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Evaluating the Knowledge, Attitudes and Practices of Healthcare Workers towards Adverse Drug Reaction Reporting in a Public Tertiary Hospital

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Evaluating the Knowledge, Attitudes and Practices of Healthcare Workers Towards Adverse Drug Reaction Reporting at a Public Tertiary Hospital

Abstract

Background

Spontaneous reporting of adverse drug reactions (ADRs) is a method of monitoring the safety of drugs post-marketing, providing a way to discover new, rare or unnoticed ADRs. Despite its importance, there is widespread underreporting of ADRs by health care professionals in South Africa.

Objectives

The study assessed the knowledge, attitudes and practices (KAP) of health care professionals on ADR reporting at a public hospital.

Methods

The questionnaire consisted of 21 questions (5 demographics; 7 knowledge; 1 attitude; 7 practices of the participant). Hard copies of the questionnaire were completed by doctors, nurses and pharmacists. The results were captured on Microsoft Excel™, and imported onto Stata® 14 to conduct Pearson chi-squared and Fishers tests.

Results

297 health care professionals (87.87%) responded to the questionnaire. 50.17% had knowledge of reporting, and pharmacists were the most likely professionals to know how to report (82.61%) ($p< 0.001$). 96.88% of participants who had previously received ADR training knew how to report ADRs. 90.24% stated they would report an ADR based on the seriousness of the reaction. Lack of knowledge; managing the patient being more important than reporting; and reporting being time-consuming were some discouraging factors. 58.59% of participants had encountered an ADR before but only 16.50% had reported ($p< 0.001$).

Conclusions

Doctors, nurses and pharmacists were aware of the presence of ADRs, but were unlikely to report them. Health care professionals should be made aware of the benefits of reporting, and perhaps a culture of reporting can be adopted given an awareness of pharmacovigilance.

Introduction

The safety, efficacy and quality of medicines are essential aspects to consider when dealing with the wellbeing of patients. While medicines are intended to heal, treat and prevent ailments, there is no certainty that they won't themselves cause harm. When determining the safety of new pharmaceuticals, testing and clinical trials are conducted. These allow for a range of adverse drug reactions (ADRs) to be identified, some of which may show up frequently, and others that may be extremely rare. These ADRs are defined as the "response to a drug which is noxious and unintended, and which occurs at doses normally used in man for the prophylaxis, diagnosis, or therapy of disease, or for the modifications of physiological function"[1]. Randomized controlled clinical trials have limits on the amount of time the drug is tested and the patients on which the drug; inevitably it cannot be tested on every genetic and ethnic makeup[2,3]. Post-marketing monitoring is an important feature of pharmacovigilance (PV) as it provides a means by which rare and population specific ADRs can be identified. PV is defined as the "science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other drug-related problem"[4].

Thalidomide is synonymous with PV as it brought attention to the subject of drug safety. In the 1950's, Thalidomide was put on the market and prescribed to pregnant women after it was said to be "virtually free from side effects"[5]. However, after taking Thalidomide, thousands of expectant mothers devastatingly gave birth to babies with a congenital defect called phocomelia, in which babies are born with underdeveloped limbs[6,7,8]. Following the tragedy, at the Sixteenth World Health Assembly in 1963, the early stages of the World Health Organisation (WHO) Programme for International Drug Monitoring, was proposed[9]. In 1978, all operational responsibilities were directed through the Uppsala Monitoring Centre (UMC), which holds an international database of ADRs, and plays a prominent role in signal detection and safety research[10]. Beginning with 10 founding members (Australia, Canada, Czechoslovakia, Federal Republic of Germany, Ireland, Netherlands, New Zealand, Sweden, United Kingdom, and the United States of America), there are currently 127 full members who have functional pharmacovigilance systems and meet the minimum requirements of the organization, as laid out by the WHO[10].

In 1992, South Africa met these requirements and became the first African member of the collective. South Africa's PV activities have been directed by The Medicines Control Council (MCC), which was the "statutory body" responsible for national safety and quality of medicines[11]. A new regularity authority- The South African Health Products Regulatory Authority (SAHPRA) was established in 2017 to supersede the MCC.

The MCC established The National Adverse Drug Event Monitoring Centre (NADEMC), to bridge the gap between UMC and the MCC[11], and it is responsible for the collation of data from received ADR reports, and the "assessment of causality and risk of ADRs"[12].

Separately, South Africa's National Department of Health established a National Pharmacovigilance Centre (NPC) in 2004, which plays an important role in collecting and collating programmatic reports, i.e. those relating to public health programs including TB and HIV[13].

The NPC acting in communication with SAHPRA (or the MCC previously) and the UMC potentially allows for the data to be fed centrally, a vital part of the system of PV in any country.

A study conducted by Ampadu et al. found that in 2015 the African continent was responsible for 0.88% of the global number of reports- a fraction of the rest of the world. In 2015, 28,609 Individual Case Safety Reports (ICSRs) were submitted by South Africa, representing 0.24% of the total global reports[14]. Data is often not fed to a national system, which is evident from fewer generated reports[12]. There is a lack of collaboration between sectors, particularly the pharmaceutical industry, which leads to a "national database that does not include data from all sources"[15]. Olsson, Pal & Dodoo conducted a review of PV in resource limited countries and described that due to the shortage of health care workers in low to middle income countries, the perception is that it's more important to focus on clinically managing the patient than filling out the paperwork involved in spontaneous reporting[16]. Spontaneous reporting refers to the passive reporting of ADRs by health care professionals or patients as they witness them[17]. The effectiveness of this voluntary type of reporting relies on the practitioner noticing an event and reporting it appropriately[18].

In the South African public sector, spontaneous reports are documented using the 'Adverse Drug Reaction and Quality Problem Report Form'. The forms are sent to the hospital or district PTC, where the data is consolidated and forwarded to the secretariat of the Safety and Quality Subcommittee, the provincial PTC's, the NADEMC and finally the MCC[19]. The reporting health care professional should be informed of progress and final outcomes in order to ensure an effective feedback cycle[19]. Strengthening pharmacovigilance has to include a focus on the importance of collaboration through continuous training[12].

Spontaneous underreporting of ADRs is a problem globally, and particularly in South Africa. This underreporting leads to incomplete data and can lead to trends in ADRs that go un-noticed. Health care professionals have a duty to report the ADRs they encounter. In order to understand the reasons for underreporting in the public sector, the knowledge, attitudes and practices of health care workers should be assessed.

The aim of this study was to evaluate the knowledge, attitudes and practices of healthcare workers in the public sector towards adverse drug reaction reporting.

Methods

Study Design

This study was a longitudinal, questionnaire-based study. A literature review was conducted to gain background knowledge on the perceptions of healthcare workers on ADR reporting globally. A questionnaire was then compiled based on similar studies[20, 21, 22]. The questions were categorised as follows: 5 questions pertaining to demographics; 7 questions on the awareness of ADR reporting; 7 questions about the professional's previous ADR reporting involvement; 1 question pertaining to the professional's general attitude towards ADR reporting and 1 question about possible future improvements that could be made. After a pilot study using a group of randomly selected pharmacists, the questions were adapted appropriately.

Site Selection

A public tertiary hospital in Johannesburg, South Africa was chosen. The hospital employs more than 4000 staff and is one of the largest teaching hospitals, serving a population of approximately 8 723 786 (in 2015). Based on a sample size calculation using the number of doctors (623), nurses (2165) and pharmacists (26) employed at the hospital (total= 2814), 338 was found to be the appropriate number of participants. Participants were made up of pharmacists, nurses and medical doctors who practiced within the main hospital pharmacy and the ten highest volume inpatient wards (i.e. Pulmonology; Oncology; ICU (neonatal and adults); Surgical; Orthopaedic; Renal; Gynaecology; Diabetes; Gastroenterology; Cardiac).

Data Collection

Participation in the questionnaire occurred over the period between July and November 2016, in which the hard copies of the questionnaires were disseminated and collected. The questionnaires were distributed to pharmacists, and to head nurses at wards, who distributed and collected the questionnaires within their departments. Participants were required to complete the informed consent form and were given appropriate instructions for filling out the questionnaire.

Data Analysis

Data was collected in the form of the hard copy questionnaire responses from pharmacists, doctors and nurses. The data was then electronically captured on to spreadsheets on Microsoft Excel™. The questionnaire responses was categorized in terms of: the demographics of the person participating; the current awareness of the participant (i.e. knowledge); the attitude of the professional towards PV; any prior PV involvement the participant may have had (i.e. practices); and the need for further PV training or other suggestions. The data captured on Microsoft Excel™ spreadsheets was imported on Stata® (Version 14). Pearson chi squared and Fishers tests were run in order to discover significant associations in the data.

Ethical Considerations

Ethics approval was granted by the University of the Witwatersrand Human Research Ethics Committee (HREC) (No. M160246).

Results

Demographics

Two hundred and ninety-seven questionnaires were returned out of the sample size calculated of 338, to yield a 87.87% response rate. The respondents were made up of 41 doctors; 230 nurses; 24 pharmacists and 2 participants did not indicate their profession. Forty-nine percent of participants were qualified professionals having already completed their internships and community service. The majority (83.84%) of participants were female.

Knowledge of the Participants

Table 1 shows the knowledge of the participants. Over 50% of participants stated they knew how to report an ADR, and 77.10% stated that they were familiar with the form. Participants chose many reasons for the importance of ADRs, with most participants checking all the options for that question.

Table 2 shows the knowledge of the participants by profession. Fifty-four percent of the nurses stated they didn't know how to report, while 53.59% of doctors and 82.61% of pharmacists know how to report.

In terms of the level of practice, more than half of the participants (53.77%) who knew how to report had been practicing as health care professionals for 6-10 years. Participants who were newest to practicing (<1 year) had little knowledge of reporting with 76.47% of participants stating they didn't know how to report. Fifty-eight percent of post-community service participants knew how to report ADRs, whereas only 23.08% of interns knew how to report ADRs.

Attitudes of the Participants

Table 3 shows the frequency distribution of the results pertaining to the attitudes of the participants towards PV. Over ninety percent of the participants (90.24%) stated they would report an ADR based on the seriousness of the reaction. Various factors such as not knowing how to report; not knowing where to report; managing the patient being more important than reporting; and reporting being time-consuming, made up most of the factors that discouraged participants from reporting. Figure 1 shows participant's opinions on which health profession should be held responsible for reporting ADRs. Ninety-three percent of participants felt medical practitioners should be held responsible, followed by 88.89% for nurses and 76.77% for pharmacists. Two percent of participants chose "other" which was made up of the response "patients".

Practices of the Participants

Table 4 shows previous PV activity in which participants may have been involved, of which only 10.77% of participants had received previous PV training. Of the 58.59% of participants who encountered an ADR in practice, only 16.50% reported the encountered ADR. The vast majority of participants (73.74%) submitted <1 ADR per year.

Discussion

Knowledge of Health Care Professions On ADR Reporting

Participants in this study had some awareness of pharmacovigilance, side effects and adverse drug reactions. Health care professionals have demonstrated a relative awareness for the presence of ADRs in studies similar to this one, including that of Fadare et al.[23], and Pimpalkhute et al.[21]. However, these studies also found a lack of awareness of the process of reporting. Fadare found that although 93.8% of participants had knowledge of reasons to report ADRs, only 39.5% of participants were aware of the actual reporting form[23]. Similarly, according to Suyagh, Farah and Farha, only 28.6% of hospital pharmacists were aware of the reporting system in Jordan[22]. In this current study, the questionnaire results showed that 50.17% of participants knew how to report ADRs, and 77.10% were aware of the yellow reporting form.

In terms of knowledge of the pharmacovigilance reporting system, 59.26% of participants identified NADEMC as the place to report ADRs, while only 48.82% chose the PTC as an option. Fadare et al. found a similar figure (44.6%) of participants who were aware of the existing hospital committee[23]. Although the NADEMC is the national monitoring centre, the PTC should also be recognised as an important channel for communication within the institution. Provincial PTCs play a significant role in the collection of ADR reports. Ideally, the gathering of reports for provincial PTCs is a function that happens through the Safety and Quality Subcommittee, which physically gathers and collates the data, looking for potential concerning trends. Communication and integration among all health care professionals may help to give holistic care, and in many ways can make the involved persons more motivated.

The study found different levels of knowledge among the different professions. Nurses had the least knowledge of how to report (46.46%) , followed by doctors (53.49%) and then pharmacists (82.61%) ($p< 0.001$). De Angelis et al. concluded that “Nurses are not fully aware of their role in adverse drug reaction reporting”[24], and Hanafi et al. had a similar finding with 89% of nurses preferring to refer the report to the doctor for completion[25].

Health care professional’s knowledge of the flow of reporting as well as their awareness of who should take responsibility of reporting need to be enforced. This brings up the need to train heath care professionals more constantly, through the use of in-service training and more formalised classroom-based learning at the undergraduate level. This study also found a statistical association between knowledge of ADR reporting and the years of experience of participants. Participants who are newer to practicing as health care professionals seemed to have knowledge of the importance of reporting, however there is a lack of knowledge of the process itself (p-value = 0.000). Only 23.08% of interns knew how to report ADRs, yet 61.45% had seen the reporting form before ($p< 0.001$). These findings were consistent with that of Elkami et al. who found that deficiencies in the undergraduate curriculum lead to a lack of knowledge about pharmacovigilance[26].

Attitudes Of Health Care Professionals On ADR Reporting

Attitudes in this study were measured by the factors that encouraged and discouraged health care workers, as well as the cases in which they were most likely to report ADRs. These factors accounted for some of the gaps between knowledge and practice. Believing that ADR reporting is important is an inevitable start to reporting ADRs, and this study found that only 21.89% of participants chose “did not think it was important to report” as a reason for underreporting. Similarly, Gupta and Udapa found that 89.5% of doctors thought reporting was an important part

of their profession[27], and Joubert and Naidoo found that 79.4% of participants "regarded PV as a valuable tool"[17].

A range of factors discouraged participants from reporting, with "managing the patient was more important than reporting", "do not know how to report", and "do not know where to report" being the most frequently answered. "Ignorance about the reporting system" found in this study was consistent with the results of Desai et al[20]. Most health care professionals cited the seriousness of the ADR (90.24%) as the main encouraging factor in deciding whether to report an ADR, comparable to the 88.9% found by Gupta and Udapa[27].

Practices of Health Care Professionals on ADR Reporting

The practices of health care professionals were assessed through responses based on encountered ADRs versus reported ADRs. 58.59% of participants had encountered an ADR in practice, yet only 16.50% reported the encountered ADR ($p<0.001$). Fadare et al. discovered that although more than 80% of participants had previously witnessed an ADR, 42.7% chose not to report it[23].

Vallano et al. found the availability of reporting forms to be a major barrier of reporting[29]. In this study, although 59.26% of participants stated the forms were easily available to them in practice. This issue is one that should be addressed at each institution and brings up the need for heads of department to play a role in integrating pharmacovigilance into the topics discussed at routine meetings.

Suggestions and Future Recommendations

Education should remain a priority in the field of pharmacovigilance, and the idea of training was a fundamental point of discussion during focus group sessions. Over 96% of participants who had previously attended a training seminar stated they knew how to report ADRs. Similarly, De Angelis et al[24]; Lopez-Gonzalez[30]; Backstrom et al.[31]; Sevene et al.[32]; and Cereza et al.[33] found increases in reports after training, and higher rates of reports from health care professionals with a higher level of education. Sevene et al.[32]; and Kaselekela Oscar & Boyd[34] focused on pharmacovigilance in resource-limited countries, and mentioned continuous training, public awareness and the importance of feedback in reporting ADRs.

Training should be consistent starting from the undergraduate level and continuing into routine training sessions in the workplace[35, 36].Pimpalkhute noticed gaps in "undergraduate training" (2012, p. 60), while Olsson, Pal and Dodoo noted the importance of introducing PV training into undergraduate studies[21]. An approach targeted at students saw a "student- run pharmacovigilance programme" being piloted in the Netherlands[37]. This ideas allows for students to learn in a more practical way the importance of PV, which they can then carry into their professions.

Post-graduation, there is a need to renew the skills of PV. A possible idea for this, while also utilising the idea of incentives, is the allotment of Continuous Development Points (CPDs) to reporting healthcare workers. A study conducted in India found positive results following the implementation of this idea. Sixty-seven percent of healthcare workers had no awareness of ADR reporting prior to the study, but results showed an increased rate of reporting after the program was introduced[38]. Similarly, an idea implemented in the UK in the form of "e-learning modules" allows healthcare professionals to familiarise themselves with ADR reporting[39]. This allows for a continuous platform for training on ADRs, as well as the added incentive of receiving CPD credits.

Health care professionals also want to be kept up to date and involved, and so PV bulletins and meetings may be of great use once the culture of reporting is established.

