

The availability of persons nominated for adverse drug reporting and associated challenges in Gauteng regional and district public hospitals

A mini-dissertation submitted by

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*in partial fulfilment of the requirements for the degree of M.Sc.
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ABSTRACT

Background and Objectives: The reporting of adverse drug reactions (ADRs) is a major public health necessity. It is estimated that only six to 10 percent of all ADRs are reported worldwide. This number is far less than the actual cases of ADRs which occur in healthcare facilities. There appears to be lack of knowledge, awareness and willingness of healthcare professionals to report ADRs, which prompted some countries to nominate a person for ADR reporting in facilities. The objectives of this study were to ascertain which facilities had a nominated person or committee for ADR reporting, describe the knowledge and training of these individuals, describe the processes followed by the facilities for ADR reporting, determine the most commonly reported ADRs and causative drug classes, and, determine the factors which facilitate or hinder ADR reporting.

Method: This was an exploratory, multicenter study. A structured questionnaire with closed and open-ended questions was used for data collection. The study was conducted in Gauteng province, where stratified non-random sampling was used to collect data in the selected regional and district public hospitals.

Results: Six regional hospitals and five district hospitals participated in the study. Five (45.5%) of these hospitals had a person nominated for ADR reporting, of which all were pharmacists. All the respondents nominated for ADR reporting stated their knowledge and confidence in identification of ADRs as average and above. One (20%) of the nominated persons for ADR reporting did not have pharmacovigilance training. The reported number of ADRs over the past 12 months ranged between zero and 199. Only two (40%) of the hospitals with a nominated person for ADR reporting received feedback on the submitted reports from a committee.

Only one (16.7%) of the six hospitals that did not have a nominated person or committee for ADR reporting had plans to nominate a person for this function. ADR reporting in these hospitals were performed by the pharmacy that collated the identified ADRs into a report and distributed these to the Pharmacy and Therapeutics Committee (PTC) and South African Health Products Regulatory Authority (SAHPRA).

Only one hospital out of all the hospitals (n=11) did not use the national ADR reporting form and rather used an incident report. Out of all the participating hospitals, only two (18.2%) of the hospitals had an algorithm in place to assist with the identification of ADRs. The researcher went through the file where ADR reporting forms were kept for the past 12 months, and reported that the most commonly reported ADR type across participating facilities was allergic reactions such as rash and angioedema reported by eight of the facilities, followed by administration errors and quality issues each from three facilities. While the most frequently reported drug class associated with these ADRs included antiretrovirals

(ARVs) and angiotensin converting enzyme (ACE) inhibitors reported at eight and six facilities, respectively.

The most common challenge to ADR reporting at participating facilities was non-reporting of ADRs, followed by fear of litigation and patient's unwillingness. Although all the hospitals in this study had facility PTCs, only one hospital had a pharmacovigilance subcommittee and the others included ADRs as an agenda point of the PTC meetings.

Conclusion: Less than half of the facilities had a person nominated for ADR reporting. Pharmacists and the pharmacy were synonymous with ADR reporting as all nominated persons were pharmacists and in facilities where there was no nominated person, the responsible pharmacist was identified as the contact person for ADR reporting. Although all hospitals had PTCs, there was rarely a subcommittee dedicated to pharmacovigilance or ADR reporting, which culminated in a lack of feedback to healthcare workers that could promote it in the facility. Underreporting of ADRs by health care workers was the major challenge to effective ADR reporting as this function was considered to be too time consuming.



DECLARATION

I declare that this thesis that I now submit for assessment for the programme of study leading to the degree Master of Science in Pharmacy Administration and Policy Regulation has not been submitted for the purpose of a degree at this or any other higher education institution. It is entirely my own work and has not been taken from the work of others save to the extent that such work has been cited and acknowledged within the text of this work.

I agree to deposit this thesis in the University of Western Cape's library and Healthcare-Learning's institutional repository and or allow these institutions to do so on my behalf, subject to South African and British Copyright Legislation and the University of Western Cape's conditions of use and acknowledgement.

Signed.......... Dated.....



DEDICATION

To my late mother Yvonne Modau, I will always miss you. Every milestone I reach in life is dedicated to you. Life has not been easy without you and I hope I make you proud. To my father and sister, Moses and Refilwe Modau, I really appreciate your motivation and encouragement. Last but not least, the newest member of the family, Atlegang Lethabo Modau, I hope I inspire you to achieve far more than I have.



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LIST OF ABBREVIATIONS AND ACRONYMS

ACE	Angiotensin Converting Enzyme
ADE	Adverse Drug Event
ADR	Adverse Drug Reaction
AE	Adverse Event
AMS	Antimicrobial Stewardship
ARV	Antiretroviral
CEO	Chief Executive Officer
CHC	Community Health Centre
CNS	Central Nervous System
DoH	Department of Health
GDP	Gross Domestic Product
GI	Gastrointestinal
HOD	Head of Department
HCP	Health Care Professional
MCC	Medicines Control Council
NADEMC	National Adverse Drug Events Monitoring Centre
OTC	Over-the-counter
PMDS	Performance Management and Development System
PTC	Pharmacy and Therapeutics Committee
PV	Pharmacovigilance
QA	Quality Assurance
SA	South Africa
SAE	serious adverse drug event
SAHPRA	South African Health Products Regulatory Authority
SMS	Short Message Service
US	United States
WHO	World Health Organization

1. CHAPTER 1: INTRODUCTION

Pharmacovigilance has been defined by the World Health Organization (WHO) as: “*The science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other possible drug-related problems*” (WHO, 2006). An adverse drug reaction (ADR) is defined by the WHO as a drug response, that is noxious, unintended and occurs at normal doses of medicine used in man (WHO, 2002). The reporting of ADRs is a major public health necessity. This means that it requires organised efforts of the society to protect, promote and restore patient’s health as it may have a significant impact on mortality and morbidity caused by drugs (WHO, 2006; Mouton *et al.*, 2015).

ADR reporting is especially of value for newly registered drugs, because safety information gathered during the early phases of drug development, has significant limitations on the rare but serious adverse reactions, chronic toxicity, use in special groups or interaction with other drugs. This warrants the need for phase 4 of drug development namely, post-marketing surveillance (WHO, 2002). Post-marketing surveillance may be defined as the continuous monitoring of drugs after they reach the market in real clinical settings, taken by a variety of patients with various co-morbidities, over a prolonged period to detect previously unrecognized drug related effects, positive or negative (Vlahovic-Palcevski and Mentzer, 2011). In the United States, there has been much focus on pharmacovigilance strategies especially with a trend towards expedited drug registrations (Carroll, 2005). Accordingly, in 1993, the European law introduced the requirement for a qualified person nominated for pharmacovigilance in each pharmaceutical company (Brown, 2005).

However, the effectiveness of post-marketing surveillance is directly dependent on ADR reporting by healthcare professionals and patients in clinical practice (Palleria *et al.*, 2013). Historically, spontaneous reporting of ADRs played a vital role in the detection, evaluation, understanding and prevention of unsuspected, serious and unusual ADRs (Wysowsky and Swartz, 2005). Spontaneous reporting, also known as voluntary reporting is the passive surveillance of product safety where ADRs are reported by healthcare workers and patients, subsequent to administration of a medicinal product (Al Dweik, *et al.*, 2016). Successful spontaneous reporting of ADRs has been linked to a health care worker’s knowledge of the importance of pharmacovigilance, coupled with the skills necessary to identify and report ADRs (Ruud *et al.*, 2010). In addition, all clinical settings have a team of health care workers and ADRs can be identified by any member of this team. The coordination between team members regarding who will report the identified ADR is a crucial link for an effective pharmacovigilance effort.

ADRs vary in their classification from minor to serious. Patients presenting with serious ADRs usually end up in hospital, which illustrate the need for an active, more responsive pharmacovigilance system for hospital settings. Indeed, several studies conducted in a variety of international settings indicated a range between two and 21% of patients were being admitted to hospital with ADRs (Lobo *et al.*, 2013; Brandao and Vasconcelos, 2000; Einarson, 1993). The WHO introduced Pharmacy and Therapeutics Committees (PTCs) in hospitals to serve several functions which include, but not limited to the selection of efficacious and cost-effective medicine, efficient procurement practices, reduction of medicine wastage, ensuring efficient prescribing practices in accordance with standard treatment guidelines/protocols and dispensing practices (WHO, 2003). In addition, PTCs are encouraged to establish subcommittees to support them in their functions and one of the essential subcommittee's is the pharmacovigilance or safety and quality committee, which includes ADR monitoring (Strengthening Pharmaceutical Systems, 2012).

In 2006, countries such as Italy issued a Legislative Decree that all hospitals should have a nominated person for ADR reporting, where healthcare professionals are bound by duty to report all suspected ADRs using an appropriate form and send it to the nominated pharmacovigilance person, who verifies the completeness, accuracy and consistency of the reported information (Mazzitello *et al.*, 2013). In general, the nomination of a responsible person for ADR reporting is an important step towards building robust pharmacovigilance systems in the clinical setting (Khan *et al.*, 2013). In cases where such a person does not exist, it has been recommended that PTCs be approached to nominate such a person (Jobson, 2003).

In addition to single facility reporting, pharmacovigilance activities need to be collated at higher levels in order for it to give an overall picture of a drug. Efforts have thus been made for all countries to collaborate at an international level for drug monitoring. In the year 2002, more than 65 countries came together and formed the Uppsalla Monitoring Centre (UMC), which is coordinated by the WHO Collaborating Centre for International Drug Monitoring (Jeetu and Anusha, 2010). The main function of this centre is to manage the international ADR reports database received from national centres (Olsson, 1998). National Pharmacovigilance Centres have a crucial role in increasing public awareness on drug safety. Countries such as New Zealand, Sweden, United States of America and the United Kingdom have strategically placed national and regional pharmacovigilance centres in medical schools, hospitals or poison and drug information centres rather than housing them within the confines of a drug regulatory authority (Jeetu and Anusha, 2010).

1.1 Problem Statement

It is estimated that only six to ten percent of all hospital ADRs are reported globally (Wysowsky and Swartz, 2005). Indeed, the number of reported ADRs is far less than the actual number of cases which occur in health facilities (Wysowsky and Swartz, 2005; Khan *et al.*, 2013). Underreporting of ADRs is a global issue and in South Africa, there appears to be lack of knowledge, awareness and willingness of healthcare professionals for ADR reporting (Ampadu *et al.*, 2016; Bogolubova *et al.*, 2018). In South Africa, the Medicines Control Council (MCC), now known as the South African Health Products Regulatory Authority (SAHPRA) has a unit called the National Adverse Drug Events Monitoring Centre (NADEMC) which was established to manage the ADR database, however, the reporting rates are still low (Terblance, 2018; Bongolubova *et al.*, 2018).

Developing and underdeveloped countries such as South Africa obtain pharmacovigilance information of new drugs from developed countries which have effective pharmacovigilance systems already in place. However this may not be appropriate as factors such as cultural, genetics, geographical and other local factors need to be taken into consideration (Toklu *et al.*, 2016). Traditionally, pharmacovigilance activities were limited to spontaneous reporting of ADRs, which has been the mainstay of regulatory pharmacovigilance activities for many years (Mehta, 2011; Mehta *et al.*, 2014).

Key informants actively involved in pharmacovigilance in India, Uganda and South Africa have reported that lack of human resources was the biggest challenge to ADR reporting (Maigetter *et al.*, 2015). In addition, much of the data that had been collected and sent to the National Adverse Drug Events Monitoring Centres (NADEMCs) were not made use of due to insufficient capacity for analysis (Maigetter *et al.*, 2015). There was a work backlog of approximately three years due to bureaucratic delays at these centres. Pharmacovigilance, in general, was perceived mainly as an administrative task since the pharmacists working at the national pharmacovigilance program did not have enough administrative staff, which meant that they were spending more time doing administrative tasks such as capturing data, following-up on incomplete forms and catching-up on a backlog of three years, than analysing and interpreting the collected data (Maigetter *et al.*, 2015). Lack of man power was a challenge with only one chief pharmacist employed full-time at NADEMC, while the experts were remunerated on an hourly basis (Maigetter *et al.*, 2015). Other concerns that the NADEMCs had to deal with included; uncoordinated report submission due to fragmentation between non-governmental organisations not coordinating with the national system resulting in duplicate reports, under-reporting for anti-tuberculosis and anti-retroviral drugs, and, inconsistent use of the standard ADR reporting as other non-standard forms were also accepted, which resulted in omission of patient details required and an inability to track a report. In South Africa, there were also poor communication between the NADEMC and healthcare workers doing the reporting as doctors

complained that they did not receive feedback concerning the reported ADRs while the Medicines Control Council (MCC) responded that there were too many reports on which to provide feedback (Maigetter *et al.*, 2015; Alsaleh *et al.*, 2017; Valliano *et al.*, 2005).

One of the primary problems in the South African health care system is that it is fragmented into the public and the private health services. The public healthcare system is funded by the government and serves more than 70% of the South African population for free (GDoH, 2016). Most of these patients are low to medium income earners, and cannot otherwise afford private healthcare (Harris *et al.*, 2011). As such, public health care is burdened with a high number of patients and limited resources, including health care workers. This results in the prioritisation of direct patient care activities with the limited time and the deprioritisation or neglect of administrative tasks, of which ADR reporting is perceived as one.

Additionally, it is not considered mandatory to report ADRs as there are no policies in place which clearly state the responsibility of who should report ADRs (NDoH, 1996). This responsibility could have been addressed in the National Drug Policy (NDP) health objectives, but this policy was focused on the adequate and reliable supply of safe, cost-effective medicine of acceptable quality and rational use by all. The roles of pharmacists, pharmacy support staff, doctors and nurses are outlined in this policy but there is no direct inference to their role in ADR reporting (NDoH, 1996). Despite the lack of responsibility for ADR reporting, it has also been found that ignorance, insecurity, legal diffidence and complacency contribute to poor ADR reporting practices (Toklu *et al.*, 2016; Maigetter *et al.*, 2015).

There is a high number of patients served by the public sector, with long queues, shortage of staff, demanding working hours which often overburden healthcare workers, and ultimately impacts negatively on the quality of care and patient counselling (Visser *et al.*, 2018). This leads to inappropriate use of medicine which might be related to the origin of an ADR and/or failure by patients to recognize ADRs and report them to health care workers. In addition ADR reporting requires a multidisciplinary approach that involves collaboration amongst healthcare workers, which is problematic in most settings (Toklu *et al.*, 2016; Khan *et al.*, 2013). There seems to be an absence of literature on the availability of persons nominated for pharmacovigilance in any of the hospitals in South Africa.

In South Africa, an observational study was conducted in a secondary teaching hospital in Somerset West, Cape Town where hospital admissions due to ADRs were found to be 6.3%. In addition, 41% developed while the patients were in hospital (Mehta *et al.*, 2008). The same study reported that 46% of these ADRs that developed while the patients were admitted in the hospital were preventable. These alarming results prompted the researchers to conduct another study to evaluate healthcare workers' knowledge on ADR reporting, where 50% of the

respondents expressed that ADR reporting was time consuming, 38.24% did not know how to report, 35.29% did not know where to report to, 27.45% said that the ADR form was not user friendly, while 17.65% indicated that there was no financial incentive (Joubert and Naidoo, 2016). South Africa's national pharmacovigilance and ADR reporting systems are not yet functioning optimally.

1.2 Rationale for the study

South Africa became a member of the WHO International Drug Monitoring Programme in 1992, which made South Africa the first country in Africa to become a member (Maigetter *et al.*, 2015). The National Drug Policy (NDP) has advocated for the establishment of PTCs which will ensure efficient, rational and cost-effective supply and use of medicine (NDoH, 1996; Strengthening Pharmaceutical Systems (SPS), 2012). One of the important responsibilities of the PTCs is to manage ADRs and rectify medication errors, or nominate a subcommittee or a dedicated person for this function (Vang *et al.*, 2006). However, there is no clear policy on this function and this has resulted in differences in the objectives and functioning of PTCs across facilities in South Africa (Systems for Improved Access to Pharmaceuticals and Services (SIAPS), 2014).

The South African MCC, now referred to as SAHPRA, released a guideline for the purpose of ADR reporting by pharmaceutical companies (MCC, 2016), which require holders of certificates for the registration of medicines (pharmaceutical companies) to nominate a qualified person for pharmacovigilance. However, in order for this person to perform their duties, they require end-users of the pharmaceutical product to report all suspected and confirmed ADRs (MCC, 2016). ADR reporting is thus dependent on the actions of patients and healthcare professionals in practice. This limits the ability of pharmaceutical companies to comply with these guidelines.

In the year 2010, The South African National Department of Health compiled the revised National Core Standards for health establishments in the country to set the standards for quality service, avoid risk to poor quality care and reduce their impact. According to these National Core Standards domains, healthcare establishments should ensure quality nursing and clinical care and ethical practice, reduce unintended harm, prevent or manage problems or adverse events which should be routinely analysed and managed to prevent recurrence. However, the implementation of the national core standards has not been officially linked to performance measurement (NDoH, 2011).

