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Knowledge, Attitudes and Practices of Nurses and Pharmacists towards Adverse Drug Reaction Reporting in the Private Sector

Sophia Bogolubova

Research Dissertation

Supervised by Mrs Neelaveni Padayachee and Prof Natalie Schellack

2018



Submitted in fulfilment of the requirements for the degree of Masters in Pharmacy (MPharm) in the School of Pharmacy and Pharmacology at the University of the Witwatersrand

Declaration

I, Sophia Bogolubova, declare that this dissertation hereby submitted to the University of Witwatersrand for the degree Masters in Pharmacy has not previously been submitted to this or any other university for any other purpose. This dissertation is entirely and completely my own work, except for cases in which the work of others has been cited and duly acknowledged within the context of the dissertation.



05/02/2018

Sophia Bogolubova **Date**

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To my parents and family, who never expected anything less.

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To Natalie, for her wisdom and inspiration.

To Yashmay, for never letting me be left behind.

Abstract

Background: Pharmacovigilance is an important tool not only in protecting patients from potentially harmful effects of medicines, but it plays a role in providing good quality of care and monitoring efficacy of drug products within a population. Spontaneous reporting is a system of reporting adverse drug reactions (ADRs) practiced worldwide as part of the WHO Programme for International Drug Monitoring. Unfortunately, the major drawback of this system is the underreporting of ADRs.

Methodology: A cross-sectional questionnaire-based survey was conducted amongst pharmacists and nurses in six private hospitals in Gauteng. A pre-designed and structured multiple choice questionnaire containing 20 close-ended questions was used to assess demographics (four questions), knowledge (six questions), attitudes (five questions) and practices (five questions) of participants. E-mail and manual questionnaires were provided to target as many nurses and pharmacists as possible. Electronic responses were captured as they were submitted, while manual responses were collected by the principle investigator from a contact person identified within each hospital. The data obtained was analysed using appropriate statistical analysis through Microsoft Excel 2010 and Google Forms software.

Results: A total of 233 healthcare professionals participated in the study. Although three quarters of participants believed ADR reporting to be important, most had received no previous pharmacovigilance training and did not know how to report an ADR. 87.1% of participants believed that all ADRs should be reported, with 75.5% of participants believing they would report all ADRs they encountered in the future provided they had sufficient training and knowledge. The major factors discouraging participants from reporting was a lack of awareness with respect to the process of reporting as well as a lack of access to the ADR reporting form.

Conclusion: This study indicates that the majority of participants require further training regarding ADR reporting. Although the knowledge of most participants was acceptable, the transition into practice needs to be improved.

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Acronyms

ADE	Adverse Drug Event
ADR	Adverse Drug Reaction
CEM	Cohort Event Monitoring
EDL	Essential Drugs List
EDP	Essential Drugs Programme
EMA	European Medicines Agency
FDA	Food and Drug Administration
HCP	Health Care Professional
HIV	Human Immunodeficiency Virus
ICMRA	International Coalition of Medicines Regulatory Authorities
ICSR	Individual Case Safety Report
MCC	Medicines Control Council
MRA	Medicines Regulatory Authority
NADEMC	National Adverse Drug Event Monitoring Centre
NCC MERP	National Coordinating Council for Medication Error Reporting and Prevention
NPC	National Pharmacovigilance Centre
OTC	Over The Counter
PHC	Primary Health Care
PIDM	Programme for International Drug Monitoring
PTC	Pharmacy and Therapeutics Committees
PV	Pharmacovigilance
SAHPRA	South African Health Products Regulatory Authority
SANC	South African Nursing Council
SAPC	South African Pharmacy Council
SOP	Standard Operating Procedure
SRS	Spontaneous Reporting System
STG	Standard Treatment Guidelines
TB	Tuberculosis
TSR	Targeted Spontaneous Reporting
UMC	Uppsala Monitoring Centre
WHO	World Health Organisation

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CHAPTER 1

INTRODUCTION

1.1. INTRODUCTION

This introductory chapter describes the background to and rationale for the study. The primary research question as well as the aims and objectives are provided. Additionally, the significance of the study is discussed. Lastly, an outline of the dissertation will conclude the chapter.

1.2. BACKGROUND AND RATIONALE

Adverse drug reactions (ADRs) affect a number of patients worldwide, irrespective of age, gender, location or occupation, and can affect patients with varying magnitudes leading to morbidity and mortality (Pirmohamed et al, 2004). Lazarou and colleagues estimated in 1998 that ADRs can be considered to be the 4^{th} – 6^{th} leading cause of death in the United States (Lazarou et al, 1998). It is estimated that the burden of ADRs in developing countries such as South Africa is even higher than in developed countries due to the high prevalence of self-medication, fake and unadulterated medicines, and traditional and herbal therapies (SPS, 2011). Additionally, diseases such as Human Immunodeficiency Virus (HIV), tuberculosis (TB) and malnutrition, which are highly prevalent in South Africa, are widely known to increase the risk of ADRs in certain populations of patients.

Underreporting of ADRs is considered to be a global issue. In South Africa, where pharmacovigilance (PV) and other regulatory aspects of medicine use are not yet fully developed, ADR reporting rates are still very low. South Africa has submitted a total of 28 609 reports to VigiBase® since an official PV system begun functioning in 1992 (Ampadu et al, 2016). This amounts to approximately 27 reports per million people per year. Because South Africa has a population of approximately 52 million, this figure is expected to be higher (Stats SA, 2017).

Literature indicates that a lack of awareness and appreciation of the magnitude of the problem of ADRs and ADR underreporting, as well as misclassification of ADRs, is partially to blame for this epidemic. Many ADRs are considered to be preventable with more rational prescribing, administration and use. Frameworks for evaluating the safety of medicines in clinical use are vital, and therefore a functional PV system is of utmost importance (Mehta, 2011, Dheda et al, 2013).

The private healthcare sector in South Africa is a seldom studied field of healthcare. Most studies conducted in the country tend to focus on public sector facilities and patients. Public sector patients make up the majority of the population (42 million people in public vs. 8.2 million people in private) and are useful in investigating public health issues(Jobson, 2015). However, approximately 17% of the population are members of a private medical scheme and hence benefit from private sector healthcare services (Stats SA, 2017). Healthcare expenditure in the private sector amounted to R 151.21 billion in 2016 (CMS, 2017). Medical scheme benefits in 2016 for medicines amounted to approximately R 24 billion accounting for approximately 16% of total healthcare benefits paid (CMS, 2017). Meanwhile, only R 74 million was allocated to medicine procurement in the public sector in 2015 (National Treasury, 2015). However, it is important to keep in mind that the prices of medicines procured in the public sector are often supplied at drastically reduced prices when compared to prices charged for procurement and supply in the private sector.

1.3. RESEARCH QUESTION

What are the current knowledge, attitudes and practices of nurses and pharmacists towards adverse drug reaction reporting in the private sector?

1.4. PURPOSE OF THE STUDY

1.4.1. Aim

This study aimed to evaluate the knowledge, attitudes and practices of pharmacists and nurses in the private hospital sector towards ADR reporting.

1.4.2. Objectives

I. Assessed the knowledge of private sector HCPs regarding the ADR reporting process in South Africa.
II. Assessed the attitudes of private sector HCPs towards ADR reporting and varying components of ADR reporting.
III. Evaluated ADR reporting practices of private sector HCPs.
IV. Established factors that contributed to differences in both knowledge and attitudes towards ADR reporting.
V. Explored trends that interfered with effective ADR reporting.

1.5. IMPORTANCE/SIGNIFICANCE OF THE STUDY

This is the first study of its kind targeting the South African private sector specifically. Most PV or ADR studies in the country have thus far been focused on individual public sector facilities (Isah et al, 2012; Joubert& Naidoo, 2016; Mouton et al, 2015; Mouton et al, 2016;

Roux, 2014; Ruud et al, 2010). Although the private sector represents a minority of the population (approximately 17%), it cannot be neglected when reviewing current PV frameworks and practices. Regardless of sector of employment, health care professionals (HCPs) have the responsibility and duty to play an important role in the detection, assessment and reporting of ADRs (Khalili et al, 2012).

Spontaneous and voluntary reporting is an integral component of any PV program, and is the cheapest and most effective method of obtaining information on ADRs. It has contributed significantly to the knowledge and understanding of safe and effective medicine use worldwide. However, due to the low reporting rate in South Africa, the understanding of the safety profiles of medicines are often delayed, resulting in patients often being exposed to medicines that are either unsafe, or that have an uncertain safety profile (Mehta, 2011).

In order to improve ADR reporting rates in South Africa, an analysis of the current state of PV activity needs to take place. This study attempted to establish a baseline evaluation in order to understand whether or not HCPs are making PV a priority activity in the clinical management of their patients. Based on the final results of the study, recommendations will be made with respect to education and practices of HCPs with the aim of improving overall ADR reporting rates. Improved knowledge of the magnitude of the ADR problem might lead to better and more motivated attitudes in implementing and internalising PV in every day clinical practice.

1.6. OUTLINE OF THE DISSERTATION

This dissertation consists of six chapters. Chapter 1 is an introductory chapter, introducing the background to and rationale for the study. It also states the research question, and aims and objectives of the study. A brief discussion of the significance of the study is also included. Chapter 2 is a literature review including a discussion on the current state of PV in South Africa and worldwide, the incidence of and costs related to ADRs, medication errors as a source of ADRs and types of ADR reports. It will also discuss underreporting of ADRs based on available literature in both a global and local context. Chapter 3 discusses the methodology of the study. It elaborates on the study design population, development of the questionnaire used in the study, data collection and analysis, and reliability and validity. Ethical considerations and limitations of the study are also included. Chapter 4 presents the results of the study in both narrative and descriptive format, followed by Chapter 5 that discusses the results presented in the previous chapter. Chapter 6 concludes the dissertation by including recommendations for future studies and a conclusion. *Figure 1.1* provides a short illustration of the layout of this dissertation.

Figure 1.1. Layout of the dissertation



CHAPTER 2

LITERATURE REVIEW

2.1. INTRODUCTION

In this chapter, an overview of the published literature is provided. The chapter begins with a background into PV, as well as a discussion about PV within a South African context. The incidence of ADRs, ADR related costs, and the role of medication errors with respect to ADRs is also described. A brief discussion of the type of ADR reports is also included. Finally, a summary of underreporting in a global context is provided, including an overview of the literature regarding the knowledge, attitudes and practices of HCPs in various settings.

2.2. PHARMACOVIGILANCE

Pharmacovigilance (PV) is defined as the "*science and activities relating to the detection, assessment, understanding and prevention of adverse drug effects or any other drug-related problem*" (WHO, 2002). This definition has since been extended to include all aspects of medicine development, manufacturing, registration, warehousing, logistics, prescribing, dispensing, use and destruction of expired stock, thereby spanning the complete product life cycle.

2.2.1. PHARMACOVIGILANCE: A GLOBAL ISSUE

In 1968, after the global thalidomide disaster, the World Health Organization (WHO) sought to establish an international collaborative effort with regards to medicines' safety through the collection of worldwide ADR data (Pirmohamed et al, 2007). This effort was named "The WHO Programme for International Drug Monitoring (PIDM)", and in 1978, the Uppsala Monitoring Centre (UMC) was established as the operational body responsible for carrying out the functions of global ADR collation and monitoring (Pirmohamed et al, 2007). The WHO PIDM launched VigiBase® in 2001. It is the largest database of its kind, containing over 15 million individual case safety reports (ICSRs) of suspected adverse drug reactions. In 2015, the WHO launched VigiAccess™ - a web application that allows anybody to access the ADR information stored in VigiBase®, and is aimed at encouraging the reporting of ADRs.

Figure 2.1: Minimum Requirements for a Functional National Pharmacovigilance System (WHO, 2010)



There are 127 countries that have joined the WHO PIDM, with 28 additional countries having associate membership. These associate members are still considered to be in the early stages of establishing their PV systems. An analysis conducted by Aagard and colleagues of the WHO PIDM data concluded that high-income countries are more likely than low-income countries to have a larger number of reports in VigiBase® (*Table 2.1*).They concluded that this was as expected as the majority of these high income countries have had established PV systems for a long time (most since 1968) (Aagard et al, 2012). Even for medicines that have a higher prevalence of use in lower income countries, such as anti-malarials, reporting rates for these medicines were still seen to be higher in higher income countries (Kuemmerle et al 2011)

Table 2.1: Comparitive rankings of selected PIDM affiliated countries according to total number of ADR reports submitted to VigiBase® during 2000 – 2009 (Aagaard et al, 2012).

Country	Year of affiliation	Number of ADR reports	Reporting rate per million people per year
United States	1968	406 274	132
United Kingdom	1968	142 555	233
Italy	1975	37 681	65

Sweden	1968	30 819	333
Japan	1972	17 782	14
Cuba	1994	29 932	261
Mexico	1999	9 573	9
Chile	1996	6 313	38
South Africa	**1992**	**5 518**	**11**
Greece	1990	1 734	16
Ghana	2001	501	2
India	1998	362	<1
Russia	1998	165	<1
Zimbabwe	1998	57	1

2.2.2. PHARMACOVIGILANCE IN SOUTH AFRICA

Pharmacovigilance in Africa is still largely considered to be in its infancy. Improving access to life saving medicines took precedence over PV in low to middle income countries, especially in most African countries, before the availability of global funding improved accessibility to these medicines. This improved access increased the risk of treatment-related adverse effects, especially in communities with limited education and few trained healthcare professionals (Olsson et al, 2015). However, with the emergence of a larger middle class that are able to pay for their medications, particularly for non-communicable ailments such as hypertension, national development programs shifted their focus towards the establishment of safety and quality surveillance systems for these medicines (Ampadu et al, 2016).

In 1992, South Africa met the minimum requirements to become the first African member state of this collective (see *Figure 2.1*) (Mehta, 2014). Pharmacovigilance in South Africa is a responsibility shared with the medicine regulatory authority, public health programmes, the pharmaceutical industry and the essential drugs program (EDP). The establishment of the National Adverse Drug Event Monitoring Centre (NADEMC) in Cape Town in 1987 by the South African National Department of Health Medicines Regulatory Authority (MRA) is acknowledged as the official start of pharmacovigilance in South Africa.

As of 2015, there are 35 African countries actively involved in the WHO PIDM. Together, they have submitted 103 449 ADR reports to VigiBase®, the WHO's global Individual Case Safety Report (ICSR) database (Ampadu et al, 2016). *Table 2.2* is sourced from Ampadu and colleagues research in 2015 and depicts South Africa's standing with regard to ICSRs submitted to VigiBase® within an African context.

Within a more global context, South Africa seems to lag behind. Although it is difficult to find literature comparing total number of reports submitted since affiliation to the PIDM, over a ten year period (2000 – 2009) South Africa ranked 23rd behind countries such as the United States, Sweden, Japan, Cuba, Mexico, and Thailand (*Table 2.1*) (Aagaard et al, 2012).

Table 2.2: African countries' participation in the WHO PIDM (Ampadu et al, 2016)

Country	Year of joining	No. Of ICSRs to 2015	No of ICSRs per million person years*
Angola	2013	239	5.48
Benin	2011	29	0.71
Botswana	2009	103	8.60
Burkina Faso	2010	76	0.92
Cameroon	2010	46	0.42
Cape Verde	2012	247	165.67
Congo, the Democratic Republic of	2010	5 558	16.90
Côte d'Ivoire	2010	28	0.28
Egypt	2002	8474	8.62
Eritrea	2012	1 982	104.31
Ethiopia	2008	803	1.28
Ghana	2001	2 900	9.07
Guinea	2013	31	1.30
Kenya	2010	8 440	39.07
Liberia	2013	42	4.83
Madagascar	2009	1 087	8.23
Mali	2011	80	1.33
Mauritius	2014	39	31.22
Morocco	1992	17 231	25.38
Mozambique	2005	797	3.36
Namibia	209	1 604	119.25
Niger	2012	39	0.72
Nigeria	2005	10 590	6.70
Rwanda	2013	29	1.21
Senegal	2009	181	2.44
Sierra Leone	2008	1 272	30.97
South Africa	**1992**	**28 609**	**27.22**

Sudan	2009	38	0.20
Swaziland	2015	27	19.02
Tanzania, United Republic of	1993	1 360	1.68
Togo	2008	311	6.86
Tunisia	1993	6 990	32.14
Uganda	2008	1 871	7.59
Zambia	2010	218	3.09
Zimbabwe	1998	2 155	9.77

*Data from VigiBase® to 30 September 2015. Cumulative population to 2014 was used as 2015 data were not yet available.

While South Africa is leading African pharmacovigilance with the greatest number of total reports submitted since PIMD affiliation, the number is still low when considering the population size. With an average number of 27 reports per million people per year, considering that 7.03 million people are currently living with HIV, 454 000 living with TB (as at 2015), as well as a high and increasing prevalence of non-communicable diseases, one would expect the figures for South Africa to be higher (Stats SA, 2016; WHO, 2015).

2.2.3. SOUTH AFRICAN PHARMACOVIGILANCE STRUCTURES

Guideline 2.3.3. Reporting of Post-Marketing Adverse Drug Reactions to Human Medicinal Products in South Africa (December, 2015), published by the MCC, places the responsibility of ADR reporting on the holders of the certificate of registration of medicines. It makes no provision to place responsibility on health care professionals (such as doctors, nurses or pharmacists) to report ADRs, despite these professionals being the most likely point of first contact. Although HCPs are encouraged and professionally obliged to report ADRs, how much information is gathered, and consequently reported, is dependent on the awareness and assertiveness of the health care professional (Pimpalkhute et al. 2012).

Currently, there are a number of PV systems in South Africa. PV is a mandated function of the MCC and they are responsible for the regulatory aspects of PV, i.e. signal detection, ensuring provision of safe, effective and quality medicines, post marketing surveillance, instituting appropriate remedial action, and establishing the risk-benefit profile of all registered medical products (Maigetter et al, 2015). The other PV system is that of the National Pharmacovigilance Center (NPC), which is responsible for coordinating PV in public health programmes, particularly at Primary Health Care (PHC) level. This decentralization aims to increase the interest of PHC workers with respect to medicines and medicine safety.

In addition to the MCC and the NPC, there are a number of separate entities such as the Adverse Event Following Immunization System, the Operational Plan for Comprehensive HIV/AIDS Care, as well as non-governmental organizations such as the Wits Health Consortium, that have developed their own pharmacovigilance programmes that do not always feed into the national NADEMC system (Essack et al, 2011). Although the MCC is responsible for the management of these systems, there is no formal relationship between the MCC and other pharmacovigilance centers, nor is there any system of peer review of the responsible units (Essack et al, 2011).