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Tables and Figures

Table 1: Frequency Distribution of Participants Knowledge of PV (N=297)

Responses	Frequency (%)	Percentage (%)
Knowing how to report an ADR		
Yes	149	50.17
No	145	48.82
Total	294 (*=3)	
Familiar with the reporting form		
Yes	229	77.10
No	65	21.89
Total	294 (*=3)	
Where to report ADRs		
The National Adverse Event Monitoring Centre (NADEMC)	176	59.26
Pharmaceutical and Therapeutics Committee (PTC)	145	48.82
The Medicines Control Council (MCC)	143	48.15
Medical Supply Depot (MSD)	38	12.79
The Safety and Quality Subcommittee	70	23.57
Other	12	4.04
"Doctor and Pharmacy in Hospital"	3	
"Pharmaceutical Company"	1	
"The Drug Controller"	2	
"Supplier"		
Total	584	
Why it's important to report ADRs		
To identify new ADRs	1375	92.59
To improve patient safety	1401	94.34
To measure the incidence of ADRs	1376	92.66
To share information about ADRs with colleagues	1347	90.71
To identify relatively safe drugs	1357	91.38

It is a requirement	1315	88.55

Table 2: Knowledge of How to Report ADRs by Profession (N=292)

	Profession of Participant			
Response	Doctor	Nurse	Pharmacist	All
Yes	23	105	19	147
	(53.49%)	(46.46%)	(82.61%)	(50.34%)
	(15.65%)	(71.43%)	(12.93%)	(100%)
No	18	121	4	143
	(41.86%)	(53.54 %)	(17.39%)	(48.97%)
	(12.59%)	(84.62%)	(2.80%)	(100%)
Invalid Response	2	0	0	2
	(4.65 %)	(0.00%)	(0.00%)	(0.68%)
	(100%)	(0%)	(0%)	(100%)
Total	43	226	23	292
	(100%)	(100%)	(100%)	(100%)
	(14.73%)	(77.40%)	(7.88%)	(100%)

Pearson Chi-square = 23.1900, p-value = 0.000, Fisher's exact for scores <5 = 0.000 ***(p<0.001)***

Table 3: Frequency Distribution of Participant's Attitudes (N=297)

Response	**Frequency (N)**	**Percentage (%)**
Cases most likely to report ADR		
Seriousness of the ADR	268	90.24
Unusualness of the reaction	160	53.87
Involvement of a new drug	139	46.80
Level of certainty that it is an ADR	85	28.62
None of the above	2	0.67
Total	654	
Factors discouraging participants from reporting ADRs		

Do not know how to report	97	32.66
Not knowing where to report	96	32.32
Did not think it was important to report	65	21.89
Managing the patient was more important than reporting ADRs	115	38.72
Lack of access to ADR reporting form	49	16.50
Patient confidentiality	46	15.49
It is time-consuming	95	31.99
There is a lack of feedback after forms have been submitted	65	21.89
Other	7	2.36
"Inexperience"	1	
"No discouraging factors"	2	
Total	635	
ADRs that should be reported		
None	1	0.34
All ADRs	182	61.28
All serious ADRs	132	44.44
ADRs to new drugs	59	19.87
Unknown ADRs to old drugs	47	15.82
ADRs to herbal and non-allopathic drugs	23	7.74
ADRs to vaccinations	28	9.43
Other	3	1.01
Total	475	
Professionals who should report ADRs		
Medical practitioners	275	92.59
Nurses	264	88.89
Pharmacists	228	76.77
Other	7	2.36
"Patient"	2	
Total	774	
Reference materials participants would use		
Textbook	177	59.60

Colleague	211	71.04
Internet	236	79.46
Package Insert	224	75.42
Other	3	1.01
Total	851	

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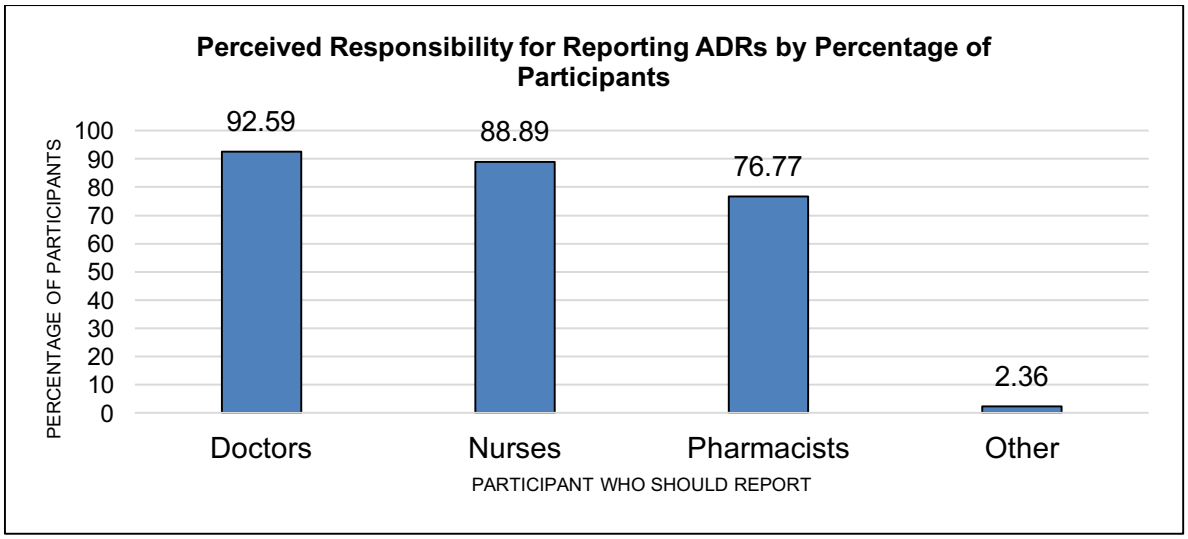


Figure 1: Perceived Responsibility for Reporting ADRs

Table 4: Frequency Distribution of Previous PV Activity (N=294)

Response	Frequency (N)	Percentage (%)
Any previous training seminars/workshops on ADR reporting?		
Yes	32	10.77
No	262	88.22
Total	294 (* =3)	
Are ADR reporting forms easily available to you in practice?		
Yes	176	59.26
No	93	31.31
Total	269 (* =28)	
Have you ever encountered an ADR in practice?		
Yes	174	58.59

No	115	38.72
Total	289 (* =8)	
Have you ever reported an ADR that you encountered?		
Yes	49	16.50
No	238	80.13
Total	287 (* =10)	
How many ADR reports have you submitted on average?		
<1/ year	219	73.74
1-10/ year	23	7.74
<1/month	5	1.68
1-10/ month	2	0.67
Total	249 (* =48)	

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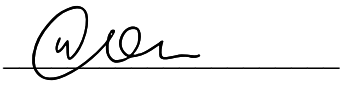
Table 5: Participants who Encountered ADRs versus those that Reported the Encountered ADR (N=285)

	Reported an Encountered ADR		
Encountered an ADR	**Yes**	**No**	**Total**
Yes	47 (27.17%) (95.92%)	126 (72.83%) (53.39%)	173 (100%) (60.70%)
No	2 (1.79%) (4.08%)	110 (98.21%) (46.61%)	112 (100%) (39.30%)
Total	49 (17.19%) (100%)	236 (82.81%) (100%)	285 (100%) (100%)

Pearson Chi-square= 30.7645, p-value= 0.000 *(p<0.001)*

CANDIDATES DECLARATION

I declare that this dissertation is my own unaided work. It is being submitted or the degree of Master of Pharmacy at the University of the Witwatersrand, Johannesburg. It has not been submitted for any other degree or examination at any other University.



Yashmay Gordhon

22 day of **JANUARY** in the year **2018**

ABSTRACT

Introduction and Objectives

Spontaneous reporting of adverse drug reactions (ADRs) is a method of monitoring the safety of drugs post-marketing, providing a way to discover new, rare or unnoticed ADRs. Despite the importance of this, there is widespread underreporting of ADRs by health care professionals in South Africa. This study was used to assess the knowledge, attitudes and practices (KAP) of health care professionals on ADR reporting at a public tertiary hospital as a way to evaluate reasons for underreporting and suggestions for future improvement.

Materials and Methods

The study was conducted at 10 wards and the pharmacy. The baseline assessment consisted of a questionnaire of 21 questions (5 demographics; 7 knowledge; 1 attitude; and 7 pertaining to practices of the participant). Hard copies of the questionnaire were provided and completed by doctors, nurses and pharmacists. The results were captured on Microsoft Excel™ spreadsheets, and then imported onto Stata® 14 to conduct Pearson chi-squared and Fishers tests. Following this, 4 focus group sessions were conducted with nurses and pharmacists in order to assess reasons for under-reporting and thoughts and opinions on how to improve the system of reporting at CMJAH.

Results

A total of 297 health care professionals (87.87%) responded to the questionnaire, the majority of which were nurses (77.44%). 50.17% said they knew how to report an ADR, and pharmacists were the most likely professionals to know how to report ADRs (82.61%) ($p< 0.001$), but explained a lack of reporting due to time-constraints during daily practice. 96.88% of participants who had previously received ADR training knew how to report ADRs. 90.24% of participants stated they would report an ADR based on the seriousness of the reaction. Lack of knowledge; managing the patient being more important than reporting; and reporting being time-consuming were listed as discouraging factors. 58.59% of participants had encountered an ADR before but only 16.50% had reported ($p< 0.001$). Training and education was noted as the primary way to improve the reporting rate, but it was also suggested that one person be put in charge of pharmacovigilance in each department, in order to manage time-related issues.

Conclusions

Doctors, nurses and pharmacists were aware of the presence of ADRs, but were unlikely to report them mostly due to a lack of training. Health care professionals need to be made more aware of the benefits of reporting, and perhaps a culture of reporting can be adopted given an awareness of PV.

KEYWORDS

Pharmacovigilance; adverse drug reactions; reporting; spontaneous report; knowledge; attitude; practices; health care professionals

ACKNOWLEDGMENTS

A special thanks goes to my supervisors Neelaveni Padayachee and Belinda Strydom for their continuous support, guidance and expertise throughout the research process.

To my family, I appreciate all of you and I am grateful for all that you do for me. I hope to continue to make you proud.

Finally, thank you to all who chose to participate in this research.

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ABBREVIATIONS USED IN THIS DOCUMENT

ADR	Adverse Drug Reaction
ARV	Antiretroviral
CEO	Chief Executive Officer
CME	Cohort Event Monitoring
ICSR	Individual Case Safety Report
ICIUM	International Conference on Improving Use of Medicines
ICU	Intensive Care Unit
MCC	Medicines Control Council
MSD	Medical Supply Depot
NADEMC	National Adverse Drug Event Monitoring Centre
NDOH	National Department of Health
NPC	National Pharmacovigilance Centre
PTC	Pharmaceutical and Therapeutics Committee
PV	Pharmacovigilance
SANC	South African Nursing Council
SAPC	South African Pharmacy Council
TB	Tuberculosis
UMC	*the* Uppsala Monitoring Centre
WHO	World Health Organization

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CHAPTER I: INTRODUCTION

Rational use of medicines has become an important topic of focus within the health science industry, with access to medicines and medical knowledge continuing to improve into the 21st century. The need to provide safe and effective medicines remains essential, and the role of health care professionals in safeguarding the use of medicines should remain a priority. Side effects, defined as "any unintended outcome that seems to be associated with treatment, including negative or positive effects" (UMC, 2017), are inevitable consequences to the use of medicines. Adverse effects can lead to life threatening ailments in more serious cases. The World Health Organization (WHO) defines an adverse drug reaction (ADR) as "a response to a drug which is noxious and unintended, and which occurs at doses normally used in man for the prophylaxis, diagnosis, or therapy of disease, or for the modifications of physiological function" (WHO, 1972).

The registration of medicines is a rigorous process and medicines go through various phases of clinical trials in which many of the risks of taking the drug are evaluated and become recognized. However, due to the limitations that exist within these controlled clinical trials, including the limited amount of time allocated to testing (Wiktorowicz Lexchin & Moscou, 2012), some effects may go un-noticed, especially those that only become present after an extended time period. Once on the market, drugs tested on certain patient populations will inevitably be used by a wider variety of people with differences in genetics and ethnicity (Eliasson, 2006). Therefore, it is vital that measures be put in place to monitor patients post-marketing. Post marketing surveillance provides a means by which rare and population specific ADRs can be identified.

The impact of ADRs on health can be devastating, especially when they are not identified timeously. Polypharmacy (taking an assortment of drugs concurrently) often leads to a situation where it is not clear what the causative agent of a given reaction may be (Nobili et al., 2011). The growing practice of self-medication and the lack of awareness of ADRs increases the likelihood that ADRs will go undetected with dire consequences. A study conducted by Hakkarainen et al. in 2012 discovered that 52% of the ADRs experienced by outpatients, and 45% of ADRs experienced by hospital patients were preventable (Hakkarainen). The awareness

of health care professionals, as well as the empowerment of patients in noticing adverse effects, is not only important but potentially life-saving (Mehta, 2011).

Together with the harm caused to a patient's health by a drug intended for treatment, ADRs also manifest themselves as a substantial economic burden. In one German study, it was found that treating an ADR cost an average of 382 Euros per ADR and 58% of these total costs lead to hospitalization (Stark, John & Leidl, 2011). A cross sectional study performed in four South African hospitals found 8.4% of hospital admissions to be ADR related (Mouton et al., 2016). The costs incurred from hospital admission; prolonged hospitalization and any further therapy that may be required can add significantly to patient costs and discomfort.

The reporting of ADRs allows for a way to monitor the safety of medicines and enable global awareness of the potential harms of certain drugs. A study conducted by Onakpoya, Heneghan & Aronson reviewed market withdrawals that occurred between 1950 and 2013, and discovered that 95 drugs were withdrawn as a result of death (2015). A subsequent study found 462 drugs withdrawn from the market as a result of an adverse drug reaction (Onakpoya, Heneghan & Aronson, 2016). Post-marketing surveillance in the form of ADR reporting acts in an effort to avoid delayed action in ensuring safety of drugs on the market. Through the implementation and adherence to a pharmacovigilance system, potential risks to patient health can be detected, and medicines not deemed safe enough for use can be removed. Pharmacovigilance is defined as the "science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other drug-related problem" (WHO, 2010, p.1). The WHO defines a Pharmacovigilance Reporting System as: "the core data-generating system of pharmacovigilance, relying on healthcare professionals and patients to identify and report any suspected adverse effects from medicines to their local or national pharmacovigilance centre or to the manufacturer" (UMC, 2017, n.p) and this gives way to a method of monitoring potential health risks.

Adherence to a Pharmacovigilance Reporting System differs between countries, often based on income and thus, resources. A study exploring the patterns of reporting ADRs found that reporting rates are higher in high income countries than they are in low income countries. (Aagard, 2012). The same study found South Africa to have a reporting rate of 11, compared to that of the United Kingdom with 233 (reports/million inhabitants/ year). Within a health care

setting like the one in South Africa, the public sector often lacks the necessary resources and infrastructure that enables higher income countries to gather data efficiently. In recent years, global funding has also increased access to medicines in developing countries. This has caused a further need for the proper training and education of health care professionals in these countries, who may have had little focus on PV in the past (Olsson et al., 2015).

It is essential for healthcare workers to assume responsibility for monitoring the safety of medicines, and it should be viewed as a professional obligation. Reasons for under-reporting globally have been well researched and largely relate to issues pertaining to the knowledge, attitudes and practices of health care professionals. The perceptions of health care workers, especially those in direct contact with patients, should be enhanced in order to effectively increase the rate and quality of reporting, possibly leading to fewer hospital admissions and improved patient safety.

CHAPTER II: LITERATURE REVIEW

2.1 A BRIEF HISTORY OF PHARMACOVIGILANCE

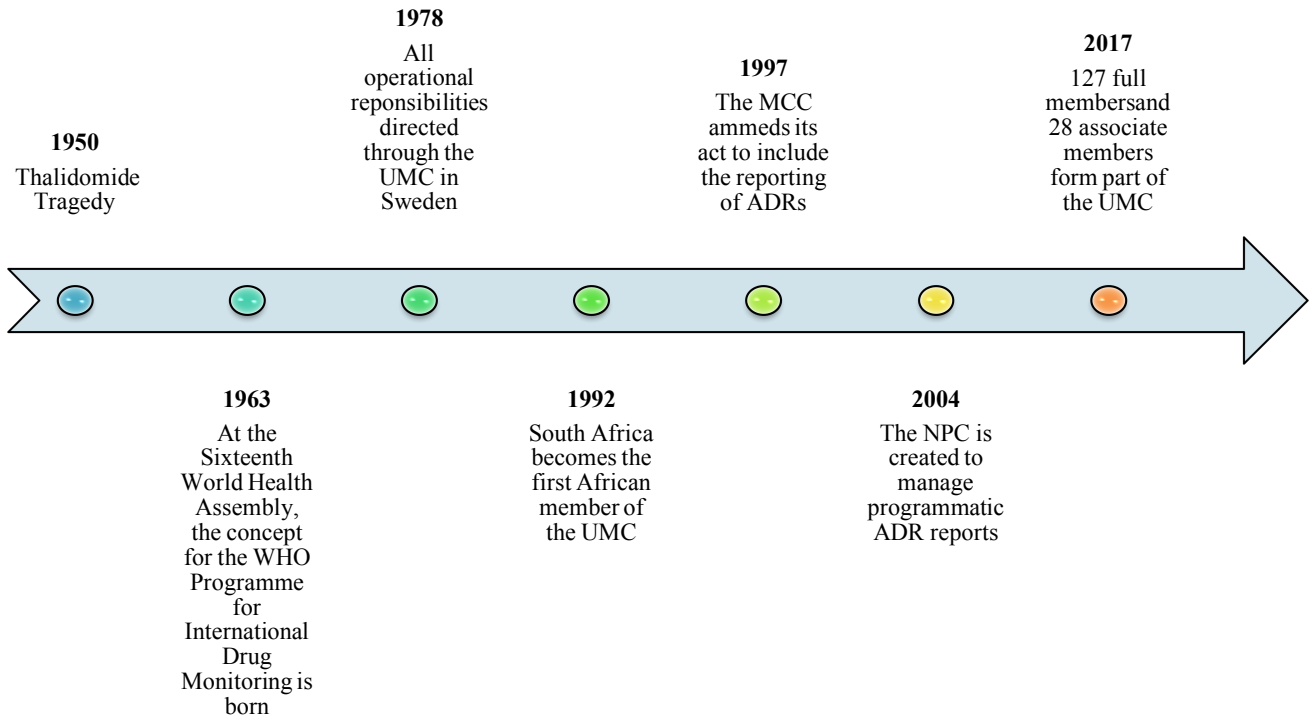


Figure 2.1: Timeline of the Basic Events of Pharmacovigilance in the South African Context

Drug disasters throughout modern history, including the Thalidomide tragedy in the 1950's-1960's in many ways led to the development of the field of PV. Before being put on the market, Thalidomide underwent clinical trials and was claimed to be "virtually free from side effects" (Lenz, 1988, pp.1). However, expectant mothers, who took the drug, devastatingly gave birth to babies with a congenital defect called phocomelia, in which babies are born with underdeveloped limbs (Kumar, 2010; Miller, 1991; McBride, 1961). This disaster brought attention to the issue of medicine safety, and the need for stricter regulations globally. In an effort to proactively avert such drug disasters, at The Sixteenth World Health Assembly, a pilot concept was born and this later became known as the World Health Organisation (WHO) Programme for International Drug Monitoring (WHO, 2002). The concept of PV then became widely recognised, encompassing the following as defined by the WHO: "drug monitoring; pharmaceutical

preparations- adverse effects; adverse drug reaction reporting; product surveillance, post marketing (and) legislation" (WHO, 2002).