1.3 Purpose of the study

1.3.1 Research Question

What is the status of ADR reporting structures, in terms of human and other resources, in public sector hospitals and what are the factors that help or hinder the effectiveness of ADR reporting within the existing structure?

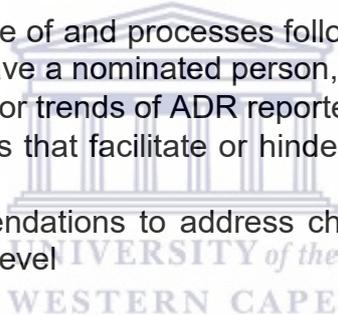
1.3.2 Aim of the study

The aim of this study was to explore the factors affecting ADR reporting at regional and district public sector hospitals in the Gauteng province.

1.3.3 Objectives of the study

The objectives of the study were to:

- Ascertain which facilities had(a) nominated person(s) responsible for ADR reporting,
- Describe the knowledge and training of person(s) nominated for ADR reporting,
- Describe the structure of and processes followed for ADR reporting at each facility that did not have a nominated person,
- Obtain statistics and/or trends of ADR reported by all facilities,
- Determine the factors that facilitate or hinder ADR reporting for the facility, and,
- To provide recommendations to address challenges associated with ADR reporting at hospital level



2. CHAPTER 2: LITERATURE REVIEW

This chapter will start with a review of national and facility-based pharmacovigilance structures as recommended by WHO, how pharmacovigilance fit into patient care at a health facility, and, adverse drug reaction classifications. This chapter concludes with the description of factors that affect ADR reporting in health facilities.

2.1 Pharmacovigilance structures

Pharmacovigilance (PV) is a relatively new science and public health activity in most underdeveloped and developing countries, when compared to developed countries (Ampadu *et al.*, 2016). In South Africa, this function is primarily driven by three main stakeholders: regulators and the pharmaceutical industry who are focused chiefly on healthcare products; public health programmes, responsible for the systems; and healthcare providers, who are focused on patients. All these stakeholders have a goal of minimising drug-related harm to the patient (Mehta *et al.*, 2017). The WHO together with its regional offices play an important role in supporting countries in promoting the establishment and building of sustainable monitoring systems for pharmacovigilance (Maigetter *et al.*, 2015).

The global pharmacovigilance basis is reliant on spontaneous reporting systems, which involves the systematic collection of reports, collation, analysis and evaluation of the data which enables the detection of signals, their communication and risk management (WHO, 2015). At a local level, these reports are collected either from healthcare workers, patients or pharmaceutical companies. The data is then sent to the relevant regional or national centres for collation and evaluation. This information is then further analysed and forwarded to the WHO individual case safety report (ICSR) database – VigiBase. The national pharmacovigilance centres receive significant feedback since findings are promptly communicated to them by the WHO Collaborating Centre for International Drug Monitoring, Uppsala, Sweden (UMC) for appropriate action (WHO, 2015).

The ICSR reporting to VigiBase is an important indicator to measure and analyse the national pharmacovigilance activities of countries (WHO, 2015). It is also important to realise that pharmacovigilance is not only focused on spontaneous ADRs and ICSR collections and submission, but it also encompasses activities such as medication errors, pharmacoepidemiological studies, clinical and product quality, products of compromised integrity, including counterfeit and substandard medicines (Ampadu *et al.*, 2016; WHO, 2015). The rate of reporting varies significantly between underdeveloped, developing and developed countries, which

are more advanced and have enough resources to facilitate the process of ADR reporting (WHO, 2015). While in South Africa, being a developing country has only submitted a total of 28 609 reports to the VigiBase between 1992 and 2014 (Ampadu *et al.*, 2016).

2.1.1 National level structures

In 2010, WHO in consultation with its advisory committees agreed on the core minimum requirements that should be present for a functional national pharmacovigilance system, which included:

- A national pharmacovigilance centre with designated staff,
- A national spontaneous reporting system with an available national ADR reporting form,
- A national database or system for collating and managing ADR reports,
- A national advisory committee, that is able to provide technical recommendations on safety issues and regulatory actions, validate causality and evaluate risk; and when necessary, participate in crisis management including crisis communication, and,
- A communication strategy that is clear for both routine and crises communication (Maigetter *et al.*, 2015).

To support and transform the activities of pharmacovigilance and enhance safety of patients, every country must have a national pharmacovigilance centre, with independent expertise to ensure that safety information on all available drugs is adequately collected, impartially evaluated and made accessible to all. Adequate nonpartisan financing must be available to support the system. Exchange of data and evaluations among countries must be encouraged and supported (Khan *et al.*, 2013; Jobson, 2003).

In SA, the function of pharmacovigilance has been undertaken by the National Adverse Drug Events Monitoring Centre (NADEMC) at the University of Cape Town. The NADEMC was set up as a partnership between the MCC and the WHO (Joubert and Naidoo, 2016; Jobson, 2003). Figure 2.1 illustrates the flow of ADR information from individuals (i.e. healthcare professionals or customers) right through to decision making by the regulatory authorities and other involved stakeholders (SPS, 2010).

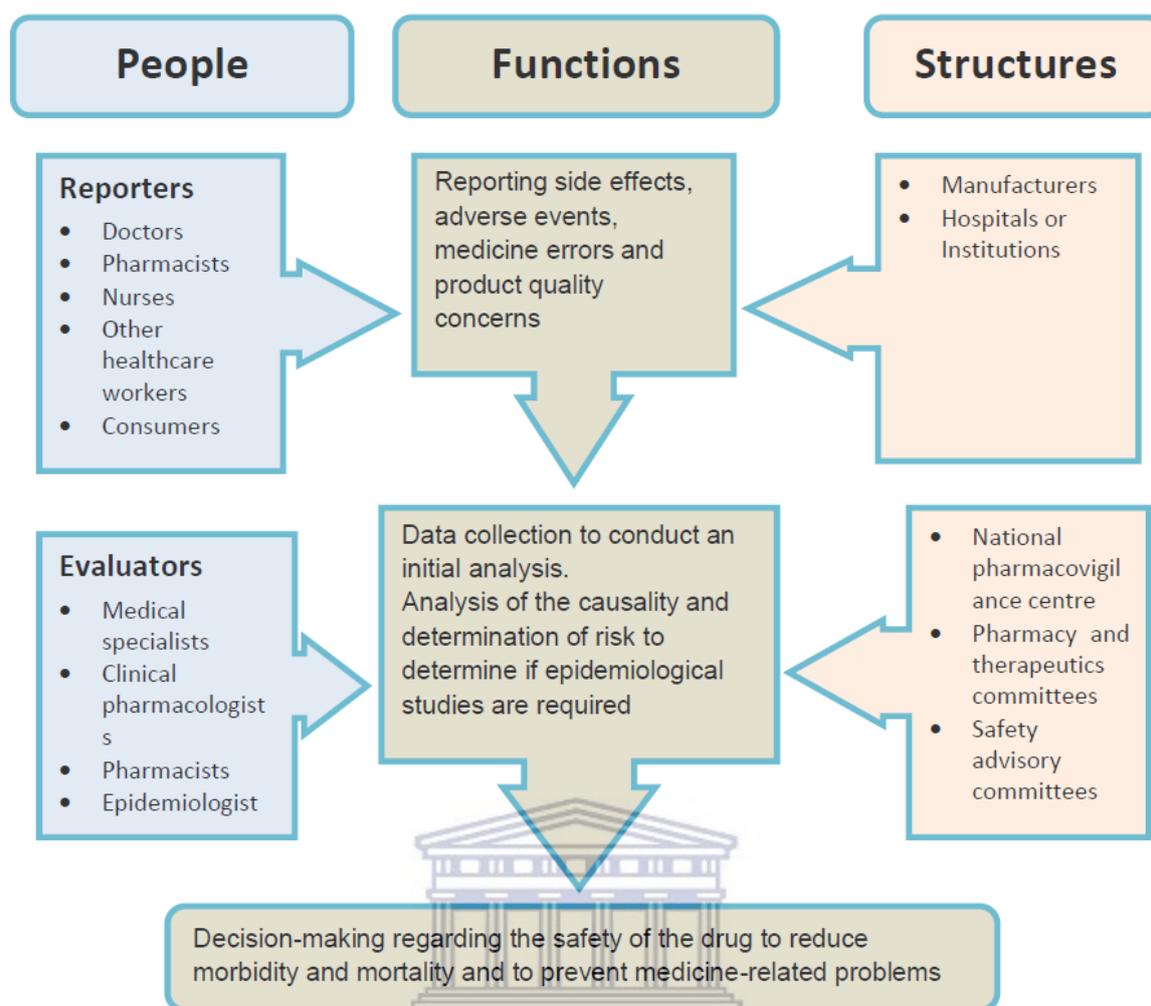


Figure 2. 1 The pharmacovigilance flow of information framework (adapted from SPS, 2010)

Spontaneous reporting is essential for the identification of new signals and/or adverse drug reaction trends. This is supported by the use of a nationally available ADR reporting form as recommended by the WHO. South Africa is one of the many countries which have a national ADR reporting form (see Appendix 1). A previous study by Banderkar *et al.* (2010) assessed both the variables included on the form and the completeness of data capturing (Maigetter *et al.*, 2015; Banderkar *et al.*, 2010). Based on the results and recommendation of this study that ADR form was updated to include all 18 variables which are considered to be crucial in identifying and enabling appropriate assessment of the reported ADRs. These include patient details, description of the reaction and outcomes, dechallenge and rechallenge information, format of the form, encompassing the flow of information, adequate space and columns, etc. as per Table 2.1.

Table 2.1 Evaluation of the South African ADR reporting form (Banderkar *et al.*, 2010).

Criteria	Available/Comment
Patient's information	✓
Pregnancy status	X
Allergic status	✓
Diagnosis	✓
Description of reaction	✓ With less space
List of suspected drugs	Six drugs, including concomitant medication
Dose, frequency of drugs	✓
Space for concomitant drugs	✓ No separate space available, but included in suspected drug column
Start date and stop date of suspected drugs	✓
Relevant history of patients	✓
Actions taken	X
Severity	X
Causality	X
Outcome	✓
Dechallenge	X
Rechallenge	✓
Treatment of ADR	✓
Lot no, expiration date	X

Pharmacovigilance (PV) should be a structured process with ongoing data which is vital to ensure safety and effectiveness of medicines and to provide information concerning regulatory actions such as drug safety alerts, labelling changes to the product information, drug recalls or withdrawal of a drug from the market (Palleria *et al.*, 2013; Jeetu and Anusha, 2010). The process of pharmacovigilance may generate large volumes of data, with the cooperation of healthcare professionals in practice and this requires expertise from the pharmacovigilance centre in order to manage this data, respond and update the reporters and avoid uninformed discontinuation of a drug from the market (Jeetu and Anusha, 2010).

The large volume of data generated through the process of pharmacovigilance needs to be collated via a national database or a system for collating and managing ADR reports (Maigetter *et al.*, 2015). In South Africa, this function is carried out by the NADEMC, which manage the collection and evaluation of spontaneous ADR reports from the stakeholders (Mehta, *et al.*, 2017).

The WHO also advised on having a national advisory committee. South Africa has met this requirement by establishing a pharmacovigilance expert committee within the MCC in 2003. This committee is composed of a pharmacist and six external experts from various institutions (Maigetter *et al.*, 2015). The role of this committee

was to advise on post-marketing related safety issues, review complaints, ADRs, make recommendations regarding registration conditions of medicine and to communicate actions to be taken for crisis management, as well as routine communication strategy that is clear for both customary and crises communication (Mehta *et al.*, 2017; Maigetter *et al.*, 2015). Communication must be prioritised to ensure the success and sustainability of pharmacovigilance. Poor communication and feedback are a major challenge and weakness to pharmacovigilance systems. It has been suggested that a national pharmacovigilance website should be established to facilitate information sharing amongst relevant stakeholders (Mehta *et al.*, 2014).

2.1.2 Facility based structures and processes and pharmacovigilance

In addition to the overarching national pharmacovigilance systems discussed previously, the WHO has additionally advocated for the establishment of PTCs in healthcare institutions (WHO, 2003). The PTCs should be a multidisciplinary forum which includes prescribers, pharmacists, nurses, administrators, quality improvement managers and other healthcare workers involved in the medication use process (Tyler, *et al.*, 2008). The main function of the PTC is to maximise and promote the rational use of medication. This role is achieved through the development and evaluation of medicine-related policies and procedures and advice on their implementation; assessment and selection of essential and vital medicines for the institution's formulary on an ongoing basis to support continuous and sustainable access to medicines; monitoring and evaluation of medicine use, safety and quality; and to advise on the implementation of preventative and corrective action of ADRs, particularly those which are potentially avoidable and often predictable (Vang *et al.*, 2006; NDoH, 2015; Schatz and Weber, 2015).

The national Department of Health has adopted the WHO's approach to the promotion of rational medicine use by establishing a PTC in healthcare institutions. However, there is lack of policy detailing the standards of the structure, role and functions of this committee and consequently, this resulted in differences in the objectives and functioning of PTCs across facilities (NDoH, 2015). Nonetheless, these committees are empowered with the responsibility for decision making and coordinating in a hospital setting (NDoH, 2015). It is easier to maintain surveillance of ADRs in a hospital setting where there is a PTC available (Rishi, 2008).

PTCs may elect a subcommittee which manage specific tasks within the facility. Strengthening Pharmaceutical Systems, (2012) stated that the establishment of subcommittees enhances simultaneous functioning of the main PTC, however there is no policy indicating which subcommittees should be appointed in the facilities. The PTC is expected to evaluate the needs of the institution and based on the speciality and expertise available, several subcommittees may be

appointed and these may include; antimicrobial stewardship, procurement advisory, pharmacovigilance, rational medicine utilisation, safety and quality committees, etc. (Strengthening Pharmaceutical Systems, 2012).

2.2 Pharmacovigilance and patient care at a health facility

Patient care is defined as services rendered by healthcare professionals for the benefit of a patient (Yorke, 2016). The process of patient care commences with the diagnosis - to determine the need for medical care, this could be an assessment of a symptom or a laboratory test or more complex investigations. Subsequent to the diagnosis, there should be planning, implementation and assessment of the treatment, this is known as the therapeutic process (Williamson, 1971). Quality and safety is of utmost importance in the diagnostic and therapeutic processes. Unfortunately, in everyday practice, not all patients receive the best care. There is often deprivation of care, unnecessary, outdated or even harmful care where there is overuse, underuse or misuse of care (Bodenheimer, 1999; Ward *et al.*, 2017). There are various terms used to explain inappropriate care and adverse outcomes experienced by patients during diagnostic and therapeutic processes. Table 2.2 describes the most commonly used terms to describe inappropriate care (Andrews *et al.*, 1997).

Adverse drug events are described as any unpleasant medical incidents related to the use of a drug, rather than the underlying medical condition, which should be reported for the benefit of the public rather than the individual (Griffin and Resar, 2009). The term adverse effect and adverse drug reaction are similar and both occur at any dose, however they are not synonymous. Adverse drug reactions are usually detected by clinical manifestations or laboratory investigations while adverse effects are not. It is, however important to distinguish the two from adverse drug event, which is directly linked to the injury or death of a patient, while adverse drug reaction and adverse effects are characterised by suspicion of the link between the drug and the reaction and includes all adverse events associated with the administration of a drug irrespective of the aetiology (Nebeker *et al.*, 2004). There are different types of aetiologies, and only a part of these are immune-mediated hypersensitivity reactions, while most are non-immune mediated and related to pharmacological properties of the medicine or individual predisposition of the patient (Hausmann *et al.*, 2012).

Errors and medication errors are often confused, it is important to recognise that errors include medication errors, whereas medication error requires the administration of a drug. Negligence and malpractice are closely related terms which are usually incorrectly used interchangeably, in reality, malpractice is a

subcategory of negligence and it is considered to be more serious than negligence (Grober and Bohnen, 2005).

The number of deaths resulting from medication errors has increased. This increase is not a surprised as in recent years, newer drugs have been introduced, medical care has become more complex and specialised and the population has aged (Aronson, 2009). An important strategy on how to improve errors in health care was to identify medication errors regardless if they were associated with an adverse event or not, hence strengthening pharmacovigilance. Safety advocates have made a recommendation to identify and report all adverse events, irrespective of whether or not they are associated with harm as this will lead to a safer environment of patients (Naessens *et al.*, 2009).