The current PV framework in South Africa is complex and convoluted due to the many possible arms of reporting, altering the direction of reporting and creating uncertainty for health care professionals. Although a PV framework exists for reporting, the communication on where the report should go is unclear. The trend is that data is often not fed to a national system, or not being fed centrally, which is evident from fewer generated reports (Maigetter et al, 2015). Without a full understanding of the flow of reporting, practitioners may fail to see why reporting ADRs is worth the time invested. The lack of awareness regarding the process of reporting to a national ADR reporting system is cited as a common barrier to reporting (Suyagh et al, 2014).

2.2.4. SOUTH AFRICAN HEALTH PRODUCTS REGULATORY AUTHORITY (SAHPRA)

In 2015, the *Medicines and Related Substances Act Amendment Act, 72 of 2008* was passed and made provision for the establishment of a new medicines regulatory authority. This new body was dubbed the South African Health Products Regulatory Authority (SAHPRA) and its board was announced in October 2017. SAHPRA intends to eventually replace the MCC as the medicine regulatory authority in South Africa. It has been described as being based on a similar model as the Food and Drug Administration (FDA) in the United States in that it is an independent body, falling outside of the South African Department of Health and will therefore not be at risk of political interference. As a more stringent and independent authority, SAHPRA hopes to improve pharmacovigilance monitoring in the country. So far, it aims to make the process of registration more transparent, i.e. different stages of registration will be more readily accessible to the South African public (Rogers and Langbridge, 2016).

One of the biggest improvements to SAHPRA, when compared to the MCC, is that it will also be responsible for the registration and regulation of medical devices as well as more stringent regulation of complementary medicines. Complementary medicines have been called up for registration in 2014 and have until 2019 to be registered with the regulatory

authority. Companies that manufacture medical devices had until August 2017 to register themselves, while medical devices themselves will be called up in 2018 (Goemans, 2017).

As a result of all the above improvements and upgrades, SAHPRA will aim to increase pharmacovigilance monitoring in South Africa within a space of ethics versus science. By having already aligned itself with agencies such as the FDA, European Medicines Agency (EMA) and the International Coalition of Medicines Regulatory Authorities (ICMRA), SAHPRA will hopefully be able to provide South Africa with an improved ADR reporting and monitoring system in line with more developed countries (Spotlight, 2016).

2.3. ADVERSE DRUG REACTIONS

An adverse drug reaction (ADR) is defined by the Medicine Control Council (MCC) as "*a response to a medicine in humans or animals, which is noxious and unintended, including lack of efficacy, and which occurs at any dosage and can also result from overdose, misuse or abuse of a medicine*" (MCC, 2014). The difference between an ADR and an adverse drug event (ADE) is aptly summarised as an ADE being used to refer harm incurred by appropriate or inappropriate use of a drug, whereas an ADR is a direct subset of these events with harm being caused by use of a drug under appropriate circumstances and at normal doses (Nebeker et al, 2004). ADEs may include medication errors (during prescribing, dispensing or administration), non-adherence or incorrect dosages (Nebeker et al, 2004). According to the definition provided by the MCC, both ADEs and ADRs are required to be reported. There are a number of different types of reports currently acceptable in the South African PV framework, broadly divided into voluntary and non-voluntary reports, and will be discussed in more detail later in this chapter.

2.3.1. CLASSIFICATION OF ADVERSE DRUG REACTIONS

ADRs can be classified in a number of different ways:

- Onset of event: Acute (<60 minutes); Sub-acute (1 – 24 hours); Latent (>2 days)
- Type of reaction: Type A, B, C, D, E, F, G, H, U (see *Table 2.3* below)
- Severity: Minor, Moderate, Severe, Fatal

Table 2.3. Wills and Brown ADR Classification (Angeline & Perumaloo, 2015)

Type	Description	Examples
A (Augmented)	A dose dependent, predictable reaction based on the pharmacology of the	Beta-blockers → bradycardia Warfarin → bleeding

	drug. Usually alleviated with a dose reduction	
B (Bizarre)	Not dose dependent and cannot be predicted based on the pharmacology of the drug. Predisposition is usually dependent on individual patient factors	Penicillin → anaphylaxis Anticonvulsant → hypersensitivity
C (Chemical)	Biological or biochemical reactions based on the chemical structure of the drug/metabolite	Paracetamol → hepatotoxicity Paclitaxel → extravasation
D (Delayed)	Occur after many years of drug exposure – may be due to an accumulation of metabolites in the body	Chemotherapy → secondary tumours Antipsychotics → tardive dyskinesia
E (Exit)	Occur on abrupt withdrawal of a drug	Phenytoin → seizures Corticosteroids → adrenocortical insufficiency
F (Familial)	Occur only in patients with genetic predispositions	Primaquin→ haemolytic anaemia in G6PD deficiency
G (Genotoxicity)	Irreversible genetic damage	Thalidomide → teratogenicity ACE-Inhibitors → hypoplasia of organs
H (Hypersensitivity)	An immune mediated response. Can be classified into Type I (immediate, anaphylactic); Type II (Cytotoxic antibody); Type III (serum sickness); Type IV (delayed hypersensitivity)	Penicillin → anaphylaxis Methyldopa → haemolytic anaemia
U (Unclassified)	Reactions in which the mechanism is unclear	Simvastatin → taste disturbances

2.4. INCIDENCE OF ADVERSE DRUG REACTIONS

2.4.1. GLOBAL AND LOCAL FIGURES

ADRs affect a number of patients worldwide, irrespective of age, gender, location or occupation, and can affect patients with varying magnitudes leading to morbidity and mortality (Pirmohamed et al, 2004). Lazarou and colleagues estimated in 1998 that ADRs can be considered to be the 4th – 6th leading cause of death in the United States, with the incidence having remained stable over the previous 30 year period (Lazarou et al, 1998). This placed ADRs as a cause of death ahead of diseases such as pneumonia and diabetes (Lazarou et al, 1998). Additionally, a meta-analysis conducted by Wiffen of 69 prospective and retrospective studies worldwide involving 419 000 patients concluded that ADRs were responsible for approximately 6.7% of all hospitalizations (Wiffen, 2002). It is estimated that the burden of ADRs in developing countries such as South Africa is even higher than in developed countries due to the high prevalence of self-medication, fake and unadulterated medicines, and traditional and herbal therapies (SPS, 2011).

A recent study conducted in four hospitals in South Africa by Mouton and colleagues found that 1 in 12 hospital admissions were due to an ADR (Mouton et al, 2016). 58% of these patients were taking more than 5 drugs at time of admission (range 1 – 17 drugs) and 39% of admitted patients were HIV positive (Mouton et al, 2016). South African patients tend to provide the perfect landscape for ADRs as a result of the cocktail of medications prescribed for the treatment of HIV, TB and non-communicable diseases (Mehta, 2011). Additionally, herbal and traditional medicines are a popular choice for many South Africans due to their low cost and free availability. The market for these medicines is estimated at approximately R 3 billion with at least 27 million people consuming herbal or traditional medicines annually (Essack et al, 2011; BMI, 2010). The use of herbal and traditional medicines raises concerns about safety as their contents are often not well known and may consist of potentially harmful ingredients (Isah et al, 2012).

2.4.2. REASONS FOR HIGH INCIDENCE

Harmful self-medication practices are a cause for concern with respect to ADRs. Easily accessible over-the-counter (OTC) medicines, as well as prescription-only drugs, are often procured from uneducated and uninformed persons in the informal sector (Isah et al, 2012). Additionally, the use of “gift” medicines from friends and family as well as the sharing of medicines without appropriate medical supervision often leads to harm, the magnitude of which is not yet quantified (Isah et al, 2012).

Not all effects of medicines, whether beneficial or harmful, can be identified during clinical trials and other pre-marketing phases of drug development. This is usually due to the small number of patients, short term use, co-morbidities, pharmacogenetics with respect to both heterogenous and homogenous populations, and concomitant use of other medications, foods, and herbal remedies (Smith et al, 2013; Wiktorowicz et al, 2012). Pharmacogenetics plays a big role in determining the beneficial or adverse response to a medicine. Data emerging from clinical trials is based on a small, often homogenous population making it difficult to extrapolate safety data to a more genetically diverse population, such as the one found in South Africa. For example, McDowell and colleagues performed a meta-analysis on the link between ethnicity and adverse drug reactions to cardiovascular drugs. They found a previously unpublished threefold increase in the risk of angioedema in black patients taking angiotension converting enzyme inhibitors (ACE-Is), when compared to non-black patients (McDowell et al, 2006). ACE-Is are often first-line therapy for the treatment of hypertension in South Africa and therefore a need to monitor outcomes, including ADRs, should be a priority activity.

There have been several studies and meta-analyses such as Mouton and colleagues all over the world in attempts to quantify the impact of ADRs on healthcare in both an individual and societal capacity. Literature both confirms that ADRs are a global health problem and suggests that more care needs to be taken in the avoidance of ADRs.

2.5. MEDICATION ERRORS

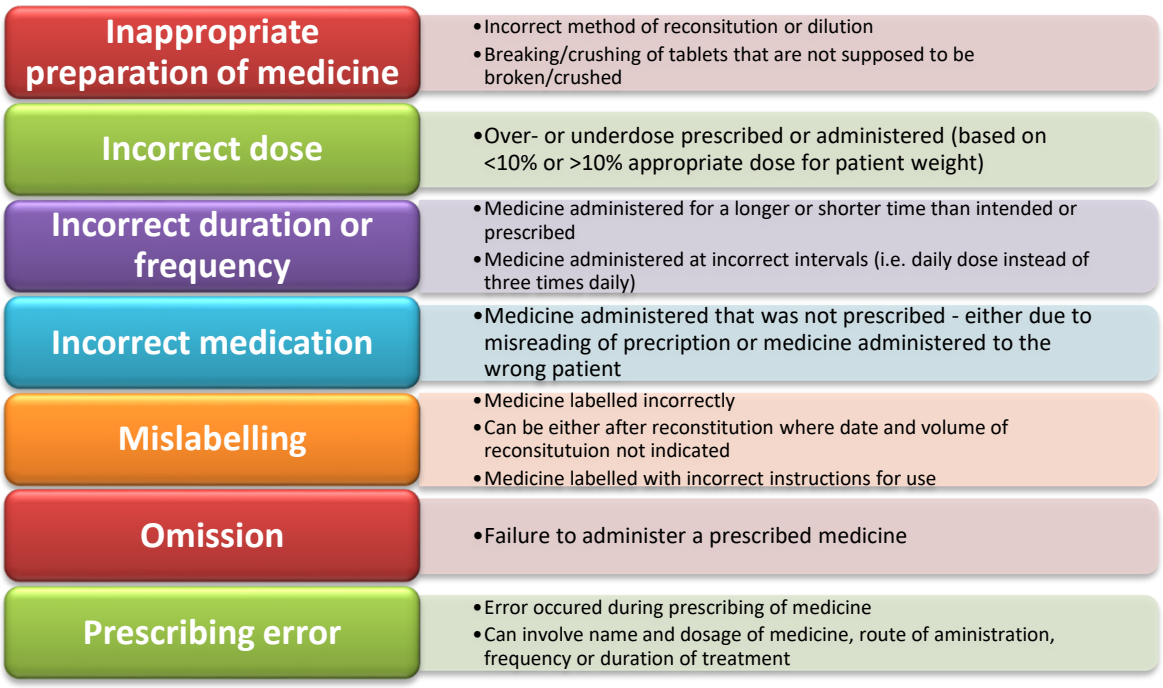
2.5.1. DEFINITION

Because the definitions of PV and ADRs include the use of medicines in a prescribing, dispensing and administration capacity, medication errors in the context of pharmacovigilance need to be addressed. The National Coordinating Council for Medication Error Reporting and Prevention (NCC MERP) is an international body that aims to maximise the safe use of medicines and increase awareness of medication errors in order to prevent them occurring. The NCC MERP defines a medication error as, "…*any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of the health care professional, patient, or consumer. Such events may be related to professional practice, health care products, procedures, and systems, including prescribing, order communication, product labeling, packaging, and nomenclature, compounding, dispensing, distribution, administration, education, monitoring, and use."*

2.5.2. CLASSIFICATION OF MEDICATION ERRORS

Medication errors can be classified according to the way in which the error occurred. This is important in the context of PV as it can emphasise the need for vigilant and competent HCPs, as well as to distinguish whether an adverse effect of a medicine is due to a medication error or as a result of the drug itself.

Figure 2.2. Classification of Medication Errors (adapted from Truter et al, 2017)



2.5.3. CATEGORISATION OF MEDICATION ERRORS

Medication errors are categorised according to their potential to cause harm to the patient and the extent of potential harm that can be caused. The information obtained from classifying a medication error allows the HCPs caring for the patient to formulate the best management plan.

Table 2.4. Categories of Medication Error (Agency for Healthcare Research and Quality, 2012)

Category	Description	Example
A	No error or potential to cause error	N/A
B	Error that did not reach the patient	N/A
C	Error that reached the patient	Multivitamin not prescribed

		but unlikely to cause harm (including omissions)	but still administered
	D	Error that reached the patient and could have necessitated monitoring and/or intervention to prevent harm	Regular release metoprolol was prescribed but extended release was administered
	E	Error that could have caused temporary harm	Blood pressure medication was accidently not prescribed and therefore not administered
	F	Error that could have caused temporary harm requiring hospitilisation	Warfarin administered daily instead of every alternate day
	G	Error that could have resulted in permanent harm	Immunosuppressant medication unintentionally prescribed and administered at a quarter of the required dose
	H	Error that could have necessitated intervention to sustain life	Anticonvulsant therapy that was accidently omitted
	I	Error that could have resulted in death	Beta-blocker not prescribed post-operatively

2.5.4. ADVERSE DRUG REACTIONS AS A RESULT OF MEDICATION ERRORS

The NCC MERP has published a list of “dangerous abbreviations” to be aware of during the prescribing, dispensing and administration phases of drug use in order to minimise medication errors and medication error-related ADRs (*Table 2.5*).

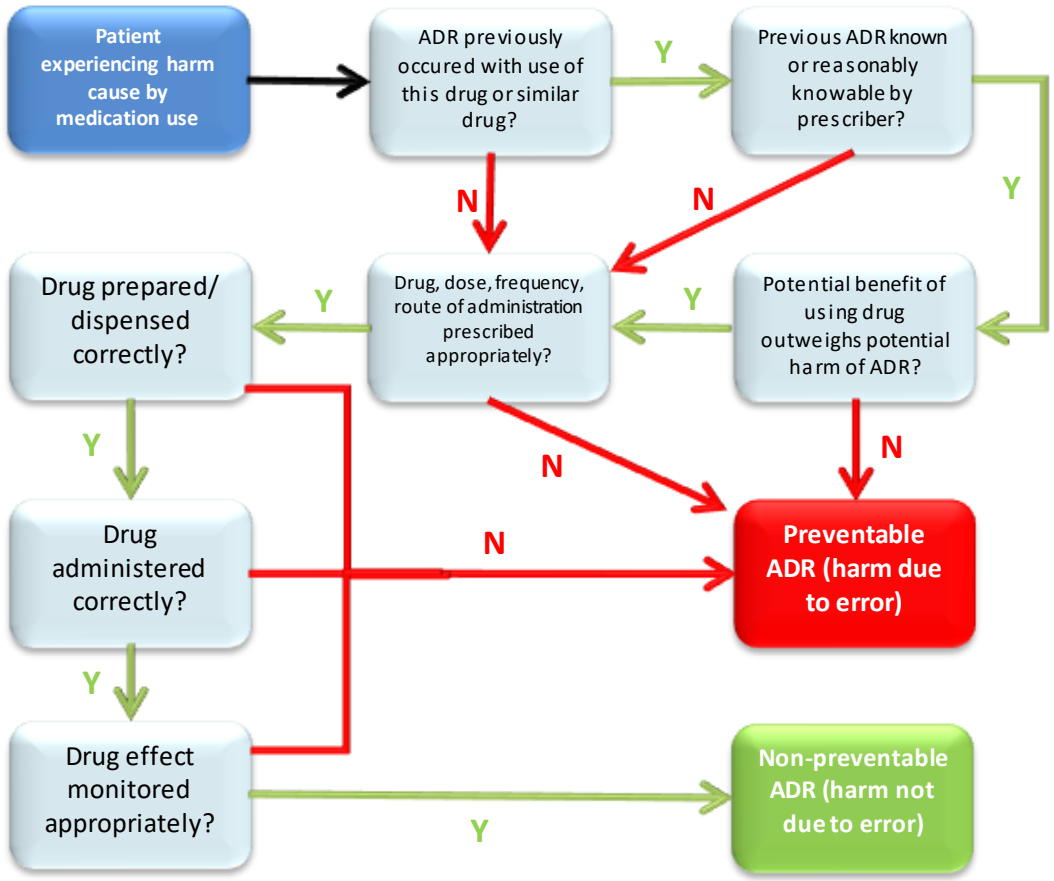
Table 2.5.Examples of Dangerous Abbreviations (NCC MERP, 2017)

Abbreviation	Intended Meaning	Common Error
U	Units	Mistaken as a zero or a four (4) resulting in overdose. Also mistaken for "cc" (cubic centimeters) when poorly written
µg	Micrograms	Mistaken for "mg" (milligrams) resulting in an overdose

SC or SQ	Subcutaneous	Mistaken as "SL" (sublingual) when poorly written
cc	Cubic centimeters	Mistaken as "U" (units) when poorly written.
AU, AS, AD	Latin abbreviation for both ears; left ear; right ear	Misinterpreted as the Latin abbreviation "OU" (both eyes); "OS" (left eye); "OD" (right eye)
IU	International Unit	Mistaken as IV (intravenous) or 10(ten)
MS, MSO4, MgSO4	Confused for one another	Can mean morphine sulfate or magnesium sulfate

In order to assist HCPs in determining whether an ADR was caused by a medication error or is in fact a result of the drug itself, the NCC MERP has also published an algorithm to assist with this determination. *Figure 2.3* is adapted from the adverse drug event algorithm published by the NCC MERP.

Figure 2.3. Adverse Drug Reaction Algorithm (adapted from NCC MERP)



Evans and colleagues published a study in 2006 where they found that 80.9% of doctors in their study thought they should always report when a patient receives the wrong treatment.

However, only 57.3% believed they should report when a patient does not receive the necessary treatment. This is a significant finding as acts of omission have actually been implicated in twice as many adverse events as acts of commission (Wilson et al, 1995).

A report published by the US Institute of Medicine in 1999 supported this finding by reporting that over one million preventable ADRs occurred each year in the US, with 44 000 – 98 000 of these being fatal, and over 7 000 being due to medication errors (Kohn et al, 1999). These numbers are supported by a more recent South African study mentioned earlier conducted by Mouton and colleagues in 2013 where an alarming number of ADRs that caused hospital admission and deaths could have been prevented.