The WHO Programme for International Drug Monitoring began with 10 founding members in 1968: Australia, Canada, Czechoslovakia, Federal Republic of Germany, Ireland, Netherlands, New Zealand, Sweden, United Kingdom, and the United States of America, before directing all operational responsibilities through the Uppsala Monitoring Centre (UMC) in 1978. The Uppsala Monitoring Centre became the controlling body, taking on the responsibility for collecting reports and information on ADRs, and supporting member countries in their pharmacovigilance activities (UMC, 2017). Currently, the UMC holds an international database of Adverse Drug Reactions (ADRs), known as "Vigibase", and plays a prominent role in signal detection and safety research (UMC, 2017). Signal detection is the "notice of an early concern or hypothesis about a possible medicines safety problem, with evidence and arguments to support it" (UMC, 2017, n.p). It aims to discover and communicate pertinent information about the risks of medicines (UMC, 2017). The members of the UMC have grown in number over time and there are currently 127 full members and 28 associate members, who are on their way to developing a functional pharmacovigilance system (UMC, 2017). The UMC consolidates reporting data from member countries, which comply with the "minimum requirements for a functional pharmacovigilance system" (WHO, 2010). The following is a list of said requirements as laid out by WHO (2010):

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

1	A national pharmacovigilance centre with designated staff (at least one full time), stable basic funding, clear mandates, well defined structures and roles and collaborating with the WHO Programme for International Drug Monitoring.
2	The existence of a national spontaneous reporting system with a national individual case safety report (ICSR) form i.e. an ADR reporting form.
3	A national database or system for collating and managing ADR reports.
4	A national ADR or pharmacovigilance advisory committee able to provide technical assistance on causality assessment, risk assessment, risk management, case investigation and, where necessary, crisis management including crisis communication.
5	A clear communication strategy for routine communication and crises communication.

2.2 SOUTH AFRICA'S COMPLIANCE TO THE WHO MINIMUM REQUIREMENTS FOR A FUNCTIONAL PHARMACOVIGILANCE SYSTEM

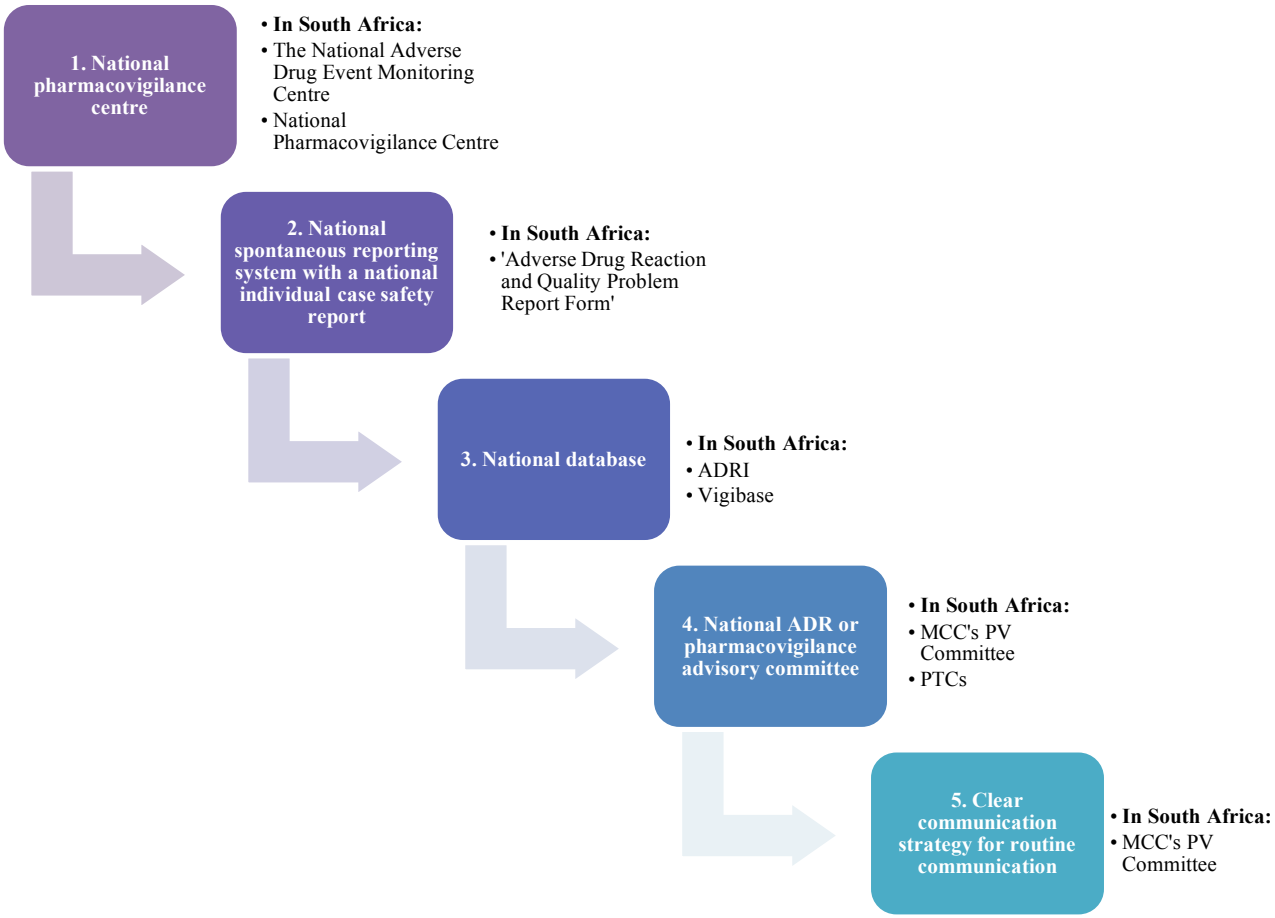


Figure 2.2: South Africa's Compliance with WHO Minimum Requirements
(Mehta, 2011; Mehta, 2014; WHO, 2010)

South Africa met these minimum requirements and became a member country of the UMC in 1992, before any other African country (Mehta, 2014). South Africa's PV activities are directed by The Medicines Control Council (MCC), which is the "statutory body" responsible for national safety and quality of medicines (Mehta, 2011, p.248). The MCC amended its act (Medicines and Related Substances Control Act 10 of 1965) in 1997 by adding Regulations 34 (Conduct of Clinical Trials for Humans) and 37 (Adverse Drug Reactions) (MCC, 1997). Regulation 34 makes provision for the application required to be completed upon desire to conduct any clinical trial, and the requirements to be fulfilled by potential investigators (MCC, 1997). Regulation 37

directly makes provisions for the holder of the registration of a medicine to timeously report suspected ADRs to the MCC, emphasizing the importance of ADR forms and collected data (MCC, 1997).

The MCC consequently published guidelines on reporting ADRs titled: 'Reporting Adverse Drug Reactions in South Africa', outlining clearly the relevant terminology pertaining to ADRs, as well as the process of reporting (MCC, 2014). It also makes provision for pharmaceutical companies to have at least one full time employee to manage pharmacovigilance affairs, and to report information to the NADEMC. According to the guidelines, serious and non-serious ADR reports should be submitted within 15 days of a witnessed reaction, using the prescribed national individual case safety report (ICSR) form. In South Africa, the preferred form is the 'Adverse Drug Reaction and Quality Problem Report Form' (Appendix A), however, individual forms used by institutions are also accepted, as long as the relevant information is provided.

The MCC established The National Adverse Drug Event Monitoring Centre (NADEMC), to bridge the gap between UMC and the MCC (Mehta, 2011), and it is responsible for the collation of data from received ADR reports, and the "assessment of causality and risk of ADRs" (Maigetter, 2010), thus fulfilling the role of managing the national database.

South Africa's National Department of Health (NDOH) subsequently established a National Pharmacovigilance Centre (NPC) in 2004, which plays an important role in collecting and collating programmatic reports, i.e. those relating to public health programs including TB and HIV (Dheda, 2016). The NPC acting in communication with the MCC and the UMC potentially allows for the data to be fed centrally, a vital part of the system of PV in any country.

On a clinical level, the development of PV advisory committees, which can report to the national centre, allows for ease of communication and the ability to deal with issues within the hospital environment. It was suggested at the First International Conference on Improving Use of Medicines (ICIUM) that hospital committees be developed (WHO, 2003). In South Africa, these hospital committees are termed Pharmaceutical and Therapeutics Committees (PTC's), and they deal with "problems of drug selection, procurement, distribution and use" (WHO, 2003). PTC's are responsible for managing ADRs and managing medication errors, as well as "evaluating the clinical use of drugs" and "managing the formulary" (WHO, 2003). These forums provide a way

in which public sector institutions can integrate gathered information, and then report this information to national centres. They also serve as a potential platform for feedback on ADR management at a clinical level. PTC's have proven effective in improving rational drug use when utilized effectively, and the WHO is committed to promoting the functioning of these committees in developing countries (WHO, 2003). 'The National Policy for the Establishment and Functioning of Pharmaceutical and Therapeutics Committees in South Africa' (2015) published by the National Department of Health outlines the goals, and policies that should be adhered to in order to have an effective PTC. Members of a PTC have a "range of expertise and skills" (National Policy, 2015, pp. 8) to provide a holistic advisory committee. The emphasis on communication between health care professionals is important as it allows for thorough clinical problem solving and thus improved patient care.

South Africa has established the necessary framework to meet the minimum requirements. As a member of the UMC, South Africa is also obligated to keep the system updated and submit ICSRs to the UMC at least quarterly (UMC, 2017).

Table 2.2: Summary of the Functions of PV Authorities

WHO	UMC	MCC	NADEMC	NPC
Responsible for directing PV globally through the WHO Collaborating Centre for International Drug Monitoring	Created by the WHO as the operational body responsible for PV; holds an international database of ADRs	The MCC is medicine regulatory authority in South Africa, and is responsible for the regulatory aspects of PV	Established by the MRA to collate ADR reports, and acts in communication with UMC	Primarily responsible for collating reports pertaining to public health programmes such as HIV and TB

(Dheda, 2016; Mehta, 2011; WHO, 2010; UMC, 2017)

2.3 REPORTING RATES IN SOUTH AFRICAN VS THE REST OF THE WORLD

A study comparing the reporting rates of developed and developing countries showed that between 2000 and 2009, the USA and the UK generated an average of 40,6274 and 14,2555 reports per year respectively. Compared with South Africa and India, which generated 5518 and 362 reports per year respectively, significant differences between developed and developing countries seem to exist (Aagaard et al., 2012). An important consideration is the disease burden in the country, as well as the type of treatments patients use outside of western medicine such as traditional medicine. In South Africa, HIV and TB account for a large patient demographic, and a high incidence of ADRs a result of the corresponding treatment, leading to a further need to monitor patients on their treatment (Mehta et al., 2008).

A study conducted by Ampadu et al. found that in 2015 Africa as a continent was responsible for 0.88% of the global number of reports- significantly lower than the rest of the world. In 2015, 28,609 ICSRs were submitted by South Africa, representing 0.24% of the total global reports (Ampadu, 2015). The trend is that data is often not fed to a national system, which is evident from fewer generated reports (Maigetter et al., 2015). There is a lack of collaboration between sectors, particularly the pharmaceutical industry, which leads to a "national database that does not include data from all sources" (Ouma & Abwao, 2012, p.9). Olsson, Pal & Dodoo conducted a review of PV in resource limited countries and described that because there is a shortage of health care workers in low to middle income countries, the perception is that it's more important to focus on clinically managing the patient than filling out the paperwork involved in spontaneous reporting (2015).

2.4 TYPES OF REPORTING: SPONTANEOUS, TARGETED AND COHORT EVENT MONITORING

ADR data gathered largely consist of spontaneous reports, which has been the mainstay approach to ADR reporting globally for many years. Spontaneous reports refer to passive reporting of ADRs by health care professionals or patients as they witness them (Joubert & Naidoo, 2016). The effectiveness of this voluntary type of reporting relies on the practitioner noticing an event

and reporting it appropriately (Mulatu & Worku, 2014). Provided its framework is adhered to, "spontaneous reporting systems provide the highest volume of information at the lowest maintenance cost" (Pal et al., 2013, p.75).

Targeted reporting is a different system of reporting, in which ADRs are noticed by monitoring particular groups of patients through active surveillance (Pal et al., 2013). This type of reporting involves the analysis of prescription data and the completion of questionnaires by health care practitioners, detailing all relevant information (Härmark & van Grootheest, 2012). Targeted reporting aims to minimize the "under-reporting" that may occur from the reliance on the voluntary nature of spontaneous reporting (Härmark & van Grootheest, 2012, p.10), however it is also a valuable tool when used in conjunction with spontaneous reporting. In response to a signal generated by spontaneous reports, targeted reporting could provide more specific information about particular groups of patients, such as those with critical illnesses (Pal et al., 2013).

Similarly, Cohort Event Monitoring (CME) programmes are established to monitor the safety and efficacy of medicines, and are based on the conduction of "prospective observational cohort" studies (Pal et al., 2013). In South Africa, CME has been used often in the field of ARV's, as well as TB. The aim is to continuously gather patient data in order to improve the treatment outcomes of patients on lifelong therapy (Vusi, 2014).

2.5 SPONTANEOUS REPORTING IN SOUTH AFRICA

In South Africa, ADR reports are documented via the 'Adverse Drug Reaction and Quality Problem Report Form' (Appendix A) - a product of the NADEMC. This form is completed with attention given to patient information; a full description of the reaction; details of the treatment including dosage and duration and details of the outcome. In the public sector, the forms are sent to the hospital or district PTC, where the data is consolidated and forwarded to the secretariat of the Safety and Quality Subcommittee, the provincial PTC's, the NADEMC and finally the MCC (Guidelines for Implementation of Pharmaceutical and Therapeutics Committees in Gauteng Province, 2013). The reporting health care professional should be informed of progress and final

outcomes in order to ensure an effective feedback cycle (Guidelines for Implementation of Pharmaceutical and Therapeutics Committees in Gauteng Province, 2013). However, the information between channels is often not fed back, which may lead to a lack of available data, as well as demotivated health care workers. Strengthening pharmacovigilance has to include a focus on the importance of collaboration through continuous training (Maigetter, et al., 2015).

2.6 KNOWLEDGE, ATTITUDE AND PRACTICES OF HEALTH CARE PROFESSIONALS

A standard of reporting can be adhered to given the right attitudes and knowledge of health care practitioners, who have a duty to adopt a "culture of reporting" when monitoring patients during their treatment process (Pimpalkhute et al., 2012, p.56). How much information is gathered and duly reported largely depends on the awareness and assertiveness of the professional (Pimpalkhute et al., 2012). The reasons for the underreporting of ADRs by health care professionals have been researched globally. Isah et al. list the following reasons for underreporting in Africa: "inability to recognize ADRs, ignorance of the reporting requirements, lack of reporting forms, feeling of guilt following the occurrence of adverse effects and fear of litigation" (2011). These factors cause health care professionals to not adhere fully to the framework of reporting, which leads to inadequate or incomplete data.

ADRs can lead to serious and even fatal consequences, shown by the "high prevalence of hospital admissions" worldwide (Suyagh, Farah & Farha, 2014, p.147-148). The future of medicine safety cannot be improved if ADRs are not adequately reported (Fadare et al., 2011). It is vital that the approach to PV is one that collaborates efforts from "drug regulatory authorities, pharmaceutical industry and all healthcare providers" (Kshirsagar, Olsson & Ferner, 2010, p.65). In the future, education and training for all involved parties can possibly enhance the reporting rate and the quality of reporting in developing countries (Elkami et al., 2011). Particularly in South Africa, it is evident that healthcare workers need more education and a better understanding of the frameworks (Mehta, 2011). Providing knowledge on the importance of ADRs and its impact on downstream costs, time spent, and the overall livelihood of the patient may be the catalyst to improving reporting habits.

2.7 AIM OF THE STUDY

The aim of this study was to determine the knowledge, attitudes and practices of pharmacists, doctors and nurses at a tertiary hospital.

2.8 RESEARCH OBJECTIVES

- To assess the current levels of knowledge of doctors, nurses and pharmacists on ADR reporting.
- To assess the attitudes of doctors, nurses and pharmacists towards ADR reporting.
- To assess the practices of doctors, nurses and pharmacists with regards to ADR reporting.
- To identify trends and relationships between knowledge, attitudes and practices on ADR reporting.

CHAPTER III: METHODOLOGY

3.1 SELECTION OF INSTITUTION

The study was conducted at a public tertiary hospital, which is a teaching hospital in the Gauteng Province. The hospital employs more than 4000 staff and serves a population of approximately 8 723 786, along with another large teaching hospital in the area. The institution was chosen to conduct the study within the main hospital pharmacy, and inpatient wards, chosen based on the trends of inpatient volume from 2015. The ten wards with the highest inpatient intake in 2015 were Pulmonology; Oncology; ICU (neonatal and adults); Surgical; Orthopaedic; Renal; Gynaecology; Diabetes; Gastroenterology; and Cardiac.

3.2 STUDY DESIGN

The study is a longitudinal, sequential explanatory study, a type of mixed-methods study beginning with a quantitative aspect (i.e. questionnaire), followed by a qualitative aspect (i.e. focus groups), used to find reasons for trends in responses (Creswell, 2003). A stratified sampling method was applied and only doctors, nurses and pharmacists from the chosen sites were invited to participate.

3.3 POPULATION AND SAMPLE SIZE

In 2016, the hospital employed a total of 623 medical doctors, 2165 nurses and 26 pharmacists. This is a total of 2814 permanent health care professionals. The following formula was used to calculate an appropriate sample size:

Sample Size:

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

Correction for Finite Population:

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

Where:

Z = Z value (e.g. 196 for 95% confidence level)

p = percentage picking a choice, expressed as decimal

(0.5 used for sample size needed)

c = confidence interval, expressed as decimal

(e.g., 0.04 = ±4)

pop = population

Using a confidence interval of 0.05 and a 95% confidence level, the appropriate sample size for this study was 338 health care professionals.

3.4 INCLUSION CRITERIA

- All qualified and registered medical doctors, nurses and pharmacists practising in the ten chosen wards in 2016/ 2017, including interns and those conducting community service.
- Participants who consented participation in the study.

3.5 EXCLUSION CRITERIA

- Health care professionals other than doctors, nurses and pharmacists were excluded from the study.

- Basic and post-basic pharmacists were not included in the study.
- Those who did not consent to participate were not included in the study.

3.6 QUESTIONNAIRE AND FOCUS GROUP DESIGN

A literature review was conducted between January and March 2016 to gain background knowledge on the perceptions of healthcare workers on ADR reporting globally. A questionnaire was then compiled consisting of questions relating to knowledge, attitudes and practices of health care professionals. A total of 21 questions were used based on 3 similar studies (Desai et al., 2011; Pimpalkhute et al., 2012; Suyagh, Farah & Farha, 2014). In order to achieve the aim of the study, the questions were categorised as follows: 5 questions pertaining to demographics; 7 questions on the awareness of ADR reporting; 7 questions about the professional's previous ADR reporting involvement; 1 question pertaining to the professional's general attitude towards ADR reporting and 1 question about possible future improvements that could be made.

