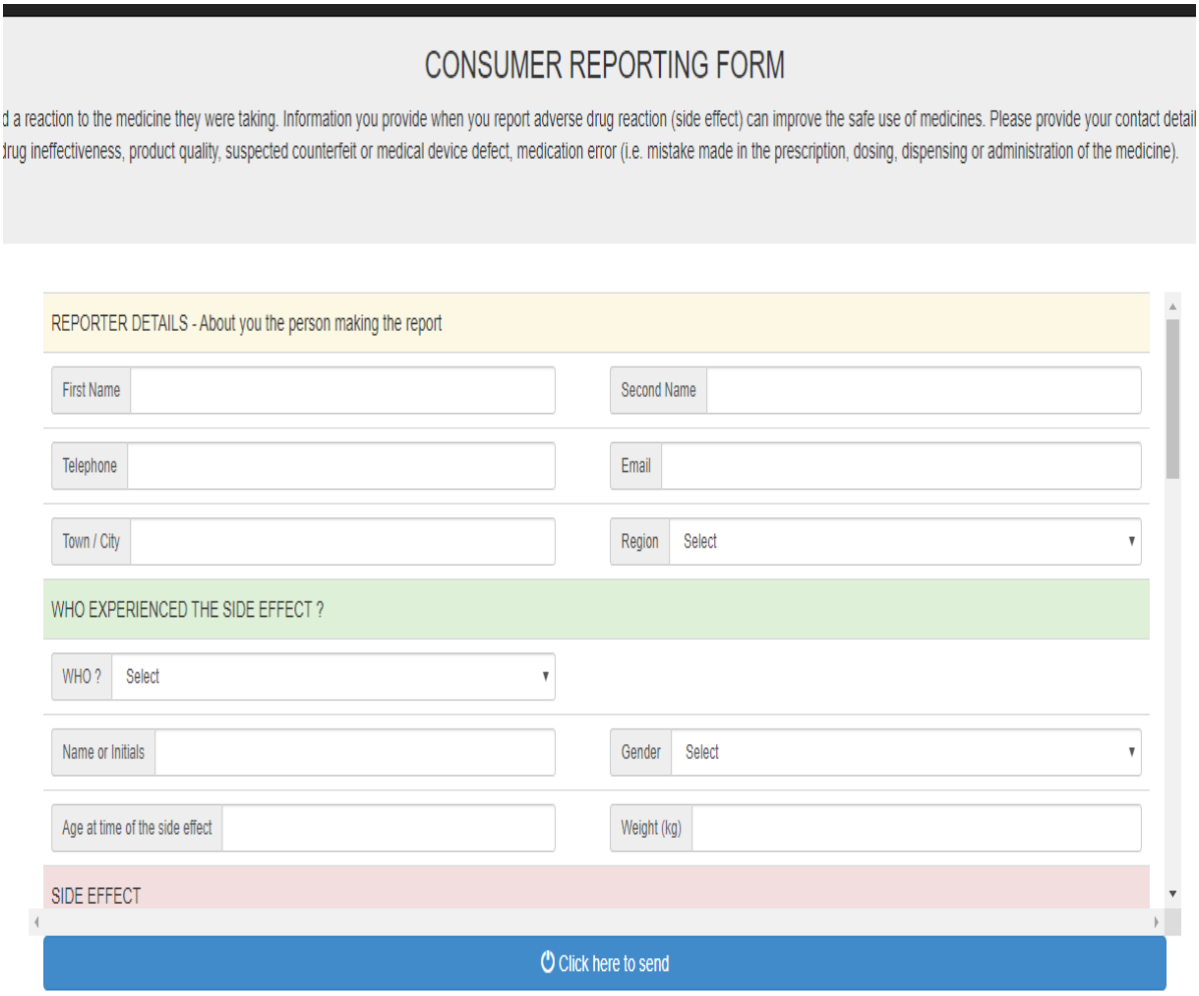
Make sure you have completed all the lines marked *

Please turn over ➡

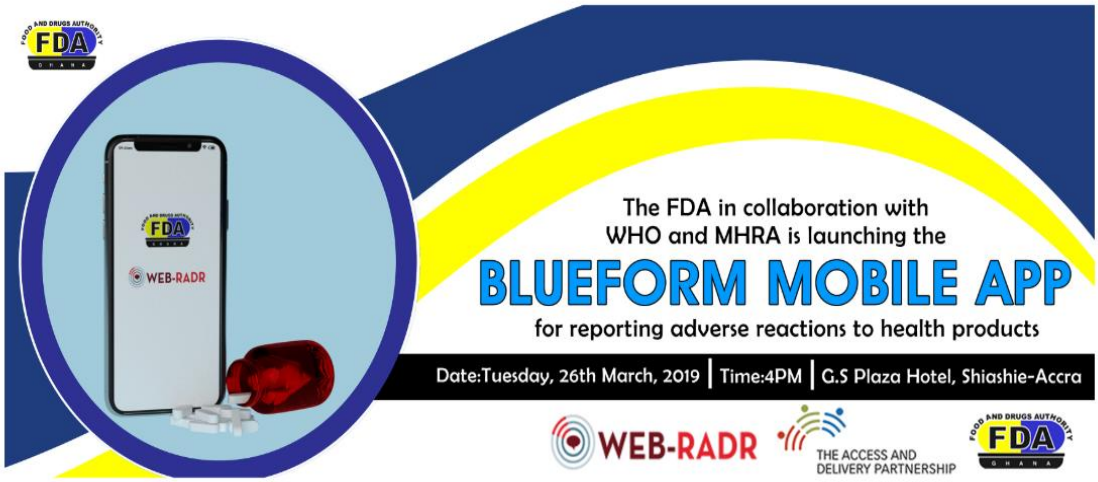
Appendix L : Healthcare Professional Electronic Reporting Portal.



Appendix M: Electronic Consumer/Patient reporting portal



Appendix N: Launch Poster of a New Mobile Application by the FDA for patient/consumer Reporting



Appendix O: Ethical Approval Letter

GHANA HEALTH SERVICE ETHICS REVIEW COMMITTEE

In case of reply the number and date of this Letter should be quoted.

Research & Development Division
Ghana Health Service
P. O. Box MB 190
Accra
Tel: +233-302-681109
Fax + 233-302-685424
Email: ghserc@gmail.com

MyRef. GHS/RDD/ERC/Admin/App 1716
Your Ref. No.

Walter-Rodney Nagumo
The University of Sheffield
School of Health and Related Research
UK

The Ghana Health Service Ethics Review Committee has reviewed and given approval for the implementation of your Study Protocol.