Table 2.6. Characteristics of Most Common ADRs Causing Hospital Admission in Four Hospitals in South Africa (Mouton et al, 2013)

	Renal Impairment	**Hypoglycaemia**	**Drug-Induced Liver Injury**	**Hemorrhage**	**Blood Dyscrasias**
Number of ADR-related admissions	24	22	20	19	14
Drugs associated with the ADR	TDF; ACE-I;co-trimoxazole; rifampicin; co-amoxiclav and ibuprofen	Insulin; metformin; sulfonylurea; unspecified hypoglycaemic agent	Rifampicin; efavirenz only; co-trimoxazole; enalapril; various combinations of ATT, NNRTIs, co-trimoxazole, erythromycin	warfarin; acetylsalicylic acid; unspecified NSAIDs; diclofenac	co-trimoxazole; zidovudine; lamivudine; stavudine; methotrexate; chloroquine; allopurinol; colchicine; rifampicin; isoniazid; amoxicillin; valproic acid
Proportion preventable (%)	73%	77%	13%	58%	30%
Reasons for preventability (%): Inappropriate drug	29%	32%	10%	0%	0%
Inappropriate dose	4.2%	18%	0%	21%	0%
Inadequate monitoring	17%	36%	0%	26%	7.1%

History of ADR	0%	18%	5%	21%	0%
Interaction	0%	4.6%	0%	26%	0%
Drug concentration	0%	0%	0%	0%	0%
Compliance	0%	14%	0%	0%	0%
Combined all-cause mortality (%)	50%	18%	35%	16%	21%
TDF = tenofovir; ACE-I = angiotension converting enzyme inhibitor; ATT = anti-tubercular treatment; NNRTI = non-nucleoside reverse transcriptase inhibitor; NSAID = non-steroidal anti-inflammatory drug					

2.6. ADVERSE DRUG REACTION RELATED COSTS

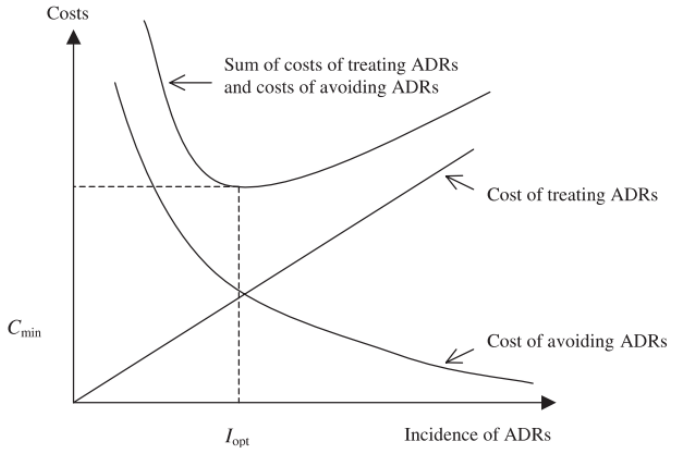
Several studies have concluded that the cost of managing ADRs places a significant burden on health care budgets, not to mention the economic burden suffered by individuals and communities due to hospitalisation or mortality (Lundkvist & Jönsson, 2004). Some countries reportedly spend up to 15 - 20% of their hospital budgets managing drug complications (White, 2009). However, it has proved difficult to exactly quantify the economic burden of ADRs due to the vast number of factors involved. For example, one would need to consider days taken off work, additional doctors visits, and additional medications purchased or used for the management of complications.

Lundkvist and Jönsson (2004) have surmised that in order to determine the economic impact of ADRs, it is necessary to look at two perspectives: the costs related to treatment of ADR outcome, and the cost of ADR avoidance. A number of studies aim to quantify the cost of "drug-related problems" rather than the cost of ADRs specifically (Philip et al, 1995; Johnson & Bootman, 1995). These estimates range from $1.5 million to $130 billion. In another study, ADR management during hospitalisation has been estimated to increase hospital costs by $2595 in 1997 (this figure can be presumed to be much higher now due to inflation and rising costs of hospitalisation (Classen et al, 1997).

Figure 2.4 describes a situation where the decision to have higher costs for ADR avoidance reduces the probability of ADR occurrence. Lundkvist and Jönsson name four key role players involved in drug utilisation for whom ADRs could have an economic impact: patients (whom might obviously be affected by the cost of managing an ADR related disease or illness, or for the cost of revisiting physicians or the purchasing of different drugs to avoid ADRs), physicians (who operate in an environment where time spent with a patient, as well as number of patients seen within a given time period, is directly related to the amount of money they will earn. It is therefore not necessarily in a physician's best monetary interest to

spend more time with a patient, explaining side effects and other effects of the drug), pharmacists (the management and other subsequent drug-related effects might lead to higher medicine-related spending for the management of these ADRs) and drug manufacturers (for whom an unexpected serious ADR might lead to a massive economic loss, but for whom spending more money and resources during clinical trials might lead to a loss in investment and time on market).

Figure 2.4. Lundkvist and Jönsson's comparison of cost of treating ADRs vs. cost of ADR avoidance (C_{min}: minimum total costs; I_{opt} optimal incidence of ADRs (Lundkvist and Jönsson, 2004)



It is also necessary to consider smaller but not insignificant ADR related economic impacts on individual patients. For example, the management of opioid-related ADRs. A patient that experiences constipation from licit or illicit opioid use might spend more money on laxatives and related products (including foods high in fibre, etc) to ease the constipation. To explore a more socio-economic perspective, a patient that becomes addicted to opioid painkillers and later begins to experience other addiction related behaviours (such as theft, unemployment, heroin-use, methadone-treatment, etc) will suffer a diverse variety of economic setbacks that is difficult to quantify but vital to understand in the greater setting of ADR-related costs.

2.7. TYPES OF ADVERSE DRUG REACTION REPORTS

There are a number of methods of ADR reporting currently employed both in South Africa and abroad.

The most common and efficient method is the Spontaneous Reporting System (SRS), also known as ICSRs whereby HCPs or patients/consumers report an ADR to their respective pharmacovigilance centers when they become suspicious of a reaction (Joubert & Naidoo, 2016). It is a voluntary, passive form of reporting that is extremely cost-effective and can be

a powerful tool to improve the safety of medicines worldwide provided that all HCPs actively participate. The SRS not only allows for the identification of new and rare ADRs (such as the fatal severe rhabdomyolysis seen with cerivastatin leading to its withdrawal in 2001) but allows for the continuous monitoring of all medicines used in “real life” situations (such as the recent finding that ACE-Is increase the risk of angioedema threefold in black patients compared to non-black patients) (Furberg & Pitt, 2011; McDowell et al, 2006).

Other methods of reporting include Cohort Event Monitoring (CEM) and Targeted Spontaneous Reporting (TSR). CEM is a prospective, observational, cohort study of adverse events associated with one or more medicines. A CEM program is an observation of a new medicine in routine clinical practice in the early post-marketing phase, although it may also be used for older medicines. TSR is a methodology that builds on the principles of the SRS but is applied in a defined setting. TSR may be adapted either to report all suspected reactions in a defined population (such as in a nursing home or palliative care facility), or to focus only on specific reactions of particular concern (such as the monitoring of ADRs when trialling a new TB regimen). This serves to limit the reporting workload associated with adverse events that are most significant to individuals and programmes in question. CEM can be an expensive initiative, while TSR required complete commitment from HCPs (Pal et al, 2013). Identifying specific risk factors and high-risk groups, as well as providing valid clinical characteristics of problems associated with specific medicines, requires methods of greater scientific rigour (Pal et al, 2013).

2.8. UNDERREPORTING

Underreporting of ADRs and the reasons for it has been well documented in literature. Studies around the world have targeted HCPs (doctors, nurses and pharmacists) to gain a better understanding of their knowledge, attitudes and practices regarding ADR reporting. Studies depicting the knowledge, attitudes and practices of HCPs regarding ADR reporting vary widely. in general, doctors in developed countries (such as the UK, USA and the Netherlands) tend to have a better understanding of their respective ADR reporting systems than their counterparts in developing countries (such as India, Nigeria and Uganda) (Oshikoya et al, 2009). Interestingly, studies within the same country also produced different results. For example, the findings of a 2009 study in Nigeria in a teaching hospital concluded that doctors had inadequate knowledge regarding ADR reporting (Oshikoya et al, 2009). However, a similar study being performed at the same time yet in a different region of Nigeria, surmised that doctors did indeed have a good level of ADR reporting knowledge (Enwere et al, 2008). Inconsistencies such as these demonstrate the underlying issues

plaguing effective PV systems worldwide. It is not enough for one hospital or one region to excel in their PV efforts while the reporting rate for the country overall is not yet acceptable.

2.8.1. KNOWLEDGE OF PHARMACISTS

Literature indicates that one of the major reasons for pharmacists having insufficient knowledge regarding ADR reporting is the lack of presence of national pharmacovigilance centres (NPCs). Pharmacists in countries such as South Africa, Turkey and Nepal cite a lack of feedback and involvement on the part of their respective NPCs as their reasons for inadequate knowledge (Ruud et al, 2010; Toklu et al, 2008; Palaian et al, 2011). Because of the lack of presence, pharmacists are ether unsure or unaware of the location of their NPCs, procedures to follow for getting in contact, or what happens to an ADR report if it is in fact submitted (Palaian et al, 2011).

2.8.2. KNOWLEDGE OF NURSES

Although ADR reporting was not considered to be a professional obligation for nurses until recently, several studies conducted in Iran, China and Australia have concluded that nurses have an acceptable level of overall ADR reporting knowledge (Hajebi et al, 2010; Li et al, 2004; Evans et al, 2006). A finding by Evans and colleagues in Australia concluded that nurses had a higher degree of ADR reporting knowledge than doctors (81.9% vs 49.7%) (Evans et al, 2006).

One of the biggest factors affecting the level of ADR reporting knowledge of nurses worldwide is the lack of visibility and awareness of PV centres. Numerous studies surmise that many HCPs, including nurses, are either completely unaware of a national PV centre/authority, or are aware of its existence but not of its location, purpose or function (Ganesan et al, 2016; Palaian et al, 2011; Irujo et al, 2007; Hanafi et al, 2012; Raza and Jamal, 2015).

2.8.3. ATTITUDES OF PHARMACISTS

The reasons for low reporting of ADRs by HCPs have been well researched. Lopez-Gonzalez and colleagues released a systematic review mentioning ignorance (95%), diffidence (72%), lethargy (77%), indifference and insecurity (67%) and complacency (47%) as the primary reasons for underreporting (Lopez-Gonzalez et al, 2009). The paperwork involved with such reporting seems to discourage the desire to produce data of any sort, especially because those responsible perceive the data as irrelevant to their immediate clinical needs (Ruud et al, 2010). This is aptly illustrated by a finding from a study conducted in Nigeria where over 40% of pharmacists stated that patients had reported an ADR to them

in the preceding month, while only 20% of those pharmacists had reported the ADR (Oreagba et al, 2011).

However, in developed countries, there seems to be a more positive attitude specifically amongst pharmacists towards ADR reporting as they considered it to be their professional obligation (Belton et al, 1995; Evans et al, 2006). Bearing this in mind, in a hospital environment, pharmacists are not always present by a patients bed side and directly monitoring their health outcomes in the same manner that doctors and nurses do. In this respect, inexperienced or unaware HCPs that lack the sound clinical judgement needed to determine a causal relationship between an adverse or unexpected event and a drug could pose as a great challenge (Suleman, 2010).

2.8.4. ATTITUDES OF NURSES

Largely, nurses seem to have the most positive attitude towards ADR reporting of all health care professionals including pharmacists (Evans et al, 2006; Wilson et al, 2008, Hajebi et al, 2010).

An interesting point to make is the difference in attitude between nurses in developed and developing countries. While nurses from all socioeconomic backgrounds believe ADR reporting to be an important aspect of medicine management, those from developed countries tend to have more motivation to monitor effects to new/experimental drugs when compared to those from developing countries (Green et al, 2001; Bateman et al, 1992; Belton et al, 1995; Desai et al, 2011; Mulatu and Worku, 2014; Suyagh et al, 2015). As stated previously in this chapter, this could be due to developed countries having had PV structures in place for a longer period of time and therefore have had more time to establish more sophisticated frameworks that actively include and educate all HCPs.

2.8.5. PRACTICE OF PHARMACISTS

Factors relating to processes for reporting, such as inadequate feedback, long forms and insufficient time to report, are often identified as major barriers to reporting (Uribe et al, 2002). A pharmacist interviewed in a study conducted by Ruud and colleagues aptly stated, *"…you report in a vacuum. You give it to somebody and you never hear again. And it's nice to get feedback, from whoever who are collecting these ADRs to say, look, this is what we're looking for, this is not what we're looking for.*" (Ruud et al, 2010). This statement is supported by a previous study conducted by Evans and colleagues whereby 58% of HCPs involved in the study cited a lack of feedback as a self-perceived barrier to reporting (Evans et al, 2006). Within a South African context, pharmacists in a study conducted by Joubertand

Naidoo in 2016 felt PV centres to be inaccessible with little to no personal contact (Joubert & Naidoo, 2016). Other self-perceived barriers included the form taking too long to complete, a lack of time, not wanting to take responsibility for the report and believing that the report will not make any difference (Evans et al, 2006).

2.8.6. PRACTICE OF NURSES

While ADR reporting practices of nurses vary, it would appear that reporting still remains a challenge worldwide. During completion of surveys, most nurses state that they have never encountered an ADR before (Hajebi et al, 2010; Li et al, 2004; Evans et al, 2006; Wilson et al, 2008). This figure is difficult to believe considering the number of patients seen to and the volume of medicines used in the presence of nurses within a hospital environment. However, this may be attributed to a lack of training with regards to the identification of ADRs (Suleman, 2010).

However, many nurses do informally report ADRs to consulting doctors, nursing managers and pharmacy with varying extents.

2.9. CONCLUSION

As illustrated by the literature discussed, ADRs are an imminent and immediate public health threat. Unfortunately, there are many drugs that will not have a favourable benefit to risk ratio. However, by utilising effective PV systems, it will be possible to minimise the risks experienced by patients through ensuring that the medicines they use have an established safety profile. The biggest challenge when it comes to the management of ADRs is their underreporting by HCPs. In many countries, patients are allowed and even encouraged to submit their own ADR reports if they suspect that they are experiencing an ADR. However, many patients are simply unaware that they are able to do this and therefore rely on their HCPs to take action when there is a suspected ADR. In countries such as South Africa, where the population is large and extremely diverse, the safety profile of each medicine will not necessarily be the same across the population. It is therefore vital that HCPs in all healthcare sectors begin to integrate PV into their daily clinical practice and begin to consider ADR reporting as a professional obligation.

A systematic review conducted by Onakpoya and colleagues in 2016 cited 462 medicinal products withdrawn worldwide due to ADRs with case reports and anecdotal evidence of ADRs used as evidence of withdrawal in 71% of cases from 1953 – 2013 (Onakpoya et al, 2016). This median interval for withdrawal after the first report was 8 years, and the rate of withdrawal was significantly lower in African countries than on other continents. As

supported by *Table 2.2*, this highlights the lack in regulatory co-ordination between medicine regulatory authorities and medicine use.

Considering that case reports are so important in removing drugs from the market where the risk profile significantly outweighs the benefits, it is vital that reporting of ADRs by HCPs be encouraged.

CHAPTER 3

METHODOLOGY

3.1. INTRODUCTION

This chapter covers the general design of the study as well as the development and distribution of the questionnaire used. The study population, study setting and data instruments are described. It further elaborates on how validity and reliability models were utilised at various stages of the study. Lastly, this chapter elucidates on the limitations of the study as well as ethical committees that approved the research.

3.2. AIMS AND OBJECTIVES

3.2.1. AIM

This study aimed to evaluate the knowledge, attitudes and practices of pharmacists and nurses in the private hospital sector towards ADR reporting.

3.2.2. OBJECTIVES

I. Assessed the knowledge of private sector HCPs regarding the ADR reporting process in South Africa.
II. Assessed the attitudes of private sector HCPs towards ADR reporting and varying components of ADR reporting.
III. Evaluated ADR reporting practices of private sector HCPs.
IV. Established factors that contributed to differences in both knowledge and attitudes towards ADR reporting.
V. Explored trends that interfered with effective ADR reporting.

3.3. STUDY DESIGN

This study was a cross-sectional, observational, questionnaire-based study that involved registered nurses and hospital pharmacists working in the private sector within a single hospital group.

3.4. STUDY POPULATION

This study was conducted in six private hospitals and clinics within a single hospital group in Johannesburg, South Africa. These hospitals were selected as a result of a purposive sampling method as each hospital offers a variety of wards and specialties (i.e. maternity,

paediatrics, oncology, ICU, neurology, psychiatry, gynaecology, orthopaedics, neonatology and surgery), and provides both in- and out-patient facilities. It was therefore possible to include a study population with varying training and specialties, and therefore a broader spectrum of results was achieved.

While there have been previous studies exploring the knowledge, attitudes and practices of HCPs towards ADR reporting, these have so far all been conducted in the public sector (Dheda, 2013; Nlooto & Sartorius, 2015; Dheda et al, 2016; Joubert & Naidoo, 2016; Segomotso, 2011; Roux, 2014). The private sector has seldom if ever been studied in this way. The Department of Health Master Procurement Catalogue 2017 identifies 476 medicines available in the public sector (to be amended when necessary at the discretion of any relevant Pharmacy and Therapeutics Committees (PTC) in line with the WHO Essential Drugs List (EDL) guidelines). The private sector, on the other hand, is not limited by the Standard Treatment Guidelines (STG), EDL or state tenders, and therefore the number of medicines available for use by patients is larger and more varied. The private sector sees a larger number of originator medicines, wider range of generic medicines, greater quantity and distribution of new medicines, as well as higher usage of experimental drugs compared to the public sector. This increase in availability of medicines may lead to an increase in the incidence of ADRs, and therefore a greater effort to target post-marketing surveillance in this sector should be made.

Hospital pharmacists and registered nurses were selected as the study population due to their roles within the multi-disciplinary health care team. Registered nurses have twenty four hour access to the patient and are directly involved in their care. They are responsible for drug administration and are usually the first point of contact when a patient experiences a beneficial or harmful response to a drug. Hospital pharmacists have the pharmaceutical and/or clinical knowledge to detect or manage ADRs by virtue of their profession. Additionally, because many private hospitals in South Africa also provide retail pharmacy services, and therefore are able to supply chronic and over the counter (OTC) medicines, hospital pharmacists do tend to have direct access to patients. Because of the multi-disciplinary health care model employed in most hospitals globally, it is important to evaluate the knowledge, attitudes and practices of both these professions towards ADR reporting. Doctors were excluded from this study due to a lack of willingness to participate during piloting.