Following the results from the questionnaire, a focus group guide was designed to address the various trends that developed relating to the perceptions held by healthcare workers about ADR reporting. These open-ended questions aimed to address the health care professional's perceptions of ADR monitoring, including the patient's awareness of ADR reporting; the professional's general attitude towards ADR reporting; the professional's previous ADR reporting involvement; and the possible improvements that could be made (see Appendix C).

3.7 BASELINE ASSESSMENT: QUESTIONNAIRE

Participation in the questionnaire phase of the study occurred in the period between July and November 2016, in which the hard copies of the questionnaires were disseminated and collected. The questionnaires were distributed to pharmacists, and to head nurses at wards, who distributed and collected the questionnaires within their departments. Reminders were sent to heads of department beforehand to ensure that staff members were made aware of the study. Those who choose to participate were required to complete the informed consent form and were given appropriate instructions for filling out the questionnaire. They were guaranteed anonymity with

regards to their questionnaire responses, in that no personal or identifiable information was asked to be disclosed. Only the researchers involved had access to the questionnaires after they were completed.

3.8 FOCUS GROUPS

Focus groups are used widely in the field of health science for their unique ability to "seek explanations for behaviour" (Lakshman, 2000). Following the questionnaire phase of the study, the focus group phase was aimed at understanding the reasons behind certain trends in questionnaire responses. The focus group platform was intended to provide further insight, possibly even drawing on the opinions expressed in the questionnaires. For purposes of continuity from the questionnaires to the focus groups, nurses and pharmacists were exclusively chosen to participate, as they represented a combined 86% of the questionnaire participants.

Nurses and pharmacists in the participating wards were subsequently invited via email and in person to attend focus groups (12-20 nurses and 12-20 pharmacists). It was unknown whether participants of the focus group had also participated in the questionnaire, due to the anonymity of the questionnaire. The groups (nurses and pharmacists) were randomly divided in half (6-10 participants per group), and 1 group of pharmacists and 1 group of nurses received training during their focus group discussion, while the others only received a brief training session at the end. Training sessions were conducted during focus groups because the size of the groups, and the unique setting provided a favourable platform for training. It utilised the effects of group dynamics as a teaching tool, allowing participants to involve themselves and bounce ideas off one another, in order to develop understanding of the material. This also allowed for a variety of themes to develop during the sessions.

The focus groups were based on a broad set of questions (Appendix C), but deviated depending on responses from participants. Each focus group took an average of 1 hour. Information gathered during the focus groups did not disclose any personal or identifiable information.

The training material used during focus groups addressed the concepts of PV and ADRs; details of the reporting process; and benefits of reporting. The aim of the material is to communicate both the process and the importance of reporting ADRs to healthcare professionals.

3.9 DATA ANALYSIS

Data was collected in the form of questionnaire responses from pharmacists, doctors and nurses. The data was then electronically captured on to spreadsheets on Microsoft Excel™. The questionnaire responses was categorized in terms of the following:

- The demographics of the person participating.
- The current knowledge and awareness of the participant.
- The attitude of the professional towards PV.
- Any prior PV involvement the participant may have had (i.e. practices).
- The need for further PV training or other suggestions.

The data captured on Microsoft Excel™ spreadsheets was imported on Stata® (Version 14). Pearson chi squared and Fishers tests were run in order to discover significant associations in the data, at a significance level of $p<0.001$. The principles of Braun and Clarke (2006) were applied to the qualitative data from the focus groups. The original focus group recordings were transcribed once and then confirmed for accuracy. The transcriptions were then coded based on emerging concepts and ideas, and finally analysed in terms of the themes and subthemes that developed during each focus group discussion.

3.10 VALIDITY OF THE STUDY

3.10.1 External Validity and Transferability

The sample for the study was all participating medical doctors; nurses and pharmacists working within the 10 chosen wards and the hospital pharmacy, representing the overall study population of the healthcare workers at the study site. Conclusions drawn in this study are specific to the hospital site, and therefore generalisations made pertain only to the study population.

3.10.2 Construct Validity

Face and content validity were evaluated in this section. Face validity was achieved in that the objectives of the study were appropriately measured using the methodology, which was adapted from previous similar studies. The questionnaire was validated using a group of 10 randomly selected pharmacists, who were not included in the study. The questionnaire was piloted once, and again one month later in order to ensure validity and eliminate bias. All the questionnaire responses were analysed to yield an understanding of relevant and irrelevant questions. The questionnaire was adjusted appropriately to obtain a final version for distribution.

3.10.3 Internal Validity and Credibility

The primary consideration in this section was the effects of social interaction on the study. The study assessed three separate groups of health care professionals (doctors; nurses and pharmacists) in the questionnaire, and then two groups (nurses and pharmacists) in the focus groups. Knowledge that the study was happening may have affected the participants responses in anticipation of what the study involved. Those that chose to respond to the questionnaire or participate in the focus groups may have done so with some level of bias.

3.10.4 Conclusion Validity

With regards to relationships among quantitative data, chi-squared tests were used to prove the statistical significance of any relationship that occurred between variables. With regards to the focus group, the quantitative data from the questionnaire was taken into consideration to look for continuity or lack thereof. These are explained in the results and discussion chapters.

3.11 RELIABILITY AND DEPENDABILITY OF THE STUDY

The study could be easily reproduced in a different study population in order to assess the knowledge, attitudes and practices of health care professionals in other settings. However, it is not necessarily expected that the results will be consistent in another setting, although similarities may occur, based on the literature review of similar studies and their results.

3.12 ETHICS

The questionnaire remained anonymous and confidential throughout, with only the researcher having access to the forms. The focus groups were recorded and participants were required to sign a recording consent form. No personal or identifying information was associated with the recording or the transcript. Only the researcher, supervisors and ethics committee, if necessary, may listen to the recordings, which will be destroyed after the appropriate time (see Appendix D and Appendix E).

Ethics approval was granted by the University of the Witwatersrand Human Research Ethics Committee (HREC) **(No. M160246)** (see Appendix F).

CHAPTER IV: RESULTS AND DATA ANALYSIS

4.1 QUESTIONNAIRE RESULTS

Two hundred and ninety-seven questionnaires were returned out of the sample size calculated of 338, giving a 87.87% response rate. The respondents were made up of 41 doctors; 230 nurses; 24 pharmacists and 2 people did not indicate their profession (Table 4.11). The female gender represented more than 83% of the sample, which is a statistically significant difference in gender *($p<0.001$)* (Table 4.1.2).

Figure 4.1.1 shows the distribution of health care professionals in the wards, with most participants who stated "other" practising in the pharmacy and not in the wards.

4.1.1 Demographics Of Participants

Table 4.1.1: Frequency Distribution of the Demographics of Participants (N=297)

Demographic Characteristics	Frequency (N)	Percentage (%)
Gender		
Male	48	16.16
Female	249	83.84
Total	**297**	
Profession		
Doctor	41	13.80
Nurse	230	77.44
Pharmacist	24	8.08
Total	**295 (*= 2)**	

Demographic Characteristics	Frequency (N)	Percentage (%)
Level of Practice		
Intern	27	9.09
Community Service	28	9.43
Post- community service	144	48.48
Total	**199 (*= 98)**	
Ward		
Pulmonology	20	6.73
Oncology	26	8.75
ICU	38	12.79
Surgical	56	18.86
Orthopaedic	39	13.13
Renal	40	13.47
Gynaecology	34	11.45
Diabetes	16	5.39
Gastroenterology	48	16.16
Cardiac	37	12.46
Other	24	7.10
"Theatre"	1	
"Pharmacy"	9	
"Paediatric oncology"	1	
"Anaesthesiology"	1	
"Haematology"	1	
Total	**378**	
Years of Practice		
< 1 year	34	11.45
1-5 years	83	27.95
6-10 years	106	35.69
> 10 years	68	22.90

Total	**291 (* = 6)**

*= missing data

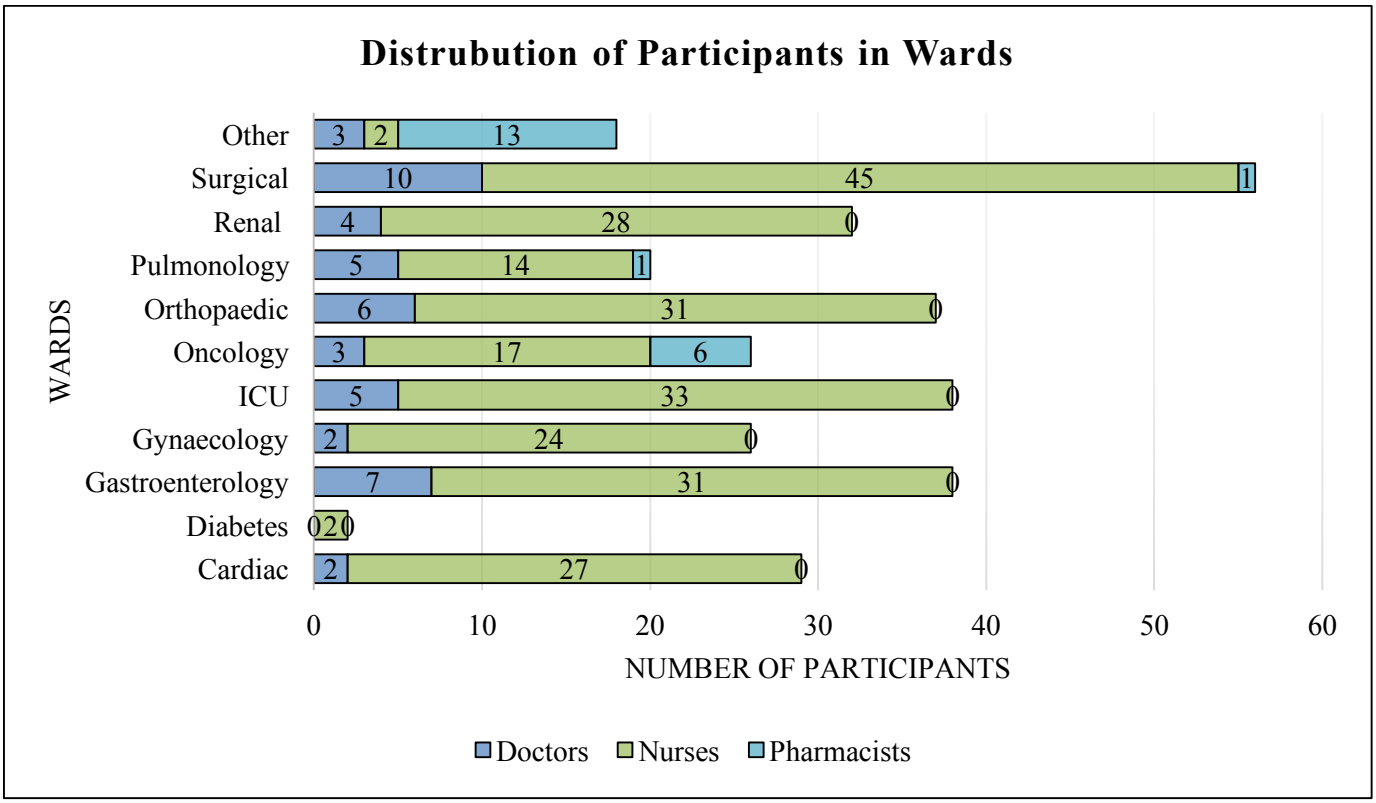


Figure 4.1.1: Distribution of Participants in Wards

Table 4.1.2: Gender of Participants Versus Profession of Participants (N=297)

	Profession of Participants			
Gender	**Doctor**	**Nurse**	**Pharmacist**	**All**
Female	25 (58.14%)	209 (90.87%)	15 (62.50%)	249 (83.84%)
Male	18 (41.86%)	21 (9.13%)	9 (37.50%)	48 (16.16%)
Total	43 (100%)	230 (100%)	24 (100%)	297 (100%)

Pearson Chi-square = 37.4158, p value = 0.000

The results are significant at p<0.001

4.1.2 Knowledge of the Participant

Fifty percent of the participants stated they knew how to report an ADR, and 77.10% stated that they were familiar with the form. Fifty nine percent of the participants identified the NADEMC as the primary place to report ADRs, shown by Figure 4.1.2. Participants chose many reasons for the importance of ADRs, with most participants checking all the options for that question shown by the distribution in Figure 4.1.3.

Table 4.1.3: Frequency Distribution of Participants Knowledge of PV (N=297)

Responses	Frequency (%)	Percentage (%)
Knowing how to report an ADR		
Yes	149	50.17
No	145	48.82
Total	294 (*=3)	
Familiar with the reporting form		
Yes	229	77.10
No	65	21.89
Total	294 (*=3)	
The National Adverse Event Monitoring Centre (NADEMC)	176	59.26
Pharmaceutical and Therapeutics Committee (PTC)	145	48.82
The Medicines Control Council (MCC)	143	48.15
Medical Supply Depot (MSD)	38	12.79
The Safety and Quality Subcommittee	70	23.57
Other	12	4.04
"Doctor and Pharmacy in Hospital"	3	
"Pharmaceutical Company"	1	
"The Drug Controller"	2	
"Supplier"		
Total	584	

Table 4.1.4: Frequency Distribution of Participants Knowledge of PV (N=297)

Continued

Responses	Frequency (%)	Percentage (%)
Why its important to report ADRs		
To identify new ADRs	1375	92.59
To improve patient safety	1401	94.34
To measure the incidence of ADRs	1376	92.66
To share information about ADRs with colleagues	1347	90.71
To identify relatively safe drugs	1357	91.38
It is a requirement	1315	88.55

*= missing data

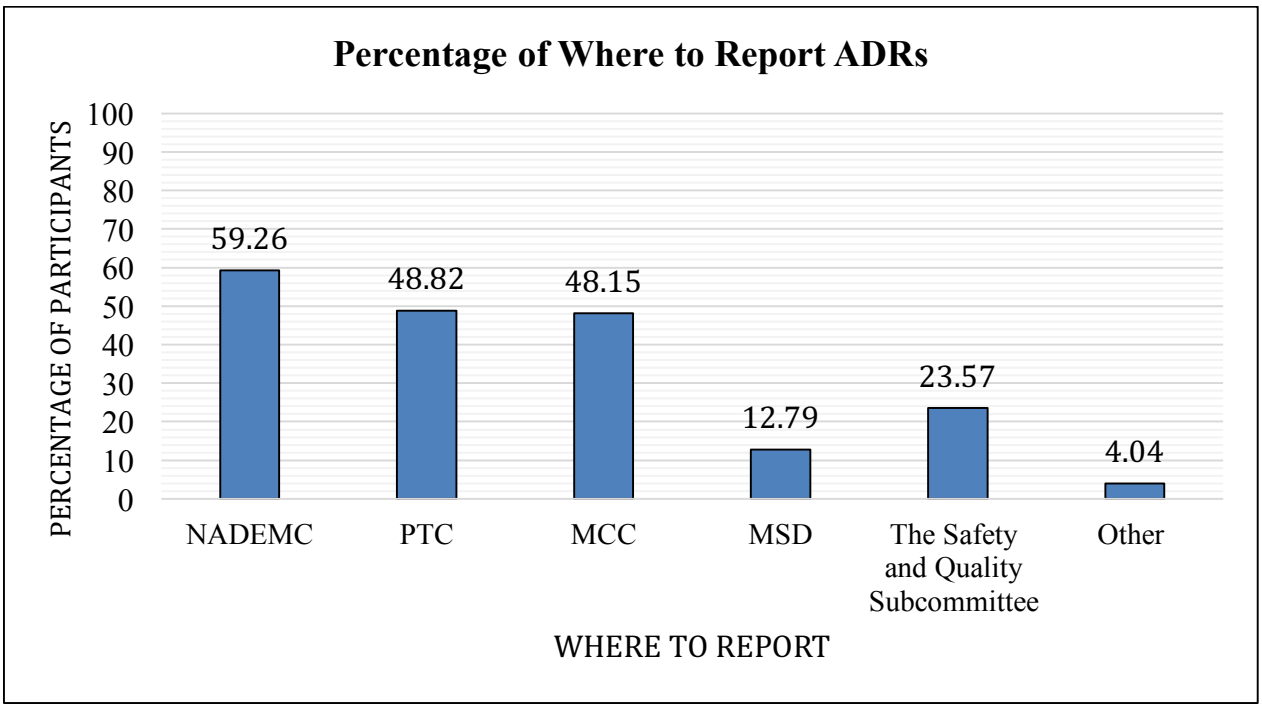


Figure 4.1.2: The Percentage of Where to Report ADRs

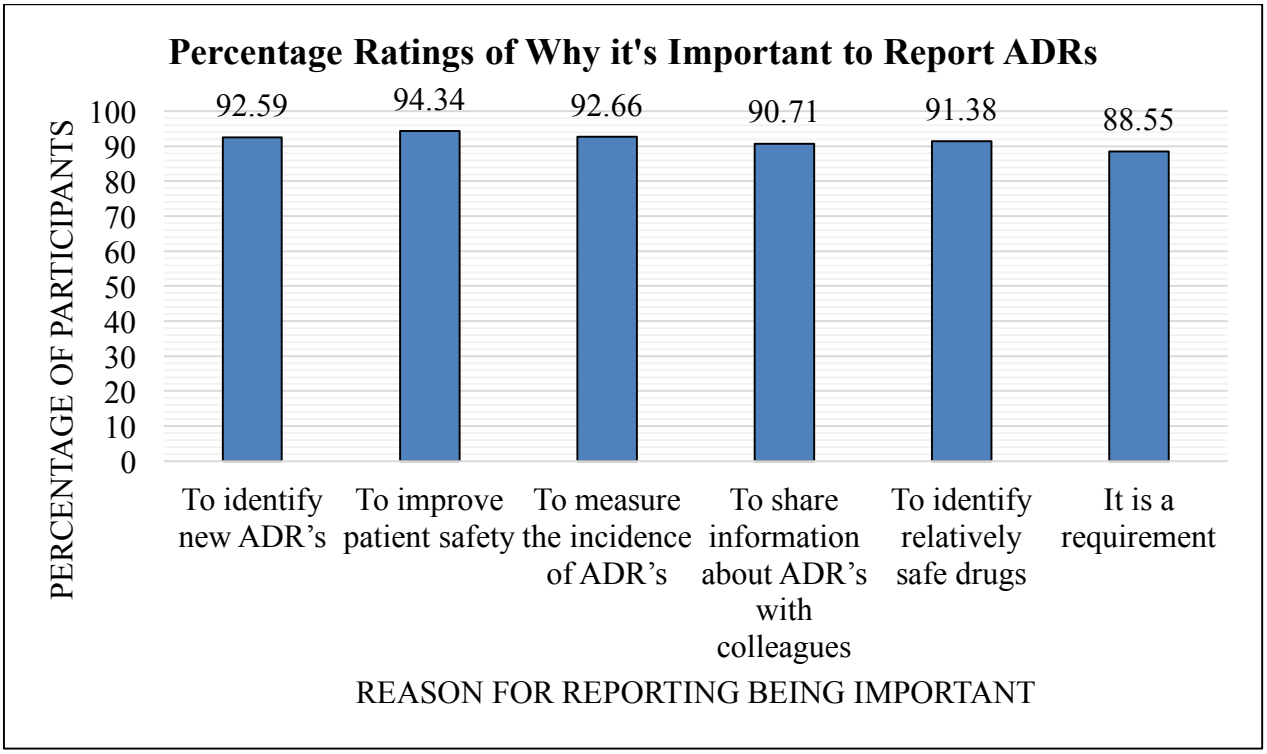


Figure 4.1.3: Percentage Ratings of Why It's Important to Report ADRs

There was a statistical difference in the knowledge of how to report ADRs by profession *(p<0.001).* Fifty percent of the nurses stated they didn't know how to report, while 53.59% of doctors and 82.61% of pharmacists knew how to report (Table 4.1.4). This is depicted visually in Figure 4.1.4 with the responses ("yes" or "no") shown by profession.