GHS-ERC Number	**GHS-ERC: 001/07/17**
Project Title	Investigating Factors Affecting Spontaneous Adverse Drug Reaction Reporting among Healthcare Professionals in Northern Ghana
Approval Date	31st August, 2017
Expiry Date	30th August, 2018
GHS-ERC Decision	**Approved**

This approval requires the following from the Principal Investigator

- Submission of yearly progress report of the study to the Ethics Review Committee (ERC)
- Renewal of ethical approval if the study lasts for more than 12 months,
- Reporting of all serious adverse events related to this study to the ERC within three days verbally and seven days in writing.
- Submission of a final report **after completion** of the study
- Informing ERC if study cannot be implemented or is discontinued and reasons why
- Informing the ERC and your sponsor (where applicable) before any publication of the research findings.

Please note that any modification of the study without ERC approval of the amendment is invalid.

The ERC may observe or cause to be observed procedures and records of the study during and after implementation.

Kindly quote the protocol identification number in all future correspondence in relation to this approved protocol

SIGNED.....
DR. CNYTHIA BANNERMAN
(GHS-ERC CHAIRPERSON)

Cc: The Director, Research & Development Division, Ghana Health Service, Accra

Appendix P: Survey Instrument (Questionnaire)

The University Of Sheffield.

School of Health and Related Research (ScHARR)

Factors affecting Spontaneous Adverse Drug Reactions (ADR) Reporting

Please complete all questions, using a pen or pencil in the appropriate place. This questionnaire should take not more than 20 minutes to complete. **(you may keep pencil).**

PART1: DETAILS ABOUT YOU

1. Your age (please select only one box):

20-30 [ ]
31-40 [ ]
41-50 [ ]
51-60 [ ]
60+ [ ]

2. Your gender (please select only one box):

Male [ ]
Female [ ]
Prefer not to say [ ]

3. In which department or unit do you mainly work?.....

4. Have you rotated to a different unit or department in the pass one year?

Yes [ ] No[ ]

5. Highest Level of education

Masters Degree [ ]
Bachelors Degree [ ]
Diploma [ ]
Certificate [ ]
Other..... [ ] (please state).....

6. Years of practice/service (please select only one box):

0-5 years [ ].
6-10 years [ ].
11 -15 years [ ].
16-20 years [ ]
Over 20 years [ ]

1

7. On average, how many patients would you see per day relating to your main work **(please select only one box):**

0-10 [ ]
11 – 20 [ ]
21-30 [ ]
31 – 40 [ ]
41-50 [ ]
51-60 [ ]
More than 60 [ ],
Don't know [ ]

8. Which best describes your pattern of work **(please select only one box):**

Full time [ ]
Part-time [ ]
Other [ ] **If so, please state what:** .....

9. Do you work on locum basis elsewhere?

Yes [ ] No [ ] prefer not to say [ ]

10. Do you use a smart phone

Yes [ ] No [ ]

PART 2: ABOUT YOUR CURRENT PRACTICE

11. Are forms for reporting ADRs available in your unit/department?

Yes [ ] No [ ] not sure [ ]

12. How often do you recall observing ADRs from medicines in patients?

Daily [ ] weekly [ ] monthly [ ] every three months [ ] every 6 months [ ] once a year [ ] **never [ ] can't tell [ ]**

13. How often do you report a Adverse Drug Reaction from medicines?

Daily [ ] weekly [ ] monthly [ ] every three months [ ] every 6 months [ ] once a year [ ] never [ ] **(skip to 18)** **can't tell [ ] (skip to 18)**

14. Did you complete a form for the Adverse Drug Reaction from the medicine you observed?
Yes [ ] No [ ] Not sure [ ]

15. How many ADRs have you reported this year **(select one option)**
nil [ ]
1-5 [ ]
6-10 [ ]
11- 20 [ ]
More than 20 [ ]

16. Whom did you report to?.....

17. Where did you record it?.....

18. Do you recall having received any training about reporting ADRs ?
Yes[ ] No[ ] **(skip to 21)** not sure [ ] **(skip to 21)**

19. If yes, please indicate when you last had training

month ago [ ] three months ago [ ] 6 months ago [ ] a year ago [ ]
two years ago [ ] Not sure [ ]

20. Do you feel you were more likely to report an ADR after the training?
Yes [ ] No [ ] Not sure [ ]

21. How often are you approached with products from pharmaceutical company representatives?
Every month [ ] Every three months [ ] Every six months [ ]
never [ ] can't remember [ ]

22. Where do you regularly get medication safety information from? **(please select any that apply)**
TV [ ] Radio [ ] Social Media [ ] Poster [ ] newsletters[ ]
Internet [ ] drug inlay sheet [ ] other [ ] please state.....

23. Do you read the FDAs newsletter, the DrugLens?
Yes [ ] No [ ] not sure [ ]

3

PART 2: ABOUT YOUR CURRENT PRACTICE (continue)

24. If yes where do you get your copy from? .....

25. Do you get feedback when you send ADR reports to authorities?

Yes [ ] Sometimes [ ] No [ ] **(skip to 27)** can't remember [ ] **(skip to 27)**

26. If **yes or sometimes** where did you access the feedback from **(tick all that apply)**

Food and Drug Authority (FDA)	[ ]
Pharmaceutical company	[ ]
Hospital Pharmacy Directorate	[ ]
Hospital Medical Directorate	[ ]
Nursing Directorate	[ ]
Other (please state).....	[ ]

PART 3: CONTEXTUAL FACTORS

27. Are there any policy guidelines in your facility to enforce ADR reporting?
Yes [ ] No [ ] don't know [ ]

28. Have you seen there any adverts or posters about ADR reporting in your hospital?
Yes [ ] No [ ] don't know [ ]

29. Do you have an institutional contact person responsible ADR reporting?
Yes [ ] No [ ] don't know [ ]

PART4: EXTERNAL FACTORS

30. Do your patients report to you when they experience ADRs or side effects of medicines?
Yes [ ] No [ ] sometimes [ ]

31. Are you able give education to patients on possible ADR's during working hours?
Yes [ ] No [ ] sometimes [ ]

32. Which do you think is the most convenient method for reporting ADR in your facility (**please select one**)

a. Paper based reporting [ ]
b. Telephone hotline [ ]
c. Online reporting directly on FDA website [ ]
d. Social Media (Whatsapp, Facebook, twitter, Instagram) [ ]
e. Electronic patient records [ ]
f. Reporting to Pharmacist on duty [ ]
g. Reporting to prescriber/ Doctor on duty [ ]
h. Others (please state)..... [ ]