The definition of pharmacovigilance has been expanded to include: Herbals, traditional and complementary medicines, blood products, biologicals, medical devices and vaccines (WHO, 2004). Many other issues are also of relevance to the science of pharmacovigilance: substandard medicines, medication errors, reports of lack of efficacy, use of medicines for indications that are not approved and for which there is inadequate scientific basis, case reports of acute and chronic poisoning, assessment of drug-related mortality, abuse and misuse of medicines, adverse interactions of medicines and food (Jobson, 2003).

Table 2.2 Terms used to describe inappropriate patient care and adverse outcomes

Term	Definition
Medication Errors	Failures in the process of therapeutic care, that did not proceed as intended and is not directly linked to harm, an example is when the doctor's prescription is misread or a dangerous dose is administered to a patient
Adverse drug events	Noxious and unintended drug effects, occurs at therapeutic doses for prophylaxis, diagnoses, therapy, or modification of physiologic functions and are directly linked to harm done by the drug rather than the disease
Adverse event	Any negative or harmful occurrence that takes place during treatment, which may or may not be associated with a medicine. <i>Note.</i> A fall could be such an event that may – or may not – have any association with a medicine.
Adverse effect	Related to the use of a drug leading to dangerous, unintended reactions, it also includes medication errors and commonly referred to as 'side effect'. Some adverse effects may occur during initiation, dose-adjustments or discontinuation of treatment. Unlike adverse drug events, adverse effects occur at any dose and can be foreseen by healthcare workers. The main difference between adverse effect and adverse drug reaction is that the latter is usually detected by clinical investigations and laboratory tests
Adverse drug reaction	Indicates a response to a medicinal product which may be toxic or used accidentally. This also includes overdose, misuse, abuse and lack of efficacy of a drug used. They differ from adverse effect because they are usually detected by clinical manifestations (signs and symptoms)

Term	Definition
Mal-occurrences	When an individual does not respond well to a drug or experiences an adverse reaction as a result
Complications	An unexpected result which occurs subsequent to a treatment, medical procedure or illness. It is termed so because it 'complicates' the situation
Medical Injuries	Harm or hurt to the body, that may result in a prolonged hospital stay, disability or death
Errors	An unintended act by a healthcare worker, which results in unintended outcomes, these include omissions
Negligence	Preventable adverse events or failure to meet the minimum standard of care
Mal-practice	An act or omission which varies from the defined norms of practice and cause injury to the patient, this term is closely related to negligence
Harm	Unintended physical injury resulting from or contributed to by medical care that requires additional monitoring, treatment or hospitalisation, or that result in death
Near Miss	Errors that did not result in injury to the patient but could have resulted in adverse consequences. Also referred to as potential adverse events or close calls

(Griffin and Resar, 2009; WHO, 2003; Naessens *et al.*, 2009; Grober and Bohnen, 2005; La Pietra *et al.*, 2005; Gagnon *et al.*, 2012; Nebeker *et al.*, 2004)

ADRs are classified into six (A, B, C, D, E and F). A - (augmented) dose related, B – (bizarre) non-dose related, C – (chronic) dose - and time – related, D – (delayed) time-related, E – (end of use) withdrawal and F – (failure) lack of efficacy or failure of treatment (Edwards and Arson, 2000). Other sources classify these reactions into two, namely type A reactions and type B reactions. Type A reactions are predictable reactions since they relate to the dose and chemical processes for which they are understood, they also known as pharmacological reactions, while type B reactions are not well understood and are unpredictable and not related to the dose, they are also referred to as idiosyncratic reactions. Some people experience these idiosyncratic reactions as allergic reactions due to their genetic makeup (Edwards and Arson, 2000; Rawlins and Thompson, 1991).

2.3 Factors affecting ADR reporting in health facilities

Prescriptions are usually written by doctors and clinical nurse practitioners in the public health primary health care sector. However that does not mean that they are solely responsible for pharmacovigilance. Pharmacists and nurses have a vital role in recognizing, evaluating, monitoring and reporting drug related problems to generate knowledge on undesirable drug effects at individual and population level (Toklu *et al.*, 2016).

An observational study conducted in India has outlined that underreporting of ADRs is fuelled by the fear of litigation, lack of knowledge and inability to recognize these events, ignorance, lack of financial incentives, time constraints and the belief that other healthcare workers should be the ones to report the ADR (Khan *et al.*, 2013). Underreporting is a great concern and has a negative impact on public health, limiting the identification of risk and further assessment of monitoring drug efficacy and safety post-marketing (Mazzitello *et al.*, 2013; Alsbou *et al.*, 2017).

The concern with underreporting and drug safety is fuelled by the fact that South Africa has the world's highest roll-out of antiretroviral drugs (ARVs), with the highest tuberculosis incidence globally (UNIADS, 2013; WHO, 2013). The concurrent use of ARVs and other treatment to manage or prevent opportunistic infections places the patients at greater risk of adverse drug reactions (Mouton, *et al.*, 2015). In a resource limited country like South Africa, these reactions are not reported (Mouton *et al.*, 2015). Several attempts have been proposed to improve pharmacovigilance activities with minimal success, and no one is willing to take this responsibility (Khan *et al.*, 2013).

The attempts which have been made to improve ADR reporting include educational interventions and refresher courses on ADRs for healthcare professionals who are presently working, including pharmacovigilance in undergraduate training, establishment of an ADR committee, encourage all healthcare workers to report all suspected ADRs, irrespective of the level of seriousness, increasing the awareness of national pharmacovigilance programmes while countries such as India have modified its ADR reporting form to make it easier for the healthcare professional to fill-in, with clear objectives on what to report (Khan *et al.*, 2013).

Table 2.3 was adapted from a questionnaire based cross-sectional study done by Khan *et al* in 2013 to investigate the knowledge and attitudes of doctors to ADR reporting and it shows the long-term and short-term interventions to promote spontaneous ADR reporting. The results highlighted some of the short-term measures which will improve reporting, which included raising awareness, encouraging reporting and training healthcare workers on pharmacovigilance. Long-term measures included nominating a person dedicated specifically for pharmacovigilance, improving the ADR form to make it more concise, teaching pharmacovigilance in universities as well as providing feedback on past reports to highlight the significance of reporting (Khan *et al.*, 2013)

Table 2.3 Short and long-term interventions to promote spontaneous ADR reporting (Khan *et al.*, 2013; Aronson, 2009).

SHORT-TERM MEASURES	LONG-TERM MEASURES
Raise awareness of ADR reporting	Have someone solely for ADR reporting, like an ADR reporting champion in the hospital
Encourage reporting of all suspected ADRs, regardless of the level of association with the interventions	Minimise administrative work, by making ADR forms more concise and objective on what to report as well as introducing computerised systems
Training in PV, emphasizing the risk perceptions of medicines. Including newly marketed drugs, over-the-counter drugs, herbals, traditional and complementary medicines	Change attitudes through discussions and trainings, where ADR reporting is seen as an integral part of medical practice. There should be a blame-free and non-punitive environment, provide feedback as well on past reports to illustrate its importance
Encourage the reporting of all suspected ADRs, whether known or unknown, common or uncommon, serious or non-serious	Pharmacovigilance should be an important part in undergraduate and post graduate curricula and not be an elective



3. CHAPTER 3: METHODOLOGY

3.1 Study design

This study was an exploratory, multicentre study. A structured questionnaire with closed and open-ended questions was used for data collection. Figure 3.1 provides a schematic representation of the process.

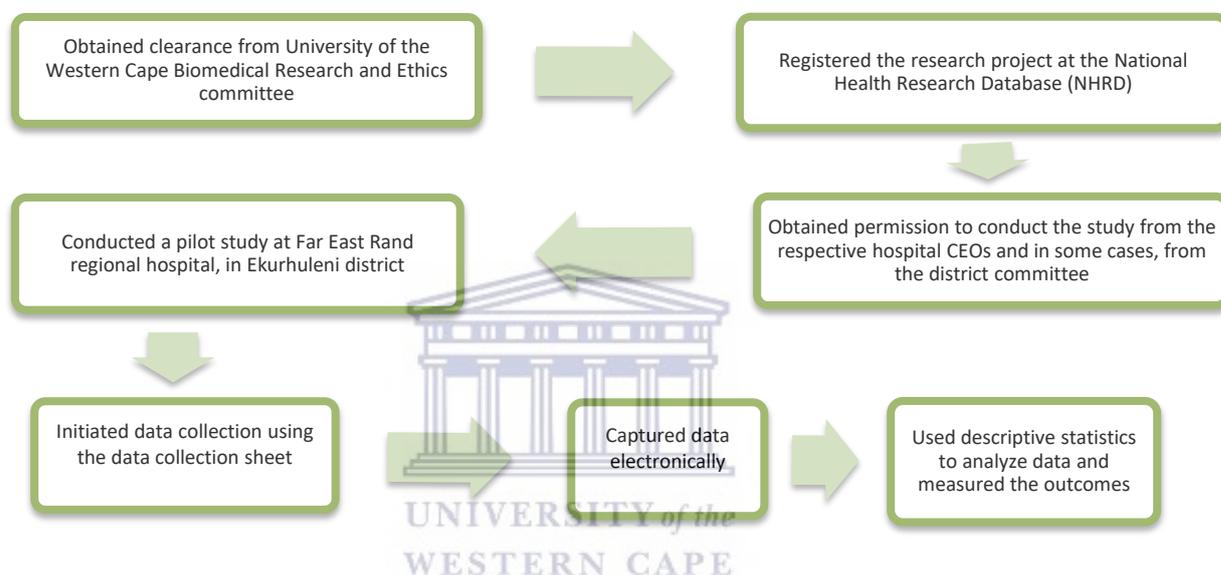


Figure 3.1 An overview of the research process

3.2 Study setting

There are nine provinces in South Africa, with the Gauteng province being a densely populated urban area with approximately 13.2 million people contributing to 24% of the South African population. Approximately 71.8% of Gauteng's population was reliant on the government for healthcare services in 2015, this number has increased from the 66% reported in 2008 (GDoH, 2016). There are 11 district hospitals, nine specialised hospitals, nine regional hospitals, three tertiary hospitals and four central hospitals (GDoH, 2016). This study was conducted in regional and district public hospitals, which fall under the five districts, namely City of Johannesburg, City of Tshwane, Ekurhuleni, Sedibeng and West Rand, situated in the Gauteng province as shown on the Figure 3.2.

The districts include; the City of Johannesburg Metropolitan Municipality, Ekurhuleni Metropolitan Municipality, City of Tshwane Metropolitan Municipality, West Rand District Municipality and Sedibeng District Municipality (GDoH, 2016). Tertiary, central and specialised hospitals were excluded. The reason for this exclusion was mainly because these three types of hospitals usually have systems in place which are only applicable to their facility and cannot be applied elsewhere (South Africa, 2012; GDoH, 2016). In addition to this, tertiary and central hospitals are linked to universities which consistently evaluates, monitors and implements new systems (South Africa, 2012).



Figure 3.2 Gauteng province district map

3.3 Study site selection and target population

3.3.1 Study site selection

All the regional (n=9) and district (n=11) public hospitals situated in the Gauteng province were included. Stratified non-random sampling was employed to select the sample of regional and district hospitals in each of the five districts. The following inclusion and exclusion criteria were applied:

3.3.1.1 Inclusion criteria

- All regional and district public hospitals within the Gauteng Province.

3.3.1.2 Exclusion criteria

- Specialised, tertiary and central hospitals were excluded as they usually have systems in place which are unique to their particular setting, and,
- Clinics, community healthcare centres and regional pharmacies, irrespective of being state or privately owned and being within the Gauteng province.

The stratified non-random sampling used in this study is defined as sampling drawn from a population, which is divided into several groups or 'Strata' (Neyman, 1934). The strata in this study was the Gauteng health districts, which each contained both regional and district hospitals. The researcher sent out permission letters to all the facilities and selection was done on a first response first selected basis for each particular district. The selection process also provided that both regional and district hospitals be presented in each district. All the facilities had equal opportunity to be selected, because all invitations were sent out simultaneously. For logistic purposes, a target sample of about 50% of the hospitals was set to participate in the study.

3.3.2 Target population and recruitment

Access to each selected facility was acquired through the submission of a letter of intent (Appendix 2) to the hospital chief executive officer (CEO). The CEO was requested for permission to access the facility and assist with the identification of the person(s) to be interviewed. The target population for interviews included any health care personnel employed at the selected facilities and involved in facility-based pharmacovigilance activities and in particular ADR reporting. Preference was given to interview nominated persons for pharmacovigilance or ADR reporting in the facility.

In cases where more than one person were identified to be interviewed, all were to be interviewed and data collated for that particular facility. In cases where it would be difficult to identify person(s) for the interview, the PTC representative or the pharmacovigilance subcommittee would be approached. In cases where the hospital did not have any of these committees, the pharmacy manager or supervisor would be interviewed as they were expected to be part of the multidisciplinary team of the PTC, together with nurses, quality-improvement managers, physicians and other healthcare professionals and staff who participate in the medication use process.

An appointment was set up with the person(s). The study information sheet (Appendix 3) and data collection sheet (Appendix 4) was sent to each person prior

to the interview in order for them to prepare for the questions that would require them to go through the facility's pharmacovigilance records.

3.4 Data collection

On the day of the interview, data collection commenced subsequent to the signing of the informed consent form (Appendix 5) by the interviewee after they had time to ask questions about the study. In addition to the interviewer taking field notes of the interview, an audio recorder was used to ensure the capturing of complete information.

The data collection instrument was a questionnaire which was developed by the researcher and adapted from the following studies: Toklu *et al.*, 2016; Hadi *et al.*, 2017. The questionnaire contained three sections; A, B and C. Section A was designed for facilities that had a nominated person(s) for pharmacovigilance, or, a subcommittee responsible for pharmacovigilance, while section B was for facilities which did not have a nominated person(s) or subcommittee for pharmacovigilance. Section C was compulsory for all facilities.

Section A of the questionnaire generated information regarding the nominated person or committee, the type of pharmacovigilance training that these persons had and details on the, the types and frequency of ADRs recorded and reported. Section B collected information on the reason the facility did not have a nominated person or committee for pharmacovigilance, process which was followed for ADR reporting and if there were any plans to nominate a person or committee in future for pharmacovigilance. Section C gathered information on pharmacovigilance documents used and produced by the facility. This included examples of the ADR report form, algorithms used to identify ADRs, ADR reports, challenges to ADR reporting and /or committee meeting agendas and minutes.

Data collection extended over a period of six weeks, and was captured electronically to be analysed. The data collection process is illustrated in Figure 3.1.

3.5 Pilot study

Prior to commencement of data collection, following ethical approval of the study, the data collection instruments were pilot-tested at a regional hospital located at Ekurhuleni district to determine the reliability and validity of the data collection tools and familiarise the researcher with the data collection process. This aided the researcher with obtaining an overview of the actual study in terms of how the interviewees interpreted and responded to the questions, the type of responses received as to how they address the aims and objective of the study, and ultimately assisted in making the necessary changes to the data collection instruments, as well as improve the questionnaire. The researcher had the opportunity to evaluate whether the questions were appropriate to elicit the desired

information based on the results of the pilot study. Subsequent to the pilot study, there were no changes made to the data collection instruments. The data that were collected from the pilot site were not used in the findings of this study.

3.6 Data capturing and analysis

The closed-ended question responses were captured on a Microsoft Excel™ spread-sheet and were checked for accuracy by an independent master's graduate. Quantitative data from Microsoft Excel™ was analysed using descriptive statistics functions. Categorical variables were summarised by frequency counts and percentages.

The open-ended question responses were transcribed verbatim from the audio recordings of the interviews. These transcriptions were sent to the participant for verification and any further explanations that might not have been clear on the day of the interview. The qualitative data were coded and thematically analysed.

3.7 Reliability and validity of data

Reliability is the extent to which results are consistent over time or a consistency of a measurement, or the degree to which an instrument measures the same way each time it is used under a similar methodology. In short, it is the repeatability or reproducibility of a measurement (Golafshani, 2003). Validity refers to the extent to which a research design is scientifically sound or appropriate (Struwig and Stead, 2013). Validity can be either internal or external. Internal validity refers to the extent to which the study design and data obtained allowed the researcher to draw accurate conclusions about the associations within the data (Leedy and Ormrod, 2001). External validity refers to the extent to which the results obtained during the study could be generalized to other contexts (Leedy and Ormrod, 2001). The validity of the data collection form was increased by the pilot study, which was conducted prior to the commencement of the study. Reliability and validity of the data was ensured by using the same data collection tool for the whole period of this study.

3.8 Bias

Bias is defined as any tendency that prevents unprejudiced consideration of a question. In research, bias occurs when one outcome or answer over another is selected by introducing systematic error into sampling or testing. Bias can occur at any phase of research, including study design or data collection, as well as in the process of data analysis and publication (Pannucci and Wilkins, 2010). In this study, bias was minimised as the data collection sheet was filled together with the respondent(s) and the researcher did not, under any circumstance, alter the response once the interview has ended. The transcripts were sent to the participants for verification and they had an opportunity to address any inaccurately captured information. This means that the researcher's views and

preferences did not factor in the data collected. The protocol methodology was strictly followed and there were no deviations without prior approval.