Inclusion criteria for participants were as follows:

- Registered nurse or hospital pharmacist employed at the facility (locum and agency staff included)

- Willingness to participate (signed informed consent and/or completed questionnaire)

Exclusion criteria were as follows:

- Non-willingness to participate
- Enrolled nurses (i.e. have not yet completed their qualification)
- Support pharmacy staff (i.e. assistants, technicians and drug controllers)

According to a study conducted by Econex on behalf of the South African Private Practitioners Forum (SAPPF) and Healthman (Pty) Ltd, The South African Private Healthcare Sector: Role and Contribution to the Economy, there were an estimated 77 569 nurses and 2 984 pharmacists working within the South African private sector, as at 2013 statistics (Econex, 2013). Assuming a ratio of approximately 0.9 registered nurses to enrolled nurses applicable throughout both public and private sectors (obtained from the South African Nursing Council Annual Statistics for Persons on the Register 2015), an estimated 72 000 registered nurses can be identified working within private institutions in South Africa. Similarly, South African Pharmacy Council Statistics show 290 private institutions registered in South Africa in 2016. Assuming that each private institution employs at least one pharmacist, at least 290 pharmacists can be identified as hospital pharmacists in the private sector.

Therefore, a sample size of 382 was calculated, using a confidence interval (CI) of 5 and a confidence level (Z) of 95%, as per the formula below:

Sample Size:

$$ss = \frac{Z^2 \times p \times (1-p)}{C^2}$$

Correction for finite population:

$$Newss = \frac{ss}{1 + \frac{ss-1}{pop}}$$

Where:

ss = sample size

Z = Z-value (e.g. 1.96 for 95% confidence level)

p = percentage picking a choice expressed as a decimal (0.5 used for sample size needed)

C = confidence interval expressed a decimal (e.g. 0.05 = ± 5)

pop = population

3.5. QUESTIONNAIRE DEVELOPMENT

A self-administered questionnaire was used as the primary data collection tool. It had been adapted from similar studies investigating the knowledge, attitudes and practices of ADR reporting amongst HCPs and modified to suit a South African private sector setting (Jose et al, 2014; Rajiah et al, 2016; van Hunsel et al, 2010; Gupta &Udupa, 2011; Kiran, 2014).

The questionnaire contained 20 close-ended questions, with four of these providing an opportunity for an open-ended answer in the form of a "Other – please specify" option.

The questionnaire was designed to capture the following information, and can be found in Appendix A:

- **Participant information and demographic (four questions)**. This included gender, age, profession and years of experience. This was to determine whether differences in these variables contribute to differences in knowledge, attitude or practice (i.e. distinguishing between different demographics might indicate the extent to which they place predicate on ADR reporting).
- **Background knowledge of the participant with regard to ADR reporting (six questions)**. This included previous training received, knowledge of ADR reporting form, where the ADR reporting form is located, and where reports should be submitted. This was to determine the baseline knowledge of each participant towards ADR reporting and the ADR reporting process. This also aided in determining the level of previous exposure of each participant to ADRs and/or ADR reporting.
- **Participant perceptions towards ADR reporting (five questions)**. This included each participant's perceived importance of ADR reporting in general, important or not important reasons for ADR reporting, factors that encouraged or discouraged the participant to report an ADR, and which kind of ADRs the participant thought should be reported. This was to aid in determining the general attitudes of the participants towards ADR reporting and attempted to identify factors outside of the participants' knowledge that may contribute to low reporting rates.
- **ADR reporting practices of participants (five questions).** This included whether the participant had come across an ADR previously, whether they have previously reported an ADR, the likely circumstances under which the participant would submit an ADR report, and which medical professional the participant deems responsible for submitting ADR reports. This was to gain an understanding of the current ADR reporting practices of each participant in order to determine how it can be improved.

3.6. QUESTIONNAIRE DISTRIBUTION

The questionnaire was distributed to potential participants during the period June 2016 and December 2016. The questionnaire was distributed in two ways: electronically via e–mail to participants with regular computer and e-mail access at their workplace, and manually via hard copies to participants without regular access to a computer or e-mail at their workplace.

3.6.1. ELECTRONIC DISTRIBUTION

A list of e-mail address for potential participants was obtained from the Pharmacy and Nursing Managers of each respective hospital. A total of 83 potential participants were identified for electronic questionnaire distribution, and included pharmacists, locum pharmacists and registered nurses. The registered nurses identified for electronic distribution all held senior or managerial positions. All other nurses did not have regular access to computer or e-mail at their workplace and were thus considered for manual questionnaire distribution.

An e-mail detailing the nature of the study in the form of an information sheet (Appendix B), informed consent document (Appendix C), and a link to the questionnaire was sent to each potential participant. Participation was completely voluntary and no incentives were offered.

3.6.2. MANUAL DISTRIBUTION

Hard copy questionnaires (including information sheet and informed consent document) were distributed to all potential participants without regular access to computer or e-mail at their workplace after holding a brief meeting with the staff of every unit/department in each identified hospital. The meeting served to provide each potential participant with the same information contained in the information sheet and informed consent document (Appendix B and C). An excess number of questionnaires were provided to the manager of each unit/department for distribution to night staff and staff that were on leave or were otherwise absent. Potential participants included pharmacists, registered nurses, and agency staff (nurses that were not directly employed by the hospital group but were outsourced from a nursing agency). Participants were provided with a period of one month to complete the questionnaire. A total of 360 questionnaires were involved in the manual distribution. Participation was completely voluntary and no incentives were offered.

3.7. DATA COLLECTION

Electronic questionnaires were captured onto Google Forms™ as they were completed.

For manually distributed questionnaires, a contact person was identified in each hospital (either the Senior Pharmacist or the Pharmacy Manager) from whom all the questionnaires were collected. Regular e-mails were sent to the managers of each unit/department to remind their staff to complete the questionnaire should they wish to participate, hand in the questionnaires to the relevant contact person at their hospital, and to remind both managers and staff to contact the principal investigator should there be any questions or concerns.

3.8. VALIDITY AND RELIABILITY

Validity and reliability will be discussed in terms of the theories and criteria laid out by Maxwell (1992), Polit&Hungler (1997) and Onwuegbuzie& Johnson (2006) for evaluating qualitative, quantitative and mixed research methodologies.

Table 3.1. Threats to Internal Validity

Threat	Definition	Applicability to current study	What was done to minimise the effect
Implementation bias	Occurs when the designed protocol is not followed in the intended manner	Can occur if the protocol used for administration of questionnaire is not the same for all HCPs (i.e. time of administration, method of administration)	An electronic platform, Google Forms™, was used to collect data for suitable participants while paper questionnaires were used for all other participants. Completion of questionnaires was entirely voluntary and participants were able to complete them at a time suited to them.
Attrition	Occurs when participants who have been selected to take part in the study do not take	Can occur when potential research participants forget to complete the questionnaire.	All participants were reminded on a weekly basis to complete the questionnaire. Data

	part at all, or partially or completely fail to take part in various stages of the research process.		collection took place over a period of six months.
Researcher bias	Occurs when the researcher has a personal bias/preference towards a technique	The researcher may create a predetermined hypothesis regarding the results that were obtained with the various testing procedures.	Two types of data collection instruments were used – an electronic platform (Google Forms™) and paper questionnaires.
Content validity	Refers to how accurately an assessment tool represents the various aspects of the specific construct in question.	Can occur when questions included in a questionnaire are too vague or broad.	Questions were selected and adapted based on previously conducted similar studies measuring the same outcomes in different settings.
Face validity	The degree to which a test subjectively measures what it is supposed to measure.	Can occur when questions might appear ambiguous, double-barrelled or otherwise difficult for the study population to answer	The questionnaire was piloted on a represation (i.e. four locum pharmacists, one clinical pharmacist, ten agency nurses). Amendenments and adjustments to the questionnaire were made accordingly after receiving feedback.
Sample integration legitimation	Refers to situations where the researcher	Can occur when the study population is	Locum pharmacists and agency nurses

	would want to make statistical generalizations from the study population to a larger target population.	restricted to one geographical region or contextual setting.	were included in the study population that perform their services in a variety of settings and locations. An assumption was also made that at least a small portion of participants had been previously employed and/or had worked in a region other than that included in this study.
Inside-outside legitimation	The extent to which the researcher accurately represents an insider's view and an observer's view for purposes of descriptive and interpretive validity.	Can occur when a researcher is ethnocentric or becomes too involved with the population being studied.	A peer-review methodology to analyse raw data and the interpretation of raw data. An emic viewpoint was obtained from a clinical pharmacist initially used for questionnaire piloting in the employ of the hospital group, while the etic viewpoint was supplied by two colleagues at the University of the Witwatersrand.
Conversion legitimation	Refers to the inferences made after qualitising or	Can occur when counts of observed data are taken out of	Data was presented in more than one profile (i.e.

	quantitising data	context, over-counted, lead to an over-generalization or over-/under-weighting	comparative profile, modal profile, normative profile) in order to provide a narrative description that was as accurate as possible.
History effect and maturation	Refers to events that occur external to the test (i.e. events in the environment) as well as physical or psychological changes in the participants.	Can occur when the environment of the population is not adequately controlled nor are the participants adequately monitored.	It is not possible to exclude collusion, collaboration and cooperation between and amongst participants during the completion of the questionnaire. Additionally, there was no method of preventing participants from researching "correct" answers to the questionnaire prior to completion.

Table 3.2. Threats to External Validity

Threat	Definition	Applicability to current study	What was done to minimise the effect
Population validity	Refers to the extent to which the findings can be generalised from the sample group towards a larger population.	Due to external factors, the sample may not be representative of the population. Convenience and purposive sampling was used by the	*(See Sample Integration Legitimation)*

		researcher.	
Ecological validity	The extent to which findings from a given study can be generalised across settings, conditions, variables and contexts.	The data and final results in the study are dependent on the setting and location in which it is obtained.	*(See Sample Integration Legitimation)*

3.9. DATA ANALYSIS

All data was captured by entering into Google Forms™ and then exported into Microsoft Excel 2016™. Descriptive data analysis was conducted using Microsoft Excel 2016™. Each variable category as coded with a number for ease of analysis. Pearson chi-squares were used for a test of association, as well as cross-tabulation methods for bivariate analysis.

Results are presented by means of percentages and/or graphs depending on their appropriateness to the variable in question. The relationship between different variables (e.g. age of respondent vs. previous exposure to ADRs) was determined using a Pearson chi-square at $p < 0.05$. Frequency analysis was also employed to assess differences in attitudes, knowledge and practices.

3.10. LIMITATIONS

An important limitation of the study was participant bias, i.e. only those who agreed to participate were able to fill in the questionnaire. The use of both e-mailed and paper questionnaires were each a limitation. E-mailed questionnaires were a limitation in that not every e-mailed potential participant had regular access to their e-mail. Additionally, the e-mails might have been ignored, automatically sent to the spam folder, and/or sent to an e-mail address that is no longer in use. The paper questionnaires proved to be a limitation in that hospital staff tend to shy away from paperwork of any sort due to an already heavy administrative workload, and therefore did not complete the questionnaire.

3.11. ETHICAL CONSIDERATIONS

Ethics clearance was obtained from the University of the Witwatersrand Human Research Ethics Committee to conduct this study (*Ethics No. : M160238*) (Appendix D). Clearance was also obtained from the hospital group involved in the study on condition of confidentiality (*Approval number: 20160620-01*) (Appendix E). Each potential participant was provided with

an information sheet detailing the nature of the study and any benefits or risks to choosing to participate (Appendix B). All potential participants were informed that should they decide to withdraw or not complete the study, no repercussions, consequences or penalties would be applied. Informed consent was obtained from each participant prior to completion of the questionnaire, either electronically or manually (Appendix C).

CHAPTER 4

RESULTS

4.1. INTRODUCTION

This chapter presents the results obtained in the study firstly in a descriptive fashion, and later using descriptive statistics. Results are presented mostly in the form of frequencies and appear in either tabular or graphic form. A test of association was conducted utilising a Pearson chi-square with $p < 0.05$. Bivariate analysis is used to present relevant data where applicable and appropriate. A total of 443 questionnaires were distributed – 83 via electronic distribution and 360 via manual distribution. Of these, only 233 responses were obtained, providing a sample response rate of 52.59%.

4.2. DEMOGRAPHICS

A total of 233 HCPs completed the questionnaire. The majority of participants were registered nurses, and approximately a fifth were pharmacists. Table 4.1 elaborates on the demographics of the participants.

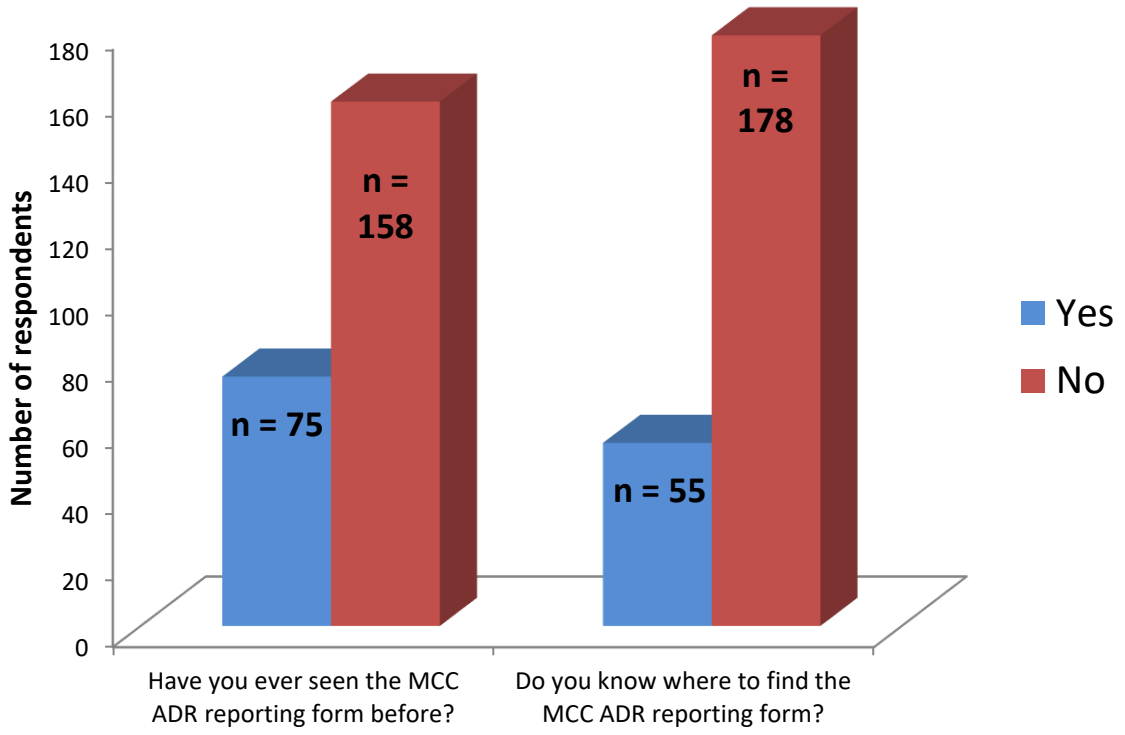
Table 4.1: Frequency distribution of demographic characteristics (N = 233)

Demographic Characteristics	Frequency (N)	Percentage (%)
Profession		
Registered Nurse	183	78.5%
Hospital Pharmacist	50	21.5%
TOTAL	**233**	**100%**
Gender		
Male	23	9.9%
Female	210	90.1%
TOTAL	**233**	**100%**
Age		
18 – 29 years old	49	21.0%
30 – 39 years old	71	30.5%
40 – 49 years old	61	26.2%

50 years and older	52	22.3%
TOTAL	**233**	**100%**
Years of experience		
Less than 1 year	17	7.3%
1 – 5 years	42	18.0%
5 – 10 years	63	27.0%
Longer than 10 years	111	47.6%
TOTAL	**233**	**100%**

4.3. KNOWLEDGE

Figure 4.1. Participants' Knowledge of ADR Reporting Form



Only 32.19% of participants had previously seen the ADR reporting form, while 76.39% did not know where it was located. Of those that had previously seen the form before, 60% knew where it could be located. Only 6.3% of participants that had not seen the form before knew where it could be found. Table 4.2 (a - b) elaborates on the difference in knowledge between pharmacists and nurses.

Table 4.2. Participants' Knowledge of ADR Reporting Form: (a) Have previously seen the MCC ADR form; (b) Know where to find MCC ADR form

(a) Seen MCC ADR form	Nurses N (expected cell total) [chi-square statistic)	Pharmacists N (expected cell total) [chi-square statistic)	Total N (%)
Yes	40 (58.91) [6.07]	35 (16.09) [22.21]	**75 (32.18%)**
No	143 (124.09) [2.88]	15 (33.91) [10.54]	**158 (67.81%)**
Total	183	50	**233 (100.00%)**

Chi-square = 41.6973; DF = 1; p = 1.066^{-10}

Therefore, the result is extremely significant at p < 0.05

(b) Know where to find MCC ADR form	Nurses N (expected cell total) [chi-square statistic)	Pharmacists N (expected cell total) [chi-square statistic)	Total N (%)
Yes	21 (43.2) [11.41]	34 (11.8) [41.75]	**55 (23.61%)**
No	162 (139.8) [3.52]	16 (38.2) [12.9]	**178 (76.39%)**
Total	183	50	**233 (100.00%)**

Chi-square = 69.5776; DF = 1; p = 7.346^{-17}

Therefore, the result is extremely significant at p < 0.05

Over three quarters of participants had never received any type of pharmacovigilance or ADR reporting training (Table 4.3). Of those that had, 17 were pharmacists and 37 were nurses.

Table 4.3: Previous pharmacovigilance/ADR reporting training received (N = 233)

Pharmacovigilance Training Received	Nurses N (expected cell total) [chi-square statistic)	Pharmacists N (expected cell total) [chi-square statistic)	Total N (%)
Yes	37 (42.41) [0.69]	17 (11.59) [2.53]	**54 (23.18%)**
No	146 (140.59) [0.21]	33 (38.41) [0.76]	**179 (76.82%)**
Total	183	50	**233 (100.00%)**

Chi-square = 4.1891; DF = 1; p = 0.040685

Therefore, the result is significant at p < 0.05

Over half of the participants did not know the process to follow when submitting an ADR report (Table 4.4). Despite the form being titled the MCC ADR reporting form, approximately a quarter of participants stated that reports should be submitted to the MCC (Table 4.6 and 4.7).