PART 5: YOUR KNOWLEDGE ON ADR REPORTING

33. Are you aware of the National Pharmacovigilance Center in Ghana?
Yes [ ] No [ ] don't know [ ]

34. What is the Food and Drugs Agency SMS text short code reporting ADRs? **(Please select one)**
1540[ ] 4015[ ] 0154 [ ] 1234[ ] don't know [ ]

35. All ADRs should be reported within how many days?
7 calendar days [ ]
15 calendar days [ ]
30 calendar days [ ]
28 calendar days [ ]
don't know [ ]

36. Serious suspected and serious unexpected ADR associated with the use a product in Ghana should be reported to the authorities within how many days?
7 calendar days [ ]
5 calendar days [ ]
30 calendar days [ ]
28 calendar days [ ]
don't know [ ]

37. What basic information is required on the ADR form?**(please select one)**

Pharmaceutical company details, FDA details, medication details, hospital details [ ]
Patient details, suspected drug, suspected reaction and reporter details [ ]
Test results, allergies, abnormalities and date ADR was collected [ ]
Drug Dosage, route, batch and drug brand [ ]
Other (please state): ..... [ ]
Don't know [ ]

PART6A:YOUR ATTITUDE TOWARDS REPORTING

38. Which group of healthcare professionals has the potential to send the **most** number of reports?

Nurses [ ]

Doctors [ ]
Pharmacist [ ]
Physician/Medical Assistants [ ]
All [ ]
Other (please state).....

39. Who has the **ultimate** responsibility to report ADR?

Nurses [ ]

Doctors [ ]
Pharmacist [ ]
Physician/Medical Assistants [ ]
All [ ]
Other (please state).....

WHAT IS YOUR OPINION ON THE FOLLOWING STATEMENTS (PLEASE TICK ONE).

PART 6 B: YOUR OPINIONS	Strongly Disagree	Disagree	Neither agree or disagree	Agree	Strongly agree
40. I feel the reporting process in my hospital is efficient.	[ ]	[ ]	[ ]	[ ]	[ ]
41. I feel only safe drugs are allowed in the market.	[ ]	[ ]	[ ]	[ ]	[ ]
42. I feel the ADR form is complex to complete.	[ ]	[ ]	[ ]	[ ]	[ ]
43. I feel that reporting ADR leads to investigations by the health department which can affect my job.	[ ]	[ ]	[ ]	[ ]	[ ]
44. I feel guilty for ADR that occurred because of a drug I administered or prescribed	[ ]	[ ]	[ ]	[ ]	[ ]
45. I keep ADRs report so that I can collect case series and publish to better my career.	[ ]	[ ]	[ ]	[ ]	[ ]
46. I don't think I should report an ADR when I am not sure of the causality between the reaction and the drug.	[ ]	[ ]	[ ]	[ ]	[ ]
47. I feel there are so many patients to handle and we don't have time, so ADRs become unimportant.	[ ]	[ ]	[ ]	[ ]	[ ]
48. I would report more ADRs if there were monetary gain or percentage increase in salary.	[ ]	[ ]	[ ]	[ ]	[ ]
49. I feel there is lack of knowledge AND unawareness of the reporting process involved in submitting an ADR report.	[ ]	[ ]	[ ]	[ ]	[ ]
50. I feel ADRs can increase healthcare cost in my facility.	[ ]	[ ]	[ ]	[ ]	[ ]
51. I feel only serious ADRs should be reported.	[ ]	[ ]	[ ]	[ ]	[ ]
52. I feel ADR reporting in my hospital is generally effective.	[ ]	[ ]	[ ]	[ ]	[ ]
53. I feel patient safety in my hospital can be improved by reporting ADRs.	[ ]	[ ]	[ ]	[ ]	[ ]

PLEASE INDICATE TO WHAT EXTENT YOU AGREE OR DISAGREE WITH THE FOLLOWING SUGGESTED WAYS OF IMPROVING ADR REPORTING IN YOUR FACILITY (PLEASE TICK ONE FOR EACH CHOICE)

PART 6C: YOUR OPINIONS	Strongly Disagree	Disagree	Neither agree or disagree	Agree	Strongly agree
54. Organizing continuous medical education, training and refresher courses for staff on ADR reporting.	[ ]	[ ]	[ ]	[ ]	[ ]
55. Encouraging feedback among patients, prescribers and dispensers of medicines.	[ ]	[ ]	[ ]	[ ]	[ ]
56. Regular reminder visits from a qualified person for pharmacovigilance (QPPV).	[ ]	[ ]	[ ]	[ ]	[ ]
57. Increased communication among different healthcare professional cadres	[ ]	[ ]	[ ]	[ ]	[ ]
58. Increased multi-media publicity about the reporting scheme at various healthcare facilities.	[ ]	[ ]	[ ]	[ ]	[ ]
59. Increasing awareness about new drugs in health facilities.	[ ]	[ ]	[ ]	[ ]	[ ]
60. Encouragement from heads of departments.	[ ]	[ ]	[ ]	[ ]	[ ]
61. Forming an ADR reporting network	[ ]	[ ]	[ ]	[ ]	[ ]
62. Introduction of mobile phone application for online reporting. 63. Having an ADR focal person in every unit/department	[ ] [ ]	[ ] [ ]	[ ] [ ]	[ ] [ ]	[ ] [ ]
	8				

PART 6C: YOUR OPINIONS (cont.)	Strongly Disagree	Disagree	Neither agree or disagree	Agree	Strongly agree
64. Make ADR reporting a compulsory obligation for all healthcare professionals	[ ]	[ ]	[ ]	[ ]	[ ]
69. Making ADR forms available and accessible in every department/unit	[ ]	[ ]	[ ]	[ ]	[ ]
65. Providing an ADR drop box in all units/departments.	[ ]	[ ]	[ ]	[ ]	[ ]
66. Could you suggest other ways of improving ADR reporting in your healthcare facility?	....				

THANK YOU FOR ANSWERING THESE QUESTIONS.