3.9 Ethical considerations

Ethical approval was obtained from the University of Western Cape Biomedical Research Ethics Committee (BM18/6/15). A letter of intent to conduct the study at a particular facility was submitted to each of the hospital's chief executive officer (CEO) and respective districts research committees for permission to gain access to the hospitals following the Registration of the research project at the National Health Research Database (NHRD ref: GP_201808_041), which serves as a repository of health-related research conducted in South Africa. Furthermore, some district hospitals required approval of a committee in addition to the CEOs permission. The hospital CEOs were requested to assist in identifying health care workers in the facility who were involved in pharmacovigilance or ADR reporting for the facility. Subsequent to the identification of potential interviewees, an appointment was set up with the person(s). The study information sheet (Appendix 3) and data collection sheet (Appendix 4) was sent to each person prior to the interview in order for them to prepare for the questions that would require them to go through the facility's pharmacovigilance records.

When considering the principles of autonomy, the participating hospital facility pharmacovigilance representatives were duly informed about the intentions of the study subsequent to the administration of the study information sheet (Appendix 3) together with the informed consent (Appendix 4) which were signed once the participants were assured of confidentiality and that they were able to withdraw from the study at any time, without any consequences for them and they knew what was expected of them. The identities of the facilities were blinded by referring to the facilities using codes, this was to ensure that the reputation of the facility was not at stake.

The signed consent forms with the identifying information were kept separate from the data collection sheets and were available only for senior researchers involved in the study. After the study is completed i.e. research reports and publications written, the electronic databases and paper data collection tools will be deleted and destroyed by the principal researcher.

The risks for study participants were minimal as the anonymity protection ensured confidentiality. No direct benefits for the study participants were anticipated.

4. CHAPTER 4: RESULTS

4.1 Gauteng Public Hospitals

The data collection process started in August 2018, and it was spread over a period of six weeks, until October 2018. Only public sector hospitals situated in one of the following five districts in the Gauteng province were included in this study.

Table 4.1 Gauteng Province districts and regional hospital totals and those that participated in the study

District	Regional Hospitals Number (participated)	District Hospitals Number (participated)
West-Rand District Municipality	1 (1)	2 (1)
City of Johannesburg Metropolitan Municipality	2 (1)	2 (1)
Ekurhuleni Metropolitan Municipality	4 (2, 1*)	1 (0)
City of Tshwane Metropolitan Municipality	1 (1)	4 (2)
Sedibeng District Municipality	1 (1)	2 (1)

Key: * pilot site

Table 4.1 illustrates the districts and number of hospitals situated in each district, where the facilities used in the study are indicated in brackets. There were 11 district hospitals spread over the five districts in the province of which five (45.5%) were selected for this study using stratified non-random sampling. Similarly, there were nine regional hospitals which were spread over the five districts of the Gauteng province. From the nine regional hospitals, six (66.7%) were selected for participation in this study and one was used as the pilot site. The pilot site's results were excluded from the study.

4.2 Hospitals that had a person(s) or committee nominated for ADR reporting

Five (45.5%) of the 11 hospitals had either a person or committee nominated for ADR reporting. This was spread over two (33.3%) of the regional hospitals and three (60%) of the district hospitals as shown on Table 4.1. All the hospitals indicated that their nominated persons were pharmacists as depicted in Table 4.2.

Table 4.2 Availability of person(s) or committee responsible for pharmacovigilance

Is there a person or committee nominated for adverse drug reactions reporting	District Hospital	Regional Hospital
Yes	3	2
No	2	4

Table 4.3 Facilities which had a nominated person(s) or committee responsible for pharmacovigilance

	District (n=3)	Regional (n=2)
The qualification of the nominated person	3	2
<ul style="list-style-type: none"> • Pharmacist 		
Knowledge of ADR reporting	1	0
<ul style="list-style-type: none"> • Average • Good • Excellent 	1 1 1	1 1
Confidence to identify an ADR	1	1
<ul style="list-style-type: none"> • Average • Good • Excellent 	1 1 1	0 1
Received any pharmacovigilance training	2	2
<ul style="list-style-type: none"> • Yes • No 	1	0
When was pharmacovigilance training received	0	1
<ul style="list-style-type: none"> • Within the last 12 months (2017) • 1-2 years ago (2015-2016) • More than 2 years ago (before 2015) 	2 0	0 1
Was the training adequate	2	2
<ul style="list-style-type: none"> • Yes 		

4.2.1 Knowledge on ADR reporting and confidence in the ability to identify ADRs

Table 4.3 demonstrates the self-reported knowledge on ADR reporting and confidence to identify an ADR of the persons nominated for ADR reporting. The Likert-scale was used to determine whether their ratings were poor, fair, average, good or excellent. One pharmacist rated his/her knowledge on ADR reporting as average, while two pharmacists rated their knowledge as good and another two as excellent. The same respondents rated their confidence in identifying an ADR as

average (2 participants), good (1 participant), and excellent (2 participants), respectively.

4.2.2 Pharmacovigilance training of persons nominated for ADR reporting

Four (80%) of the nominated persons for ADR reporting indicated that they had training on pharmacovigilance as depicted in Table 4.3. All four respondents who had training stated that the training which was received was adequate. One of the respondents last received training on pharmacovigilance in 2017, two in 2016, while the other received it in 2014. Training was received from the following providers; Johannesburg district, Right-to-care, National Department of Health (nDoH) National Road Show and Pulse Health Solution. One of the nominated persons for ADR reporting completed a master's degree in ADR reporting, where she implemented new strategies to improve ADR reporting. Only one person nominated for pharmacovigilance had not received any pharmacovigilance training, because she was only recently appointed for this role. Those who received training on pharmacovigilance stated that the training included ADR reporting, how to report, how to identify ADRs, who should report, why reporting is done, as well as medication errors.

4.2.3 Previously reported ADRs by nominated person for ADR reporting

All the nominated persons provided a file containing all the ADR reporting documentation for their facility. The number of identified and reported ADRs over the past 12 months in each hospital was obtained by going through the files which were provided. The district hospital, HOSD1 did not identify nor report any ADRs, HOSD2 had five ADRs, while HOSD3 had three ADRs. All the district hospitals (HOSD1, HOSD2 and HOSD3) did not have any deaths due to ADRs, while the regional hospitals (HOSR1 and HOSR2) had 10 and 199 ADRs identified and reported over the past 12 months respectively. Whereas in the hospital HOSR1 had 1 death - where streptokinase IV was the cause, while hospital HOSR2 had less than 10 deaths due to ADRs, the exact number could not be confirmed as there were patients who were not followed up.

4.2.4 Feedback from committees on reported ADR

All facilities had a Pharmacy and Therapeutics Committees (PTC), which are audited annually as per the requirements of the national core standards. Only two (40%) of the five hospitals that had a person nominated for pharmacovigilance indicated that they received feedback from either their institutional pharmacovigilance or antimicrobial stewardship (AMS) subcommittees of the hospital PTCs, respectively. The hospital with the AMS committee, only provided feedback on ADRs caused by antimicrobials, i.e., antibiotics, antifungal,

antiparasitic or antiviral agents. The subcommittees in both these institutions met monthly.

The functions of the pharmacovigilance subcommittee was to set the norms and monitor medication errors, adverse drug events and poor product quality use in order to promote rational medicine use and the safety use of pharmaceutical products, blood and blood products; to develop and implement protocols and guidelines regarding the prevention and reporting of medication errors and adverse drug events; to conduct regular audits on the reporting of medication errors and adverse drug events; and to provide feedback and other appropriate measures in order to correct safe and effective use of pharmaceutical products, blood and blood products. The function of the AMS subcommittee was to draft antibiotic policies which will improve quality of patient care and safety, reduce antimicrobial resistance, optimise therapy, reduce adverse effects and treatment failures, with increased cure rates, manage adverse events related to the use of antimicrobials, implement infection control practices and provide feedback to the hospital PTC.

4.3 Hospitals that did not have a person(s) or committee nominated for ADR reporting

There were six hospitals that did not have a person(s) or committee nominated for ADR reporting, the hospital CEOs recommended that the pharmacy managers complete the study questionnaires, because the hospitals' ADR forms were sent to the pharmacy following the identification and reporting of an ADR. No other healthcare personnel were identified for the purpose of ADR reporting and it was decided with the CEO and the pharmacy managers that only the pharmacy managers would participate in the study.

The hospitals were asked for reasons for not having a nominated person or committee for ADR reporting and most of the hospitals stated that there is a lack of volunteers for this role:

“There is no one to take the initiative and no one wants to volunteer.” – HOSD5

Shortage of staff was also one of the prevalent reasons for not having a committee or a person for ADR reporting, hospital HOSR4 stated that *“The burden is high and there is not enough staff”*. Similarly, the hospitals expressed that the rate of reporting is low and therefore there is no need to have such a person or committee as stated by HOSR6. While hospital HOSR5 believed that there is no need for such a person or committee, and said *“it is supposed to be everyone’s responsibility”*. The hospitals also stated that there are too many committees and they do not want to add more, they are waiting for a directive from National to

instruct them to form this specific committee or nominate such a person, there is lack of time, training and resources to support this particular function, while HOSD5 also added that *“it is not remunerated and it is too administrative”*.

None of the hospitals had attempted to nominate a person or committee for ADR reporting in the past. Only one of the six hospitals had plans to nominate a person or a committee for ADR reporting in future, and this person was the store pharmacist.

4.3.1 The process of ADR reporting

The hospitals which did not have a person nominated for ADR reporting were asked to describe the steps which they follow when ADRs have to be reported and the various description are stated below:

4.3.1.1 The process of reporting for HOSD4

There were ADR reporting forms available in the wards which were kept in a designated box. Once an ADR was identified, the doctor had to complete the form or instructed the assisting nurse to do so. After the form had been completed, they were either taken to any of the PTC members, to the pharmacy or they were left in a designated box where a pharmacy staff member collected the forms and took them to the pharmacy. They would then be discussed in the hospital PTC and then scanned by the pharmacy manager and forwarded to the district office. The district office would then send these forms to SAHPRA.

4.3.1.2 Process of reporting for HOSD5

The nurses in the wards were expected to identify the ADRs since they were the ones who administered medicine to the patient. Once an ADR was identified, an ADR reporting form would be completed and sent to the pharmacy manager who took them to the PTC for discussion. The infection control committee was consulted if there were any antimicrobials involved. Following the PTC discussion, the forms were sent to SAHPRA using the email address provided on the forms.

4.3.1.3 Process of reporting for HOSR3

This hospital was able to provide an algorithm which they used to identify ADRs. Only serious ADRs were reported to the CEO, who reported to the provincial quality assurance director within 24 hours via Short Message Service (SMS). The serious adverse drug reactions are those which results in death, life threatening experience or require hospitalisation or prolongation thereof. The CEO would then initiate an investigation through the Serious Adverse Drug reactions committee of the district (City of Johannesburg). A preliminary report would be sent by the CEO within seven days to the Head of the Department that reported the ADR. Within 25 days, a comprehensive QA investigation report was to be submitted. The Serious Adverse drug Event (SAE) was then either closed or referred to NADEMC and for ratification by the province. This algorithm is provided as appendix 9.

4.3.1.4 Process of reporting for HOSR4

ADRs were reported from the wards/pharmacy using the national ADR reporting forms. These forms were then submitted to the pharmacy manager who would include them in the agenda for the PTC, as this also formed part of quality assurance. The ADRs would then be discussed in the PTC and a resolution made. Feedback would then be given to those who reported the ADR. The forms would then be sent to SAHPRA via email.

4.3.1.5 Process of reporting for HOSR5

In this hospital, following the identification of an ADR, doctors and nurses would bring the forms to the pharmacy. The pharmacy manager collated these forms, added ADR's to the agenda for the PTC and they were discussed in the PTC and simultaneously sent to the provincial district and to SAHPRA.

4.3.1.6 Process of reporting for HOSR6

In this hospital, following the identification of an ADR, the treating doctor completed the national ADR form and sent them to the pharmacy manager, who worked closely with the pharmacy store supervisor and together they collated the forms received and added them to the agenda for the PTC to be discussed and concurrently sent the forms to the provincial PTC. If it was a quality issue, the query was sent to the medical supplies depot and included the batch number of the concerned product. The medical supplies depot then forwarded the query to the respective company, samples were retained in the pharmacy stores in case a sample was requested for testing.

The processes described above have similarities, even though the order might be different. ADRs were identified, the ADR reporting form completed and submitted to the pharmacy manager. The pharmacy manager ensured that the ADRs were reported to the facility PTC and in some cases the provincial PTC. Depending on the hospital resources which were available, some hospitals did not send their reports to the provincial PTC as they were able to make resolutions within the facility's PTC. The pharmacy manager also sent these forms to SAHPRA which reviews the reported ADR. None of the hospitals reported that they sent their ADR reports directly to the National Adverse Drug Event Monitoring Centre (NADEMC) Which is a unit of SAHPRA established to assist with the collection and management of the national ADR database (Maigetter, *et al.*, 2015; Mehta, 2011).

4.4 Status of ADR reporting at all participating hospitals

4.4.1 Adverse Drug Reaction reporting forms

The responses from the hospitals with a person or committee responsible for ADR reporting were compared with those without a person or committee responsible for ADR reporting. All the hospitals (n=5) with a person/committee responsible for

ADR reporting reported that they used the national ADR reporting forms, while five (80%) of the hospitals without a person or committee responsible for ADR reporting were using the national ADR reporting forms. The only hospital that did not use the national ADR form, rather used a nurses' incident report to record and report ADRs (Appendix 9). The reason why they were not using the national ADR reporting form was because the incidence report form was more comprehensive and less restricting; it also covered other non-treatment related aspects that were related to patient care. This hospital decided not to have too many forms and rather used one form which had enough space for the reporter to narrate the report/incident.

All the hospitals reported that they kept the ADR reporting forms either at the pharmacy and in the wards or consulting rooms, as demonstrated on Table 4.4. In addition, all healthcare professionals had access to the forms, except for Hospital HOSR3, where only nurses had access. This was also the only hospital which did not use the national ADR reporting form.

To verify the use of the national ADR reporting forms, hospitals were asked to produce at least three of the previously completed ADR forms for the researcher to view. All hospitals were able to produce these and they were using the latest version (version 4.0 07/16), with the exception of hospital HOSR3, which did not use the national ADR reporting form. However hospital HOSR3 was able to provide the researcher with a blank form used in the facility.

Table 4.4 Status of ADR reporting at all participating hospitals (n=11)

	Facilities with a nominated person (n=5)	Facilities without a nominated person (n=6)
Use of national ADR reporting form		
• Yes	5	5
• No	0	1
Where are the ADR reporting forms kept		
• Consulting areas	2	0
• Pharmacy and wards	3	4
• Wards only	0	2
Who has access to the ADR reporting forms		
• All healthcare personnel	5	5
• Nurses only	0	1
Use of ADR trigger tools/ algorithms		
• Yes	1	1
• No	4	5
ADR reporting in the facility is:		

• Compulsory	3	5
• Voluntary	2	1
• Remunerated	0	0
Facilities able to provide three completed ADR reporting forms		
• Yes	5	6
• No	0	0

4.4.2 Use of algorithms and trigger tools for ADR identification and reporting

Only two (18.2%) hospitals used algorithms and/or trigger tools to identify ADRs, one of these had a person/committee responsible for ADR reporting and the other one did not. Hospital HOSR3 was using the serious adverse drug events (SAE) algorithm, where following the identification of a SAE, they would immediately complete an incident report and inform the person in charge or operational manager, who would then report to the CEO, this report would escalate to the SAE committee who would then provide a resolution back to the CEO. The second hospital which used an algorithm/information poster was HOSR2, this hospital had a person responsible for ADR reporting. The algorithm/information poster contained information on what an ADR was and how to recognise an ADR, as well as the contact details of the person responsible for ADR reporting. This hospital had by far the highest reported number of ADRs (n=199), followed by hospital HOSR3 which had a total of 10 reported ADRs over the past 12 months, making it the second highest.

4.4.3 Commonly reported ADR types

All respondents allowed the researcher to go through the facility files that contained the documentation of the facilities' ADR reporting activities for the past 12 months (October 2017 and October 2018). The documentation consisted of completed ADR forms and reports with a notable absence of feedback reports from any committee or SAHPRA. The individual reported ADRs were first classified into categories which included administration errors, allergic reactions, quality issues, endocrine effects and others. These types were then assigned per facility to identify those ADR types which were most frequently reported across facilities (the unit of analysis in this study was thus the facility). The most frequently reported ADR types identified across facilities is summarised in Figure 4.1. The most frequently identified ADR type reported at participating facilities was allergic reactions, reported by eight of the facilities, which presented as angioedema and rash. Two of these facilities had a nominated person for ADR reporting. Other frequently reported ADR types at facilities without a nominated person or committee included quality issues (n=3) and administration errors (n=2). The hospitals described administration errors as any deviations from the written prescription and included administering the wrong dose, wrong medicine, omission

of medicines, using the incorrect route of administration, reconstituting with the wrong diluent/solvent/additive, or administering at the wrong time. Quality issues included deteriorated medicine, impurities present in the medicine, faulty packaging, incorrect tablet count or volume of medicine.