Table 4.1.5: Knowledge of How to Report ADRs by Profession (N=292)

	Profession of Participant			
Response	**Doctor**	**Nurse**	**Pharmacist**	**All**
Yes	23	105	19	147
	(53.49%)	(46.46%)	(82.61%)	(50.34%)
	(15.65%)	(71.43%)	(12.93%)	(100%)
No	18	121	4	143
	(41.86%)	(53.54 %)	(17.39%)	(48.97%)
	(12.59%)	(84.62%)	(2.80%)	(100%)
Invalid Response	2	0	0	2
	(4.65 %)	(0.00%)	(0.00%)	(0.68%)
	(100%)	(0%)	(0%)	(100%)
Total	43	226	23	292
	(100%)	(100%)	(100%)	(100%)
	(14.73%)	(77.40%)	(7.88%)	(100%)

Pearson Chi-square = 23.1900, p-value = 0.000, Fisher's exact for scores <5 = 0.000
The results are significant at p<0.001

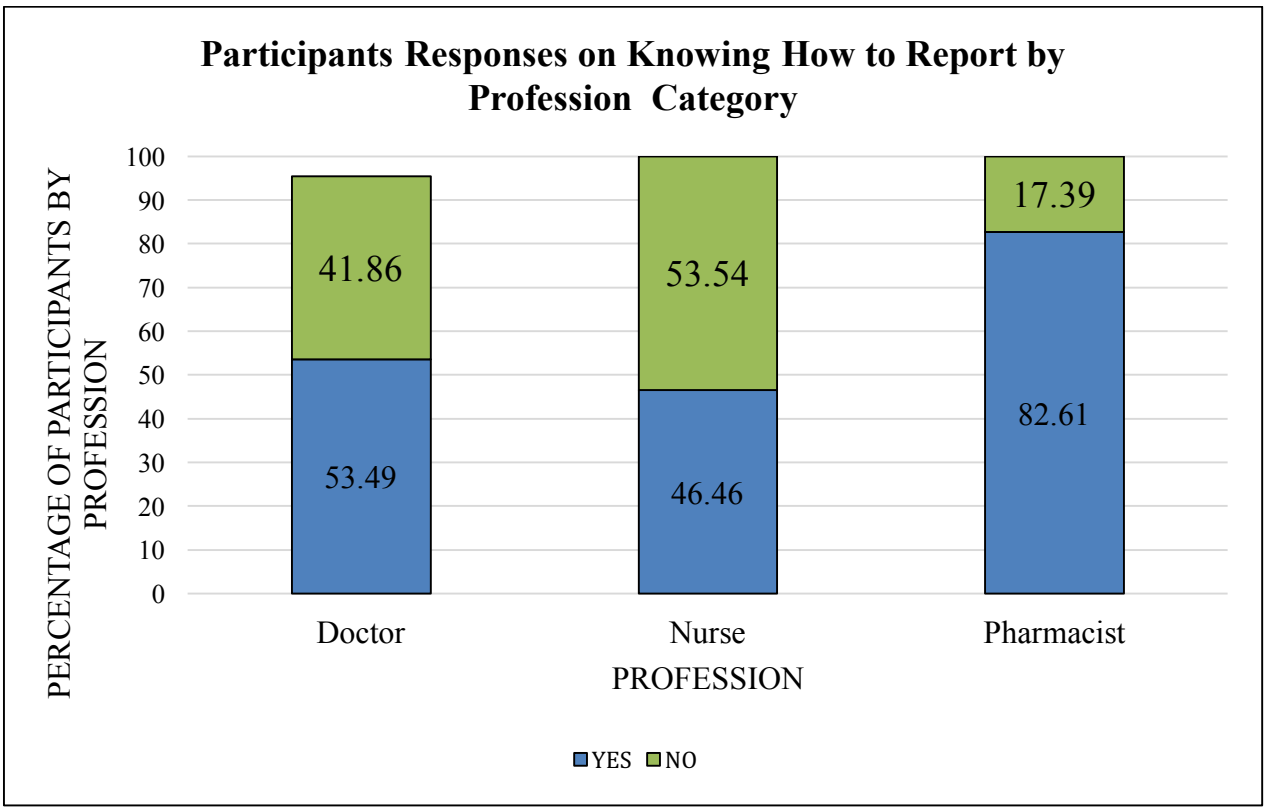


Figure 4.1.4: Knowledge of Reporting by Profession

Table 4.1.5 and Table 4.1.6 below show the participants knowledge of how to report by the years of experience and level of practice respectively. Fifty-four percent of participants who knew how to report had been practising as health care professionals for 6-10 years. Statistically, participants who were newest to practising (<1 year) had little knowledge of reporting with 76.47% of participants stating they didn't know how to report *($p<0.001$)*. Fifty-eight percent of post-community service participants knew how to report ADRs, whereas only 23.08% of interns knew how to report ADRs *($p<0.001$)*.

Table 4.1.6: Knowledge of How to Report ADRs by Years of Experience of Participants (N=288)

	Years of Experience of Participants				
Response	**<1 year**	**1-5 years**	**6-10 years**	**>10 years**	**All**
Yes	6 (17.65%) (4.08%)	34 (41.46%) (23.13%)	57 (53.77%) (38.78%)	50 (75.76%) (34.01%)	146 (51.04%) (100%)
No	26 (76.47%) (18.71%)	48 (58.54%) (34.53%)	49 (46.23%) (35.35%)	16 (24.24%) (11.51%)	139 (48.26%) (100%)
Invalid Response	2 (5.88%) (100%)	0 (0.00%) (0.00%)	0 (0.00%) (0.00%)	0 (0.00%) (0.00%)	2 (0.69%) (100%)
Total	34 (100%) (11.81%)	82 (100%) (28.47%)	106 (100%) (36.81%)	66 (100%) (22.92%)	288 (100%) (100%)

Pearson Chi-square- = 47.2773, p-value = 0.000, Fisher's exact for scores <5 = 0.000
The results are significant at p<0.001

Table 4.1.7: Knowledge of How to Report ADRs by Level of Practice of Participant (N= 195)

	Level of Practice of Participants			
Response	**Intern**	**Community Service**	**Post- Community Service**	**All**
Yes	6	12	82	100
	(23.08%)	(42.86%)	(58.16%)	(51.28%)
	(6.00%)	(12.00%)	(82.00%)	(100%)
No	18	16	59	93
	(69.23%)	(57.14%)	(41.84%)	(47.69%)
	(19.35%)	(17.20%)	(63.44%)	(100%)
Invalid Response	2	0	0	2
	(7.69%)	(0.00%)	(0.00%)	(1.03%)
	(100%)	(0.00%)	(0.00%)	(0.00%)
Total	26	28	141	195
	(100%)	(100%)	(100%)	(100%)
	(13.33%)	(14.36%)	(72.31%)	(100%)

Pearson Chi-square= 22.7846, p-value = 0.000, Fisher's exact for scores <5 = 0.001
The results are significant at p<0.001

With regards to the knowledge of the reporting form, participants were asked if they had seen the form previously after seeing an example of one in the questionnaire. The table below (Table 4.1.7) shows that 77.89% of participants had seen the form before. Eighty-one percent of doctors, 75.00% of nurses and all (100%) of the pharmacists had seen the form before. The chi-squared test conducted shows that there was an insignificant difference between professions in this regard ($p>0.001$).

Table 4.1.8: Knowledge of Reporting Form by Profession (N= 294)

	Profession of Participants			
Response	**Doctor**	**Nurse**	**Pharmacist**	**All**
Yes	35	171	23	229
	(81.40%)	(75.00%)	(100%)	(77.89%)
	(15.28%)	(74.67%)	(10.04%)	(100%)
No	8	57	0	65
	(18.60%)	(25.00%)	(0.00%)	(22.11%)
	(12.31%)	(87.69%)	(0.00%)	(100%)
Total	43	228	23	294
	(100%)	(100%)	(100%)	(100%)
	(14.63%)	(77.55%)	(7.82%)	(100%)

Pearson Chi-square= 7.9417, p-value = 0.019, Fisher's exact for scores <5= 0.007
The null hypothesis is true at a significance level of p<0.001

Table 4.1.8 shows the knowledge of the reporting form by the level of practice of participants. In line with knowledge of how to report, 86.01% of post-community service professionals were familiar with the reporting form. However, although there was a low percentage of interns who knew how to report an ADR, more than 60% (61.54%) of interns had seen the form before.

Table 4.1.9: Knowledge of Reporting Form by Level of Practice of Participants (N=197)

Level of Practice

Response	Intern	Community Service	Post-Community Service	All
Yes	16	15	123	154
	(61.54%)	(53.57%)	(86.01%)	(78.17%)
	(10.39%)	(9.74%)	(79.87%)	(100%)
No	10	13	20	43
	(38.46%)	(46.43%)	(13.99%)	(21.83%)
	(23.36%)	(30.23%)	(46.51%)	(100%)
Total	26	28	143	197
	(100%)	(100%)	(100%)	(100%)
	(13.20%)	(14.21%)	(72.59%)	(100%)

Pearson Chi-square= 19.3007, p-value= 0.000, Fisher's exact for scores <5 = 0.000

The results are significant at p<0.001

Similarly, Table 4.1.9 shows the participants knowledge of the reporting form by the years of experience. Participants who had been practising longer were more familiar with the form, with 91.8% of people practising for >10 years having previously seen the form. Only 21.03% of participants were unfamiliar with the reporting form, with 44.12% of participants practising <1 year. There is an association between the years of experience and familiarity with the reporting form *(p<0.001)*.

Table 4.1.10: Knowledge of Reporting Form by Years of Practice of Participants (N=290)

	Years of Experience of Participants				
Response	**<1 year**	**1-5 years**	**6-10 years**	**>10 years**	**All**
Yes	19	59	89	62	229
	(55.88%)	(71.08%)	(84.76%)	(91.18%)	(78.97%)
	(8.30%)	(25.76%)	(38.86%)	(27.07%)	(100%)
No	15	24	16	6	61
	(44.12%)	(28.92%)	(15.24%)	(8.82%)	(21.03%)
	(24.59%)	(39.34%)	(26.23%)	(9.84%)	(100%)
Total	34	83	105	68	290
	(100%)	(100%)	(100%)	(100%)	(100%)
	(11.72%)	(28.26%)	(36.21%)	(23.45%)	(100%)

Pearson Chi-square= 22.2389, p-value= 0.000, Fisher's exact for scores < 5 = 0.000
The results are significant at p<0.001

4.1.3 Attitudes of the Participants towards PV

Table 4.1.10 shows the frequency distribution of the results pertaining to the attitudes of the participants towards PV. Ninety percent of participants stated they would report an ADR based on the seriousness of the reaction, shown by Figure 4.1.5 with the other cases most likely to be reported by participants. Factors such as not knowing how to report; not knowing where to report; managing the patient being more important than reporting; and reporting being time-consuming, made up most of the factors that discouraged participants from reporting. Figure 4.1.6 shows participant's opinions on which health profession should be held responsible for reporting ADRs. Ninety-three percent of participants felt medical practitioners should be held responsible, followed by 88.89% for nurses and 76.77% for pharmacists. Two percent of participants chose "other" which was made up of the response "patients". This was further broken down in Figure 4.1.7, which shows the profession of participant and corresponding

response of who should report. Nurses, pharmacists and doctors themselves believed doctors should be held responsible for reporting before other health care professionals.

Table 4.1.11: Frequency Distribution of Participant's Attitudes (N=297)

Response	Frequency (N)	Percentage (%)
Cases most likely to report ADR		
Seriousness of the ADR	268	90.24
Unusualness of the reaction	160	53.87
Involvement of a new drug	139	46.80
Level of certainty that it is an ADR	85	28.62
None of the above	2	0.67
Total	654	
Factors discouraging participants from reporting ADRs		
Do not know how to report	97	32.66
Not knowing where to report	96	32.32
Did not think it was important to report	65	21.89
Managing the patient was more important than reporting ADRs	115	38.72
Lack of access to ADR reporting form	49	16.50
Patient confidentiality	46	15.49
It is time-consuming	95	31.99
There is a lack of feedback after forms have been submitted	65	21.89
Other	7	2.36
"Inexperience"	1	
"No discouraging factors"	2	
Total	635	
ADRs that should be reported		
None	1	0.34
All ADRs	182	61.28
All serious ADRs	132	44.44

Response	Frequency (N)	Percentage (%)
ADRs that should be reported (continued)		
ADRs to new drugs	59	19.87
Unknown ADRs to old drugs	47	15.82
ADRs to herbal and non-allopathic drugs	23	7.74
ADRs to vaccinations	28	9.43
Other	3	1.01
Total	475	
Professionals who should report ADRs		
Medical practitioners	275	92.59
Nurses	264	88.89
Pharmacists	228	76.77
Other	7	2.36
"Patient"	2	
Total	774	
Reference materials participants would use		
Textbook	177	59.60
Colleague	211	71.04
Internet	236	79.46
Package Insert	224	75.42
Other	3	1.01
Total	851	

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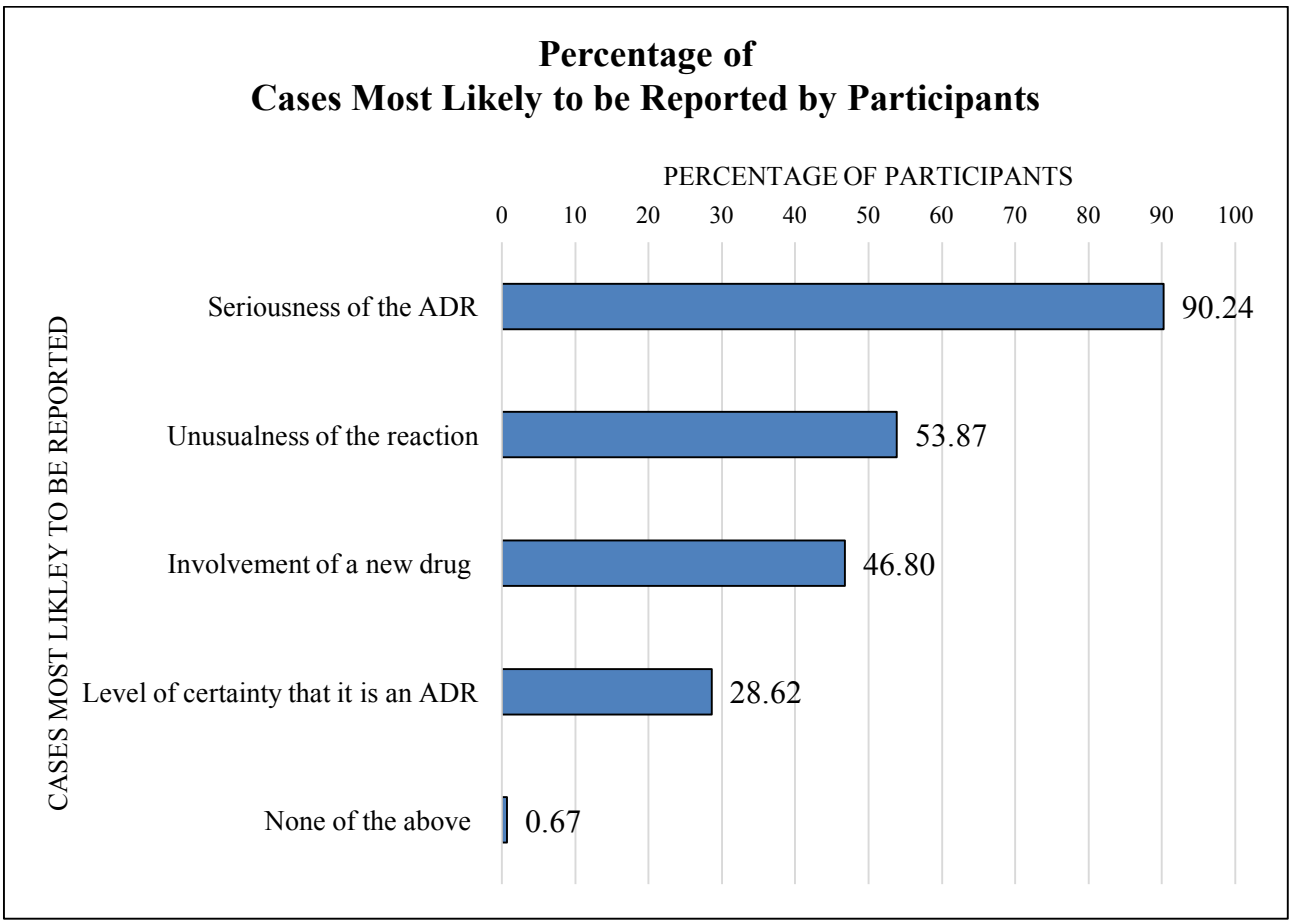