If you have any comments about any of the questions we have asked, please add them here

_____

_____

_____

_____

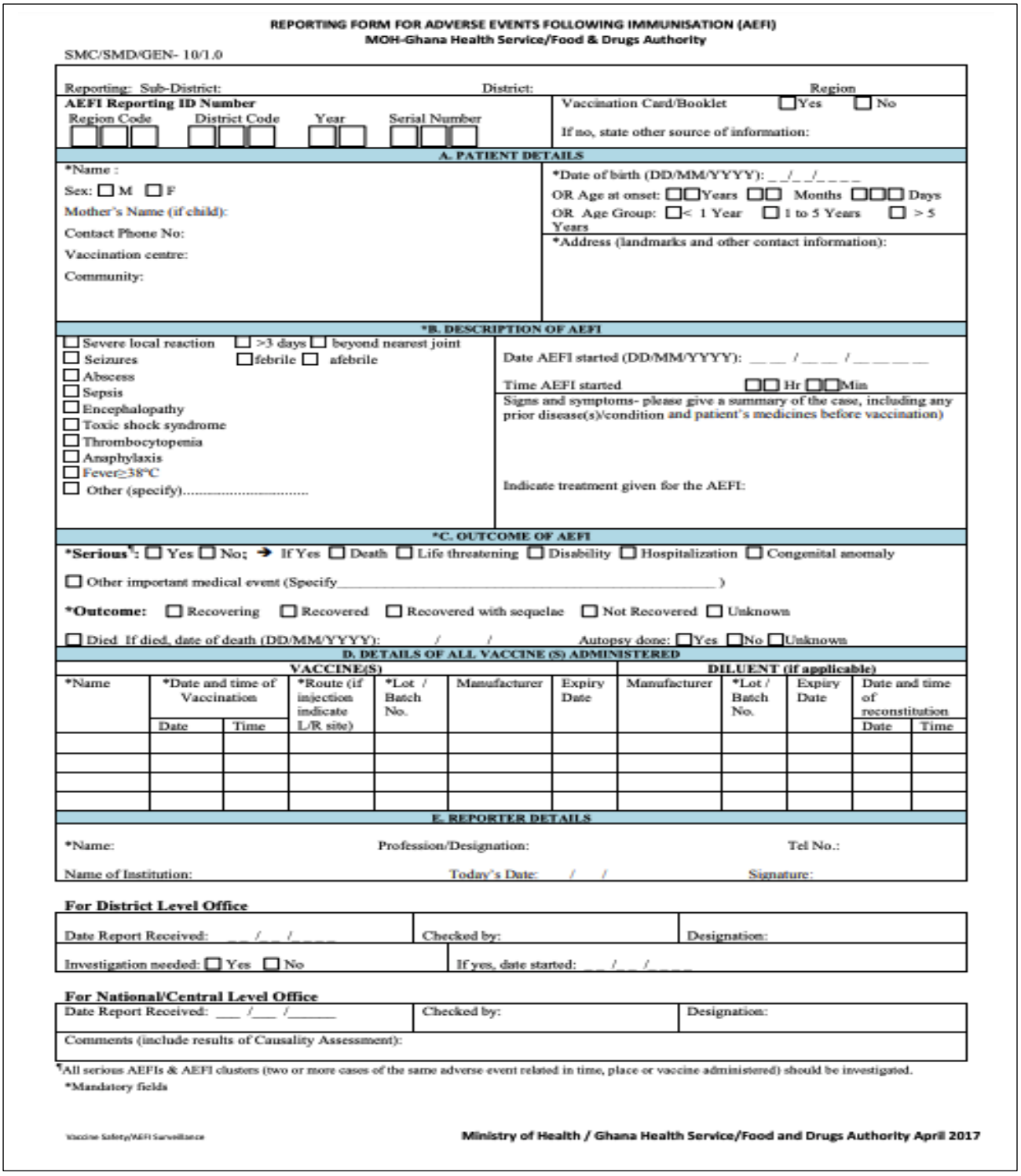
If you wish to find out the results of this questionnaire, or you would like to discuss any aspect of this questionnaire please email wnagumol@sheffield.ac.uk

Please provide your name and contact telephone number and explain your reason for emailing.

Please return your questionnaire, consent form and invitation letter in your given envelope to the Research Assistant OR TTH Research Unit (2nd Floor Admin.)OR In-Charge for collection.

THANK YOU VERY MUCH FOR YOUR GREAT CONTRIBUTION TO KNOWLEDGE!!

Appendix Q: Adverse Event Following Immunization (AEFI) reporting



REPORTING FORM FOR ADVERSE EVENTS FOLLOWING IMMUNISATION (AEFI)
MOH-Ghana Health Service/Food & Drugs Authority

SMC/SMD/GEN- 10/1.0

Reporting: Sub-District: District: Region

AEFI Reporting ID Number
Region Code ☐☐☐ District Code ☐☐☐ Year ☐☐ Serial Number ☐☐☐

Vaccination Card/Booklet ☐Yes ☐No
If no, state other source of information:

A. PATIENT DETAILS

*Name :
Sex: ☐ M ☐ F
Mother's Name (if child):
Contact Phone No:
Vaccination centre:
Community:

*Date of birth (DD/MM/YYYY): _ _/_ _/_ _ _ _
OR Age at onset: ☐☐Years ☐☐ Months ☐☐☐ Days
OR Age Group: ☐< 1 Year ☐ 1 to 5 Years ☐ > 5 Years
*Address (landmarks and other contact information):

***B. DESCRIPTION OF AEFI**

☐ Severe local reaction ☐ >3 days ☐ beyond nearest joint
☐ Seizures ☐febrile ☐ afebrile
☐ Abscess
☐ Sepsis
☐ Encephalopathy
☐ Toxic shock syndrome
☐ Thrombocytopenia
☐ Anaphylaxis
☐ Fever≥38°C
☐ Other (specify).....

Date AEFI started (DD/MM/YYYY): __ __ / __ __ / __ __ __ __
Time AEFI started ☐☐ Hr ☐☐Min
Signs and symptoms- please give a summary of the case, including any prior disease(s)/condition and patient's medicines before vaccination)

Indicate treatment given for the AEFI:

***C. OUTCOME OF AEFI**

***Serious**[¶]: ☐ Yes ☐ No; ➔ If Yes ☐ Death ☐ Life threatening ☐ Disability ☐ Hospitalization ☐ Congenital anomaly
☐ Other important medical event (Specify_____)
***Outcome:** ☐ Recovering ☐ Recovered ☐ Recovered with sequelae ☐ Not Recovered ☐ Unknown
☐ Died If died, date of death (DD/MM/YYYY): / / Autopsy done: ☐Yes ☐No ☐Unknown

D. DETAILS OF ALL VACCINE (S) ADMINISTERED

VACCINE(S)							DILUENT (if applicable)				
*Name	*Date and time of Vaccination		*Route (if injection indicate L/R site)	*Lot / Batch No.	Manufacturer	Expiry Date	Manufacturer	*Lot / Batch No.	Expiry Date	Date and time of reconstitution	
	Date	Time								Date	Time