Gynaecomastia was reported at two facilities which had a person or committee for ADR reporting, while the following reactions were reported at one facility and they included CNS effects, visual effects, gastrointestinal effects, cough and fatigue.

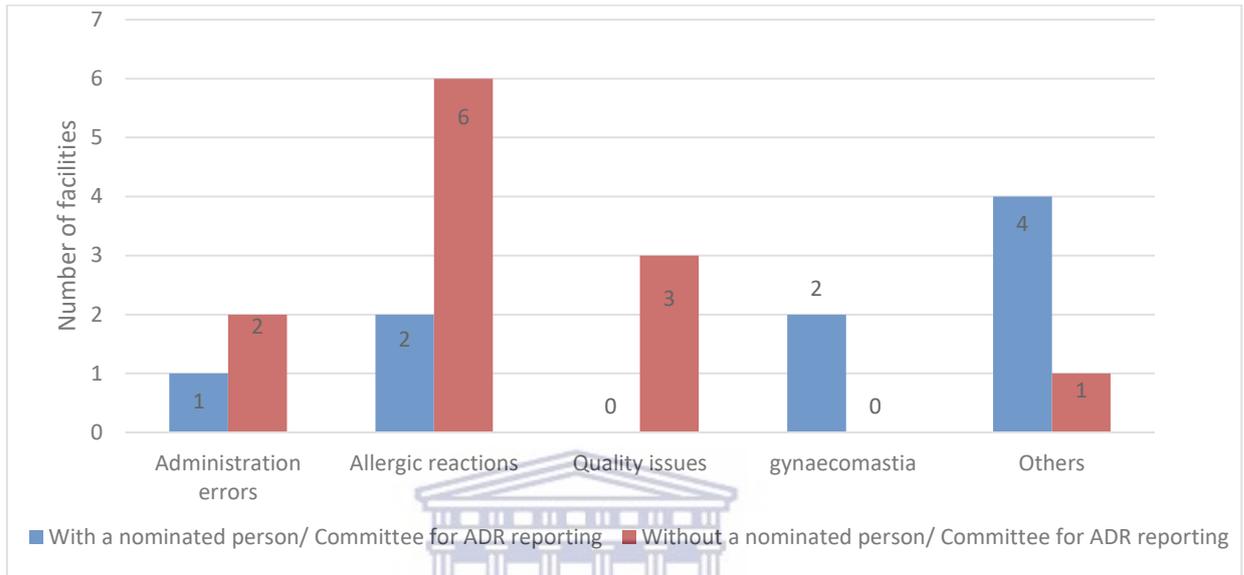


Figure 4.1 Frequently reported ADR types in hospitals with (n=5) and without (n=6) a nominated person for ADR reporting over the past 12 months

4.4.4 Most commonly reported class of drugs

Figure 4.2 illustrates the most frequently reported drug classes implicated in previously identified and categorised ADR types in the facilities over the past 12 months. ADRs due to antiretroviral drugs (ARVs) were prevalent in eight of the 11 hospitals. Five of these hospitals did not have a person or committee for ADR reporting. The second most common class of drugs to produce ADRs was ACE inhibitors (n=5). Enalapril was by far the most frequently prescribed ACE inhibitor at these facilities. There were two Central nervous system (CNS) drugs at hospitals with a person or committee for ADR reporting as shown on the Figure 4.2 and these included anticonvulsants, while hospitals without a person or committee for ADR reporting had anaesthetics and antipsychotics under the CNS drugs. Other drugs included reports on lubricants (KY Jelly), antibiotics and streptokinase which resulted in death of a patient. All of these reported cases never received any form of feedback from SAHPRA.

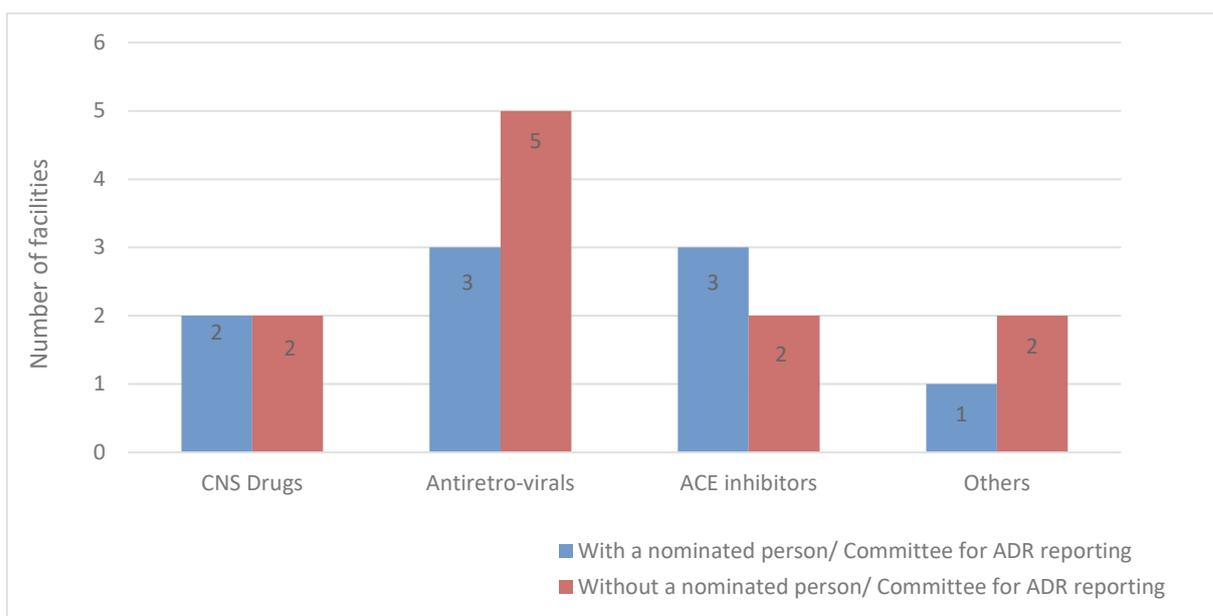


Figure 4.2 Commonly reported drug classes causing ADRs in hospitals with (n=5) and without (n=6) a nominated person for ADR reporting

4.4.5 Challenges with ADR reporting in the facilities

Table 4.5 lists some of the challenges associated with ADR reporting which were reported by the facilities. The most common challenge for facilities with and without a nominated person for ADR reporting was prevalent ADRs not being reported. The second most common challenge for both facility types were high workload, being short staffed or lack of time. Facilities with a person for ADR reporting further listed fear of litigation. While, facilities without a person nominated for ADR reporting listed additional challenges such as patient's unwillingness to participate in ADR reporting, too administrative, lack of understanding and lack of responsibility. These results show that more challenges are seen with facilities without a person or committee for ADR reporting.

Table 4.5 Challenges with ADR reporting in hospitals with and without a nominated person for ADR reporting

Theme	Quote
Too administrative	"It is admin intensive" – HOSR5 "No filling in the forms as supposed" – HOSD2
Lack of understanding	"Failure to understand if a reaction is part of the disease process or drug related" - HOSR3 "Some of the reactions are minor and not deemed necessary" – HOSR6
Patient unwillingness	"Patients do not report since most of the symptoms resolve spontaneously, they are usually not reported" – HOSR3 "Patients not willing to spend time with healthcare workers to fill-in the ADR forms" – HOSR4

Fear of litigation	“Fear of being seen as incompetent (blame and punishment)” – HOSD3
Prevalent ADRs not being reported	“Under-reporting” - HOSD3 “People do not report” – HOSR5 “Not willing to report” – HOSR6
Lack of responsibility	“Responsibility” – HOSD4
Short-staffed, high workload and lack of time	“Short-staffed, overburdened with work and not time to fill the form” – HOSD4 “Work load” – HOSR1

The facilities were asked if ADR reporting was compulsory or voluntary. According to the responses which were given by the study participants, 60% (N=3) considered ADR reporting as compulsory in hospitals with a person/committee for ADR reporting, while 83.3% (n=5) of the hospitals without a person/committee responsible for ADR reporting considered ADR reporting as compulsory. The respondents were probed for the reason why they considered ADR reporting to be compulsory or not, they stated that only life threatening and serious adverse events should be compulsory to report and the common and expected ADR should be voluntary. The respondents also indicated that they could not force a healthcare worker to report an ADR, the heads of the department should emphasize the importance of reporting ADRs in their department and it should be their responsibility to evaluate if their staff members comply.

None of the hospitals specifically remunerated those who were responsible for pharmacovigilance or those who sent in reports for ADRs. The remuneration was described as any form of reward or benefit for those who were actively involved in the ADR reporting process. One of the respondents indicated that ADR reporting was part of a healthcare workers daily activity and they could not expect to be remunerated for doing what they are expected to do. Furthermore, some of the participants felt that ADR reporting should be included in the assessment of Performance Management and Development System (PMDS) that aims to assess staff quarterly using a set of criteria related to their role.

Various strategies were employed and suggested by the participants to overcome the challenges faced by the hospitals. Hospital HOSD4 stated that ‘the responsibility of ADR reporting will be transferred to the store pharmacist’. The store pharmacist would be best suited for taking over this function as he or she was perceived to be better equipped for this role – their role is administrative in nature and they can collate the ADR reporting forms for the hospitals and will be able to do the follow-up. They are also in contact with pharmaceutical companies and medical supplies depot where they order medicines from, this gives them the ability to report and investigate quality issues.

Improving awareness on the importance of ADR reporting in the hospitals – by placing posters on the walls and emphasizing the importance of

pharmacovigilance during pharmacy week as reported by HOSD5. Using the electronic reporting application which is available from the Department of Health EML application. This makes it convenient for the reporter and eliminates the extensive paper work, i.e. the need for a scanning and/or faxing the ADR report forms as reported by HOSR4.

Conducting medication errors and ADR training, with follow-up training at regular intervals as stated by HSD3 that medication errors training was conducted for nurses and other clinical staff, with a follow-up training. Increasing accessibility of the ADR reporting forms to all health care practitioners, Hospital HOSR5 pharmacy staff goes to the wards to place forms and collection boxes on a regular basis. The heads of each department have been prompted to report any ADR which take place in their departments as reported by hospitals HOSD2, HOSR6 and HOSD5.

One strategy that seemed to work extremely well in HOSR2 was through alerting the pharmacists when a suspected ADR was identified by ward staff the pharmacist would then do the administrative work of completing the ADR form. This hospital HOSR2 had by far the highest number of reported ADRs (199) reported between September 2017 and October 2018.

4.4.6 Committees which support pharmacovigilance within the hospital

There was only one hospital (9.1%) which had a subcommittee specifically for pharmacovigilance, while 90.9% did not have subcommittees for pharmacovigilance and this function was part of the hospital's PTC. The only other facility which had a subcommittee was hospital HOSD2, which had a subcommittee for antimicrobial stewardship, and not for pharmacovigilance. The hospitals were asked to produce the agenda for the last three PTC meetings and 40% (n=2) of the hospitals which had a person or committee responsible for ADR reporting were able to produce this agenda while it was 33.3% (n=2) at hospitals without a person or committee responsible for ADR reporting. Other facilities did not provide the agenda because it could not be located (n=6) or the agenda contained confidential information (n=1), which could not be shared with researcher.

5. CHAPTER 5: DISCUSSION

The aim of this study was to explore the factors affecting ADR reporting at regional and district hospitals in Gauteng Province. This study represented just over half (55%) of the regional (6/9) and district (5/11) hospitals across the five districts of Gauteng Province. A factor that was given specific prominence was if the hospital had nominated a person responsible for ADR reporting.

5.1 Hospitals that had a person(s) or committee nominated for ADR reporting

This study found that less than half (45.5%) of the participating hospitals had a person nominated for ADR reporting. In all cases this person was a pharmacist. These results coincide with a study conducted in non-university hospitals in France, where directors and presidents of the hospitals were asked to nominate a person for pharmacovigilance and the study reported that 83% of the nominated persons for pharmacovigilance were pharmacists, 13.5% were doctors while less than 3% were nurses and hospital directors (Gony, *et al.*, 2010). Pharmacists are seen as the custodians of medicine and it is their responsibility to promote and encourage ADR reporting and improve the safety of medicine hence the person or committee to be nominated for ADR reporting should be prepared to play this role. In addition, countries such as the United States, Canada and the United Kingdom have appointed hospital pharmacists to be solely responsible for ADRs reporting (Suleman, 2010).

The five pharmacists nominated for ADR reporting in this study rated their knowledge on ADR reporting and confidence to identify an ADR ranging from average to excellent. Similarly, a pilot study on the evaluation of knowledge, attitude and practices of Indian pharmacists revealed that 95% of the respondents were indeed knowledgeable about ADRs, even though these participants were not necessarily nominated for ADR reporting at their facilities (Ahmad *et al.*, 2013). The positive self-reported knowledge and confidence ratings from the pharmacists of this study, also agrees with research which reported that pharmacists in South Africa are familiar with the concept of pharmacovigilance, conceding that they were not nominated for ADR reporting and are willing to participate in the process of ADR reporting, however they are uncertain of the role they should be playing (Joubert and Naidoo, 2016). Due to pharmacists' extensive knowledge on medicine, they have a central role in coordinating medicine safety and contribute to the identification, prevention, reporting and documentation of ADRs (Suleman, 2010). This information illustrates that pharmacists have the knowledge and ability

to drive ADR reporting in hospitals, and hence should be the nominated person(s) to ADR reporting.

Four of the five (80%) pharmacists nominated for ADR reporting in this study had received pharmacovigilance training that they described as adequate. Another South African study from one regional hospital found that 89% of healthcare personnel were interested in receiving pharmacovigilance training that included ADR reporting (Terblanche, 2018), because they believed that training improved awareness of ADR reporting. Indeed, the positive effect of training has been shown to improve ADR reporting frequency in physicians in part due to the fact that they were more confident that they have correctly identified an ADR (Figueiras *et al.*, 2006; Lopez-Gonzalez *et al.*, 2014). This improvement in ADR reporting was further proved in a systemic review study which evaluated the effect of multiple interventions to improve ADR reporting, these interventions included training, visual aids on ADR reporting, use of electronic gadgets, continuous feedback on reported ADRs, pharmacists and other key personnel involvement, where there was a greater than fivefold increase in spontaneous reporting of ADRs (Gonzalez-Gonzalez, *et al.*, 2013).

The frequency of ADR reporting for the study participants over the past 12 months, ranged between 0 and 10 for five of the participants and 199 for one participant. This information was obtained by going through the files which were provided, where all the ADR forms were kept by the hospitals. The ADR forms in the files were either filled-in by the physicians, nurses or the pharmacist. However, they were kept at the pharmacy, irrespective of which healthcare worker reported the ADR. No deaths were attributed to ADRs in the district hospitals while one and ten ADR-related deaths were reported by the regional hospital participants, respectively. These results show a significant variation in the number of ADRs reported between participants, as seen with the high variation range. The higher frequency of reporting for especially the regional hospital participants correlates more with a study conducted in one regional and three tertiary hospitals in South Africa which revealed that 2.9% of medical admissions were attributed to ADRs, while a massive 16% were ADR-related (Mouton *et al.*, 2015). The number of deaths due to ADRs was relatively low in our study and this may be because patients are usually not followed-up as mentioned by one of the hospitals. Yet, a study that followed approaches to pharmacovigilance in Europe and the United States by Wiktorowicz *et al.*, (2012) reported that more than 100 000 deaths per annum in the United States were due to ADRs and that they were amongst the top 10 leading cause of death.

Two (40%) of the five hospitals with a nominated person for ADR reporting indicated that they received some form of feedback from the institutional pharmacovigilance or antimicrobial stewardship (AMS) subcommittees, which were subcommittees, which report to the facility's PTC. Feedback and evaluation

of the decisions taken enhances PTC accountability and ensures the credibility of decisions taken (Mashaba *et al.*, 2018). Both the pharmacovigilance and antimicrobial stewardship (AMS) subcommittees met monthly. The frequency of committee and subcommittee meetings in our study relates to the study conducted by Matlala *et al.* (2018), where almost 40% of the nine Gauteng district hospitals and over 70% of the six regional hospitals had PTC meetings monthly respectively. The average number of PTC meetings ranged between four and 12 annually (Mashaba *et al.*, 2018).