Table 4.4. Participant's knowledge regarding how to fill out and submit an ADR report form

Variable	Frequency (N)	Percentage (%)
Mark the statement that applies to you:		
I know how to fill out and submit an ADR reporting form	69	29.6%
My manager deals with all ADR reports	37	15.9%
I don't know the process to follow	127	54.5%
TOTAL	**233**	**100%**

Table 4.5. Relationship between previous PV training and knowledge regarding filling out and submission of ADR report form

Pharmacovigilance Training Received	I don't know the process to follow N (expected cell total) [chi-square statistic)	I know how to fill out and submit an ADR reporting form N (expected cell total) [chi-square statistic)	My manager deals with all ADR reports N (expected cell total) [chi-square statistic)	Total N (%)
Yes	15 (29.43) [7.08]	32 (15.99) [16.03]	7 (8.58) [0.29]	**54 (23.18%)**
No	112 (97.57) [2.14]	37 (53.01) [4.83]	30 (28.42) [0.09]	**179 (76.82%)**
Total	127	69	37	**233**

Chi-square = 30.45; DF = 2; p = 2.442^{-7}

Therefore, the result is extremely significant at p < 0.05

Table 4.6 presents deceptive results as participants were able to mark more than one option when asked where ADR reports are submitted. In reality, participants are very uncertain as to where reports are submitted as depicted in Table 4.7.

Table 4.6. Participant's knowledge regarding submission of ADR report form

Variable	Frequency (N)	Percentage (%)
ADR reports are submitted to:		
Pharmacy Manager	91	39.1%
Nursing Manager	55	23.6%
Hospital Manager	7	3.0%
Head Office	20	8.6%
Medicines Control Council (MCC)	62	26.6%
National Adverse Drug Event Monitoring Center (NADEMC)	39	16.7%
I don't know	109	46.8%
TOTAL	**233**	**100%**

When asked whether the respondent believes their respective hospital submits sufficient and/or appropriate ADR reports, 78.7% said they did not know. Only 4.3% of respondents indicated that they think their hospital submits appropriate ADR reports while 17.6% said they do not believe so.

Table 4.7. Participant's knowledge regarding submission of ADR report form (expanded)

Variable	Frequency (N)	Percentage (%)
ADR reports are submitted to:		
Pharmacy Manager	28	12.0%
Nursing Manager	12	5.2%
Hospital Manager	0	0.0%
Head Office	1	0.4%
Medicines Control Council (MCC)	8	3.4%
National Adverse Drug Event Monitoring Center (NADEMC)	6	2.6%
I don't know	96	41.2%
Pharmacy Manager; Head Office; MCC	4	1.7%
Pharmacy Manager; Head Office; MCC; NADEMC	2	0.9%
Pharmacy Manager; MCC	8	3.4%
Pharmacy Manager; MCC; I don't know	3	1.3%
Pharmacy Manager; MCC; NADEMC	8	3.4%

Pharmacy Manager; MCC; NADEMC; I don't know	1	0.4%
Pharmacy Manager; NADEMC	3	1.3%
Pharmacy Manager; Nursing Manager	8	3.4%
Pharmacy Manager; Nursing Manager; Head Office	3	1.3%
Pharmacy Manager; Nursing Manager; Head Office; MCC	2	0.9%
Pharmacy Manager; Nursing Manager; Head Office; MCC; NADEMC	1	0.4%
Pharmacy Manager; Nursing Manager; Hospital Manager	2	0.9%
Pharmacy Manager; Nursing Manager; Hospital Manager; Head Office; MCC; NADEMC	5	2.1%
Pharmacy Manager; Nursing Manager; I don't know	2	0.9%
Pharmacy Manager; Nursing Manager; MCC	8	3.4%
Pharmacy Manager; Nursing Manager; MCC; NADEMC	2	0.9%
Pharmacy Manager; Nursing Manager; NADEMC	1	0.4%
Head Office; MCC	2	0.9%
MCC; I don't know	1	0.4%
MCC; NADEMC	7	3.0%
Nursing Manager; I don't know	6	2.6%
Nursing Manager; NADEMC	3	1.3%
TOTAL	**233**	**100%**

4.4. ATTITUDE

In total, three quarters of respondents thought that reporting ADRs was very important (Table 4.8). Opinions between nurses and pharmacists were similar with the exception of 3 nurses believing ADR reporting to be not important. The difference in opinion between nurses and pharmacists can be seen in Table 4.8, and experience-related difference in opinion is presented in Table 4.9.

Table 4.8. Importance placed on ADR reporting: Nurses vs. Pharmacists N (%)

Importance Placed	Nurses N (%)	Pharmacists N (%)	Total N (%)
Very Important	133 (72.60%)	44 (88.0%)	**177 (75.96%)**
Important	47 (25.68%)	6 (22.0%)	**53 (22.75%)**
Not Important	3 (1.64%)	0 (0.0%)	**3 (1.28%)**
Total	183	50	**233 (100.0%)**

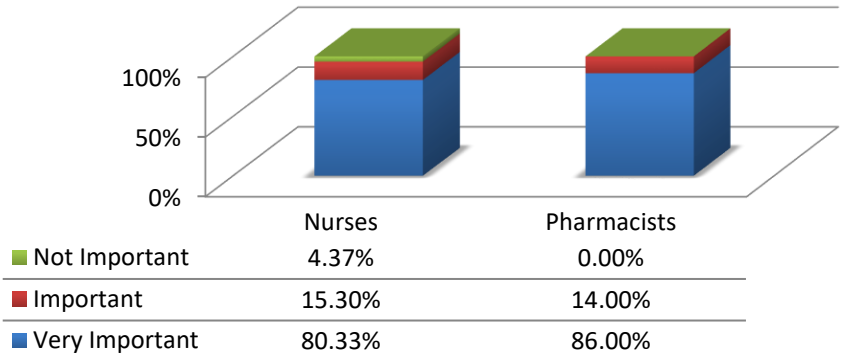
Table 4.9. Importance placed on ADR reporting: Experience related N (%)

Importance Placed	Less than 1 year N (%)	1 – 5 years N (%)	5 – 10 years N (%)	More than 10 years N (%)	Total N (%)
Very Important	17 (100%)	27 (64.3%)	47 (74.6%)	86 (77.5%)	**177 (75.9%)**
Important	0 (0%)	15 (35.7%)	16 (25.4%)	22 (19.8%)	**53 (22.7%)**
Not Important	0 (0%)	0 (0%)	0 (0%)	3 (2.7%)	**3 (1.3%)**
Total	17	42	63	111	**233**

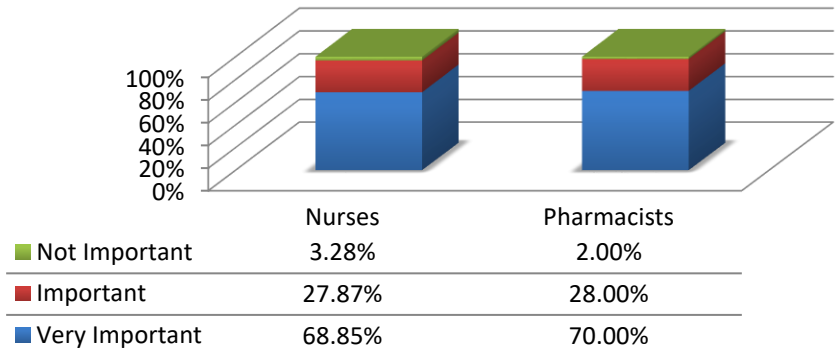
Further opinions regarding the importance of different elements of ADR reporting are presented in Figure 4.2 (a – f) below.

Figure 4.2. Differences in attitude of nurses and pharmacists towards varying elements of ADR reporting

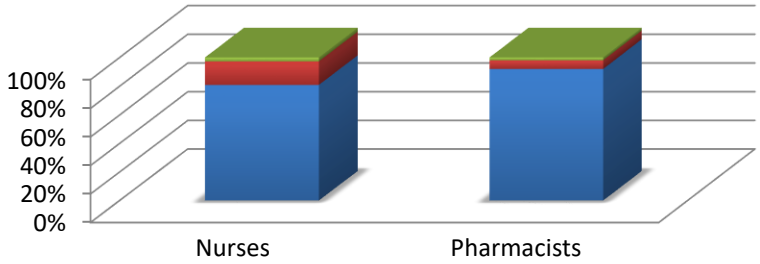
a) I think it is important to report ADRs to identify new ADRs



b) I think it is important to report ADRs to share information about ADRs with colleagues

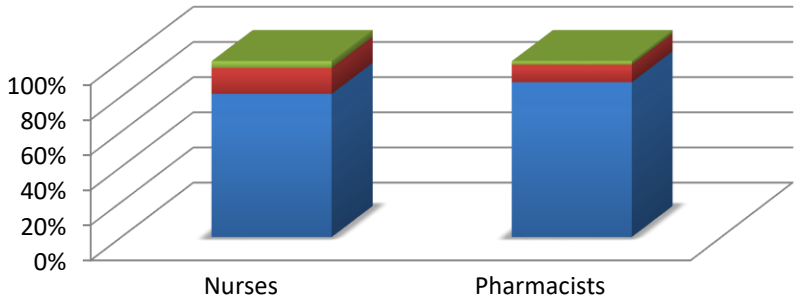


c) I think it is important to report ADRs to improve patient safety



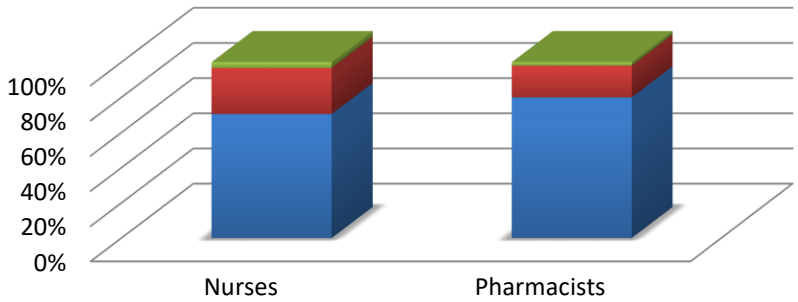
	Nurses	Pharmacists
Not Important	2.73%	2.00%
Important	16.39%	6.00%
Very Important	80.87%	92.00%

d) I think it is important to report ADRs to help establish the safety of new drugs



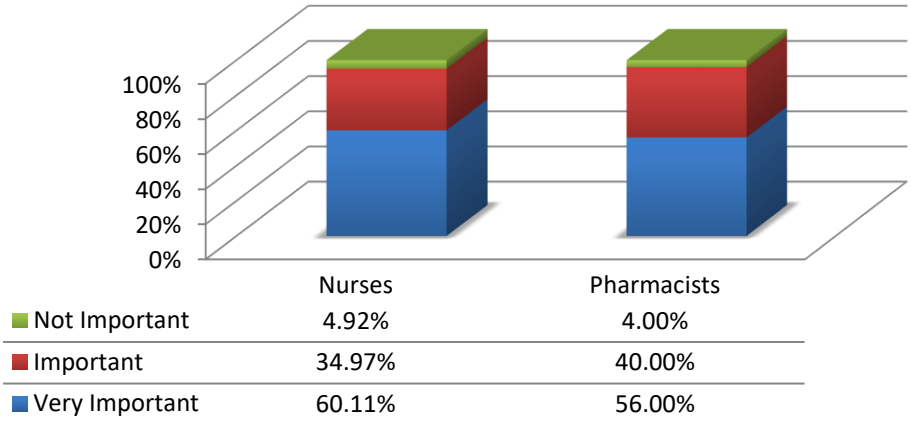
	Nurses	Pharmacists
Not Important	3.83%	2.00%
Important	14.75%	10.00%
Very Important	81.42%	88.00%

e) I think it is important to report ADRs to measure the incidence or frequency of ADRs



	Nurses	Pharmacists
Not Important	3.28%	2.00%
Important	26.23%	18.00%
Very Important	70.49%	80.00%

f) I think it is important to report ADRs because it is a legal requirement



	Nurses	Pharmacists
Not Important	4.92%	4.00%
Important	34.97%	40.00%
Very Important	60.11%	56.00%

When asked which type of ADRs should be reported, most respondents thought that ADRs to all types of drugs should be reported. Only 22.3% believe that ADRs to new drugs should be reported (Table 4.10).

Table 4.10. Which type of ADRs should be reported: Nurses vs Pharmacists

Type of ADR	Nurses N	Pharmacists N	Total N (%)
None	1	0	**1 (0.4%)**
All ADRs	169	34	**203 (87.1%)**
All serious ADRs (causing death or serious injury)	47	27	**74 (31.8%)**
ADRs to medical devices (such as pacemakers, prosthetics, etc)	24	19	**43 (18.5%)**
ADRs to new drugs	28	24	**52 (22.3%)**
ADRs to herbal, natural or traditional medicines	18	12	**30 (12.9%)**

Two respondents (both pharmacists) provided the following comments regarding which ADRs should be reported:

- *"All ADRs necessitating change of therapy."*
- *"ADRs not specified on package insert."*

Table 4.11 below presents the suggestions from HCPs regarding how to improve reporting in their hospitals.

Table 4.11. Suggestions on how the culture of reporting can be improved

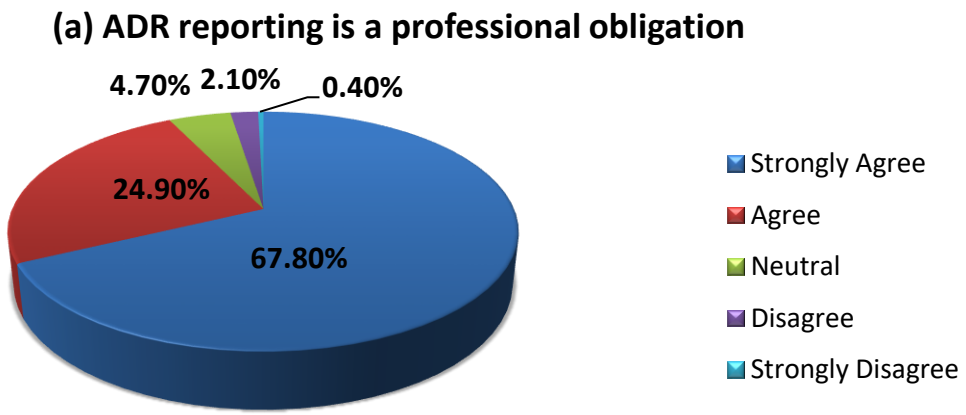
Suggestion	Number N	Percentage %
ADR reporting made mandatory (i.e. will affect my monthly performance)	40	17.2%
Workshops and seminars	130	55.8%
Pharmacovigilance teaching programmes for undergraduates, interns and postgraduates	94	40.3%
Monthly meetings discussing common ADRs that may be encountered	122	52.4%
Bring out bulletins/newsletters on ADRs	104	44.6%
Getting paid a sum of money for each ADR reported	12	5.2%
Other	4	1.7%

Four participants provided additional comments regarding how to improve ADR reporting at their hospitals:

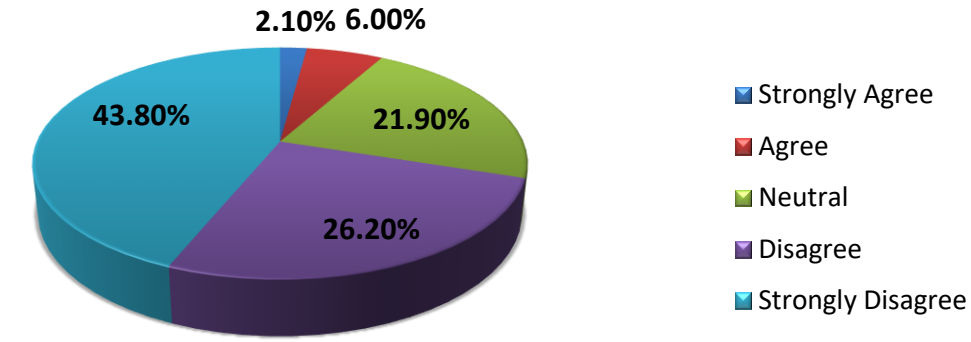
- *"When is a reaction an ADR. How to identify and determine when to report"*
- *"Online reporting"*
- *"Electronic submission process with instant feedback on status of the ADR reported"*
- *"Access of ADR forms"*

Participants were provided with a number of general statements regarding their attitudes towards ADR reporting and asked to rate them on a scale of 1 to 5, with 1 being "Strongly Agree" and 5 being "Strongly Disagree". The results are depicted in Figure 4.3 (a) – (d) below.