E. REPORTER DETAILS

*Name: Profession/Designation: Tel No.:
Name of Institution: Today's Date: / / Signature:

For District Level Office

Date Report Received: ___ /__ /_____ Checked by: Designation:
Investigation needed: ☐ Yes ☐ No If yes, date started: ___ /___ /_____

For National/Central Level Office

Date Report Received: ___ /___ /_____ Checked by: Designation:
Comments (include results of Causality Assessment):

[¶]All serious AEFIs & AEFI clusters (two or more cases of the same adverse event related in time, place or vaccine administered) should be investigated.
*Mandatory fields

Vaccine Safety/AEFI Surveillance

Ministry of Health / Ghana Health Service/Food and Drugs Authority April 2017

Appendix R : Certificate of Authorization TTH

Department of Research &Development
Tamale Teaching Hospital

TTH/R&D/SR/108
06/09/2017

TO WHOM IT MAY CONCERN

CERTIFICATE OF AUTHORIZATION TO CONDUCT RESEARCH IN TAMALE TEACHING HOSPITAL

I hereby introduce to you **Mr. Walter-Rodney Naguma,** a PhD student from the University of Sheffield. Who has been duly authorized to conduct a study on **"Factors affecting Spontaneous Adverse Drug Reaction Reporting among Healthcare Professionals".**

Please accord him the necessary assistance to be able to complete his study. If in doubt, kindly contact the Research Unit at the second floor of the administration block or on Telephone 0209281020. In addition, kindiy report any misconduct of the Researcher to the Research Unit for necessary action.

Please note that this approval is given for a period of six months, beginning from 6th of September, 2017 to 31st of March, 2018.

Thank You.

ALHASSAN MOHAMMED SHAMUDEEN
(HEAD, RESEARCH & DEVELOPMENT)

Ward HCs
Please assist
him
Doctor

Appendix S : Knowlege of ADR reporting based on demographic characteristics

KNOWLEDGE QUESTION		Age			Sex		Years of practice					Patients per day		
		20-30	**31-40**	**40+**	**M**	**F**	**≤5**	**6-10**	**11-15**	**16-20**	**≥ 20**	**≤20**	**21-40**	**≥ 40**
Aware of national PV Centre? (%)	Aware	45(37.2)	60(49.6)	16(13.2)	73(59.3)	50(40.7)	67(55.8)	36(30.0)	7(5.8)	3(2.5)	7(5.8)	59(51.8)	32(28.1)	23(20.2)
	Not aware	155(60.1)	87(33.7)	16(6.2)	124(47.5)	137(52.5)	167(65.0)	64(24.9)	5(1.9)	6(2.3)	15(5.8)	173(68.9)	68(27.1)	10(4.0)
χ^2 – Value		*X_2=18.332* df=2 P=0.000*			*X_2=4.691* df=1 P=0.030*		*X_2=5.798* df=4 P=0.215					*X_2=26.395* df=2 P=0.000*		
SMS short code for reporting ADR (%)	Correct	9 (47.4)	9 (47.4)	1 (5.3)	9 (45.0)	11 (55.0)	10 (50.0)	8 (40.0)	1 (5.0)	1 (5.0)	0 (0)	8 (44.4)	5 (27.8)	5 (27.8)
	Incorrect	190 (53.4)	136 (38.2)	30 (8.4)	186 (51.7)	174(48.3)	223 (63.2)	90 (25.5)	12 (3.4)	8 (2.3)	20 (5.7)	221 (64.4)	95 (27.7)	27 (7.9)
χ^2 – Value		*X_2=0.733* df=2 P=0.693			*X_2=0.337* df=1 P=0.562		*X_2=3.900* df=4 P=0.420					*X_2=8.722* df=2 P=0.013*		
What basic info. is required on ADR forms (%)	Correct	63(50.8)	46 (37.1)	15 (12.1)	63 (49.6)	64 (50.4)	72 (57.1)	33 (26.7)	7 (5.6)	7 (5.6)	7 (5.6)	69(58.0)	35 (29.4)	15 (12.6)
	Incorrect	130 (54.2)	95 (39.6)	15 (6.3)	128 (52.9)	114 (47.1)	153(64.8)	63 (25.7)	6 (2.5)	2 (0.8)	12 (5.1)	154(66.4)	60 (25.9)	18 (7.8)
χ^2 – Value		*X_2=3.696* df=2 P=0.158			*X_2=0.360* df=1 P=0.548		*X_2=10.224* df=4 P=0.037*					*X_2=3.204* df=2 P=0.202		
All ADRs should be reported within how many days (%)	Correct	4 (40.0)	6 (60.0)	0 (0)	6 (51.2)	4 (40.0)	7 (70.0)	3 (30.0)	0	0	0	4 (44.4)	4 (44.4)	1 (11.1)
	Incorrect	193 (53.3)	137 (37.8)	32 (8.8)	188 (51.2)	179 (48.8)	222 (61.7)	95 (26.4)	13 (3.6)	9 (2.5)	21 (5.8)	223 (63.9)	95 (27.2)	31 (8.9)
χ^2 – Value		*X_2=2.452* df=2 P=0.293			*X_2=0.300* df=1 P=0.584		*X_2=1.352* df=4 P=0.853					*X_2=1.514* df=2 P=0.469		
Serious ADRs Shoul	Correct	22 (38.6)	23 (40.4)	12 (21.1)	28 (49.1)	29 (50.9)	24 (42.1)	16 (28.1)	6 (10.5)	4 (7.0)	7 (12.3)	23 (44.2)	26 (50.0)	3 (5.8)

d Be Reported Within How Many Days (%)	Incorrect	174 (55.1)	122 (38.6)	20 (6.3)	168 (52.3)	153 (47.7)	205 (65.3)	82 (26.1)	7 (2.2)	5 (1.6)	15 (4.8)	205 (66.8)	73 (23.8)	29 (9.4)
χ^2 – Value		*X_2=14.732* df=2 P=0.001*			*X_2=0.200* df=1 P=0.655		*X_2=24.181* df=4 P=0.000*					*X_2=15.320* df=2 P=0.000*		
P>0.05														

Appendix T: Search Strategy
REVIEW TOPIC: KNOWLEDGE, ATTITUDE, PERCEPTION AND PRACTICE OF ADVERSE DRUG REACTION REPORTING