This study also found that more than half of the participating institutions did not receive feedback on the reported ADRs. Those who did receive feedback, did not receive it frequently enough as the committees meet only once a month, while decisions on patient ADR reports may require swift evaluation. Literature reiterates that frequently scheduled PTC meetings are necessary as they facilitate decision making regarding pharmacovigilance relating to the handling and reporting of ADRs, medication errors and management of product complaints (Mashaba, *et al.*, 2018). However, decision making requires a quorum at PTC meetings and Mashaba *et al.* (2018) also found that only 37.5% of the hospital meetings in their study met quorum, thus relevant decisions which feeds back to the healthcare workers were absent for about three quarters of meetings that did take place. Similarly, a survey conducted by Mehta, *et al.*, (2014) reported that poor communication and feedback were identified as major weaknesses to existing pharmacovigilance systems. Other literature stated that providing feedback is important as it improves the morale of the healthcare staff (Granás, *et al.*, 2007; Joubert and Naidoo, 2016). A study conducted in the Netherlands to examine the expectations of healthcare professionals regarding feedback on ADR reporting found that 80.3% of respondents thought feedback increased their knowledge (Oosterhuis *et al.*, 2012). Feedback and communication amongst all stake holders involved in the pharmacovigilance process should be prioritised as reported in a survey of current pharmacovigilance activities in South Africa, conducted the National Department of Health, in collaboration with the University of Cape Town, which also reported that it would be of benefit to establish a national pharmacovigilance website which will be a platform used to facilitate information sharing (Mehta, *et al.*, 2014).

The Medicines Information Centre (MIC), situated within the Division of Clinical Pharmacology, Department of Medicine, Faculty of Health Sciences in the University of Cape Town, is the only clinically based medicines information centre in South Africa (SA) and provides information to both public and private sector healthcare professionals. The MIC has established a toll-free hotline which provides healthcare personnel on all aspects concerning the treatment of HIV and TB (Swart *et al.*, 2013). A similar hotline may be established for the purpose of pharmacovigilance to provide reliable real time advice, individual and collective feedback and communication on ADR reports (Mehta *et al.*, 2017). At a provincial

level, the Gauteng provincial pharmacy and therapeutics committee has initiated a subsidiary Safety and Quality committee with an objective to manage activities relating to ADR reporting, medication errors and quality problems. The Gauteng provincial pharmacy and therapeutics committee has published the first pharmacovigilance bulletin in 2017 which promotes communication on pharmacovigilance activities (Terblanche, 2018).

5.2 Hospitals that did not have a person(s) or committee nominated for ADR reporting

There were six hospitals that did not have a person(s) or committee nominated for ADR reporting. The most common reason why these facilities did not have a nominated person or committee for pharmacovigilance was lack of volunteers for this role. None of the hospitals had attempted to nominate a person or committee for ADR reporting in the past, because the rate of ADR reporting was low, the hospitals were under resourced and they were waiting for a directive from national to instruct them to nominate such a person. Another South African study conducted in a public hospital in the North West Province, did not investigate nominated persons, yet similarly found that resource shortages were reasons assigned to challenges of the pharmacovigilance system at the hospital (Goosen *et al.*, 2015). Lack of time and resources were also given as reasons by 63.3% of participants on not having a person responsible for ADR reporting in a study done in a regional hospital in Ghana (Amedome and Dadson, 2017). The problem with not having a person nominated for ADR reporting is that this causes an overlapping of responsibility and this has led to the assumption that another healthcare personnel will report the suspected ADR (Walji *et al.*, 2011). This means that none of the healthcare personnel feels obliged to report an ADR and they cannot delegate someone to do so since there is no one who is responsible for this function.

Different hospitals followed different processes for reporting ADRs, depending on the resources they had available. Upon analysis, the processes described had similarities, even though the order might be different. ADRs were identified, the ADR reporting forms were completed by the healthcare personnel who encountered the ADR and the forms were submitted to the pharmacy manager. The pharmacy manager ensured that the ADRs were reported to the facility PTC and in some cases the provincial PTC. Depending on the hospital resources which were available, some hospitals did not send their reports to the provincial PTC as they were able to make resolutions within the facility's PTC. The pharmacy manager also sent these forms to SAHPRA for review of the reported ADRs. It is important for the hospitals to have clear and proper processes to follow when reporting ADRs because pharmacovigilance programmes around the world relies

on spontaneous reporting of ADRs and hospitals are able to provide this data (Pal *et al.*, 2013). Hospitals may have different processes when reporting ADR's and this depends on the resources they have available. Based on the efficiency of the process and the support within the facility, it may be acceptable to have different processes, provided that ADRs are ultimately being reported on a continuous basis. Only a small number of African countries, including South Africa, Mozambique, Uganda, Morocco, Tanzania, Zimbabwe, Egypt, Ghana, Togo, Nigeria and Tunisia have formal pharmacovigilance systems in place and are full members of the WHO Programme for international Drug Monitoring, however, this does not mean that the processes of reporting should be similar since there are various other factors which influence how the facilities report ADRs (Sevene *et al.*, 2008). Based on this literature, it is apparent that pharmacovigilance is not a "one size fits all" process where all facilities can adopt one process. The reporting of ADRs should be tailored for each facility and hence a need for a designated person or committee to drive this process and pharmacists are in the best position to do so. This statement is supported by Suleman, 2010, who stated that pharmacists are best fit for this role due to their ease of access to patient medical records, being experts on medicine and ensuring safe use of medicine.

5.3 Status of ADR reporting at all participating hospitals

All the hospitals (n=5) with a person/committee responsible for ADR reporting reported that they used the national ADR reporting forms, while five (80%) of the six hospitals without a person or committee responsible for ADR reporting were using the national ADR reporting forms. The only hospital that did not use the national ADR form rather used a nurses' incident report to record and report ADRs. The reason why they were not using the national ADR reporting form was because the incidence report form was more comprehensive and less restricting; it also covered other non-treatment related aspects that were related to patient care. This hospital decided not to have too many forms and rather used one form which had enough space for the reporter to narrate the report/incident. However, not using the national ADR form may be problematic, because it has been noted in literature that different reporting forms may lead to different reporting styles and loss of important information (Bandekar, *et al.*, 2010). The Department of Health of South Africa has used the WHO standards to develop the current national ADR reporting forms, to facilitate identification and evaluation of drug reactions which promotes safe use of medicines, improves patient and public health (nDoH, 1996).

All the hospitals reported that they kept the ADR reporting forms either at the pharmacy or in the wards or consulting rooms. In addition, all healthcare professionals had access to the forms, except for Hospital HOSR3, where only nurses had access. Literature recommends that sufficient resources should be made available to facilitate and encourage reporting. Goosen, *et al.*, (2010) has stated that adequate ADR reporting forms and a telephone line should be provided

to improve the system. All hospitals that used the national ADR form were able to produce at least three previously completed ADR forms, which were also the latest version (version 4.0 07/16) of this form.

According to this study, only two (18.2%) of the 11 hospitals used algorithms and/or trigger tools to identify ADRs, one of these had a person/committee responsible for ADR reporting and the other one did not. The hospital which reported using an information poster (HOSR2) had a person responsible for ADR reporting. The information posters which were displayed on the corridor walls of the hospital, in the wards, patient waiting areas and at the pharmacy contained information on what an ADR was and how to recognise an ADR, as well as the contact details of the person responsible for ADR reporting. This hospital had by far the highest reported number of ADRs (n=199), followed by hospital HOSR3 which had a total of 10 reported ADRs (and used the SAE algorithm) over the past 12 months, making it the second highest. The positive effect of algorithms and trigger tools on ADR identification has been demonstrated in a study conducted in India where the reported ADRs were 18.1% over the study period where a trigger tool was being used, compared to other studies where a trigger tool was not being used and the reported ADRs were 5.42%, 9.8% and 3.31% (Ganachari *et al.*, 2013).

Pharmacists possess the skills and ability to drive ADR reporting in hospitals and one of the ways in which they can enhance this activity is by using algorithms and trigger tools, which may use suspect drugs to identify a possible ADR, suspect drugs are drugs which are commonly used as antidotes, to prevent or reverse the harmful effects of drugs received by the patient. Cavell, 2009 has defined trigger drugs as medicines which are administered to prevent harm of an adverse drug event. These medicines include antidotes such as activated charcoal, vitamin K, naloxone, acetylcysteine, flumazenil, glucagon, calcium gluconate, etc. When the pharmacy staff issue these drugs, they should follow-up with the prescriber to determine if the patient has experienced an ADR or not.

This study reports the ADR reporting frequency at the unit of analysis at the level of the facility. The most frequently reported ADR type across facilities was hypersensitivity reactions, reported at eight facilities, which presented as angioedema and rash. Two of these facilities had a nominated person for ADR reporting. These hypersensitivity reactions are classified as type B reactions, which are bizarre or idiosyncratic in nature, they cannot be predicted from known pharmacology of the medicine and the reactions are usually outward, which means that they can be easily identified by the patient and/or the healthcare worker (Kaufman, 2016). This means that healthcare workers are easily alerted of the possibility of an ADR where a type B ADR is involved, hence the high number of this type of ADR being reported (Kaufman, 2016).

Other frequently reported ADR type at facilities without a nominated person or committee included quality issues (n=3) and administration errors (n=2). Quality issues is important to report on ADR forms, because most facilities only report quality issue to their suppliers where they send the default products back to the supplier for an exchange. This deviation in product quality needs to be addressed as faulty pharmaceuticals which are released into the market may result in health problems and it is extremely important as it poses a risk in patient safety (Visacri, *et al.*, 2014). This type of ADR is relatively easy to evaluate, with common examples including absence of a label, presence of foreign bodies or colour changes (Visacri, *et al.*, 2014).

Administration errors are also as important when it comes to ADR reporting, nurses are usually involved in the administration of medicine and in some cases, they are involved in the dispensing and preparation of medicine, having a similar role to that of a pharmacist and hence it will be of benefit for the person responsible for ADR reporting to work closely with nurses and assist in identifying and reporting such cases (Armitage and Knapman, 2003).

It is difficult to compare the results from this study to studies on the prevalence of ADRs in an area or facility, because the units of analysis differ. In prevalence studies the unit of analysis is the individual patients treated at the facility, whereas in this study the unit of analysis was the facility itself. A study conducted in Malaysia, which evaluated the number of spontaneous ADR reports received by the Malaysian ADR advisory committee somewhat coincides with the results of our study as they have reported that skin and appendages are the most common ADRs (Lei, *et al.*, 2007). A similar study conducted in Nepal which looked at the number of reported ADRs reported that weight gain was the most common ADR, followed by CNS related ADRs (paraesthesia, tremor, fever, insomnia, agitation, confusion, dizziness, irritability, peripheral neuropathy and delirium), fatigue, gastrointestinal related and rash, gynaecomastia and cough once again did not feature as the studies frequently reported ADRs for patients admitted in the hospital (Rauniar and Panday, 2017).

In the African continent, a study which looked at the number of ADRs reported to the global VigiBase database from 1992 to 2015 showed that 31.14% of the ADRs were reports of skin and subcutaneous tissue, followed by administration errors 20.91%, CNS disorder with 17.48% and gastrointestinal disorder with 16.10% (Ampadu *et al.*, 2016). These results both infer that skin reactions (rash and angioedema) were the leading ADRs followed by administration errors. This study furthermore showed that antiretroviral drugs were most commonly involved in ADRs (28.63%), followed by antibiotics (5.24%), and ACE inhibitors (2.42%) (Ampadu, *et al.*, 2016). Although this was a bigger study which evaluated 35

African countries, the results were somewhat showing a trend with antiretrovirals and ACE inhibitors found in this study.

5.4 Challenges with ADR reporting in the facilities

The most common challenge identified in this study was that ADRs were not being reported. The second most common challenge was the high workload, being short staffed or lack of time. Facilities with a person for ADR reporting (n=2) further listed fear of litigation. While, facilities without a person nominated for ADR reporting listed additional challenges such as patient's unwillingness to participate in ADR reporting, too administrative, lack of understanding by healthcare workers and lack of responsibility from pharmacy staff and other healthcare workers in the hospital. A similar study conducted in a Gauteng regional hospital, looked at common challenges with ADR reporting and it reported that 37.1% of the responded stated that there was lack of time to identify and report these reactions, while 34.1% feared that they might be wrong (Terblanche *et al.*, 2018). While according to a study conducted in France in non-university hospitals, the four main challenges with ADR reporting included lack of understanding to report ADRs which are already included in the product package insert, uncertainty of the link between the drug product and the reaction, lack of time and fear of being called upon, all of which were reported in our study (Gony, *et al.*, 2010).

Most participants (72.7%) considered ADR reporting as compulsory for healthcare personnel. These results coincide with that of a study done in one of the Gauteng province regional hospitals, which reported that 82.6% of healthcare personnel considered ADR reporting compulsory (Terblanche *et al.*, 2018) and another Ethiopian study that found that 57.9% (n=77) of the respondents also stated that ADR reporting should be compulsory (Gurmesa and Dedefo, 2016). In this study, when the respondents were probed for the reason why they considered ADR reporting to be compulsory or not, they stated that only life threatening and serious adverse events should be compulsory to report and the common and expected ADRs should be voluntary. These responses tally with a study conducted in Ethiopia, where 58 of the respondents (43.6%) stated that ADR reporting was encouraged when the reaction was serious (Gurmesa and Dedefo, 2016). The respondents of this study further recommended that the pharmacy or nominated person could not force a healthcare worker to report an ADR, instead the line manager or head of the department should emphasize the importance of reporting ADRs in their department and it should be their responsibility to evaluate if their staff members comply.

None of the hospitals specifically remunerated those who were responsible for pharmacovigilance or those who sent in reports for ADRs. One of the respondents indicated that ADR reporting was part of a healthcare workers daily activity and

they could not expect to be remunerated for doing what they were expected to do. This statement was supported by a study done at Sebokeng Hospital where only 8.3% of the healthcare workers felt that ADR reporting should be remunerated (Terblanche *et al.*, 2018). Furthermore, some of the study participants from this study felt that ADR reporting should be included in the assessment of Performance Management and Development System (PMDS) that aims to assess staff quarterly using a set of criteria related to their role. In a Malaysian study that explored barriers and facilitators for ADR reporting among community pharmacists, it was reported that providing financial incentives can be beneficial in increasing the number of ADRs reported, the downside to that is that healthcare personnel will be doing this for financial gain and the quality of the reported ADRs may be of little benefit to medication safety, while providing little benefit for those who report ADRs may result in demotivation for reporting (Elkalmi, *et al.*, 2011).

5.5 Strategies used to overcome the challenges faced by the hospitals

The strategy to nominate the store pharmacist for ADR reporting seems to be a novel idea from HOSD4. To the researcher's knowledge, there is no study which has been conducted to evaluate the role of store pharmacists in ADR reporting. Due to the fact that the store pharmacist's role being more administrative in nature, collating ADR reporting forms and doing follow-ups might be easier than for pharmacists with more direct patient care activities. Store pharmacists are also in contact with pharmaceutical companies and medical supplies depot where they order medicines from, which gives them routine access to report and investigate quality issues. Bushra *et al.* (2015) agrees that the expertise of a pharmacist on drug products gives them an advantage of over other members of the healthcare team to influence changes such as getting substandard products withdrawn from the market or cause label changes. They can also emphasise the importance, seriousness, preventability and necessity to report ADRs through their interactions with other healthcare workers (Bushra *et al.*, 2015).

HOSD5 suggested improving awareness on the importance of ADR reporting by placing posters on the walls and emphasizing the importance of pharmacovigilance during pharmacy week. This strategy aligns with a study conducted by Pimpalkhute, *et al.* (2012) which evaluated the level of awareness about pharmacovigilance and ADR monitoring amongst doctors in a tertiary hospital and reported that measures such as making ADR reporting guidelines available in a form of posters and booklets has proven to be useful in increasing awareness and status of ADR reporting. Another way that pharmacists promoted ADR reporting in this study was to request healthcare personnel to call them to the ward if an ADR was suspected. The responding pharmacist would then do the administrative work of completing the ADR forms. This is the strategy used by

Hospital HOSR2 and their ADR reports was the highest at 199 reported between September 2017 and October 2018.

Conducting medication errors and ADR training, with follow-up training at regular intervals as well as increasing accessibility of the ADR reporting forms to all health care practitioners was also suggested in this study as ways to overcome the challenges of ADR reporting. Terblanche (2018) concurs with these initiatives in a research conducted in one of Gauteng province regional hospitals, where strategies such as training programmes, improved feedback, increased availability of ADR reporting forms and having a pharmacist available in the wards were some of the initiatives proposed to improve ADR reporting (Terblanche, 2018).