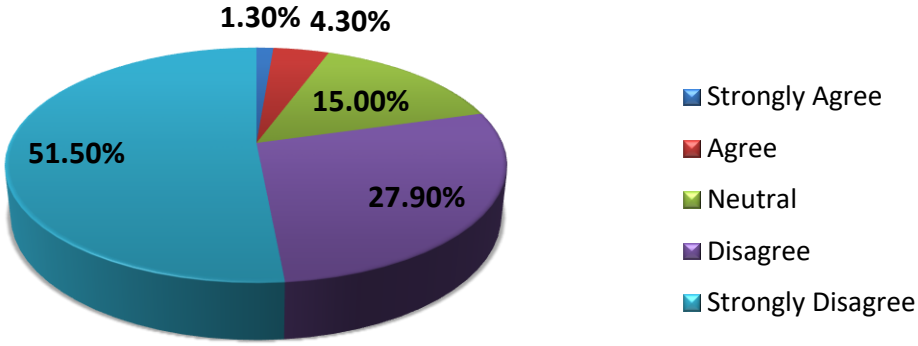
Figure 4.3. General attitudes of participants towards ADR reporting



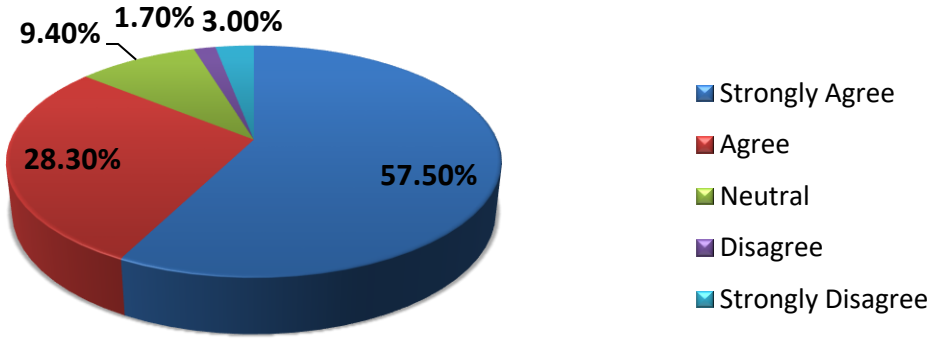
(b) ADR reporting adds up to unnecessary workload



(c) Nobody really benefits if I report an ADR



(d) I would like to receive more training on ADR reporting



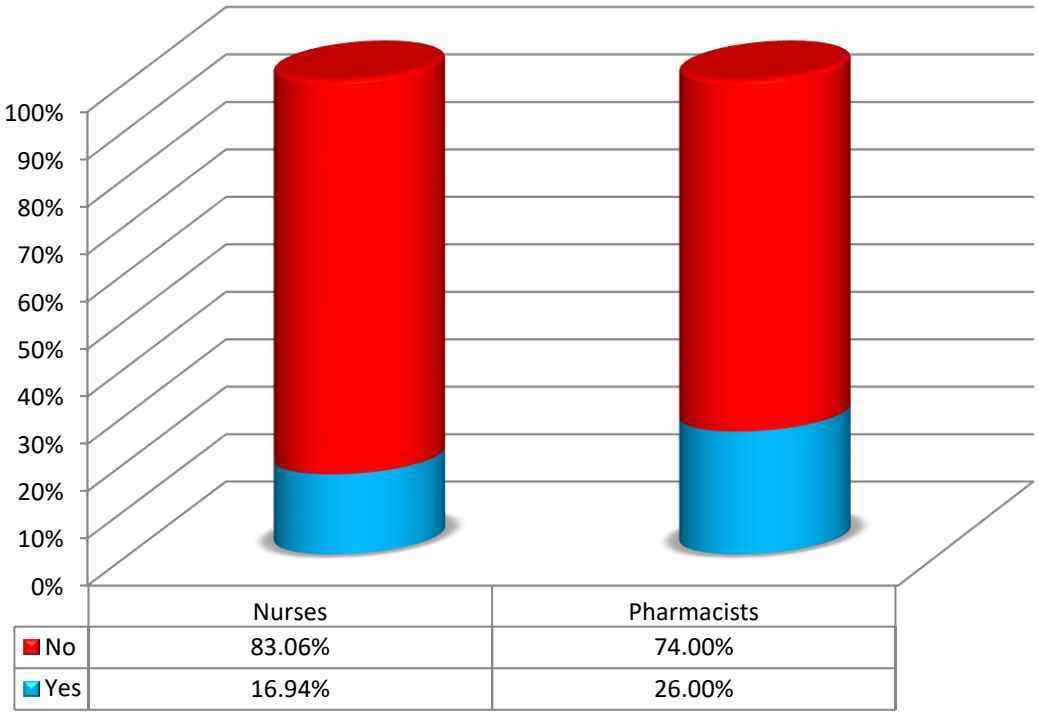
4.5. PRACTICE

Only 18.9% of participants (i.e. N = 44) stated that they had previously reported an ADR. Of these, 13 respondents were pharmacists and 31 were nurses (Figure 4.4).

When the participants were asked whether they had previously encountered an ADR and failed to report it, 13.7% of the total had indicated yes. Approximately two-thirds had marked no. The remaining 22.3% stated that they didn't know, i.e. they were not sure if they had ever encountered an ADR.

The majority of participants (75.5%) stated that they would most likely report all ADRs they encounter (Figure 4.5).

Figure 4.4. Percentage of participants that have reported an ADR: Nurses vs Pharmacists (N = 233)



Those that had previously received PV training were more likely to have reported an ADR in the past with a statistically significant result as per Table 4.12

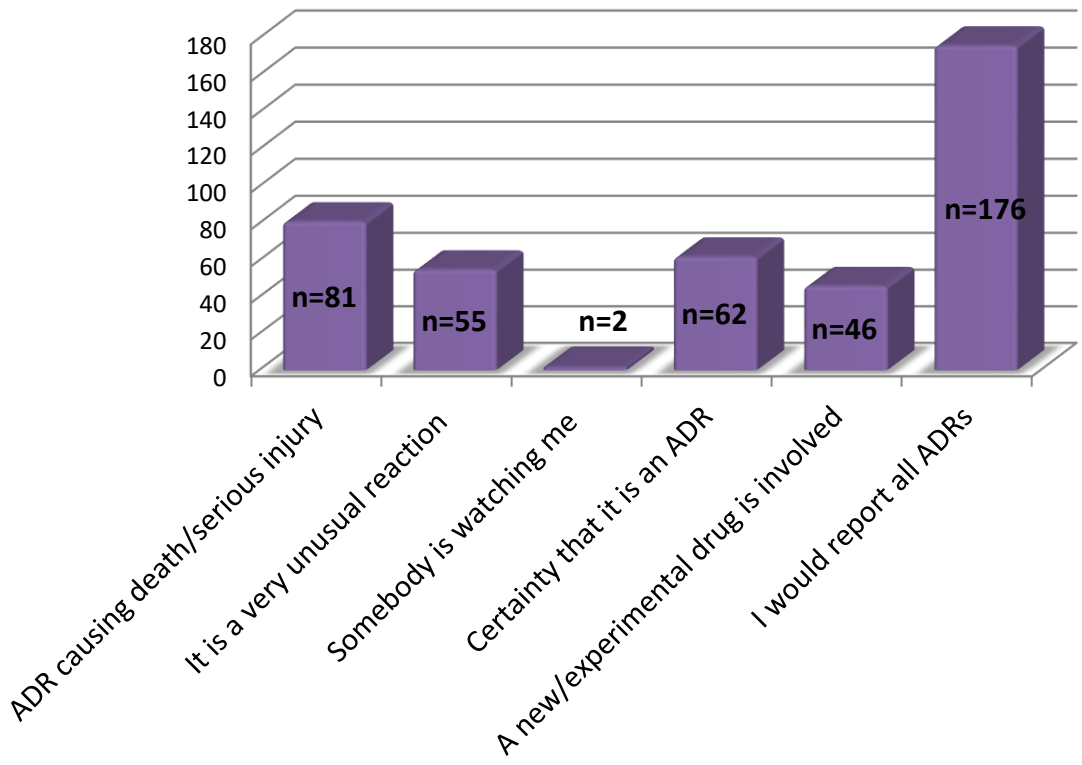
Table 4.12: Previous pharmacovigilance/ADR reporting training received vs. Likelihood of having reported an ADR in the past (N = 233)

Previous PV training received	Have reported an ADR before N (expected cell total) [chi-square statistic)	Have not reported an ADR before N (expected cell total) [chi-square statistic)	Total
Yes	19 (10.2) [7.6]	35 (43.8) [1.77]	**54 (23.2%)**
No	25 (33.8) [2.29]	154 (145.2) [0.53]	**179 (76.8%)**
Total	44	189	**233**

Chi-square = 12.1934; DF = 1; p = 0.00048

Therefore, the result is significant at p < 0.05

Figure 4.5. Likelihood that participants would report an ADR



There were a number of factors that participants stated discouraged them from reporting ADRs. The frequency of these factors varied greatly, and is summarised below in Table 4.13. In addition to the predefined factors, a number of comments were provided by participants (summarised below):

- *"Certainty as adverse reactions could be as a result of other factors not the treatment. It is difficult to know when a reaction is an ADR versus from some other cause"*

- *"Have not been in that situation yet"*

- *"Don't know how to tell if ADR"*

- *"None because I have no experience with doing such"*

- *"Lack of training regarding reporting the ADR"*

- *"This is my first time seeing the ADR form"*

- *"Not knowing what an ADR is"*

- *"No internal process for ADR"*

- *"Not sure if it might be an allergic reaction that the patient did not know"*

Table 4.13. Factors that might discourage HCPs from reporting ADRs

Factors	N (%)
Do not know how to report	108 (46.4%)
Do not know where to report	81 (34.8%)
Did not think it was important to report	18 (7.7%)
Managing the patient was more important than reporting the ADR	27 (11.6%)
Lack of access to ADR reporting form	80 (34.3%)
Patient confidentiality might be breached	10 (4.3%)
Legal liability issues	6 (2.6%)
The form is too long	19 (8.2%)
I don't receive any feedback once the form has been sent	32 (13.7%)
Other (summarised in comments above)	17 (7.3%)

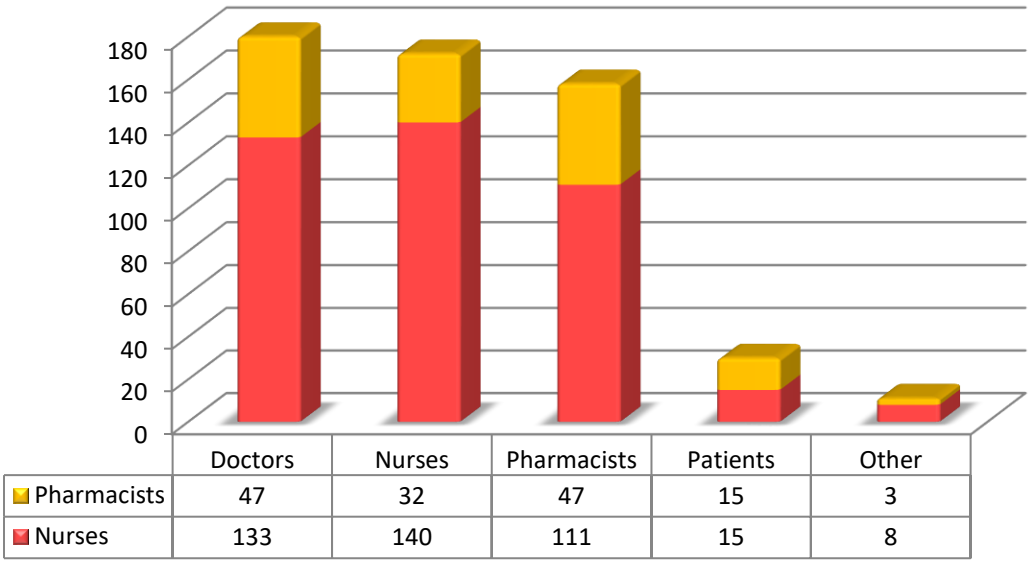
Table 4.14.highlights the discouraging factors between participants that claimed to have reported an ADR in the past versus those that had not.

Table 4.14. Discouraging factors for ADR reporting vs have previously reported an ADR

Factor	Have previously reported an ADR (%)	Have not previously reported an ADR (%)
Do not know how to report	31.8	50.3
Do not know where to report	18.2	38.6
Did not think it was important to report	20.5	8.9
Managing the patient was more important than reporting the ADR	18.2	13.8
Lack of access to ADR reporting form	40.9	33.3
Patient confidentiality might be breached	2.3	4.8
Legal liability issues	0	3.2
The form is too long	13.6	6.9
I don't receive any feedback once the form has been sent	40.9	7.4

Participants also had an opportunity to indicate who they believe should be responsible for reporting/submitting ADR reports (Figure 4.6). A small portion of participants (4.7%), in addition to marking the boxes for doctors, nurses and pharmacists, marked the box for "Other" to state that they believe all HCPs should be responsible for reporting ADRs. One participant aptly stated, *"...All the above professionals because they prescribe, dispense and administer these drugs to patients*".

Figure 4.6. People deemed responsible by the participants for reporting ADRs



	Doctors	Nurses	Pharmacists	Patients	Other
Pharmacists	47	32	47	15	3
Nurses	133	140	111	15	8

4.6 DESCRIPTIVE STATISTICS

Data was coded according to a "most correct" or "most preferred" principle. Only thirteen questions were coded in this way due to the nature of the questions. The questions that were excluded included questions regarding participant demographics and questions of a personal and opinionated nature where there could be no "most correct" answer. Table 4.15 elaborates on the coding method used for selected questions

Table 4.15. Coding used for descriptive statistics per question (selected questions used for analysis)

Question	Variable Coding
Have you ever received any pharmacovigilance or ADR reporting training?	**Yes – 1** **No - 0**
Have you ever seen the MCC ADR reporting form before? Please refer to the below form.	**Yes – 1** **No - 0**
Do you know where to find the MCC ADR reporting form?	**Yes – 1** **No – 0**
How important do you think it is to report ADRs?	**Very important – 2** **Important – 1** **Not Important – 0**

I think it is important to report ADRs to identify new ADRS	*(graded according to scale of 1 – 5 present on questionnaire)*
I think it is important to report ADRs to share information about ADRs with colleagues	*(graded according to scale of 1 – 5 present on questionnaire)*
I think it is important to report ADRs to improve patient safety	*(graded according to scale of 1 – 3 present on questionnaire)*
I think it is important to report ADRs to help establish the safety of new drug	*(graded according to scale of 1 – 3 present on questionnaire)*
I think it is important to report ADRs to measure the incidence or frequency of ADRs **I think it is important to report ADRs because it is a legal requirement**	*(graded according to scale of 1 – 3 present on questionnaire)* *(graded according to scale of 1 – 3 present on questionnaire)*
In your view, which ADRs should be reported?	**Answers containing "All ADRs" – 5** **Answers containing "All serious ADRs" – 4** **Other answers – 3** **None - 0**
Have you ever reported an ADR?	**Yes – 1** **No – 0**
Have you ever encountered an ADR and not reported it?	**No – 2** **I don't know – 1** **Yes – 0**
Please mark the statement(s) that apply to you regarding the process to follow when reporting an ADR:	**I know how to fill out an ADR report form – 2** **My manager deals with all ADR reports – 1** **I don't know the process to follow – 0**
ADR reports are submitted to:	**Answers containing "MCC" or "NADEMC" – 3** **Answers containing "Pharmacy Manager" or "Nursing Manager" – 2** **Answers containing "Hospital Manager" or "Head Office" – 1** **I don't know – 0**
In your opinion, which of these people should be responsible for reporting ADRs?	**All healthcare professionals – 3** **Singular answers – doctors, nurses or pharmacists – 2** **Patients – 1**
Do you think that your hospital submits sufficient and appropriate ADR reports?	**Yes – 2** **No – 2** **I don't know – 1**

ADR reporting is a professional obligation	*(graded according to scale of 1 – 5 present on questionnaire)*
ADR reporting adds up to unnecessary workload	*(graded according to scale of 1 – 5 present on questionnaire)*
Nobody really benefits if I report an ADR	*(graded according to scale of 1 – 5 present on questionnaire)*
I would like to receive more training on ADR reporting	*(graded according to scale of 1 – 5 present on questionnaire)*

The overall mean scores between both nurses and pharmacists were similar. However, a larger difference between the minimum and maximum scores was observed amongst nurses than pharmacists, although participants in the nursing group had the highest score. Questions utilised for coding included the assessment of knowledge, attitudes and practices of participants.

Table 4.16. Descriptive Statistics - overall

	N	Mean	Standard deviation	Standard error	95% confidence interval from mean		Minimum	Maximum
					Lower bound	Upper bound		
Nurses	183	39.44	4.43	0.33	38.79	40.09	26	51
Pharmacists	50	41.94	3.41	0.49	40.97	42.91	36	49
Total	233	39.96	4.33	0.28	39.40	40.52	26	51

Pharmacists had a better overall mean score in respect of knowledge questions (Table 4.17). This is consistent with other knowledge-related results presented above. Interestingly, the minimum and maximum scores for both nurses and pharmacists were the same.

With respect to attitude related questions, nurses actually scored higher than pharmacists did (Table 4.18). This can imply that nurses hold an overall more positive view towards ADR reporting than pharmacists.

The scores relating to practice relate questions were similar for both nurses and pharmacists. While there was a larger standard deviation seen amongst the pharmacists, improvement in this area would be valuable.

Table 4.17. Descriptive Statistics:Knowledge-related questions

	N	Mean	Standard deviation	Standard error	95% confidence interval from mean		Minimum	Maximum
					Lower bound	Upper bound		
Nurses	183	3.54	2.36	0.17	3.20	3.88	1	10
Pharmacists	50	6.86	2.84	0.40	6.05	7.67	1	10
Total	233	4.25	2.82	0.18	3.89	4.61	1	10

Table 4.18. Descriptive Statistics: Attitude-related questions

	N	Mean	Standard deviation	Standard error	95% confidence interval from mean		Minimum	Maximum
					Lower bound	Upper bound		
Nurses	183	31.72	3.06	0.23	31.27	32.17	21	40
Pharmacists	50	30.72	2.29	0.32	30.07	31.37	26	35
Total	233	31.51	2.94	0.19	31.13	31.89	21	40

Table 4.19. Descriptive Statistics: Practice-related questions

	N	Mean	Standard deviation	Standard error	95% confidence interval from mean		Minimum	Maximum
					Lower bound	Upper bound		
Nurses	183	4.16	1.01	0.07	4.01	4.31	2	6
Pharmacists	50	4.38	1.09	0.15	4.07	4.69	2	6
Total	233	4.21	1.03	0.07	4.08	4.34	2	6

CHAPTER 5

DISCUSSION

5.1. INTRODUCTION

This chapter will discuss the results obtained in the context of the study and make appropriate recommendations accordingly. It will compare results with similar studies conducted both in South Africa and internationally in order to place the study in both a local and global context. This chapter will also highlight the deficits in the knowledge, attitude and practices of HCPs in the private sector and discuss measures to improve on these deficits.

5.2. DEMOGRAPHICS

A total of 443 questionnaires were distributed – 83 via electronic distribution and 360 via manual distribution. Of these, only 233 total responses were obtained, providing a sample response rate of 52.59%. This is a lower response rate than was achieved in other similar studies (61% in India, 58.8% in Japan, 68.9% in South Africa) (Desai et al, 2011; Obara et al, 2016; Joubert& Naidoo, 2016)

The majority of participants were registered nurses (78.5%). This corresponds to statistics provided by Econex on behalf of the South African Private Practitioners Forum (SAPPF) and Healthman (Pty) Ltd, The South African Private Healthcare Sector: Role and Contribution to the Economy whereby an estimated 77 569 nurses and 2 984 pharmacists were working within the South African private sector, as at 2013 statistics (Econex, 2013).

Further, 90.1% of participants were female compared to 9.9% of participants who were male. This is consistent with South African Nursing Council Statistics for 2016 where the female to male ratio is approximately 10:1 (SANC, 2016). Although the South African Pharmacy Council statistics for 2016 provides a lower ratio of females to males at approximately 1.5:1, the lower number of pharmacists included in this study aptly contributes to the overall number of male and female participants (SAPC, 2016).

The age distribution of participants was roughly equal with the larger proportion of participants being 40 years and older, and just under half of participants were younger than 40 years old. Approximately half of the participants had been practicing for over 10 years, whereas only 7.3% had been practicing for less than a year with the majority of these being nurses. The small number of newly qualified nurses might be attributed to a finding by Armstrong and Rispel in 2015 that over the last few years, nursing as a profession has

become less attractive. It has become to be perceived as a job, rather than a vocation, with long and inflexible working hours, increased service demands, and poor salaries, thus reducing the number of students eager to study nursing (Armstrong and Rispel, 2015).