Figure 4.1.5: Percentage of Cases Most Likely to be Reported by Participants

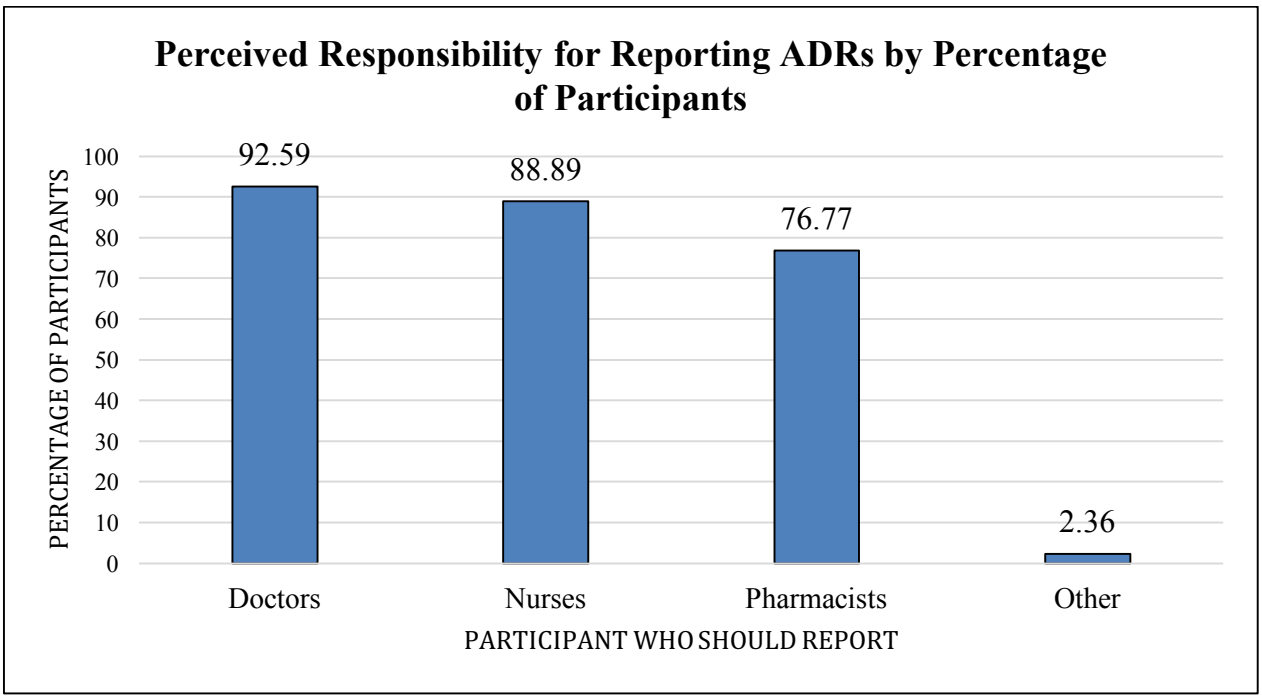


Figure 4.1.6: Perceived Responsibility for Reporting ADRs

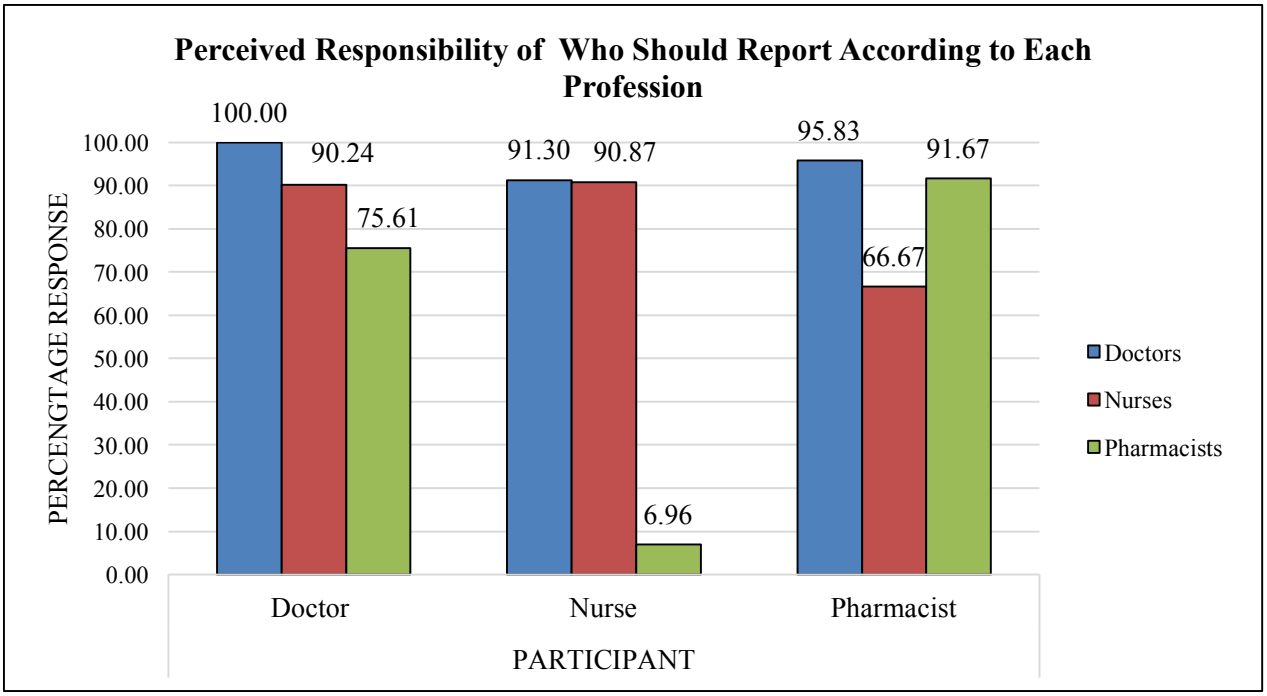


Figure 4.1.7: Percentage of who should report according to each profession

4.1.4 Previous PV Practices of Participants

Table 4.1.11 shows previous PV activity in which participants may have been involved, of which only 10.77% of participants had received previous PV training, and the majority of participants (73.74%) submitted <1 ADR per year. There was a significant difference between the percentage of participants who encountered an ADR in practice (58.59%), and those who reported the encountered ADR (16.50%) *(p<0.001)*. This information is shown in table 4.1.12 and figure 4.1.8. There was also an association between the participants who attended workshops/seminars and those who had knowledge of reporting (Table 4.1.13). Of the participants who had previously attended a seminar, 96.88% answered "yes" when asked whether they knew how to report ADRs *(p<0.001)*. This brings up the importance of training when dealing with healthcare worker's knowledge. When looking at the percentage of those having attended a workshop versus those that reported ADRs (Table 4.1.14), 48.15% reported <1 ADR per year; and 11.11% reported <1 ADR per month.

Table 4.1.12: Frequency Distribution of Previous PV Activity (N=294)

Response	Frequency (N)	Percentage (%)
Any previous training seminars/workshops on ADR reporting?		
Yes	32	10.77
No	262	88.22
Total	294 (* =3)	
Are ADR reporting forms easily available to you in practice?		
Yes	176	59.26
No	93	31.31
Total	269 (* =28)	
Have you ever encountered an ADR in practice?		
Yes	174	58.59
No	115	38.72
Total	289 (* =8)	

Have you ever reported an ADR that you encountered?		
Yes	49	16.50
No	238	80.13
Total	287 (* =10)	
How many ADR reports have you submitted on average?		
<1/ year	219	73.74
1-10/ year	23	7.74
<1/month	5	1.68
1-10/ month	2	0.67
Total	249 (* =48)	

*= missing data

Table 4.1.13: Participants who Encountered ADRs Versus those that Reported the Encountered ADR (N=285)

	Reported an Encountered ADR		
Encountered an ADR	**Yes**	**No**	**Total**
Yes	47 (27.17%) (95.92%)	126 (72.83%) (53.39%)	173 (100%) (60.70%)
No	2 (1.79%) (4.08%)	110 (98.21%) (46.61%)	112 (100%) (39.30%)
Total	49 (17.19%) (100%)	236 (82.81%) (100%)	285 (100%) (100%)

Pearson Chi-square= 30.7645, p-value= 0.000
The results are significant at p<0.001

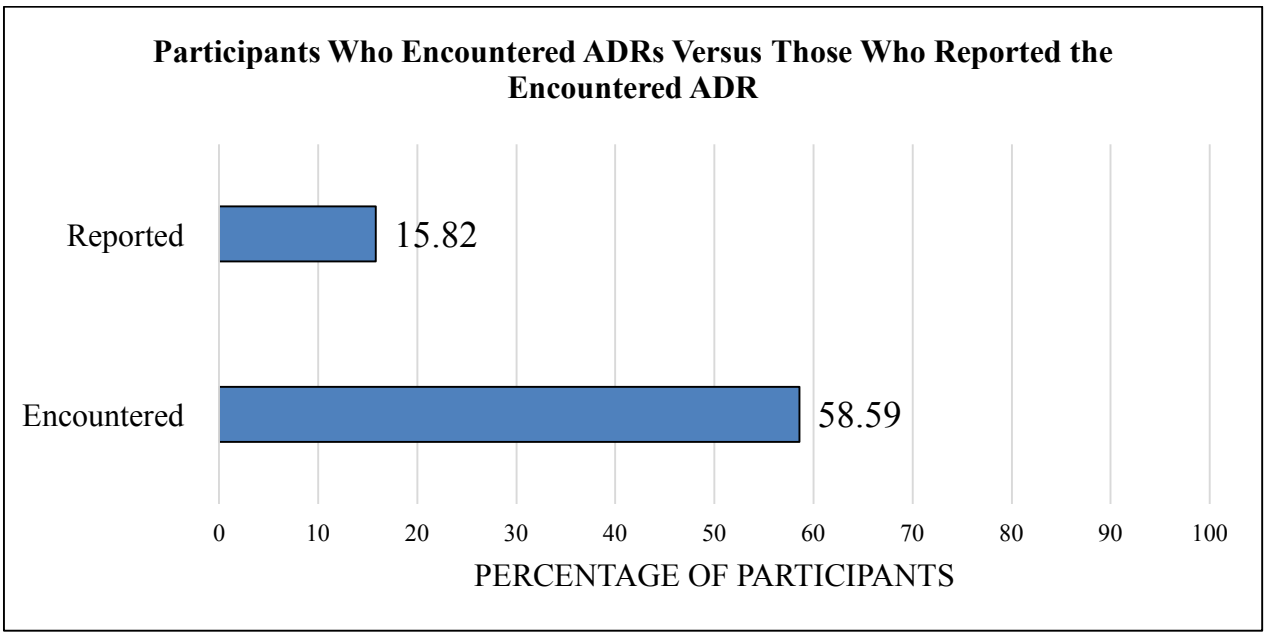


Figure 4.1.8: Participants who encountered an ADR versus those who reported the encountered ADR

Table 4.1.14: Knowledge of How to Report ADRs by Previous Training (N=292)

	Knowing how to report an ADR			
Have you previously attended an ADR Training Seminar/Workshop?	**Yes**	**No**	**Invalid Response**	**Total**
Yes	31 (96.88%) (21.09%)	1 (3.13%) (0.70%)	0 (0.00%) (0.00%)	32 (100%) (10.96%)
No	116 (44.62%) (78.91%)	142 (54.62%) (99.30%)	2 (0.77%) (100%)	260 (100%) (89.04%)
Total	147 (50.34%) (100%)	143 (48.97%) (100%)	2 (0.68 %) (100%)	292 (100% (100%)

Pearson Chi-square= 31.1291, p-value= 0.000, Fisher's exact = 0.000
The results are significant at p<0.001

Table 4.1.15: Number of ADR Reports Submitted by Previous Training (N= 248)

	Number of ADR Reports Submitted				
Have you previously attended an ADR Training Seminar/Workshop?	**<1/year**	**1-10/ year**	**<1/month**	**1-10/ month**	**Total**
Yes	13 (48.15%) (5.96%)	0 (0.00%) (0.00%)	3 (11.11%) (60.00%)	0 (0.00%) (0.00%)	27 (100.00%) (10.89%)
No	205 (92.76%) (94.04%)	12 (5.43%) (52.17%)	2 (0.90%) (40.00%)	2 (0.90%) (100.00%)	221 (100.00%) (89.11%)
Total	218 (87.90%) (100.00%)	23 (9.27%) (100.00%)	5 (2.02%) (100.00%)	2 (0.81%) (100.00%)	248 (100.00%) (100.00%)

Pearson Chi-square= 50.4708, p-value = 0.000, Fisher's exact = 0.000
The results are significant at p<0.001

4.1.5 The Need for Further PV Training or other Suggestions

Table 4.1.15 shows the participant's suggestions for improving PV, with workshops and seminars making up most of the responses (59.93%). Figure 4.1.9 shows this with a ranking of what participants chose as suggestions for improvement. Education for nurses and paramedicals (54.88%) and bulletins on ADRs (52.86%) followed closely. Figure 4.1.10 further categorises the information by years of experience, with generally equal distribution.

Table 4.1.16: Frequency Distribution of Suggestions Offered to Improve PV

Suggestions for Improvement	Frequency (N)	Percentage (%)
ADR reporting made mandatory	113	38.05
Workshops and seminars	178	59.93
Pharmacovigilance teaching programmes for undergraduates, interns and postgraduates.	136	45.79
Education for nurses and paramedicals	163	54.88
Monthly meetings of rare ADRs	118	39.73
Bring out bulletins on ADRs	157	52.86
Other	13	4.38
"Streamlined process, access to forms, access to fax"	1	
"Shorter form"	1	
Total	878	

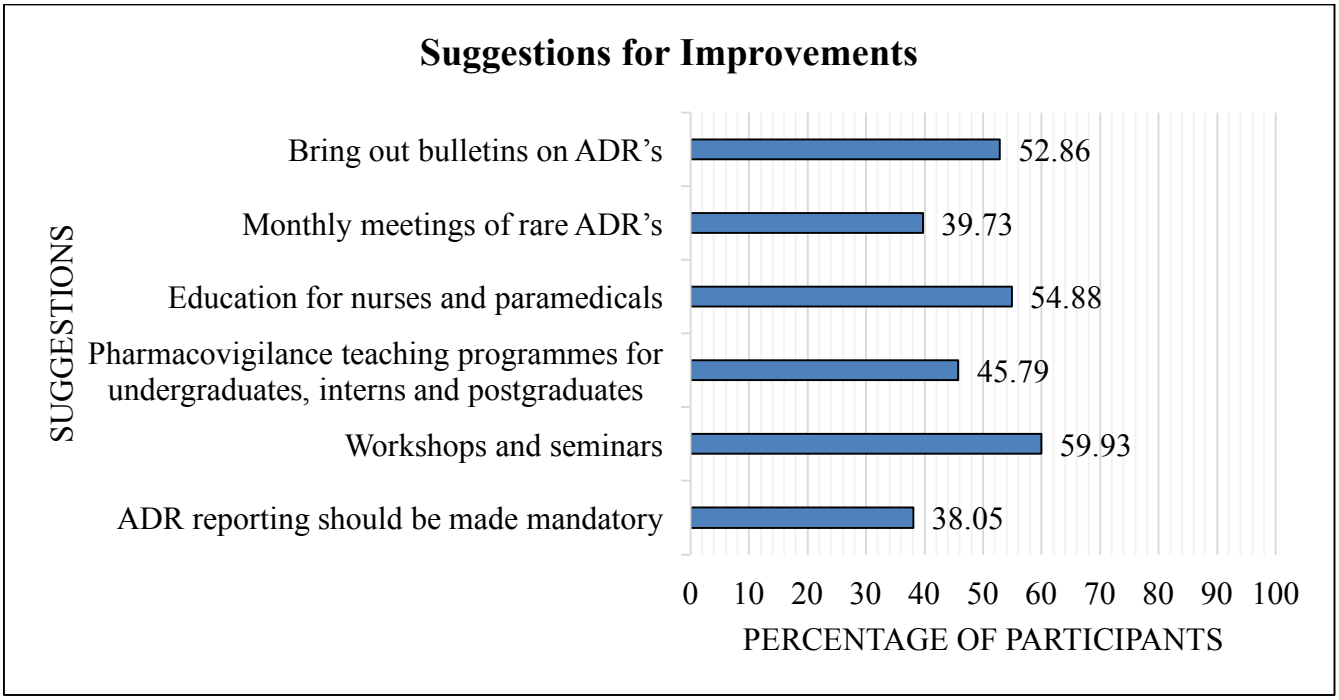


Figure 4.1.9: Suggestions for Improvement

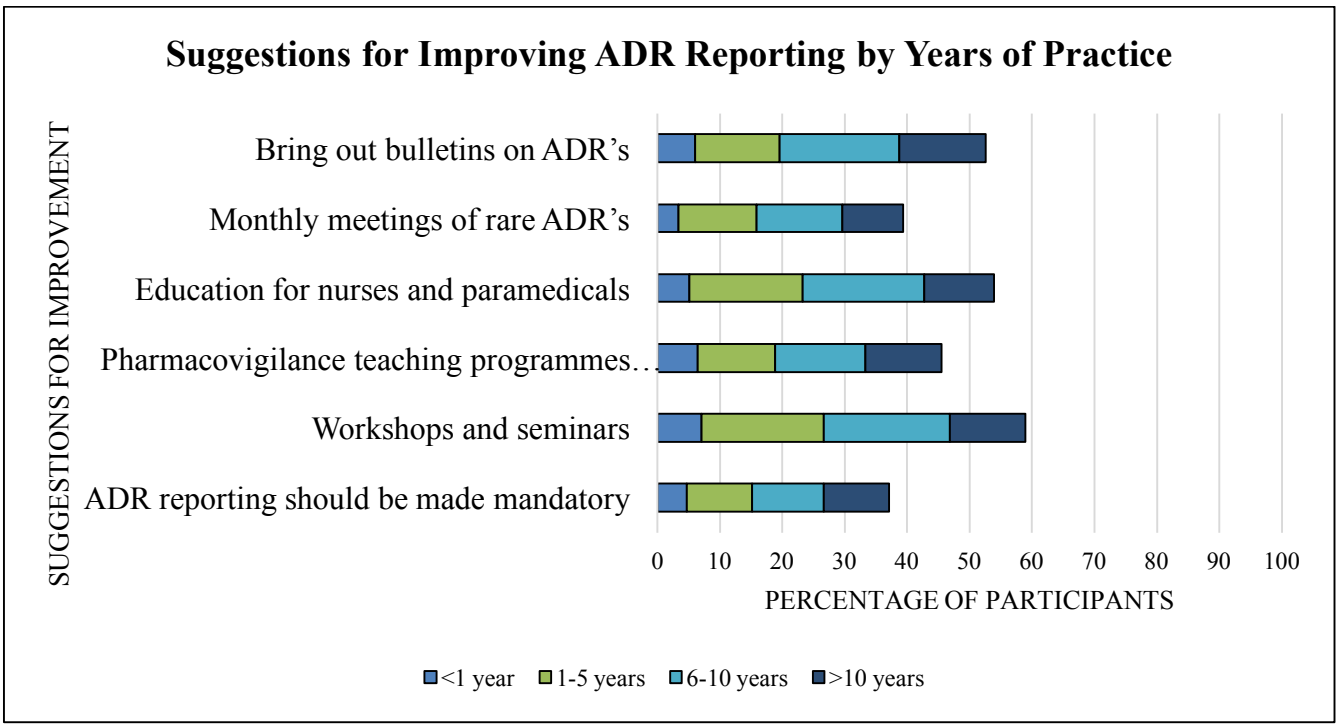


Figure 4.1.10: Suggestions for Improving ADR Reporting by Years of Practice

4.2 FOCUS GROUP RESULTS

The results of the focus group are discussed below in detail, drawing on the themes that developed during the sessions. A summary of the results obtained is tabulated below each section, categorised by the following (as for the questionnaire results):

1. Knowledge and Awareness of the Participant.
2. Attitudes of the Participants towards PV.
3. Previous PV Practices of Participants.
4. The Need for Further PV Training or other Suggestions.