Another suggestion from participants were to encourage the use of the electronic reporting application which is available from the Department of Health EML mobile application. This makes it convenient for the reporter and eliminates the extensive paper work, i.e. the need for a scanning and/or faxing the ADR report forms. This is supported by a study conducted by Ribeiro-Vaz, *et al.* (2016) who described and evaluated the use of information systems to promote ADR reporting in 15 countries globally and reported that the increasing trend of web-based software has positively improved ADR reporting numbers by more than two-fold. The above strategies to facilitate ADR reporting require collaboration amongst all those involved and these strategies may be combined with inclusion of electronic reporting aids, in addition to the Department of Health EML application, which is only available on a mobile phone and not on a computer, conducting continuous training as healthcare personnel who receive training are more likely to report ADRs with better understanding of the pharmacovigilance system (Walji *et al.*, 2011).

5.6 Committees which support pharmacovigilance within the hospital

All the facilities had functioning Pharmacy and Therapeutics Committees (PTC). This study also looked at the subcommittees which support ADR reporting and report to the PTC of which only one hospital (9.1%) which had a subcommittee specifically for pharmacovigilance. For the rest of the hospitals the pharmacovigilance function was part of the PTC. The only other facility which had a subcommittee partially related to pharmacovigilance was hospital HOSD2, which had a subcommittee for antimicrobial stewardship. Two of the hospitals which had a person or committee responsible for ADR reporting and another two hospitals that did not have a nominated person or committee were able to produce their last three PTC meeting agendas. Other facilities did not provide the agenda because it could not be located (n=6) or the agenda contained confidential information (n=1), which could not be shared with researcher. It is important for hospitals to have a

committee or a subcommittee which supports ADR reporting and provide feedback to the reporters in order to improve their confidence in reporting, communicate the findings and improve medicine safety in the facility (Schatz and Webber, 2015). Hospital HOSD3, which had a subcommittee stated that their PTC agenda was too broad and time consuming, hence their attendance was low because some PTC members only wanted to attend the meeting for specific agenda points which were applicable to them and hence there was a necessity for subcommittees which feedback to the main PTC committee. This was in contrast with Hospital HOSR6, which stated that the facility did not want to have too many committees, ADRs were an agenda point of the PTC, and therefore there was no perceived need for a separate committee. Matlala, *et al.* (2017) carried out a study to determine the percentages of tertiary, regional and district PTCs in the Gauteng province which had any subcommittees within the PTC and 25% (n=5) of the PTCs had an ADR subcommittee (Matlala, *et al.*, 2017). It is acknowledged that the results of this study are not directly relatable to our findings, however, they concur with our study that majority of the hospital PTCs do not have a pharmacovigilance/ADR reporting subcommittee.

5.7 Availability of person or committee for ADR reporting

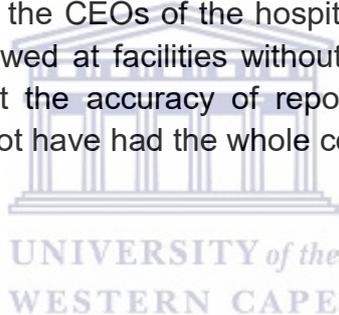
One of the objectives of this study was to determine which facilities had a person or committee nominated for ADR reporting. Countries such as Iran have introduced a guideline where each hospital has to nominate a person responsible for pharmacovigilance, the designated person may be a nurse, doctor or pharmacist and they are referred to as drug safety officer (DSO). Over 600 hospitals selected their DSO who underwent training and became a full member of WHO International Drug Monitoring Program and the number of reported ADRs increased to more than 35 000 country wide (Mirbaha *et al.*, 2015). These results could be loosely extrapolated to one of the participating hospitals (HOSR2) where there was a person nominated for ADR reporting and the rates of reporting were higher than those which did not have a person nominated for ADR reporting. However, this study cannot conclude if a nominated person really made a difference in increasing ADR reporting.

5.8 Limitations of the study

This study represented just over half (55%) of the regional (6/9) and district (5/11) hospitals across the five districts of Gauteng Province. Therefore, these results may not be reflective of the rest of South Africa, which is acceptable for an explorative study design. Furthermore, the small sample size and narrow focus (i.e. focus on nominated persons) restricted the comparability of these data to other studies which focus on ADR reporting in general. This could be attributed in part to limited time and money to perform the research.

The study was more focused on the processes and challenges with ADR reporting and not on the types of ADRs which were reported. The researcher did not observe the ADRs in the hospitals and relied heavily on the ADR forms which were available to extrapolate the types of ADRs reported by the hospital. Therefore, these types of ADRs may not be a true reflection of the actual ADRs which occur in these facilities.

Due to recommendation by the CEOs of the hospital not all personnel involved in ADR reporting was interviewed at facilities without a nominated person for ADR reporting. This might affect the accuracy of reporting in these facilities as the pharmacy manager might not have had the whole context of ADR reporting.



6. CHAPTER 6: CONCLUSION AND RECOMMENDATIONS

6.1 Conclusion

The research study aimed to explore the factors that affect ADR reporting in regional and district public hospitals in the Gauteng province and specifically focused on structures that support ADR reporting such as persons or committees nominated for ADR reporting. In general, pharmacists and the pharmacy were synonymous with ADR reporting as all nominated persons were pharmacists and in facilities where there were no nominated person, the responsible pharmacist was identified as the contact person for ADR reporting. Although all hospitals had PTCs, there was rarely a subcommittee dedicated to pharmacovigilance or ADR reporting, which culminated in a lack of feedback to healthcare workers that could promote it in the facility. Lack of feedback and communication on reported ADRs is a weakness in pharmacovigilance systems and may hinder the sustainability of ADR reporting, because feedback has been shown to increase confidence in identifying ADRs and motivation and purpose for ADR reporting.

Together with this seemingly lack of supportive structure to support ADR reporting and the pharmacy in particular, the primary challenge to ADR reporting at participating facilities was that ADRs were not being reported, which were reflected in the mostly (with the exception of one facility) very low number of reported ADRs over the last 12 months at facilities with a nominated person and perception from some facilities that ADRs was not a concern. In addition, there were very few tools available to promote the identification and subsequent reporting of ADRs at participating facilities.

These findings show a lack of structure and leadership support for adequate ADR reporting at regional and district public hospitals in Gauteng Province. However, we only interrogated the views of one person at each hospital and while it might reflect the views from mainly the pharmacy, it does not capture the views of prescribers and personnel outside the pharmacy.

This is the first study in the country to evaluate the availability of a nominated person or committee for ADR reporting in public hospitals and while this has been shown to boost ADR reporting in other countries, it remains to be seen if it will have an effect in South Africa.

6.2 Recommendations

Recommendations for practice include:

- Hospitals should take the initiative to nominate a person or a committee. This will assist healthcare workers with reporting as they will have a reliable 'go-to' person whenever they feel there is a suspected ADR or are not sure and this uncertainty leads to ADRs not being reported.
- The hospitals which have ADR reporting in their PTC agenda should make sure that they provide feedback on ADRs which have been reported in the hospital to raise awareness and share their findings to improve patient safety. Should the PTC agenda be too long, it may be necessary to form a subcommittee specifically for pharmacovigilance as seen with one of the facilities in this study.
- Hospitals should make use of algorithms and trigger tools which aid in the identification of possible ADRs. This can be as simple as pharmacy following-up on the antidotes or trigger drugs such as naloxone, acetylcysteine, flumazenil etc. as this will trigger the healthcare personnel to investigate and where necessary report if there was an ADR.
- Adverse Drug Reactions reporting should be part of the performance management and development system (PMDS). None of the hospitals remunerate ADR reporting, the reason being that ADR reporting is a professional obligation, healthcare professionals (HCP) are expected to report ADRs they encounter and this should reflect on their PMDS assessment since some of the healthcare personnel expect some form of remuneration as motivation.
- Adverse Drug Reactions reporting should be made as easy and convenient as possible, though the accessibility of ADR reporting forms was not identified as a barrier to reporting in any of our facilities, it is important to ensure that it remains that way and improve accessibility by exploring the option of web-based reporting (in addition to the mobile Department of Health - EML application which is already available).
- Training in a form of workshops, webinars, conferences and seminars will help improve knowledge and skills in ADR reporting and improve health care personnel confidence in identifying and reporting ADRs.
- The study can be further explored to implement the recommendations suggested in this study and evaluate their impact on ADR reporting.

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8. APPENDICES

APPENDIX 1: ADR Report Form



**ADVERSE DRUG REACTION (ADR)/
PRODUCT QUALITY PROBLEM REPORT FORM
(PUBLIC AND PRIVATE SECTOR)
(Including Herbal Products)**



Reports will be shared with the Pharmacovigilance Centre for Public Health Programmes (PCPHP) - 0123959506

Reporting Health Care Facility/Practice							
Tel: 012 395 8197 (MCC) 021 447 1618 (NADEMC)		Facility/Practice					
Fax: 086 620 7253		District		Tel			
E-mail: adr@health.gov.za		Province		Fax			
Patient Details							
Patient Initials		File/Reference Number		Date of Birth/Age			
Sex <input type="checkbox"/> M <input type="checkbox"/> F <input type="checkbox"/> Unk		Race		Weight (kg)		Height (cm)	
Allergies				Estimated Gestational Age at time of reaction		Pregnant? <input type="checkbox"/> N <input type="checkbox"/> Y	
Suspect Medicine(s) [Medicines suspected to have caused the ADR]							
Trade Name [Generic Name if Trade Name is unknown]		Route	Dose (mg) and Interval	Date Started/Given	Date Stopped	Reason for use	Batch Number
							Expiry Date
All other Medicines Patient was taking at time of reaction [Including over-the-counter and herbal products]							
Trade Name [Generic Name if Trade Name is unknown]		Route	Dose (mg) and Interval	Date Started/Given	Date Stopped	Reason for use	Batch Number
							Expiry Date
Adverse Drug Reaction/Product Quality Problem							
Date and time of onset of reaction		Date reaction resolved/duration					
Please describe Adverse Reaction/Product Quality Problem: (kindly add as much clinical information as possible)							
Intervention (tick all that apply) <input type="checkbox"/> No Intervention <input type="checkbox"/> Intervention unknown <input type="checkbox"/> Patient Counselling/non-medical treatment <input type="checkbox"/> Discontinued Suspect Drug; Replaced with: _____ <input type="checkbox"/> Decreased Suspect Drug Dosage; New Dose: _____ <input type="checkbox"/> Treated ADR - with: _____ <input type="checkbox"/> Referred to Hospital: Hospital Name _____ <input type="checkbox"/> Other Intervention (e.g. dialysis): _____				Patient Outcomes (tick all that apply) <input type="checkbox"/> ADR recovered/resolved; recovering/resolving <input type="checkbox"/> not recovered/not resolved <input type="checkbox"/> Patient Died: Date of death: _____ <input type="checkbox"/> Impairment/Disability <input type="checkbox"/> Congenital Anomaly <input type="checkbox"/> Patient Hospitalised or Hospitalisation prolonged <input type="checkbox"/> Life Threatening <input type="checkbox"/> Other: _____ <input type="checkbox"/> ADR reappeared after restarting suspect drug/similar drug (rechallenge)?: <input type="checkbox"/> N <input type="checkbox"/> Y <input type="checkbox"/> Not done <input type="checkbox"/> Unknown			
Laboratory Results				Additional Laboratory Results			
Lab Test	Test Result	Test Date	Lab Test	Test Result	Test Date		
Co-morbidities/Other Medical Condition(s)							
Reported by							
Name		E-mail					
Designation <input type="checkbox"/> Nurse <input type="checkbox"/> Pharmacist <input type="checkbox"/> Doctor <input type="checkbox"/> Other:		Telephone					
Date reported:		Signature					
THIS ADR REPORT IS NOT A CONFIRMATION THAT THE REPORTER OR THE SUSPECT MEDICINE(S) CAUSED THE ADR							v4.0 07/16

Accessed: October, 2018

APPENDIX 2: Letter of Intent



Mr TumeloModau Tel: 073 444 1250

Dr Mea van Huyssteen Tel: 0219592864

School of Pharmacy, University of the Western Cape, Robert Sobukwe Road, Bellville, Cape Town, 7535

Gauteng Department of Health
Chief Executive Officer
Dear Sir/Madam

RE: Permission to conduct a study at Gauteng regional and district public hospitals

I am a part-time post-graduate student at the University of the Western Cape. As part of the requirements for my masters' degree qualification, I have to conduct a research project. The title of my study is "the availability of persons nominated for adverse drug reporting and associated challenges in Gauteng regional and district public hospitals."

I therefore kindly request your permission to conduct the study in the above mentioned facility.

The study will commence once ethical approval has been granted by the University of the Western Cape Biomedical Research and Ethics Committee. Attached please find a copy of the protocol for your information.

I trust that you will find the above in order. Please feel free to contact me or my supervisors, should you require any additional information.

Sincerely,

Mr Tumelo M Modau (Student)
Tel: 073 444 1250, Email: t4modau@gmail.com

Dr M. Van Huyssteen (Supervisor)

Email: mvanhuyssteen@uwc.ac.za

Mr R. Bapoo (Co-Supervisor)

Email: rbapoo@uwc.ac.za

APPENDIX 3: STUDY INFORMATION SHEET



Mr TumeloModau Tel: 073 444 1250

Dr Mea van Huyssteen Tel: 0219592864
School of Pharmacy, University of the
Western Cape, Robert Sobukwe Road,
Bellville, Cape Town, 7535

Study title: THE AVAILABILITY OF PERSONS NOMINATED FOR ADVERSE DRUG REPORTING AND ASSOCIATED CHALLENGES IN GAUTENG REGIONAL AND DISTRICT PUBLIC HOSPITALS

Study information sheet

To: Interviewee (Participant)

You are being invited to take part in a research study conducted by Mr TumeloModau, a masters' student from the School of Pharmacy at the University of the Western Cape. As part of my master's degree in pharmacy administration and regulation, I have to conduct a research study and submit a mini-dissertation to fulfil the requirements of the degree. The study that I am conducting is titled: The availability of persons nominated for adverse drug reporting and associated challenges in Gauteng regional and district public hospitals.

Before you decide whether you wish to take part in this study, you should read the provided information sheet carefully. You are not obliged to take part in this study and failure to participate will have no effect on you. You may change your mind at any time (before the start of the study or even after you has commenced the study) for whatever reason without having to justify your decision and without any negative impact.

Purpose of the research:

The purpose of this study is to describe the status of ADR reporting structures, in terms of human and other resources, in public hospitals and to identify factors that help or hinder the effectiveness of ADR reporting within the existing structures.

Research procedure:

You have been identified by the CEO of your hospital as a person involved in ADR reporting. As such we would like to ask you to participate in the research study. You have been sent this study information sheet and the data collection sheet, in order for you to familiarise yourself with questions and facility-based records that we will be

asked for during the interview. The researcher will make an appointment to administer the questionnaire with you that will take about 45 minutes of your time in total to complete.

Confidentiality and anonymity

All information provided by you during the study will be kept confidential. No personal or identifying information with regard to your facility will be included in the final research, with all results presented in a combined form. On completion of the study, the sample data will be kept for a period of two years after which it will be destroyed by paper shredding.

Risks and benefits

This study anticipates no risks associated with participating in this study. There are no anticipated direct benefits to you as a participant. All participants enrolled in the study participate on a voluntary basis.

Voluntary participation

Participation in this study is the sole decision of the participant and your participation is completely voluntary. If you agree to partake in the study, you will need to sign a consent form before your information may be collected. You may withdraw from the study at any time. Withdrawal from the study will not affect the participant in any way. I am very thankful for your willingness to take part in this research project.

IF YOU REQUIRE FURTHER INFORMATION

Any further queries or information required may be directed to:

Mr TumeloModau
MOBILE: 073 444 1250
EMAIL: t4modau@gmail.com

OR

Dr Mea van Huyssteen
Pharmacy building, First floor Room F6, School of Pharmacy, University of the Western Cape, Robert Sobukwe Road, Bellville, 7535, South Africa.
Tel: +2721 9592864

The committee giving ethical approval for this study is the UWC Biomedical Research Ethics Committee. The biomedical research ethics administration is available in the Research Office in the New Arts Building, C-Block, Top Floor, Room 28 at the University of the Western Cape, Robert Sobukwe Road, Bellville, South Africa. If you have any problems or questions about this study you can also contact the BMREC, Research Development, Tel: 021 959 4111, email: research-ethics@uwc.ac.za.