5.3. KNOWLEDGE

Approximately three quarters of participants had never received any PV training (*Table 4.3*). This finding is similar to one in Nigeria where only a third of participants in a similar study had undergone any PV training (Osakwe et al, 2013). A larger proportion of pharmacists than nurses have previously received PV or ADR reporting training, with a statistically significant result at $p < 0.05$. This result is as expected due to the fact that pharmacists are exposed more often to concepts such as ADRs and medication management by virtue of their profession. During their undergraduate degrees, pharmacists in South Africa are exposed to between three and four years of pharmacy practice training – focusing on legal and regulatory aspects of pharmacy amongst other things – and between two and three years of pharmacology – focusing on how medicines function in the body, including toxicities (sourced from the Bachelor of Pharmacy curricula of Rhodes University, University of Witwatersrand, Nelson Mandela Metropolitan University and University of Western Cape). To compare with a country with a higher ADR reporting rate than South Africa, such as the United States (77/million population in 2011 in South Africa vs. 2803/million population in 2011 in USA (Maigetter et al, 2015; FDA, 2015)), pharmacist training is more or less equivalent regarding the number of years spent on pharmacology and pharmacy practice (sourced from PharmD curricula of the University of Southern Carolina, Ernest Mario School of Pharmacy, University of California San Francisco, and University of Maryland).

In contrast, nurses in South Africa are typically exposed to only one year of pharmacology during their undergraduate training, with an additional focus on legal and regulatory aspects relevant to the nursing profession (sourced from the Bachelor of Nursing curricula of University of KwaZulu Natal, University of Witwatersrand, University of Pretoria and Nelson Mandela Metropolitan University). Nursing training will differ vastly from pharmacy training due to the vastly different fields and focuses, each with their own importance and roles in patient care.

However, to have three quarters of participants in this study having received no PV training during their careers can be viewed as problematic. The population of patients seen in hospitals is often vulnerable and prone to the development of ADRs due to the polypharmacy often used. As illustrated by Mouton and colleagues in 2015 that ADRs contributed to the deaths of 2.9% of hospital admissions and 16% of total deaths in four South African hospitals (Mouton et al, 2015). By virtue of the type of patient presenting in a

hospital, a rudimental understanding of PV might be beneficial to these patients and to the general community as a whole.

Interestingly, the number of years of experience of the respondent doesn't present a statistically significant difference in whether any previous training has been received, but rather, the age of the participant seemed to have significance. While there is no clear trend dependent on age, respondents aged 50 years and older had a proportionally larger exposure (42.30%) to PV training. This could be intuitively attributed to simply having been in practice for a longer period of time than other respondents, however the correlation has proved to be statistically insignificant. This finding is similar to those of other studies assessing the knowledge, attitudes and practices of health care workers such as Palaian et al (2011). Other similar studies did not explore the relationship between age/number of years of experience and previous PV training. However, analysis done by Osakwe and colleagues in Nigeria found a positive relationship between previous PV training received and PV knowledge and practices. Those that had undergone PV training scored higher than those that had not in knowledge and practice (Osakwe et al, 2013).

Table 5.1. Effect of training on knowledge scores of pharmacovigilance (Osakwe et al, 2013)

Received PV Training	Good (%)	Fair (%)	Poor (%)
Yes	48.9%	18.1%	33.0%
No	17.0%	15.4%	67.6%

Table 5.2. Effect of training on practice of pharmacovigilance (Osakwe et al, 2013)

Received PV Training	Good (%)	Fair (%)	Poor (%)
Yes	26.6%	24.5%	48.9%
No	15.4%	11.3%	73.3%

Approximately a third of participants stated that they know how to fill out an ADR form (*Table 4.4*). This corresponds to the third of participants that stated that they had previously seen the ADR form (*Table 4.2*). A copy of the form was attached with the questionnaire for participants to refer. This finding has proven to be difficult to compare with other similar studies as other studies seem to assume that the HCPs they are surveying have a base knowledge of the ADR form.

Participants that had previously undergone some kind of PV training were much more likely to know the process to follow when submitting an ADR with an extremely statistically significant p-value (*Table 4.5*). They were also more likely to have had reported an ADR in the past (*Table 4.12*). This finding is supported by numerous other sources that conclude that PV training increases the likelihood that HCPs will participate in PV activities such as ADR reporting (Zolezzi&Parsotam, 2005; Kulkarni et al, 2013).

There were a small number of participants (8.5%) that had never seen the ADR form before yet marked that they knew how to complete the form. This might be attributed to the structure of the form. Bandekar and colleagues performed a review in 2010 on ADR forms from numerous countries and compiled a list of 18 points that should be present on an ADR form for it to be considered sufficient to collect data and efficient for use. ADR forms used in South Africa contain 12 of these points determined by Bandekar and colleagues (Bandekar et al, 2010). This implies that the MCC ADR form is sufficiently user-friendly, such that even a HCP that has never seen it before can complete it, and that it asks the HCP sufficient information that is readily available to them.

Table 5.3. Assessment of South Africa's ADR reporting form (Bandekar et al, 2010)

Contents	South African ADR form
Patient Information	Yes
Pregnancy Status	No
Allergic Status	Yes
Diagnosis	Yes
Description of Reaction	Yes (little space)
List of Suspected Drugs	Yes (six drugs including concomitant medication)
Dose, Frequency of Drugs	Yes
Space for concomitant drugs	Yes (no separate space available but is included in suspected drug column)
Start Date and Stop Date of Suspected Drugs	Yes
Relevant History of Patient	Yes
Actions Taken	No
Severity	No
Causality	No
Outcome	Yes

Dechallenge	No
Rechallenge	Yes
Treatment of ADR	Yes
Lot No., Expiration Date	No

The majority of participants stated that they did not know where the ADR form should be submitted. Despite the form being titled as the MCC ADR form, only about a quarter of participants noted that the form should be submitted to the MCC (Table 4.6). This finding is supported by numerous studies whereby HCPs are either completely unaware of a national PV centre/authority, or are aware of its existence but not of its location, purpose or function (Ganesan et al, 2016; Palaian et al, 2011; Irujo et al, 2007; Hanafi et al, 2012; Raza and Jamal, 2015). Joubert and Naidoo (2016) concluded in their study that pharmacists would like to see increased communication from local PV centres in South Africa. The pharmacists involved in their study viewed the PV centres as inaccessible with little to no personal contact (Joubert& Naidoo, 2016). However, there still appears to be a large amount of confusion regarding where ADR reports should be submitted as evidenced by Table 4.7. A large portion of participants in this study (approximately 40%) stated that forms should be submitted to the Pharmacy Manager. While not technically the correct response, it could be considered "most correct" as standard operating procedures (SOPs) in most institutions, including the hospitals used in this study, dictate that ADRs be reported to the Pharmacy Manager for further investigation and action. In many SOPs, it is the responsibility of the Pharmacy Manager to submit ADR reports to the medicines regulatory authority.

When asked whether the respondent believes their respective hospital submits sufficient and/or appropriate ADR reports, an overwhelming 78.1% said they did not know. This indicates that staff are largely not informed in such matters. Additionally this might indicate that there are insufficient processes in place for the handling of ADR reports. This is exemplified by a comment provided by a participant on another question, "*No internal process for ADR*". While there is an SOP for the management of ADRs within the hospital group in this study, it appears that there needs to be more awareness of it. In order to improve ADR practices in private institutions in South Africa, all HCPs should be aware and informed of the procedures for handling ADRs.

5.4. ATTITUDE

Overall, participants had a positive attitude towards ADR reporting, with most respondents considering ADR reporting, including varying elements of reporting, as important and very important. Only 3 nurses considered ADR reporting to be not important.

When asked which type of ADRs should be reported, most respondents thought that ADRs to all types of drugs should be reported. Only 22.3% believe that ADRs to new drugs should be reported. This is totally contradictory to findings in other studies conducted in developed countries where an overwhelming majority of HCPs believed ADRs to new products should be reported (99.3%, 90.4%, 91% respectively) (Green et al, 2001; Bateman et al, 1992; Belton et al, 1995). Conversely, HCPs in developing countries had a similar attitude to this study in that 34.2%, 7.7%, and 57.0% of HCPs surveyed respectively believed that ADRs to new drugs should be reported (Desai et al, 2011; Mulatu and Worku, 2014; Suyagh et al, 2015). This can be viewed as a problematic attitude as long-term harms to new drugs are often not known when they are first marketed. ADR observation and reporting should actually be considered a priority activity in the management of new drugs. 30 participants thought that ADRs to herbal, natural or traditional medicines should be reported. In South Africa, the total market for traditional medicines is estimated at approximately R 3 billion, with at least 27 million patients consuming traditional or herbal medicines annually (BMI, 2010). The contents of traditional and herbal medicines are often unknown, and in some instances contain potentially harmful ingredients (Isah et al, 2012).

Two respondents (both pharmacists) provided the following comments regarding which ADRs should be reported:

- *"All ADRs necessitating change of therapy"*
- *"ADRs not specified on the package insert"*

An important way to improve ADR reporting is to ask participants directly for suggestions on how to improve ADR reporting at their respective institutions. More than half of respondents say that workshops and seminars, monthly meetings, and publication of bulletins/newsletters would improve the ADR reporting culture. The responses indicate that HCPs would prefer "in-house" methods to improve ADR reporting at their institutions. In this way, each institution would be able to constantly remind their HCPs about ADRs and their management. A comment provided by a participant noted that training regarding identification of ADRs would be effective. This corresponds with the comments provided by participants for another question regarding the likelihood of reporting ADRs (Figure 4.5) that HCPs are simply unaware or not confident enough to make a decision as to what constitutes an ADR and what action they should take. This finding supports those obtained internationally that varying degrees of unfamiliarity with the reporting process remains one of the biggest hurdles to efficient reporting (Grootheest, 1999; Evans et al, 2002).

Additionally, several participants noted that online or electronic reporting would be effective to improve reporting rates. Many HCPs in all environments are often overwhelmed with paperwork and thus tend to shy away from any additional forms that might be regarded irrelevant to their immediate clinical needs (Rudd et al, 2010). Considering that many workplaces, including hospitals, are moving towards being a paperless environment, electronic forms could save HCPs time and energy in all areas of patient management (Kutney-Lee and Kelly, 2011).

5.5. PRACTICE

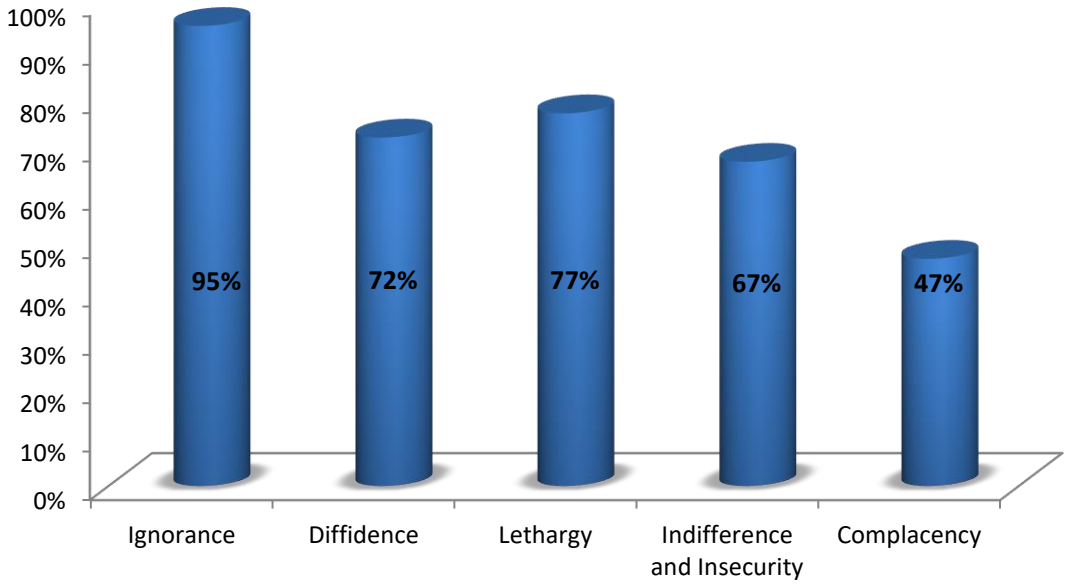
Only 44 participants (18.9%) have ever reported an ADR before. This figure is lower than in others reported in other similar findings: 33.7% in Nepal, 32.0% in Nigeria, 22.8% in China, 35.0% in the Netherlands, and 44.1% in a similar South African study (Palaian et al, 2011; Okezie, 2008; Li et al, 2004; Eland et al, 1999; Joubert& Naidoo, 2016). When the participants were asked whether they had previously encountered an ADR and failed to report it, 13.7% of the total had indicated yes. Approximately two-thirds had marked no, although this might have been attributed to the wording of the question, i.e. they had never encountered an ADR and therefore had not reported it. Regardless of how the question was perceived, it is almost impossible for such a large majority to state that they hadn't encountered an ADR, particularly being in a hospital environment. Simply by the nature of the drugs in use in a hospital setting, at least one ADR should have been encountered (e.g. morphine-induced constipation, or antibiotic-related diarrhoea and/or abdominal discomfort). The remaining 22.3% stated that they didn't know, i.e. they were not sure if they had ever encountered an ADR. In this respect, workshops that focus on common ADRs that may be encountered in a hospital setting might assist in reducing the uncertainty experienced by HCPs.

Older participants (aged 40 and older) were more likely than younger participants (aged 40 and younger) to have reported an ADR in the past (21.48% vs. 16.07%) and were more likely to know the ADR reporting process (35.54% vs. 23.21%). This corresponds to a similar study by Evans and colleagues (2006) whereby senior nurses had a higher degree of involvement in the ADR reporting process than their junior counterparts.

The majority of participants (75.5%) stated that they would most likely report all ADRs they encounter (*Figure 4.5*). Therefore, more effort to train these HCPs to report would be beneficial. If a similar intention to report all ADRs exists for the majority of HCPs, the process of reporting needs to be streamlined and made more efficient, as well as the provision of more integrated and intensive training regarding identifying and detecting ADRs.

There were a number of factors that participants stated discouraged them from reporting ADRs. The frequency of these factors varied greatly, and are summarised in Table 4.13. It is possible to surmise that the three biggest factors that prevent HCPs from reporting ADRs are not knowing how to report, not knowing where to report, and a lack of access to ADR forms. Most of the additional comments provided by participants exemplified the fact that HCPs are simply not educated and/or trained enough in the identification of an ADR. Admittedly, many ADRs might be quite subtle and difficult to distinguish from an actual clinical disease state. Sometimes it might be impossible to directly identify an ADR. In this respect, it is vital that all HCPs work together in order to utilize the expertise of all fields, i.e. clinical expertise of doctors, patient knowledge and care expertise of nurses, pharmaceutical knowledge of pharmacists. This is consistent with conclusions drawn by Lopez-Gonzalez and team in a systematic review performed to identify the determinants of ADR underreporting.

Figure 5.1. Major factors contributing to underreporting ADRs: systematic review (Lopez-Gonzalez et al, 2009)



In this present study, participants mostly correctly identified the key role players in the ADR reporting process (doctors (77.2%); nurses (73.8%); pharmacists (67.8%) (*Figure 4.6*). However, only a small number (4.72%) thought that all HCPs are responsible for ADR reporting. This finding is supported by a similar study where only 8.8% of pharmacists correctly believed that all HCPs were role players in the ADR reporting process (Joubert& Naidoo, 2016). Hospital nurses have the potential to hold an important role in ADR detection and reporting because of their proximity to patients. They are unique in their position in drug

administration and the monitoring of responses to drugs, often acting as a messenger between patients and doctors and being responsible for alerting doctors to changes or differences in patients health state (Hanafi et al, 2012). 12.87% of participants (15 pharmacists and 15 nurses) in this study thought that patients should be responsible for reporting ADRs. In practical terms, patients are not always suitably qualified to report ADRs due to a lack of knowledge or awareness and therefore better communication between patients and HCPs needs to be encouraged. In a study in Lagos, Nigeria, over 40% of pharmacists stated that patients had reported an ADR to them in the preceding month, while only 20% of those pharmacists had reported the ADR (Oreagba et al, 2011). While HCPs have the main responsibility of reporting ADRs, patients have been permitted and should be encouraged to report ADRs in countries such as South Africa in order to increase reporting rates (Khalili et al, 2012; Roux, 2014).

5.6. LIMITATIONS

The major limitation of this study was that it was conducted only within a single hospital group. It is possible that other hospital groups within South Africa, indeed even individual hospitals, place a greater emphasis on PV and ADRs. However, by including agency nurses and locum pharmacists in the study, it was assumed that they would have been exposed to other environments with other practices. Additionally, because HCPs in South Africa are required to spend at least one year in a public sector institution performing community service, it was hoped that at least some respondents would have had PV exposure during this time and carried it over into private practice. Additionally, doctors and prescribers have been excluded from this study. This was unfortunately due to a lack of willingness to participate during piloting and other pre-distribution phases of the study, and therefore, the results could have been interpreted differently if they had been including as participants.

CHAPTER 6

CONCLUSION

6.1. INTRODUCTION

This chapter will conclude the dissertation by providing a brief summary of the results obtained in context of the research question. Further, it will provide recommendations based on the obtained results and provide some ideas for further study.

6.2. SUMMARY OF RESULTS

The knowledge of the participants of this study with respect to ADR reporting is inadequate. Regardless of their profession, the participants involved in this study did not provide satisfactory answers regarding the ADR reporting form and the processes involved with it, including who should be responsible for reporting. Largely it would appear that the primary reason for participants not knowing where the form must be submitted was that they had simply never seen the form before. However, the overall knowledge of participants regarding ADR reporting could be considered as acceptable considering that only approximately a quarter of participants had ever received any previous PV training.

However, the overall attitude of participants to ADR reporting was overall quite positive. Most participants believed ADR reporting to be an important function of their job, with many of these agreeing that it was a professional obligation. A small cause for concern was the type of drugs participants believed should be reported, with only a small percentage believing ADRs to new drugs should be reported. Regardless, most respondents agreed that ADRs to all types of drugs should be reported.

Participants provided useful suggestions as to how to increase the culture of reporting at their respective hospitals. Considering that many had received no previous PV training, a large number of participants suggested “in-house” methods of training such as workshops and seminars in order to familiarise themselves with both the identification of common ADRs as well as the process of ADR reporting.

Although the overall knowledge is inadequate while the overall attitudes are quite positive, the transition into practice needs to be improved. A small percentage of participants had previously reported an ADR before. The three biggest factors that prevent HCPs from reporting ADRs are not knowing how to report, not knowing where to report, and a lack of access to ADR forms. In the greater scheme of things, these are minor issues that can be

easily rectified. Most of the additional comments provided by participants exemplified the fact that HCPs are simply not educated and/or trained enough in the identification of an ADR.