4.2.1 Knowledge and Awareness of the Participant

Overall, participant's knowledge of PV and particularly ADR reporting was mostly limited to what had been taught during undergraduate studies. Both pharmacists and nurses identified ADRs as being more serious/ severe than side effects, and as reactions that are progressive and

possibly permanent. Side effects were not seen as necessary to report, particularly because they are often known or expected to happen, as one participant explained:

> *"Normally what I would tell a patient is (that) certain rashes appear as side effects. But if it becomes severe, you just monitor that and then, well you have to stop them and report it…You know certain rashes comes and goes…I don't see that as an ADR"* (Pharmacist, Group 1, Female).

Nurses in the second group identified a few examples of ADRs, such as:

> *"For example: antibiotics, they have a lot of adverse effects. Like Stephen Johnson's syndrome- we saw a patient with that recently. Grey (baby) syndrome as well"* (Nurse, Group 2, Female)

Both nurses and pharmacists demonstrated an awareness of ADRs in practice, being able to name examples and recount recent incidences within the wards. However, this knowledge didn't necessarily extend to the reporting of ADRs. Pharmacists admitted to learning about how to report ADRs recently by a pharmacist of authority, however some pharmacist participants were unaware of where the form went after handing it to the drug controller at the pharmacy. On the other hand, nurses in one group were mostly unaware of the form, and confusion occurred between participants about where to find forms in the wards. In the second focus group of nurses, participants were unaware of the existence of the form altogether, stating they had never seen it before. Many participants felt it should be placed in patient files as that would make the process more convenient. Pharmacists showed some understanding for the role of the PTC at the hospital, having seen meetings held once a month, while nurses were not aware of the role of the PTC at the hospital.

Table 4.2.1: Knowledge of the Participant

	Pharmacist Group 1	Pharmacist Group 2	Nurse Group 1	Nurse Group 2
Knowledge of PV and ADRs	Adherence	The detection and reporting of adverse drug reactions	Serious side-effects	Not aware of the term 'pharmacovigilance'
	Different to a side effect because its unknown	Different to a side effect in that an ADR is life threatening	Defined by severity	Aware of ADRs giving examples of skin reactions; Steven Johnson's and Grey Baby Syndrome with antibiotics
	Different to a side effect because its more serious/ life threatening			Difference between side effect and adverse effect identified as side effects being unpleasant but non-life-threatening
	A reaction that comes and goes is not believed to be an ADR			
Knowledge of what to report	Report serious adverse reactions, not side effects	Reactions that are expected/ common shouldn't be reported		
	Don't report known reactions			
Awareness of the form	Not Aware	Awareness of the form only during internship or undergraduate studies, but not since	Not Aware	Not Aware
	Recently been made aware by someone of authority (i.e. drug controller)	Recently been made aware by someone of authority (i.e. drug controller)	Aware of it but its unavailable in the ward	
			Aware of it but unaware of where to find it	
			Reporting form attached to admission form, but is not put into	

			patient files	
Knowledge of how/where to report	Send patient to doctor (refer) when an adverse drug reaction is encountered	Forms ultimately sent to the NADEMC	Not Aware	No knowledge of where the form goes
	No knowledge of where the form goes	Forms referred with patient to doctor	Not Aware of the existence of a PTC	No knowledge of how to report
	Aware of the existence of a PTC			

4.2.2 Attitudes PV Practices of Participants

In each focus group, participants believed that ADR reporting was of significant importance in health care. In the first group of pharmacists, one participant explained ADRs to be:

> *"of high importance because it creates a database of what to expect"*
> (Pharmacist, Group 1, Female).

This opinion was echoed by a nurse who understood that a record of adverse effects should be kept after the drug is put on the market.

Factors found to encourage reporting included feedback being provided; certainty that what is observed clinically is an ADR; diminished patient compliance; witnessing reactions that progress rapidly; and those that are not listed in the package insert. One group of pharmacists discussed a new-found understanding that pharmacists have the ability and expertise to be able to report ADRs, and thus felt encouraged to do so. Similarly, a nurse participant felt reporting protected her as a nurse, in that it was her professional obligation to report anything that could be harmful to a patient.

During discussions on factors that discourage participants from reporting, a range of reasons were given (summarized in the tables below). These included reporting being time consuming, and a lack of patient contact time (for pharmacists); reporting not being within the scope of practice for pharmacists/ nurses; polypharmacy leading to an uncertainty of what the causative agent could be; lack of knowledge; fear of being held liable; the form being too long to complete during working hours; and the lack of communication among members of the health care team. Lack of communication and lack of feedback was a common theme that developed among the groups, as one nurse explained:

> *"I think the thing that is inhibiting people (from) recording (ADRs) is lack of communication by the multidisciplinary team members. If you report to the pharmacy, they keep the data, they don't come back to me to give you an intervention – do this or stop this drug, use this one. So maybe it's like what's the use of doing this"*
> (Nurse, Group 2, Female).

Lack of feedback after a form was submitted made the reporting health care professional less likely to report in the future, assuming reporting didn't lead to anything. A pharmacist recounted a product quality report she had previously submitted, and explained how receiving feedback from the pharmaceutical company had encouraged her to continue reporting in the future.

In terms of liability, one group of nurses feared liability and as a result refrained from claiming responsibility by signing the form. On the other hand, the second group of nurses felt as if taking responsibility for the witnessed ADR by recording what was observed further protected them and the patient involved as well. Participants who had been practising for a shorter amount of time seemed to be more likely to claim responsibility and report the ADR personally.

Also based on the years of practice, one nurse explained a lacking culture of reporting in the wards, leading to continuing lack of reporting with newer nurses:

> *"It's a vicious cycle because, because they don't do it, the next generation nobody is going to do it"*
> (Nurse, Group 2, Female).

Table 4.2.2: Attitudes of the Participants towards PV

	Pharmacist Group 1	Pharmacist Group 2	Nurse Group 1	Nurse Group 2
Importance of reporting ADRs	Of high importance because it creates a database of what to expect		Important because it prevents further complications	Important because it prevents the patient from getting the medication again
				Important because there may be an issue with the specific batch, which should be recalled
				Important because after clinical trials, there needs to be a way of recording possible adverse effects
Reasons to report	Certainty that it is an ADR	Receiving feedback is an encouraging factor to continue reporting	Any reaction that isn't listed in the package insert	Reactions that increase in frequency or severity should be reported

	If feedback is provided, reporting will be more likely in the future	All cases should be reported for the realization that they could become progressively more serious	A reaction that spreads or gets rapidly worse should be reported	Feelings that reporting what you see protects you as a nurse
	In situations where patient compliance is diminished due to the reaction	Feelings that pharmacists have the information and ability to report. Pharmacists also see patients monthly for repeats and are more likely to know of reactions experienced by outpatients		
Reasons for not reporting/ under-reporting	Time-consuming process	Mild or expected reactions don't need to be reported	A known/ expected reaction does not need to be reported	Not necessary to report a suspected/ known reaction
	Patient contact time is not enough for proper counseling with regards to ADRs	Feelings that patients only claim to have a reaction to be put on a preferred drug	Lack of knowledge	Participants identified a possible problem of nurses not feeling like it's their responsibility to report
	Any reaction that is already listed in the package insert (i.e. known or expected) does not need to be reported	Insufficient time with the patient and being short staffed	Mild reactions don't need to be reported, the reaction will resolve once the doctor changes the drug	Lack of communication between the multi-disciplinary team members, and a lack of feedback as a result
	Feelings that patients claim to have a reaction in order to get a preferred drug over the prescribed drug	Polypharmacy leads to an uncertainty about which drug caused the reaction	Nurses are not responsible for reporting as they were not the ones prescribing the medicine	Senior staff members lack of reporting leads to an unawareness of reporting
	Mild reactions don't need to be reported because they will resolve themselves	Not being aware of reactions due to insufficient patient counselling	The reporting form does not contain a "space" for a nurse to report	Participants felt that nurses will only do what is compulsory

	Pharmacist Group 1	Pharmacist Group 2	Nurse Group 1	Nurse Group 2
Reasons for not reporting/ under-reporting (continued)	Feeling as if the doctor has the authority		A lack of time	The length of the form is discouraging
	Having to report on paper versus a computer based system		Reluctance to report for fear that it would be claiming responsibility for the incident (liability)	Positive attitude towards reporting in the future, given the instructions on how and where to report; and understanding the importance of reporting
	Feeling as if no resolution is reached after a report is submitted			

4.2.3 Previous PV Practices of Participants

With regards to the participant's previous PV practices, pharmacists were able to recall a few cases of ADRs witnessed, but very few reported. These results were consistent with the questionnaire results. Most pharmacist participants were under the impression that it is more within the scope of practice of a doctor to report ADRs, and as a result most pharmacists had previously referred the patient back to the doctor with the reporting form in the event of a suspected reaction, as one pharmacist explained:

> *"Stop it immediately, go see the doctor. Report to the doctor, there is a specific form that you need to fill in with the doctor and then bring it back. Some of them go back"* (Pharmacist, Group 1, Female).

Participants in the same group also mentioned a specific case that was not reported due to a lack of knowledge about the correct channel of reporting. They further cited a lack of time and patient contact to be able to report the ADR, adding to the reason for referral. Although the pharmacists continued to refer suspected ADRs, they consistently mentioned a lack of feedback, and communication within the health disciplines:

> *"So you would actually say "take the form, go to the doctor, speak to the doctor about it. Maybe the doctor can substitute it with something else". But there is no follow up, you see,… did it help or did it not help. We are not aware of what happens next"* (Pharmacist, Group 1, Female).

One pharmacist recounted an incident of reporting in which she became more aware that reporting is within the scope of practice of a pharmacist:

> *"I sent it with the patient to the doctor…I told him to take it to the doctor and the doctor sent it back saying that even the pharmacist can do it…I had to ask him what happened, and I took the patient's details"* (Pharmacist, Group 2, Female).

The nurses similarly believed ADR reporting to be within the scope of practice of doctors, and admitted to regular patient referrals. As a result, none of the nurses within the group could recall the process of reporting, and had never submitted an ADR report.

With regards to general PV practices, both pharmacists and nurses had told patients to stop the drug and refer to the doctor to substitute the drug with another, when in the presence of a reaction of any kind. Inquiries about drug interactions were rare in both groups. The pharmacists generally seemed to check the interactions within the medicines dispensed, but didn't always ask patients about concurrent medicines taken, although acknowledging the growing trends of polypharmacy and self-medication. Herbal and traditional medicines were rarely considered when counselling a patient.

Table 4.2.3: Previous PV Practices of Participants

	Pharmacist Group 1	Pharmacist Group 2	Nurse Group 1	Nurse Group 2
Specific cases	Previous reporting didn't include reporting by pharmacist, cases usually referred to a doctor who may choose to report. Insufficient patient contact time cited as the reason for referral	Case of a rash with leflunomide was reported by the pharmacist	No previous "ADRs" claimed to be witnessed	Steven Johnson's Syndrome witnessed in the ward. Patient was discharged with oral antibiotics and was readmitted following the start of Steven Johnson's. Participants were unaware if any reporting occurred
	A patient presenting with a rash from taking a cephalosporin was not reported due to not knowing the correct port of call	Previous product complaints have been reported, and followed up by the company involved	Steven Johnson's Syndrome witnessed but not thought of as being a possible ADR	
		Swelling of the feet with amlodopine was seen and referred to the doctor, but not reported		
		Allergies to excipients		
General PV Practices	Instruct patient to stop drug, contact doctor to change the drug, but no reporting activity occurs		The package insert of a medicine is checked when a reaction occurs	When there is a known side effect with a specific drug, preventative measures are taken by participants to avoid the effect/ add to patient comfort
	No reporting activity because no training had previously been given on how to report; the last time ADRs were explained was during undergraduate training			Any reaction noticed is verbally reported to the doctor

	Pharmacist Group 1	Pharmacist Group 2	Nurse Group 1	Nurse Group 2
Promotion of patient awareness	Inform patients of possible expected reactions, or to be aware of anything out of the ordinary, and to report this to the doctor	Patients should be encouraged to be vocal about any symptoms or possible reactions that occur		
	Fear of the placebo effect when warning a patient of possible reactions			
Inquiries/ warnings about drug interactions	Drug interactions with alcohol are generally mentioned	Warnings about drug-drug interactions are limited to alcohol	Inquiries into concomitant drugs not always made	
	Interactions with ARVs always checked			
	Food-drug interactions rarely discussed			
	Interactions with complementary medicines rarely discussed			

4.2.4 The Need for Further PV Training or Other Suggestions

A few subthemes developed during the discussions on training and future suggestions. Most participants spoke about a lack of training and thus a lack of knowledge on how to report ADRs. Participants responded by saying they would be more likely to report given proper training/ instructions. One nurse recalled never having learned about ADR reporting and suggested adding it to the undergraduate pharmacology curriculum for nurses. A pharmacist mentioned the need for routine training seminars:

> *"We were aware of it…you study, you learn about it but you just stop learning. And I think the same for the nurses. So if they can just make it accessible and someone inform them, like what was done with us…"*
> (Pharmacist, Group 1, Female)

With regards to the ADR reporting form, all participants had concerns about the length of the form, as well as the accessibility of the form. Nursing participants were not entirely aware of where the form was kept, and suggested the forms form part of each patient file:

> *"Maybe it should form part of our file… when we give the medication. After or under the prescription chart, it should also be there so if you come across anything of that sort you don't start looking for the form"*
> (Nurse, Group 1, Female).

Use of mobile applications as an alternative to the paper based form were discussed with each group, with mixed opinions. Most participants felt as if it was a more convenient and efficient method, while one pharmacist felt it was a less reliable method.

One idea that was discussed in each group was having a designated person(s) in charge of PV, perhaps a pharmacist to whom all health care professionals can refer patients with suspected ADRs.

A nurse in the second group felt it would be important to get pharmacists more patient contact time through ward rounds, explaining that it would provide a way for pharmacists to use their pharmacology expertise and work with nurses to monitor patients:

> *"I also think that if there was a drive to put pharmacist on ward rounds, that that would really help"*
> *(Nurse, Group 2, Female).*

Education in the form of posters was mentioned both in terms of reminding health care professionals to report and how to report, as well as promoting patient awareness. Many pharmacists felt it was important to empower patients, so that out-patients will be more alert while on their medication, and more communicative with the pharmacist about potential problems. This was mentioned in response to issues of a lack of patient contact due to time constraints, and polypharmacy:

> *"Patients here go to multiple doctors and they independently prescribe"*
> (Pharmacist, Group 1, Female).

Therefore, patient awareness developed as a theme as pharmacists believed it would give them a more complete picture of the patient's health and medication.

Nurses felt having posters and visual aids in the wards would serve as a reminder to report, as well as a convenient guide on how and where to do so. In the same way, both pharmacists and nurses were eager to become more aware of adverse effects, with one pharmacist asking:

> *"Is there an available database for the public? Or for us as a professionals to actually have access to in terms of pharmacovigilance"*
> (Nurse, Group 1, Pharmacist).

The concept of a PV bulletin, in which all health care professionals are kept updated on PV issues and trends, was discussed in this regard. This was also seen as a way to amalgamate the different health disciplines by keeping all health professionals aware and involved in the issues of PV.

Finally, the idea of incentivizing PV was explored with nurses and pharmacists believing it should form part of professional development points.