APPENDIX 4: QUESTIONNAIRE



Mr TumeloModau Tel: 073 444 1250

Dr Mea van Huyssteen Tel: 0219592864
School of Pharmacy, University of the Western
Cape, Robert Sobukwe Road, Bellville, Cape
Town, 7535

THE AVAILABILITY OF PERSONS NOMINATED FOR ADVERSE DRUG REPORTING AND ASSOCIATED CHALLENGES IN GAUTENG REGIONAL AND DISTRICT PUBLIC HOSPITALS

Name of the facility:		Unique Study Code :				
Section A (facilities that has a nominated person or committee for ARD reporting)						
1.	Is there a person or committee nominated for ADRs reporting? (If NO, please skip this section and proceed to answer the “B” and “C” sections of the questionnaire)	YES	NO			
2.	Are you the nominated person or on the nominated committee?	YES	NO			
3.	3.1 What is your qualification:	Pharmacist				
		Pharmacist Assistant/Technician				
		Medical Practitioner				
		Professional Nurse				
		Enrolled Nurse				
		Other (Please specify):				
	3.2 How would you rate your knowledge of ADR reporting?	1 = poor; 2 = fair; 3 = average; 4 = good, 5 = excellent				
		1	2	3	4	5
	3.3 How confident are you to identify an ADR?	1	2	3	4	5
	4.1 Do you have any form of Pharmacovigilance training?	YES	NO			

<p>4.</p>	<p>4.2 If 'Yes', when was it received? </p>	<p>4.3 Who provided this training? </p>		
<p>4.4 What was the training about? </p>				
<p>4.5 Was this training adequate? If not, how should it be changed? <table border="1" style="float: right;"> <tr> <td>YES</td> <td>NO</td> </tr> </table> </p>			YES	NO
YES	NO			
<p>4.6 If no training was received, would you like to receive training on ADR reporting? Why do you say yes/no? What topics should be included? </p>		<table border="1"> <tr> <td>YES</td> <td>NO</td> </tr> </table>	YES	NO
YES	NO			
<p>5.</p>	<p>Over the past twelve months, how many ADRs did you identify?</p>			
<p>6.</p>	<p>Over the past 12 months, how many of your identified ADRs did you report?</p>			
<p>7.</p>	<p>How many of these ADRs resulted in death?</p>			
<p>8.</p>	<p>Do you receive or give feedback on ADRs reported to a certain committee in the facility?</p>	<table border="1"> <tr> <td>YES</td> <td>NO</td> </tr> </table>	YES	NO
YES	NO			
<p>9.</p>	<p>If yes, what is the name of this committee and what are its functions? </p>			
<p>10.</p>	<p>How often do this committee meet? (Weekly, bi-monthly, monthly, quarterly etc.)</p>			
<p>Kindly skip section "B" and proceed to section "C"</p>				

Section B (facilities without a nominated person or committee for ADR reporting)			
1.	What is the reason why there is no person or committee nominated for ADR reporting		
		
		
		
		
2.	What is the process followed in ADRs reporting in this facility? Please explain		
		
		
		
		
3.	Has the hospital attempted to nominate a person or committee for ADR reporting in the past?	YES	NO
	If not, what is the reason?		
		
		
		
4.	Are there any plans to nominate a person or committee for ADR reporting?	YES	NO
Section C (all facilities)			
1.	Provide a copy of the ADR reporting form you use - If different from the national ADR reporting form		
	1.1 Where are these forms kept?		
	1.2 Who has access to them?		
2.	2.1 Do you use any algorithms or trigger tools to identify ADRs?	YES	NO
	2.2 If yes, which ones?		
	(Please provide a copy of your algorithm or trigger tool)		
3.	Which type of adverse drug reaction(s) are reported mostly in the facility? (e.g.: Drug-induced liver injury, kidney injury, diarrhoea, neutropaenia, angioedema, hypotension, hyperkalaemia, etc)		

4.	Which particular class of drugs or drug is especially problematic in causing ADRs in this facility?		
5.	In the facility, ADR reporting is? Please tick the relevant box(es) relating to people who are specifically nominated.	Compulsory	
		Voluntary	
		Remunerated	
6.	Please state the challenges experienced with ADR reporting in the facility		
7.	Please state strategies used to deal with the above mentioned challenges		
8.	If, possible, please provide copies of the last three ADR reports compiled for this facility		
9.	If possible, please provide the agendas and minutes for the last 3 committee meetings that discussed ADR reports and reporting for this facility.		



Thank you for your time and cooperation

The committee giving ethical approval for this study is the UWC Biomedical Research Ethics Committee. The biomedical research ethics administration is available in the Research Office in the New Arts Building, C-Block, Top Floor, Room 28 at the University of the Western Cape, Robert Sobukwe Road, Bellville, South Africa. If you have any problems or questions about this study you can also contact the BMREC, Research Development, Tel: 021 959 4111, email: research-ethics@uwc.ac.za.

APPENDIX 5: INFORMED CONSENT FORM



Mr TumeloModau Tel: 073 444 1250

Dr Mea van Huyssteen Tel: 0219592864
School of Pharmacy, University of the
Western Cape, Robert Sobukwe Road,
Bellville, Cape Town, 7535

Study title: THE AVAILABILITY OF PERSONS NOMINATED FOR ADVERSE DRUG REPORTING AND ASSOCIATED CHALLENGES IN GAUTENG REGIONAL AND DISTRICT PUBLIC HOSPITALS

Informed Consent From participant

- I have read and understood the information given to me by the researcher. I was given the opportunity to ask questions and given adequate time to rethink my participation in the study.
- I understand that participation in this study is voluntary and that I may withdraw at any point without providing reasons for my choice.
- I understand that this study has been approved by the University of Western Cape Biomedical Research and Ethics committee.
- I am fully aware that the results of this study will be used for scientific purposes and may be published. I agree to this, provided that my privacy is guaranteed.
- I hereby give consent to participate in the study.

_____ Name of participant	_____ Signature	_____ Date /20	_____ Place
_____ Witness	_____ Signature	_____ Date /20	_____ Place

Statement by the researcher

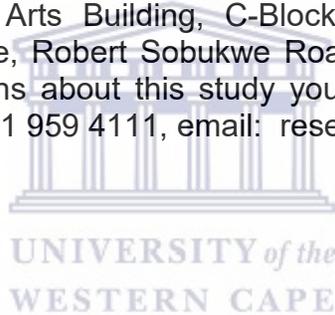
I have provided verbal and/or written information regarding this study. I agree to answer any future questions concerning the study as best as I am able to. I will adhere to the approved protocol.

Tumelo Modau

Name of researcher

Signature of researcher

The committee giving ethical approval for this study is the UWC Biomedical Research Ethics Committee. The biomedical research ethics administration is available in the Research Office in the New Arts Building, C-Block, Top Floor, Room 28 at the University of the Western Cape, Robert Sobukwe Road, Bellville, South Africa. If you have any problems or questions about this study you can also contact the BMREC, Research Development, Tel: 021 959 4111, email: research-ethics@uwc.ac.za.



APPENDIX 6: ETHICS TRAINING OF T MODAU



Certificate

This is to certify that

Modau TM

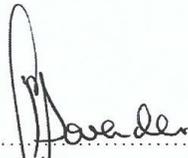
attended, satisfactorily completed and
passed requirements for

WESTERN CAPE
RESEARCH METHODOLOGY COURSE
REME 801

on

09 – 13 March 2015

at the Sefako Makgatho
Health Sciences University



Prof P. Govender
Research & Postgraduate Studies Directorate

31 March 2015
Date



SEFAKO MAKGATHO HEALTH SCIENCES UNIVERSITY
RESEARCH ETHICS COMMITTEE (SMUREC)

Certificate Of Attendance

I, the undersigned, acting as representative of the aforementioned
CPD Provider, hereby certify that

Modau TM

P38991

attended a

MREC ETHICS WORKSHOP

on

7 May 2015

at the Sefako Makgatho Health Sciences University
The approved CPD reference number of the Medical and Dental Professional
Board's is as follows:

MDB002/005/48/2015

I certify that the said practitioner qualifies for
CEU's, obtained as follows:

Level 1 (Participant)	06
Level 2 (Presenter)	00
Ethics	✓
TOTAL	06

Prof P. Govender
Research & Postgraduate Studies Directorate

7 May 2015

Date

APPENDIX 7: ETHICS CLEARANCE CERTIFICATE



OFFICE OF THE DIRECTOR: RESEARCH RESEARCH AND INNOVATION DIVISION

Private Bag X17, Bellville 7535
South Africa
T: +27 21 959 4111/2948
F: +27 21 959 3170
E: research-ethics@uwc.ac.za
www.uwc.ac.za

14 August 2018

Dr M van Huyssteen and Mr T Modau
School of Pharmacy
Faculty of Natural Sciences

Ethics Reference Number: BM18/6/15

Project Title: The availability of persons nominated for adverse drug reporting and associated challenges in Gauteng regional and district public hospitals.

Approval Period: 20 August 2018 – 20 August 2019

I hereby certify that the Biomedical Science Research Ethics Committee of the University of the Western Cape approved the scientific methodology and ethics of the above mentioned research project.

Any amendments, extension or other modifications to the protocol must be submitted to the Ethics Committee for approval.

Please remember to submit a progress report in good time for annual renewal.

The Committee must be informed of any serious adverse event and/or termination of the study.

Ms Patricia Josias
Research Ethics Committee Officer
University of the Western Cape

PROVISIONAL REC NUMBER -130416-050

APPENDIX 8: NHRD ONLINE APPLICATION

8/31/2018

NHRD - Details

RESEARCH PROPOSAL DETAILS: [GP_201808_041](#)

Research Committee



GAUTENG HEALTH RESEARCH COMMITTEE

APPLICATION DETAILS

Title of Research Project

THE AVAILABILITY OF PERSONS NOMINATED FOR ADVERSE DRUG REPORTING AND ASSOCIATED CHALLENGES IN GAUTENG REGIONAL AND DISTRICT PUBLIC HOSPITALS

Status of Application

Pending (New Application)

Status of Project

On-Going

Proposal Submission Date

2018/08/30



Comments

You will find a list of all comments made on the selected research application. The list below displays comments visible to both the Applicant and Research Committee

Comment	Comment Date	Comment By
---------	--------------	------------

PRIMARY INVESTIGATOR OF THE PROJECT/PROPOSAL

Title	Name	Surname	Role	Institution	E-Mail	Telephone No.	Mobile No.	CV/Resume
MR	Tumelo	Modau	Student		t4modau@gmail.com	0116350601	0734441250	No File
Postal Address Line 1	Postal Address Line 2	Postal Address Line 3	Postal Address Line 4	Postal Code				
25409/100 EXT 4	Sebaka-Borena Str	Mamelodi East, PO Rethabile	Pretoria	0122				

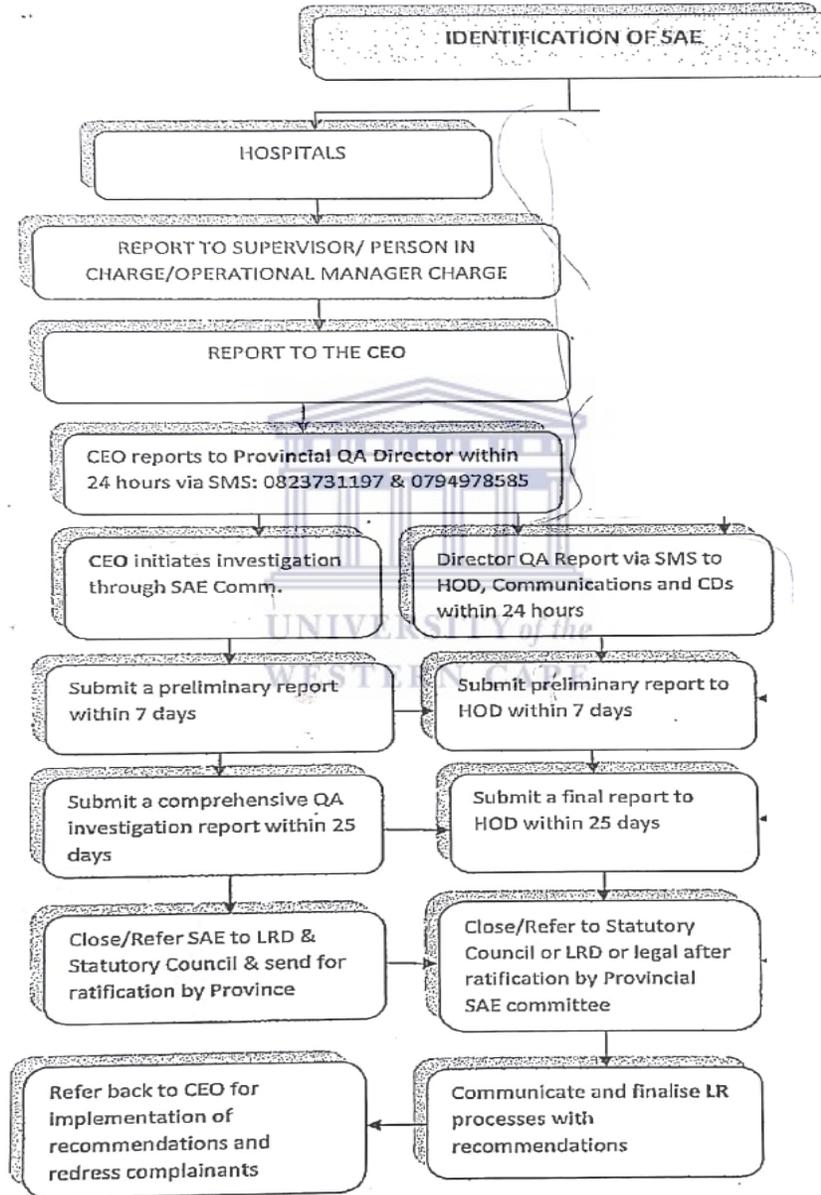
Research Staff assigned to Project/Proposal

Title	Name	Surname	Role	Institution	E-Mail	Telephone No.	Mobile No.	CV/Resume
DR	Mia	Van Huyssteen	Supervisor		research-ethics@uwc.ac.za	+27219592864	0844910531	No File
Postal Address Line 1	Postal Address Line 2	Postal Address Line 3	Postal Address Line 4	Postal Code				
SCHOOL OF PHARMACY, UNIVERSITY OF THE WESTERN CAPE	Robert Sobukwe Road	Belville	Bellville	7535				

APPENDIX 9: HOSPITAL HOSR3 ALGORITHM



SERIOUS ADVERSE EVENTS ALGORITHM



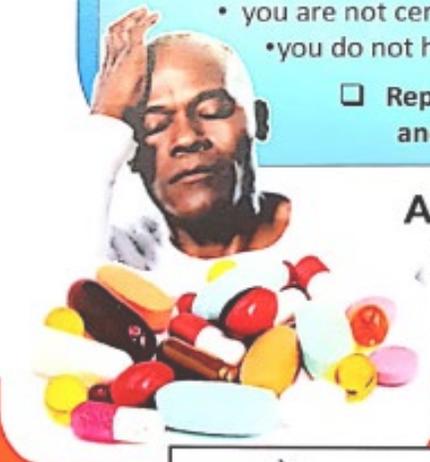
APPENDIX 10: HOSPITAL HOSR2 ADR INFORMATION POSTER

REPORT ADVERSE DRUG REACTIONS



An **Adverse Drug Reaction (ADR)** is any unexpected, unintended or harmful reaction caused by the administration of a drug. The onset of the adverse reaction may be sudden or develop over time. ADRs may occur following a single dose or prolonged administration of a drug or result from the combination of two or more drugs.

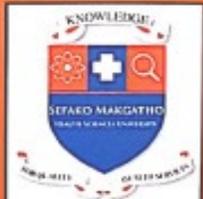
- All healthcare professionals should report suspected ADRs
- Report adverse experiences with
 - medication, vaccines and biologicals
 - medical devices (including in-vitro diagnostics)
 - complementary / alternative medicines (including traditional, herbal remedies, etc.)
- Report even if
 - you are not certain the product caused the event
 - you do not have all the details
- Reporting forms are available in the wards and at the pharmacy



ADRs reported will contribute to the improvement of medicine safety and therapy in South Africa



Contact:
[Redacted]
Cell:
[Redacted]



Layout and design from Dr. Basu (2017/2018)

Adverse Drug Reaction

Would you recognise it?

Is your patient experiencing an **UNEXPECTED** effect from a medication?

Is your patient experiencing **SIDE-EFFECTS** from one of their medications?

Is your patient experiencing an **UNDESIRED EFFECT** from drug therapy?

Are you giving your patient one medication because of the **side-effects** from another medication?

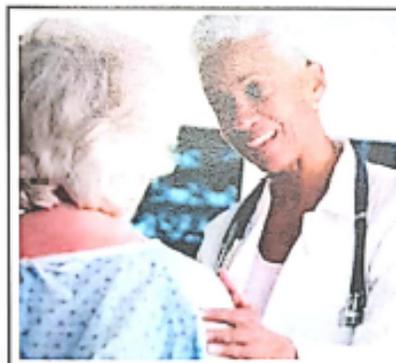
Has your patient developed a new **DRUG ALLERGY**?

Have you had to administer a reversal agent or **PRN antidote**?



If you answered **YES** to any of the above questions, then your patient may be experiencing an **ADVERSE DRUG REACTION** that needs to be reported!

Please fill out an ADR report!



Contact:



Cell:



Layout and design: Peter de Beer 082 512 5247