6.3. RECOMMENDATIONS

The biggest conclusion drawn from this study is that participants are not sufficiently exposed to PV in their careers. Therefore, the most important recommendation to be made is to emphasise PV during undergraduate studies, and to ensure that hospital staff are provided with a continuous exposure to PV or ADR workshops/seminars/training sessions. Because PV is fast becoming an integral part of managed health care worldwide, it is important that South Africa not be left behind in this regard.

Additionally, one of the biggest factors that seemed to discourage participants from reporting was a lack of access to ADR reporting forms. In this respect, it is recommended that senior staff in the hospitals ensure that ADR forms are easily available and accessible for its health care professionals. It might be logical to assume that if health care professionals have greater access to the forms, they would be reporting more often, and vice versa.

Hospital environments can be stressful and fast paced environments. The realistic likelihood of a hospital worker completing a long form that they do not perceive as important to their immediate clinical needs is small. Therefore, an online or electronic platform for the submission of ADRs is recommended. It will drastically reduce the time and energy required to complete a report and hopefully will lead to increased numbers.

The final recommendation is to encourage greater cooperation and coordination between and amongst the medicine regulatory authorities and health care professionals. The MCC, NPC and other bodies involved with PV need to determine a way to centralise and streamline the ADR reporting process. In this way, it will be possible to drastically reduce confusion or uncertainty amongst health care professionals. In addition, the MCC needs to make an effort to have a bigger presence. If ADR reporting could be actively promoted to both patients and health care professionals, the likelihood of reporting could be increased due to this increased awareness. Finally, there needs to be a greater cooperation amongst health care professionals utilising the expertise and skill of each profession. For example, pharmacists and doctors are not typically involved in the twenty four hour care of the patient, yet nurses are. Therefore, if a nurse caring for a patient notices a change in the patients state after administration of a medicine, she/he should be responsible for consulting with the doctor or pharmacist in order to determine if a potential ADR might be detected.

6.4. RECOMMENDATIONS FOR FUTURE STUDIES

Going forward, a number of different approaches could be utilised in order to effectively determine the status of PV in the South African private sector. Firstly, a similar study could be conducted in the other major hospital groups in the country in order to paint a more complete picture of the knowledge, attitudes and practices of ADR reporting in the private sector.

Alternatively, a more hands-on study could be undertaken in which an electronic platform is developed that could assist with ADR reporting rates in this particular hospital group. If something like that is not feasible in the short term, a study comparing changes in knowledge, attitudes and practices before and after the implementation of a workshop/training session could be conducted.

6.5. CONCLUSION

In reality, improving PV in South Africa is an effort that must be based at national level. However, while those at national levels are slowly implementing improvements and changes, hospitals and clinics with the ability and resources to implement their own improvements should be encouraged to do so. Generally, attitudes of “one report will not make a difference” need to be discouraged. Even if every private hospital in the country submits one report, it will make a difference in the certainty of the safety profile of a particular drug. Particularly in the private sector where there is a massive expenditure per annum on medicines, it can only benefit the population to increase the reporting rate.

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APPENDIX A:

QUESTIONNAIRE

Dear Participant:

This questionnaire may contain words that you do not understand. Please ask the investigator to explain any words or information that you do not clearly understand. For your information:

Definitions:

Adverse Drug Reaction (ADR): A response to a medicine in humans or animals, which is noxious and unintended, including lack of efficacy, and which occurs at any dosage and can also result from overdose, misuse or abuse of a medicine (MCC, 2014).

Pharmacovigilance: The detection, assessment, understanding, management and prevention of adverse reactions to medicines (WHO, 2015).

1. What is your profession?

Doctor	
Registered Nurse	
Pharmacist	

2. What is your gender?

Male	
Female	

3. How old are you?

18 – 29 years old	
30 – 39 years old	
40 – 49 years old	
50 years or older	

4. For how many years have you been practicing?

Less than 1 year	
1 – 5 years	
5 – 10 years	
Longer than 10 years	

5. Have you ever received any pharmacovigilance or ADR reporting training?

Yes	
No	

6. Have you ever seen the MCC ADR reporting form before? Please refer to the form attached on the last page.

Yes	
No	

7. Do you know where to find the MCC ADR reporting form? Please refer to the form attached on the last page.

Yes	
No	

8. How important do you think it is to report ADRs?

Very important	
Important	
Not very important	
Not important at all	

9. Why do you think it might be important to report ADRs? Please rate each point on a scale from 1 to 5, with 1 being not important at all and 5 being very important. You can use the same number more than once.

To identify new ADRs	**1**	**2**	**3**	**4**	**5**
To share information about ADRs with colleagues	**1**	**2**	**3**	**4**	**5**
To improve patient safety	**1**	**2**	**3**	**4**	**5**
To help establish the safety of new drugs	**1**	**2**	**3**	**4**	**5**
To measure the incidence or frequency of ADRs	**1**	**2**	**3**	**4**	**5**
Because it is a legal requirement	**1**	**2**	**3**	**4**	**5**

10. In your view, which ADRs should be reported?

None	
All ADRs	
All serious ADRs (causing death or serious injury)	
ADRs to medical devices (such as pacemakers, prosthetics, etc)	

ADRs to new drugs	
ADRs to herbal, natural or traditional medicines	
Other (please specify):	

11. Have you ever reported an ADR?

Yes	
No	

12. Have you ever encountered an ADR and not reported it?

Yes	
No	
I don't know	

13. Please mark the statement(s) that apply to you regarding the process to follow when reporting an ADR:

I know how to fill out an ADR form (see attached form)	
My line manager manages all ADR reports so I don't really bother	
I don't know the process to follow	

14. ADR reports are submitted to:

Pharmacy Manager	
Nursing Manager	
Hospital Manager	
Head Office	
Medicines Control Council	
National Adverse Drug Event Monitoring Centre	
I don't know	

15. When would you be most likely to report an ADR?

It is a very serious ADR (causing death or serious injury)	
It is a very unusual reaction	
Somebody is watching me	
Certainty that it is an ADR	
A new or experimental drug is involved	
I would report all ADRs	

16. What are the factors that might discourage you from reporting ADR's?

Do not know how to report	
Do not know where to report	
Did not think it was important to report	
Managing the patient was more important than reporting the ADR	
Lack of access to ADR reporting form	
Patient confidentiality might be breached	
Legal liability issues	
The form is too long	
I don't receive any feedback once the form has been sent	
Other (please specify)	

17. In your opinion, which of these professionals should be responsible for reporting ADRs?

Doctors	
Nurses	
Pharmacists	
Other (please specify)	

18. Do you think that your hospital submits sufficient and appropriate ADR reports?

Yes	
No	
I don't know	

19. Do you have any suggestions about how the culture of reporting can be improved? Please tick/cross the appropriate box(es). You can choose more than one option.

ADR reporting made mandatory (i.e. will affect my monthly performance).	
Workshops and seminars.	
Pharmacovigilance teaching programmes for undergraduates, interns and postgraduates.	
Monthly meetings discussing common ADRs that may be encountered.	
Bring out bulletins on ADRs.	
Getting paid a sum of money for each ADR reported	
Other (please specify	

20. Using a scale of 1 – 5, please indicate whether you agree or disagree with the following statements:

1 – Strongly disagree **2 – Disagree**

3 – Neither agree nor disagree **4 – Agree**

5 – Strongly agree

ADR reporting is a professional obligation	**1**	**2**	**3**	**4**	**5**
ADR reporting adds up to unnecessary workload	**1**	**2**	**3**	**4**	**5**
Nobody really benefits if I report an ADR	**1**	**2**	**3**	**4**	**5**
I would like to receive more training on ADR reporting	**1**	**2**	**3**	**4**	**5**

Thank you for your co-operation!

APPENDIX B:

INFORMATION LEAFLET AND INFORMED CONSENT

Study Number:	M160238
Study Title:	An Evaluation of Health Care Worker Knowledge, Attitudes and Perceptions to Adverse Drug Reaction Reporting in the South African Private Sector
Investigator:	Ms Sophia Bogolubova
Institution:	University of the Witwatersrand
24 Hr Contact Number:	072-212-6396

To the potential participant:
This information sheet and consent form may contain words that might need clarification. Please ask the investigator to explain any words or information that you do not clearly understand. You may take home an **unsigned copy** of this information sheet and consent form to think about or discuss with family or friends **before** making your decision.

Good day,

My name is Sophia Bogolubova, I am a pharmacist, and I am currently completing my Masters degree at the University of Witwatersrand. I would like to invite you to consider participating in a research study titled, "An Evaluation of Health Care Worker Knowledge, Attitudes and Perceptions to Adverse Drug Reaction Reporting in the South African Private Sector". Before agreeing to participate, it is important to read and understand the following regarding the purpose of the study, the procedures, and your right to withdraw from the study at any time. This information leaflet will help you decide if you would like to participate. You should fully understand what is involved before you agree to take part in this study. You should not agree to take part unless you are satisfied about all the procedures involved. If you decide to take part in this study, you will be asked to sign an informed consent letter, which confirms that you understand the study and are participating voluntarily.

The purpose of the study is to gain an understanding of the knowledge, attitude and perceptions of doctors, registered nurses, and pharmacists within Life Healthcare with respect to ADR reporting.

This study will be performed at Life Brenthurst Clinic, Life Flora Hospital, Life Fourways Hospital and Life Wilgeheuwel Hospital, and will have between 300 and 400 participants. Participants will include pharmacists, doctors and registered nurses that work at Life Healthcare. Each participant will be provided with a questionnaire composed of various multiple-choice questions. Should you wish to participate, you will have two weeks to complete the questionnaire and return it to either your Line Manager, or directly to the principle investigator.

Your participation in this study is entirely voluntary and you can choose to decline to participate, or stop at any time, without stating any reason. Non-participation or withdrawal will not result in any disadvantage to you.

This study has been approved by **Human Research Ethics Committee (HREC)** of the University of the Witwatersrand**.** In addition, this study protocol has been submitted to **Life Healthcare Research and Scientific Committee** for ethics clearance and approval.

Should you have any questions, or require any further information, below are a list of the people that are involved with and working on this study.

Name	**Role**	**E-mail**	**Tel**
Sophia Bogolubova	Principle Investigator	sophiebogolubov@gmail.com	072-212-6396
Neelaveni Padayachee	Supervisor	Neelaveni.Padayachee@wits.ac.za	(011) 717-2269
Natalie Schellack	Co-Supervisor	Natalie.Shellack@smu.ac.za	(012) 521-4312

If you require any additional information regarding your rights as a research participant, or if you have any complaints regarding this study, you may contact the Chairperson of the Human Research Ethics Committee, University of the Witwatersrand:

Prof. Cleaton Jones	011 717 2100

All information obtained during the course of this study, including personal and research data, will be kept strictly confidential. You will not be required or asked to provide any

personal information, such as your name, address, ID number, employee number, telephone number, etc. Data may be reported in scientific journals, and will not include any information that might identify you as a participant in this study. This information might be inspected by the University of Witwatersrand, Human Research Ethics Committee (HREC), and Life Healthcare. This information will only be utilized by the abovementioned parties in connected with carrying out their obligations to this study.

Thank you for taking the time to consider participating in my study.

Sophia Bogolubova

APPENDIX C:

INFORMED CONSENT

- I hereby confirm that I have been informed by the principal investigator, Sophia Bogolubova, about the nature of the study (M160238, An Evaluation of Health Care Worker Knowledge, Attitudes and Perceptions to Adverse Drug Reaction Reporting in the South African Private Sector).
- I have also received, read and understood the above written information (Information Leaflet and Informed Consent) regarding the study.
- I am aware that the results of the study, including my profession and responses, will be anonymously processed into a study report.
- In view of the requirements of research, I agree that the data collected during this study can be processed in a computerized system.
- I may, at any stage, without prejudice, withdraw my consent and participation in the study.
- I have had sufficient opportunity to ask questions and (of my own free will) declare myself prepared to participate in the study.

PARTICIPANT:

Printed Name	Signature	Date and Time

PRINCIPLE INVESTIGATOR:

I, Sophia Bogolubova, herewith confirm that the above participant has been fully informed about the nature of the above study.

Printed Name	Signature	Date and Time

APPENDIX D:

R14/49 Ms Sophia Bogolubova

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)

CLEARANCE CERTIFICATE NO. M160238

NAME: (Principal Investigator)	Ms Sophia Bogolubova
DEPARTMENT:	Pharmacy and Pharmacology Life Flora Clinic, Life Fourways Hospital Life Brenthurst Clinic Life Wilgeheuwel Hospital
PROJECT TITLE:	An Evaluation of Health Care Worker Knowledge, Attitudes and Perceptions to Adverse Drug Reaction Reporting in the South African Private Sector
DATE CONSIDERED:	26/02/2016
DECISION:	Approved unconditionally
CONDITIONS:	
SUPERVISOR:	Mrs Neelaveni Padayachee
APPROVED BY:	Professor P. Cleaton-Jones, Chairperson, HREC (Medical)
DATE OF APPROVAL:	11/07/2016

This clearance certificate is valid for 5 years from date of approval. Extension may be applied for.

DECLARATION OF INVESTIGATORS

To be completed in duplicate and **ONE COPY** returned to the Research Office Secretary in Room 10004,10th floor, Senate House/2nd floor, Phillip Tobias Building, Parktown, University of the Witwatersrand. I/We fully understand the the conditions under which I am/we are authorised to carry out the above-mentioned research and I/we undertake to ensure compliance with these conditions. Should any departure be contemplated,from the research protocol as approved, I/we undertake to resubmit to the Committee. I **agree to submit a yearly progress report**. The date for annual re-certification will be one year after the date of convened meeting where the study was initially reviewed. in this case, the study was initially review in April and will therefore be due in the month April each year.

Principal Investigator Signature Date

PLEASE QUOTE THE PROTOCOL NUMBER IN ALL ENQUIRIES

Human Research Ethics Committee (Medical)

Research Office Secretariat: Faculty of Health Sciences, Phillip Tobias Building, 3rd Floor, Office 301,
29 Princess of Wales Terrace, Parktown, 2193 Tel +27 (0)11-717-1252 /1234/2656/2700
Fax 0865557886 Private Bag 3, Wits 2050, email: zanele.ndlovu@wits.ac.za
Office email: hrec-medical.researchoffice@wits.ac.za
Website: www.wits.ac.za/research/about-our-research/ethics-and-research-integrity/

04 October 2016

Sophia Bogolubova
Department of Pharmacy and Pharmacology

Sent by email to:sophiebogolubov@gmail.com

Dear Ms Bogolubova

Re: **Protocol M160238**
Study Title: An Evaluation of Health Care Worker Knowledge, Attitudes and Perceptions to Adverse Drug Reaction Reporting in the South African Private Sector
Principal Investigator: Ms Sophia Bogolubova
Protocol Amendment: Data Collection Instrument and Procedure

This letter serves to confirm that the Chairman of the Human Research Ethics Committee (Medical) has approved the amendments on the abovementioned study, as detailed in your letter received on 16 August 2016.

Thank you for keeping us informed and updated,

Yours Sincerely,

UNIVERSITY OF THE WITWATERSRAND
OFFICE OF THE DEPUTY VICE CHANCELLOR RESEARCH
04 OCT 2016
RESEARCH OFFICE HREC (Medical)
JOHANNESBURG

Ms Zanele Ndlovu
Administrative Officer
Human Research Ethics Committee (Medical)

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)

01 March 2017

Ms Sophia Bogolubova
Faculty of Health Sciences
Department of Pharmacy and Pharmacology
Parktown
Johannesburg

Sent by email to: sophiebogolubov@gmail.com

Dear Ms Bogolubova,

Re: **Protocol Ref no: M160238**
Protocol Title: An Evaluation of Private Sector Nurse and Pharmacist Knowledge, Attitudes and Perceptions to Adverse Drug Reaction Reporting
Principal Investigator: Ms Sophia Bogolubova
Protocol Amendments : Amendments to Study Population

This letter serves to confirm that the Chairman of the Human Research Ethics Committee (Medical) has approved the protocol amendments on the abovementioned protocol, as detailed in your letter dated 20 November 2016.

The following documents were received:

- Cover Letter dated 20 December 2017.

Thank you for keeping us informed and updated.

Yours Sincerely,

L. Moeng

Mr Lebohang Moeng
Administrative Assistant
Human Research Ethics Committee (Medical)

UNIVERSITY OF THE WITWATERSRAND
OFFICE OF THE DEPUTY VICE CHANCELLOR RESEARCH
01 MAR 2017
RESEARCH OFFICE HREC (Medical)
JOHANNESBURG

APPENDIX E:

Life College of Learning
Head Office
Oxford Manor, 21 Chaplin Road, Illovo 2196
Private Bag X13, Northlands 2116
Telephone: +27 11 219 9000
Telefax: +27 11 219 9001
www.lifehealthcare.co.za

20 June 2016

ATTENTION: **S Bogolubova**

SUBJECT: **APPLICATION TO CONDUCT RESEARCH**

TITLE: **An evaluation of health care worker knowledge, attitudes and beliefs to adverse drug reaction reporting in the South African private sector.**

Our previous correspondence refers.

The Research Ethics Committee hereby conditionally approves your request.
Approval number: 20160620-01. Valid until 2017/06/30.

The approval is conditional to your agreement on the following provisos:

1. You must request permission (in writing) from the Hospital Manager and Pharmacy Manager of the Life Healthcare (LHC) facility in which you intend conducting your research, accompanied by this letter.
2. LHC will not be liable for any costs incurred during or related to this study.
3. Should patient or institutional confidentiality be compromised, LHC has the right to withdraw the permission and take legal action.
4. The researcher will provide LHC Research Ethics Committee with an update on the progress of the study every four months.
5. An electronic copy of the final research report is submitted to the Life Healthcare Research Ethics Committee ***prior*** to publication.
6. No direct reference is made to LHC or its various facilities in the research report or any publications thereafter.
7. The Company and its facilities are not in any way identifiable in the study.
8. On completion of the degree, an electronic (.pdf) copy of the research report will be provided to LHC. This copy will be uploaded to the institutional repository.
9. Kindly clear copy-right issues with your supervisor and/or Higher Education Institution prior to accepting these terms and conditions.

Please sign this letter as indicated below and return to the sender within 5 working days:

I, S Bogolubova, hereby agree to the provisos (points 1-9) as listed above.

Signature: _____

Date: _____

We wish you the best in your studies and look forward to the final results.

Yours sincerely

Aroodt.

Anne Roodt
on behalf of the Research Ethics Committee.

Life Healthcare Group (Proprietary) Limited
Reg. no. 2003/024367/07 Registered address Oxford Manor, 21 Chaplin Road, Illovo 2196, Private Bag X13, Northlands 2116
Directors: A Meyer (Chief Executive Officer), CLW Bakker, D Schaubie, PP van der Westhuizen

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