DataBases	Google Scholar, Embase, PsychInfo and Medline (via Ovid or Pubmed)
Date of Search	November, 2019 (Updated January 2020)
Outcome	"Knowledge and Attitude and Practice" OR KAP OR knowledge OR attitude OR perception* OR practice OR approach OR perspective OR understanding OR familiarity OR awareness OR recognition OR principle*
Setting	Hospital or healthcare or 'clinical facility' or clinic or 'health centre'
Intervention	**"Adverse drug reaction*"** OR PV OR ADR* OR pharmacovigilance OR Adverse reaction reporting" OR "Medicine safety" OR "drug" OR "safety reporting" OR "Drug surveillance" OR "Safety reporting" OR "Adverse drug event reporting" OR "Spontaneous event reporting" OR "Spontaneous adverse drug reporting" OR "Voluntary reporting" OR "Prescription drug monitoring" OR "Suspected adverse drug reaction"
Population 1	"**Healthcare professionals"** OR doctor OR nurse OR pharmacist OR "general practitioner" OR "medical officer" OR "medical doctor*" OR "nurse practitioner*" OR "nursing officer*" OR Prescriber

Population 2 (Africa)	(**‘‘Africa’’[MeSH] OR Africa*[tw] OR** Algeria[tw] OR Angola[tw] OR Benin[tw] OR Botswana[tw] OR ‘‘Burkina Faso’’[tw] OR Burundi[tw] OR Cameroon[tw] OR ‘‘Canary Islands’’[tw] OR ‘‘Cape Verde’’[tw] OR ‘‘Central African Republic’’[tw] OR Chad[tw] OR ComORos[tw] OR Congo[tw] OR ‘‘Democratic Republic of Congo’’[tw] OR Djibouti[tw] OR Egypt[tw] OR ‘‘EquatORial Guinea’’[tw] OR Eritrea[tw] OR Ethiopia[tw] OR Gabon[tw] OR Gambia[tw] OR Ghana[tw] OR Guinea[tw] OR ‘‘Guinea Bissau’’[tw] OR ‘‘IvORy Coast’’[tw] OR ‘‘Cote d’Ivoire’’[tw] OR Jamahiriya[tw] OR Jamahiryia[tw] OR Kenya[tw] OR Lesotho[tw] OR Liberia[tw] OR Libya[tw] OR Libia[tw] OR Madagascar[tw] OR Malawi[tw] OR Mali[tw] OR Mauritania[tw] OR Mauritius[tw] OR Mayote[tw] OR MORocco[tw] OR Mozambique[tw] OR Mocambique[tw] OR Namibia[tw] OR Niger[tw] OR Nigeria[tw] OR Principe[tw] OR Reunion[tw] OR Rwanda[tw] OR ‘‘Sao Tome’’[tw] OR Senegal[tw] OR Seychelles[tw] OR ‘‘Sierra Leone’’[tw] OR Somalia[tw] OR ‘‘South Africa’’[tw] OR ‘‘St Helena’’[tw] OR Sudan[tw] OR Swaziland[tw] OR Tanzania[tw] OR Togo[tw] OR Tunisia[tw] OR Uganda[tw] OR ‘‘Western Sahara’’[tw] OR Zaire[tw] OR Zambia[tw] OR Zimbabwe[tw] OR ‘‘Central Africa’’[tw] OR ‘‘Central African’’[tw] OR ‘‘West Africa’’[tw] OR ‘‘West African’’[tw] OR ‘‘Western Africa’’[tw] OR ‘‘Western African’’[tw] OR ‘‘East Africa’’[tw] OR ‘‘East African’’[tw] OR ‘‘Eastern Africa’’[tw] OR ‘‘Eastern African’’[tw] OR ‘‘NORth Africa’’[tw] OR ‘‘NORth African’’[tw] OR ‘‘NORthern Africa’’[tw] OR ‘‘NORthern African’’[tw] OR ‘‘South African’’[tw] OR ‘‘Southern Africa’’[tw] OR ‘‘Southern African’’[tw] OR ‘‘sub Saharan Africa’’[tw] OR ‘‘sub Saharan African’’[tw] OR ‘‘subSaharan Africa’’[tw] OR ‘‘subSaharan African’’[tw]) NOT (‘‘guinea pig’’[tw] OR ‘‘guinea pigs’’[tw] OR ‘‘aspergillus niger’’[tw])
Exclude	**NOT** “disease condition” OR cancer OR malaria OR vaccination OR hepatitis OR diabetes OR immunization OR osteopORosis OR HIV OR AIDS OR TB OR Asthma OR “clinical trials”
	NOT Drug OR **“**Clavulanic acid” OR Paracetamol OR Warfarin OR Analgesic* OR Antibiotic*OR anti-infective* OR antidepressant OR antipsychotic* OR anaphylaxis OR psychotropic*
	NOT Student* OR “pharmacy student*” OR “nurse* student*” OR dentist OR “medical student*” OR “Medical college” OR teacher* OR Patient* OR consumer OR “Community Pharmacist”

Appendix U: Summary of Review Findings of African Studies

	PUBLICATION	YEAR	SUMMARY OF FINDINGS
1.	(Ezeuko *et al.,*	2015	Knowledge was generally low, and pharmacist had better knowledge comparatively. Common reasons for non-reporting were unavailability of electronic reporting (83.6%), unavailability of reporting forms (66.4%) and ignorance (58.2%). Others of lesser importance were the bureaucratic reporting process (39.9%), no incentives (32.5%) legal implication of reporting (26.6%). Workshops and mass media were highly (62.5%) suggested to increase awareness.
2.	(Nde *et al.,* 2015)	2015	62.2% ever reported ADR and averaged of 82.5% heard about the PV System but only 40.1% could define PV. No functional PV system was available. Majority of HCPs (90%) reported ADRs to Pharmaceutical companies. Most common reason for non-reporting "was not knowing" whom to report to.
3.	(Katusiime *et al.,* 20	2015	HCPs had a fair level of knowledge (40%). 69.1% understood the concept of ADR reporting, who to report to (75.3%), knew the national PV centre (41.7%), availability of forms on wards (25.3%). Only 16.6% ever reported an ADR. Most encouraging factor was unusual reaction (91.1%) and lack of time (56.5%) was the most discouraging factor.
4.	(Ameade e*t al,* 2014	2014	Knowledge was low (36.45%) and attitude above average (59.4%). Most HCPs knew the difference between ADR and side effects (67.2%), but not the definition of ADR (21.9%). 94.4% indicated reporting was important but only 8.8% of nurses completed a form after observation. Common reasons for non-reporting were client failure to report (18.4%) and lack of knowledge (42.2%). The most commonly suggested way to prevent ADRs and increase reports was workshops (51.2%).
5.	(Bello and Umar, 20	2011	Majority (70.5%) encountered ADR but only 4.9% reported resulting in a low reporting rate of (7%) among doctors. Lack of physician awareness about the reporting channels appear to be a major cause of under-reporting.
6.	(Kiguba et al., 2014	2014	52% ever heard of PV and 31.2% were aware of the national centre. 21% suspected an ADR in the last one month, 15% reported in last 12months but only 3% submitted a report to the national centre. Most common facilitator was the ADR being serious (18%) and for patient safety (18%) and barrier being "not knowing" how to report (45%). Attitudinally 76% saw reporting as a professional obligation, majority (73.3%) disagreed it took time, or should be financially motivated to report (58.0%) or put their careers at risk (76%).
7.	(Sabblah et al., 201	2014	Doctors had excellent knowledge (51%) and 27.4% ever had training. 59.5% had seen a suspected ADR but only 20% completed an ADR form. Common reasons for non-reporting was unavailability of forms (43.1%) and lack of knowledge about the reporting process (28.5%).
8.	(Angamo *et al.,* 2	2012	76.8% had inadequate knowledge but positive attitude (75%) with majority (57.3%) agreeing reporting was part of their duty, improves healthcare (73.17%) and quality of patient care (73.17%). 51.2% agreed reporting creates workload. Practice was poor (0%) with 15.85% ever encountering ADR but no one ever reporting an ADR or noted in on record.

9. (Awodele *et al.,* 201	2011	82.9% had heard about PV and 79.3% gave correct definition. 97.6% agreed ADR reporting was essential. Only 5.6% reported ADR in the last month with 2.4% to regulatory authority and majority did not know how to report (56.2%) or where to obtain a form (71.7%).
10. (Ohaju-Obodo and I	2010	78% of doctors had inadequate knowledge about PV with 71.2% unaware about yellow forms. 92.4% observed ADRs at work but only 25.5% of cases were reported with only 7.5% of reports to the national centre. Further assessment showed 47.4% were not aware of the reporting process. Common reasons for non-reporting was lack of awareness (47.7%), commitment from regulators (12.5%) and unavailability of forms (11.9%).
11. (Elnour *et al.* 2009)	2009	81.7% had an idea about ADRs and 96.2% saw ADR monitoring to be important. Only 26.1% ever reported an ADR. Common reasons for non-reporting of ADRs was not knowing how to report (27%) and unaware of the existence of a reporting system (27.1%).
12. (Oshikoya and Awo	2009	89.9% knew they could report ADRs but only 51.5 % knew about the national PV centre and 32.3% aware of the yellow card system. Attitude was positive, as 64.6% felt reporting was a professional obligation. Factors encouraging reporting was seriousness of ADR (77.8%) it being unusual (70.7%). The most discouraging factor was the concern that report may be wrong (47.5%). Majority disagreed (66.7) lack of time discouraged reporting.
13. (Okezie and Olufun	2008	General knowledge was good with 63.5% above the knowledge mean score of 27.5 with no statistical difference in age, sex and years of practice in relation to knowledge. 58.3% had general knowledge and were aware of reporting guidelines. Most (89.5%) had observed ADRs and only 32% have ever reported. There is lack of knowledge about reporting forms. Uncertainty about causality of ADR is a limiting factor to reporting. Demographic characteristics like sex, age, faculty, cadre or years of practice were associated with reporting awareness. Efforts must be made to educate about the reporting process by using posters in wards and clinics and giving active feedback to doctors
14. (Adedeji *et al.,* 2013	2013	There was poor knowledge of reporting procedures (48.6%), national PV centre (71.4%), ADR forms (57.1%). 85.7% observed ADRs but 2.9% reported with yellow forms. Reasons for non-reporting included ADR information not being useful (85.7%), time consuming (8.6%), litigation issues (14.3%), extra workload (17.1% and negative consequences to manufacturers (11.4%).
15. (Seid *et al.,* 2018)	2018	52.9% had adequate knowledge with 66% aware of the difference between ADR and side effect, 12.1% knew the term PV, 49% knew they national reporting system. 86.3% had positive attitude and 56% encountered ADRs but only 49.1% reported with 21.4 directly to regulatory authority. Having previous training, being a nurse or health officer were associated with reporting knowledge.
16. (Muringazuva et al.,	2017	There was 100% awareness the reporting system but 79% did not see the reporting system as necessary especially if the reactions were known or minor. Only 38% were aware of reporting time frames and only 21% were aware reporting could identify new events.

17. (Mulatu and Worku	2014	34.2% had sufficient knowledge. 52.3% knew the definition of PV, aware of ADR reporting (42.9%), the yellow form (21.4%) and how to report (27.8%). Attitudinally, 95.4 agreed reporting was their duty, patient safety could be improved (93.8%) and 68.1% feared litigation issues. Non reporting was due to uncertainty about what to report (43.4%) and where to report (37.8%). 16.2% ever reported an ADR and 38.1% recorded the reports, mainly to regulatory agency (27.7%).
18. (Shanko and Abdela	2018	In terms of knowledge, 29.5% familiar with the term PV,33.6% knew the difference between ADR and side effects, 59.3% knew about the national reporting system and availability of forms (61.4%). Pharmacist were more aware than other HCPs and y10 to 14 ears of experience was associated with knowledge. Attitude was positive, 60.8% saw reporting as part of their duty, important for public health (83.4%) and important in healthcare system (73.2%). 62.4% felt reporting did not create additional workload and common reasons for non-reporting were unavailability of forms (53.9%), uncertainty about how to report (51.9%) and lack of feedback (41%). 49.2% encountered ADRs especially doctors (72.7%), 37.3% recorded in patient folder, 34.2% advice patients especially pharmacists (66.6%)
19. (Kefale *et al.,* 2017)	2017	Overall knowledge was 33%. 31% knew the term PV, the national monitoring system (36.6%), the ADR form (27.7%) and 53.5 knew the difference between ADR and side effects. Attitudinally majority agreed reporting was part of their duty (84%), needed to establish causality before report (77%), reported only serious ADRs (35.2%) and making reporting compulsory (21.4%). 36.6% saw ADRs in the last 12months and 90.2% reported. Reporting were mostly to either the head of pharmacy (37.8%) or the regulatory agency (49.8%). Also, 38.5% advice patients about ADRs.
20. (Khoza et al., 2004)	2004	Lack of knowledge on how to report (47.2%). 75.5% indicated reporting was important professional obligation. Participants agreed that non-reporting was due poor feedback (59%), inaccessibility (45.8%), one report makes no difference (46.5%). Only 16% of HCPs agreed reporting took their time and disagreed (83.3%) reporting may risk their carrier. Only 20.1% ever reported an ADR.
21. (Gurmesa and Dede	2016	KAP was generally low but doctors and pharmacist had better awareness than nurses. 62.4% heard about ADR reporting, the yellow form (37.4%), knew where to report (30.8%) and 24% reported to regulatory agency. In terms of attitude, 77.4% indicated reporting is essential, 57% wanted reporting made compulsory, fewer (43.6%) HCPs were for reporting only serious ADRs. Reason for non-reporting were uncertainty about what to report (45.5%), the reporting system (9%) and unavailable forms (40.9%). 27% observed ADRs, 38.8% reported, 78.5% reporting at most three with 50% reported to the hospitals and 14.3% to regulatory authority.
22. (Fadare *et al.,* 2011	2011	60.5% lacked knowledge about Yellow form, reporting guidelines (57%) and hospital PV committee (44.6). Ignorance about how to report (66.1%) and verbal reporting (75%) was common. Average of 69.8% observed ADRs but only 42.7% ever reported. More doctors (85.7%) observed ADRs but more nurses reported (75%) than doctors (30.8%).
23. (Terblanche *et al.* 2	2017	Knowledge was generally low (17.5%). Only 18.9% were aware of the local PV reporting system, 15.2% were aware of the forms and only 18.9 knew who to submit a completed form to. Pharmacists were more likely to be aware. Attitude

		was positive, 82.6 preferred reporting to be compulsory, 92.6 did not want remuneration for reporting and 89.4 saw reporting as their professional obligation. Only 12% reported an ADR and the two most common reason for non-reporting was uncertainty about how, where and when to report (54.5%) and lack of time (37.1%).
24. (Kamal *et al*. 2014)	2014	Doctors' awareness of PV and reporting was low/poor. Only18.9% were aware of the NPVC and only 6.9% reported and ADR. Reasons for non-report were uncertainty (50.0%), lack of time (46.0%) and not knowing how (60.0%). Attitude was positive, 81.5% said reporting was necessary and 74% wanted it made mandatory. 60.0% were concerned with patient confidentiality and were less concerned about getting involved in litigation (47.4%). Years of practice influenced knowledge and attitude.
25. (Charles*,et al* 2017)	2017	Knowledge was low (23.9%) among HCPs with an average mean score of 8.1%/20. Pharmacist were more aware (56%) of PV than physicians (32.0%) and nursing staff (30%). Main reason for non-reporting; availability of forms (70.4%) and ignorance (24.8%). Only 1.7% reported ADR and reporting rate to the NPVC was 0.65%. Attitude was positive, 94.7% said reporting was necessary.
26. (Alemu and Biru, 2(	2019	Knowledge was generally inadequate (75.4%) with nurses more likely to be poor knowledge. 50% of HCPs did not report ADRs but attitude was positive (74%). Training awareness and feedback is encouraged.
27. (Amedome and Dad	2017	On average 83.3% of HCPs aware of ADR reporting system especially pharmacists (92.2%). Attitudes were generally positive (74%) with HCPs responding that reporting was the responsibility of all HCPs and reporting would increase patient safety.
28. (Udoye *et al.,* 2018)	2018	All pharmacists were aware of PV but only 24.3% officially reported and 73.4% had seen a patient with ADR. Poor attitude and practice with reasons such as lack of time, one report makes no difference and lack of incentives. Ensure form availability and continuous education and reminders.
29. (Joubert and Naidoc	2016	Majority of pharmacists (62.8%) were familiar with PV and deemed it as valuable (79.4%) but 44.1% reported ADRs. Main barrier was that reporting was time consuming (50%) and PV centres were remote.

Appendix V: Participant Information Sheet (Survey)

The University Of Sheffield. Information Sheet

Factors Affecting Spontaneous Adverse Drug Reaction Reporting Among Healthcare Professionals in Northern Ghana

Invitation You are invited to take part in the above research project which is being undertaken by the University of Sheffield in the United Kingdom. Before you decide whether or not to participate in the research, it is important for you to understand why the research is being carried out and what it will involve and why you have been invited to take part

Purpose of the Research and why you have been selected. Adverse drug reactions (ADRs) are recognised events in all health systems and there is considerable research in many countries about their incidence and in particular what influences reporting of ADRs. Little is known about this however, in Ghana and specifically from the perspective of health professionals. This study aims to understand the experiences and views of nurses, pharmacists and doctors in different hospitals in northern Ghana in relation to ADRs and their associated reporting.

What will happen to you if you take part There are two main stages in this research and this sheet relates to the first which involves participating in a questionnaire which will take between 20 to 30 minutes to complete. You will be invited to participate in an interview if you choose to. You do not have to participate in in both stages. There are no recognised personal advantages or disadvantages associated with taking part in this research,

Do I have to take part? No. Your participation in the first questionnaire stage is entirely voluntary, as is participation in the subsequent stages which would involve further interviews. It is up to you to decide whether or not you wish to participate in this and later stages.

Will my taking part in this research be kept confidential? Yes, the questionnaire is completely anonymous, and no information will be collected that could identify you. All data will be anonymised, and you will not be identifiable in any report or publication. Personal data will be kept for 2 years once the study has ended and then destroyed. Anonymised data will be kept indefinitely and may be used in future research.

What will happen to the results of the research project? The data generated from this research will be submitted as a PhD thesis, in academic journals and abstracts will be submitted at key conferences.

Who has ethically reviewed the project? This research has been ethically approved by the Ghana Health Service Ethics Review Committee. Relevant hospital permission has also been granted ranted to carry out this research.

Who is organising and funding this research? This research is organised by the University of Sheffield and is not funded.

What if I want more information or have a complaint regarding this research? If you would like more information about his research, please contact Walter-Rodney Nagumo, the researcher, on +233208390330 / 07826136439. If you wish to raise a complaint or a concern about any aspect of this research, please contact Dr Richard Cooper (email Richard.cooper@sheffield.ac.uk, telephone +0044 1142220683). If for any reason you are not satisfied you should contact the Dean of ScHARR, Professor John Brazier (email j.e.brazier@sheffield.ac.uk phone: +0044 114 2220749.

Appendix W: Mixed Theoretical Model by Herdeiro (Herdeiro *et al.*, 2004)