Table 4.2.4: The Need for Further PV Training or Other Suggestions

	Pharmacist Group 1	Pharmacist Group 2	Nurse Group 1	Nurse Group 2
Training	No previous training given		Training seminars should be conducted regularly, particularly because shifts change	In-service training said to be the best way to approach nurses
	Future training encouraged by someone within the pharmacy			Educating/ training during undergraduate pharmacology courses. Comparisons were made to learning about antibiotic stewardship and consequently being weary of this in the wards

Suggestions	Use of a mobile application	Making reporting mandatory	The form should be made more available in daily practice	Having pharmacists on ward rounds for referral on drug interactions etc.
	Pharmacist Group 1	**Pharmacist Group 2**	**Nurse Group 1**	**Nurse Group 2**
	Forms be made more accessible	Having a pharmacovigilance pharmacist (a person in charge of PV at the pharmacy) to whom other pharmacists can refer patients	Being made aware of ADR trends in the province (i.e. bulletin)	Incentivising reporting using professional development points
	Encourage patient awareness through use of posters	Making use of a counselling room when an ADR is suspected to ensure privacy and time to assess the patient and fill out the form	The form should be made to include "reporting nurse"	Incentivising reporting using awards like certificates within the wards
	Appoint a person to be in charge of PV in the pharmacy	Encourage patient awareness through use of posters	Posters detailing how to report should be placed in the wards to remind nurses of the process	Educational posters with information about ADRs and reminders on checking patients for ADRs
	Being made aware of trends in ADRs via a bulletin	Involving all pharmacists and post-basic pharmacy assistants by discussing ADR trends within the hospital at meetings	Boxes should be placed in each ward containing blank reporting forms, and a place to put completed forms	Having a more concise form
	The use of black box warnings		It should be made mandatory to report any seen ADRs	Having one designated person for pharmacovigilance who will deal with the paperwork and referrals
			Use of a mobile application would make it more convenient to report	Using stickers/ notes on patients charts when an ADR is suspected, and then referring to the pharmacy who will report accordingly

		Using mobile applications to report quicker
		Having a computerized system which has all the patients information and medication history, which can also be used to report suspected ADRs

CHAPTER V: DISCUSSION

5.1 DEMOGRAPHICS

The questionnaire phase of the study had a response rate of 87.87%, comparable to that of previous similar studies (Pimpalkhute et al., 2012; Gupta & Udapa, 2011; Elkami et al., 2011; Mulatu & Worku, 2014). The respondents consisted of 41 medical doctors (13.80%); 230 nurses (77.44%); and 24 pharmacists (8.08%). This distribution was largely due to the number of health care professionals working at the hospital, which in 2016 consisted of 623 medical doctors, 2165 nurses and 26 pharmacists (shown in the sample size calculation in Chapter III: Methodology). The demographic of the participants was also largely female (83.84%), with 90.97% of nursing participants, and 62.50% of pharmacist participants being female. According to the South African Nursing Council (SANC) website, the number of registered nurses was totalled at approximately 55 337 (Gauteng Province) in 2016, made up of 92.68% females and 7.32% males (South African Nursing Council, 2017). Similarly, according to the South African Pharmacy Council (SAPC), there are approximately 16 340 pharmacists made up of 62.39% females and 37.61% males (South African Pharmacy Council, 2017). These statistics may serve to explain the imbalance of gender in the study.

5.2 KNOWLEDGE OF HEALTH CARE PROFESSIONS ON ADR REPORTING

Health care professionals have demonstrated a relative awareness for the presence of ADRs in studies similar to this one, including that of Fadare et al. (2011), and Pimpalkhute et al. (2012). However, these studies also found a lack of awareness of the process of reporting. Fadare found that although 93.8% of participants had knowledge of reasons to report ADRs, only 39.5% of participants were aware of the actual reporting form (Fadare et al., 2011). Similarly, Alsaleh et al. found that 72.6% of participants were able to correctly define ADRs, while only 7% were aware of the reporting system of the country (2017). According to Suyagh, Farah and Farha, only 28.6% of hospital pharmacists were aware of the reporting system in Jordan (2014).

In this current study, the questionnaire results showed that 50.17% of participants knew how to report ADRs, and 77.10% were aware of the yellow reporting form. Yet, during focus group sessions, participants did not demonstrate knowledge of the process of ADR reporting.

In terms of knowledge of the pharmacovigilance reporting system, 59.26% of participants identified the NADEMC as the place to report ADRs, while only 48.82% chose the PTC as an option. Nurses were unaware that PTCs existed, but most pharmacists knew about the role of the PTC at the hospital, which was confirmed during focus group discussions. Fadare et al. found a similar figure with 44.6% of participants who were aware of the existing hospital committee (2011). Although the NADEMC is a national monitoring centre, the PTC should also be recognised as an important channel for communication within the institution. Provincial PTCs play a significant role in the collection of ADR reports. Ideally, the gathering of reports for provincial PTCs is a function that happens through the Safety and Quality Subcommittee, which physically gathers and collates the data, looking for potential concerning trends. Communication and integration among all health care professionals may help to give holistic care, and in many ways can make the involved persons more motivated to report in the future.

The study found different levels of knowledge among the different professions. Nurses had the least awareness of how to report (46.46%) , followed by doctors (53.49%) and then pharmacists (82.61%) ($p< 0.001$). During focus group discussions, nurses drew on the theme of responsibility and accountability. Many nurses didn't believe reporting ADRs was a professional nursing obligation, and believed that referring patients who presented with a reaction was the correct step to take. De Angelis et al. concluded that "Nurses are not fully aware of their role in adverse drug reaction reporting" (2015, pp.1), and Hanafi et al. had a similar finding with 89% of nurses preferring to refer the report to the doctor for completion (Hanafi et al., 2014). With regards to perceived responsibility, nursing respondents in the questionnaire identified themselves and doctors to be mostly responsible for reporting ADRs, while placing little responsibility on pharmacists. This result was inconsistent with the focus groups, in which nurses felt least equipped to report.

Health care professional's knowledge of the flow of reporting as well as their awareness of who should take responsibility of reporting need to be enforced. This brings up the need to train heath

care professionals more constantly, through the use of in-service training and more formalised classroom-based learning at the undergraduate level. This idea was also posed by Pimpalkhute who noticed gaps in "undergraduate training" (2012, p. 60). Olsson, Pal and Dodoo noted the importance of introducing PV training into undergraduate studies (2015). An approach targeted at students saw a "student- run pharmacovigilance programme" being piloted in the Netherlands (Netherlands Pharmacovigilance Centre, 2017). This common theme of education at the undergraduate level is largely important to the field , as Rajiah, Maharajan and Nair echoed in their study (2015). These findings were also consistent with that of Elkami et al. who found that deficiencies in the undergraduate curriculum lead to a lack of knowledge about pharmacovigilance (Elkami et al., 2011).

This current study also found a statistical association between knowledge of ADR reporting and the years of experience of participants. Participants who are newer to practising as health care professionals seemed to have knowledge of the importance of reporting, however there is a lack of knowledge of the process itself ($p<0.001$). Only 23.08% of interns knew how to report ADRs, while 61.45% had seen the reporting form before ($p< 0.001$).

5.3 ATTITUDES OF HEALTH CARE PROFESSIONALS ON ADR REPORTING

Attitudes in this study were measured by the factors that encouraged and discouraged health care workers, as well as the cases in which they were most likely to report ADRs. These factors accounted for some of the gaps between knowledge and practice. Understanding the importance of ADR reporting is an inevitable start to reporting ADRs, and this study found that only 21.89% of participants chose "did not think it was important to report" as a reason for underreporting. Similarly, Gupta and Udapa found that 89.5% of doctors thought reporting was an important part of their profession (2011), and Joubert and Naidoo found that 79.4% of participants "regarded PV as a valuable tool" (Joubert & Naidoo, 2016, p.243). Focus group sessions were consistent with questionnaire findings in this regard, as most participants thought reporting was important, and were even able to list reasons as to why this is so.

A range of factors discouraged participants from reporting, with "managing the patient was more important than reporting", "do not know how to report", and "do not know where to report" being the most frequently answered. "Ignorance about the reporting system" found in this study was consistent with the results of Desai et al. Most health care professionals cited the seriousness of the ADR (90.24%) as the main encouraging factor in deciding whether to report an ADR, comparable to the 88.9% found by Gupta and Udapa (2011).

In 1996, an attitudinal survey study by Inman listed 7 of the most frequently cited reasons for underreporting of ADRs. The focus groups conducted in this study brought up many common themes, with the fear of litigation; the need for incentives; and time-related excuses being particularly mentioned in each group. With regards to fear, De Angeles et al. mentioned fear as a possible "extrinsic issue" related to the institution itself (2014). Focus group sessions shed light on this issue as participants who were newer to practising seemed to be less fearful, feeling as if reporting a patient's reaction will in fact protect them as health care professionals. Fear of being held liable is perhaps a factor that could be dealt with during in-service training of nurses, as there is a need for nurses to understand what reporting ADRs can achieve. Vallano et al. found similar problems in focus group sessions with doctors and also discovered that many doctors aren't aware of the benefits of the system of pharmacovigilance (2005).

5.4 PRACTICES OF HEALTH CARE PROFESSIONALS ON ADR REPORTING

The practices of health care professionals were assessed through responses based on encountered ADRs versus reported ADRs. Fifty-nine percent of participants had encountered an ADR in practice, yet only 16.50% reported the encountered ADR ($p<0.001$). Fadare et al. discovered that although 59.26% of participants said they knew how to report an ADR in the questionnaire, 73.74% of participants submitted <1 ADR/ year (2011).

Vallano et al. found the availability of reporting forms to be a major barrier of reporting (2005). In this study, although 59.26% of participants stated the forms were easily available to them in practice, participants in focus group sessions weren't aware of where to find the form. This issue

is one that should be addressed at each institution and brings up the need for heads of department to play a role in integrating pharmacovigilance into the topics discussed at routine meetings.

5.5 SUGGESTIONS AND FUTURE RECOMMENDATIONS

Education should remain a priority in the field of pharmacovogilance, and the idea of training was a fundamental point of discussion during focus group sessions. Workshops and seminars was the most frequently suggested improvement to make during the questionnaire phase, and this was echoed by mentions of this during focus group sessions. Nurses felt ADR reporting would become part of their daily practice given proper training and empowerment, and pharmacists acknowledged that a lack of proper training led to ignorance about reporting. 96.88% of participants who had previously attended a training seminar stated they knew how to report ADRs. Similarly, De Angelis et al (2015); Lopez-Gonzalez (2009); Backstrom et al. (2002); Sevene et al. (2008); and Cereza et al. (2010) found increases in reports after training, and higher rates of reports from health care professionals with a higher level of education. Sevene et al. (2008); and Kaselekela Oscar & Boyd (2017) focused on pharmacovigilance in resource-limited countries, and mentioned continuous training, public awareness and the importance of feedback in reporting ADRs.

Training should be consistent starting from the undergraduate level and continuing into routine training sessions in the workplace (Granas et al., 2007); (Li et al., 2014); (Rehan et al., 2002); (Rajiah, Maharajan & Nair, 2015). Furthermore, health care professionals want to be kept up to date and involved, and so PV bulletins and meetings may be of great use once the culture of reporting is established. The use of posters and other visual aids may be of some use as a quick reference during daily practice in the wards, and in the pharmacy. Nurses in particular felt this would be helpful to them, and pharmacists felt they should even be used in patient waiting areas to remind out-patients to be alert and aware of potential adverse effects. Thoughts of increasing awareness through campaigns was also mentioned by Gupta and Udapa (2011).

CHAPTER VI: PROBLEMS AND LIMITATIONS

The study was conducted in 10 wards, and the pharmacy at one institution. The data obtained and conclusions drawn were specific to this environment, however similar studies could be done in other hospitals in order to get a more complete picture of PV in South Africa.

CHAPTER VII: FUTURE RECOMMENDATIONS AND APPLICATIONS

This study was conducted at one institution, in which the following recommendations can be made:

- Training for health care professionals from the undergraduate level to in-service training in the working environment (wards; pharmacy dispensary).
- Visual aids such as posters put up around the hospital to remind health care professionals of the process of reporting; and patient-awareness posters.
- Designating one pharmacist and one nurse in each ward to be in charge of PV.

Similar studies which evaluate the pharmacovigilance system at other institutions could be performed in order to properly assess the baseline knowledge, attitudes and practices of health care professionals in other environments. From this, further recommendations could be made.

CHAPTER VIII: CONCLUSION

Low to middle income countries often lack the resources and financial backing to allow the systems of PV to function the way they do in wealthier countries. However, the nature of spontaneous reporting is such that it is inexpensive and relies on health care professionals, or in some case patients, working within the framework of manually reporting the witnessed ADR to the relevant authority. This study assessed the knowledge, attitudes and practices of health care professionals, in order to obtain an idea of the reasons for the underreporting of ADRs, as well as ways this can be improved. It was found from this study that knowledge of the process of reporting needs to be enhanced. Some participants articulated that although they once had a basic understanding of pharmacovigilance and the activity of adverse drug reaction reporting, a lack of practice and training while on the job created a culture of non-responsibility. Attitude is thus perhaps the most important factor when it comes to reporting ADRs as unless it is a mandatory professional obligation, many health care workers see little benefit in reporting. However, if the culture of reporting is instilled at the undergraduate level, and then reinforced in the workplace, the attitudes of health care professionals may improve. The safety, quality and efficacy of medicines are pivotal factors to the health science industry, and they are ones that shouldn't be ignored. Health care professionals should be made to understand the importance that lies in the post-marketing monitoring of drugs, primarily in terms of the safety and wellbeing of patients who take drugs to improve their health.

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APPENDICES

Appendix A: ADR and Product Quality Problem Report Form

ADVERSE DRUG REACTION AND PRODUCT QUALITY PROBLEM REPORT FORM

(Identities of reporter and patient will remain strictly confidential)

Department of Health Logo Here

NATIONAL ADVERSE DRUG EVENT MONITORING CENTRE

Medicines Control Council,
The Registrar of Medicines ,
Department of Health

Tel : (021) 447-1618
Fax: (021) 448-6181

In collaboration with the WHO International Drug Monitoring Programme

PATIENT INFORMATION

Name (or initials): ..... **Age:**..... **Weight (kg) :**.....
Sex:: M F **DOB :**..... / ...../ ..... **Height (cm) :**.....

ADVERSE REACTION/PRODUCT QUALITY PROBLEM

Adverse reaction[1] ☐ **and/or Product Quality problem**[2] ☐ **Date of onset of reaction: :**...../...../.....
Time of onset of reaction: .....h.....min

Description of reaction or problem (Include relevant tests/lab data, including dates):

1. MEDICINES/VACCINES/DEVICES (include all concomitant medicines)

Trade Name & Batch No. (Asterisk Suspected Product)	Daily Dosage	Route	Date Started	Date Stopped	Reasons for use

ADVERSE REACTION OUTCOME (Check all that apply)

☐ death
☐ disability
☐ congenital anomaly
☐ required intervention to prevent permanent impairment/damage .....
☐ life-threatening
☐ hospitalisation
☐ Other.....

Event reappeared on rechallenge: Y N Rechallenge not done
Treatment (of reaction)......
.....
...
.....
.....
.....

Recovered: Y N
Sequelae: Y N
Describe Sequelae:.....
.....
.....
.....

COMMENTS: (e.g. Relevant history, Allergies, Previous exposure, Baseline test results/lab data)

2. PRODUCT QUALITY PROBLEM:

Trade Name	Batch No	Registration No	Dosage form & strength	Expiry Date	Size/Type of container

Product available for evaluation?: Y N

REPORTING DOCTOR/PHARMACIST Etc:

NAME: .....
ADDRESS: .....
Date .....
TEL: (.....).....

QUALIFICATIONS:.....
....
Signature

This report does not constitute an admission that medical personnel or the product caused or contributed to the event.

ADVICE ABOUT VOLUNTARY REPORTING

Report adverse experiences with:

- medications (drugs, vaccines and biologicals)
- medical devices (including in-vitro diagnostics)
- traditional and herbal remedies
- **For Adverse Events Following Immunisation (AEFI), please follow the reporting procedure recommended by the Expanded Programme in Immunisation (EPI)**

Please report:

- adverse drug reactions to recently marketed products
- serious reactions and interactions with all products
- adverse drug reactions which are not clearly reflected in the package insert.

Report even if:

- you're not certain the product caused the event
- you don't have all the details

Report Product Quality Problems such as:

- suspected contamination
- questionable stability
- defective components
- poor packaging or labelling
- therapeutic failures

Important numbers:

Investigational Products and Product Quality Problems:

- (012) 326-4344 to fax a report
- (012) 312-0000 to report by phone

Registered Medicines and Traditional and Herbal remedies:

- (021) 448-6181 to fax a report
- (021) 447-1618 to report by phone

Adverse Events Following Immunisation:

- (012) 312 0110 to phone for information
- (012) 321 9882 to fax a report

Confidentiality: Identities of the reporter and patient will remain strictly confidential.

Your support of the Medicine Control Council's adverse drug reaction monitoring programme is much appreciated. Information supplied by you will contribute to the improvement of drug safety and therapy in South Africa.

(Medicine Control Council, n.d.)

Appendix B: Questionnaire



Please take a few minutes of your time to fill out this questionnaire about your thoughts and opinions on Adverse Drug Reaction (ADR) reporting at [redacted]. Please note this questionnaire is anonymous.

Please tick or cross the appropriate boxes.

1. What is your gender?			
Male		Female	

2. What is your profession?							
Doctor			Nurse			Pharmacist	
(Please specify level of practice)							

3. Please specify your type of practice.							
Intern			Community Service			Post- Community Service	

4. In which ward do you practice?					
Pulmonology		Oncology		ICU	
Surgical		Orthopaedic		Renal	
Gynaecology		Diabetes		Gastroenterology	
Cardiac					

5. For how many years have you been practising?			
<1 year		1-5 years	
6- 10 years		>10 years	

6. Have you ever attended a training seminar/workshop on ADR reporting?			
Yes		No	

7. Do you know how to report an ADR?			
Yes		No	

8. Have you ever seen the form shown below?			
Yes		No	

ADVERSE DRUG REACTION AND PRODUCT QUALITY PROBLEM REPORT FORM

(Identities of reporter and patient will remain strictly confidential)

Department of Health Logo Here

NATIONAL ADVERSE DRUG EVENT MONITORING CENTRE

Medicines Control Council,
The Registrar of Medicines ,
Department of Health
Tel : (021) 447-1618
Fax: (021) 448-6181
In collaboration with the WHO International Drug Monitoring Programme

PATIENT INFORMATION

Name (or initials): ..... **Age:**..... **Weight (kg) :**.....
Sex:: M F **DOB :**..... / ...../ ..... **Height (cm) :**.....

ADVERSE REACTION/PRODUCT QUALITY PROBLEM

Adverse reaction[1] ☐ **and/or Product Quality problem**[2] ☐ **Date of onset of reaction: :**...../...../.....
Time of onset of reaction: .....h.....min

Description of reaction or problem (Include relevant tests/lab data, including dates):

1. MEDICINES/VACCINES/DEVICES (include all concomitant medicines)

Trade Name & Batch No. (Asterisk Suspected Product)	Daily Dosage	Route	Date Started	Date Stopped	Reasons for use

ADVERSE REACTION OUTCOME (Check all that apply)

☐ death
☐ disability
☐ congenital anomaly
☐ required intervention to prevent permanent impairment/damage
☐ life-threatening
☐ hospitalisation
☐ Other.....
.....
.....
.....

Event reappeared on rechallenge: Y N Rechallenge not done
Treatment (of reaction)......
.....
...
.....
.....
.....

Recovered: Y N
Sequelae: Y N
Describe Sequelae:.....
.....
.....
.....

COMMENTS: (e.g. Relevant history, Allergies, Previous exposure, Baseline test results/lab data)

2. PRODUCT QUALITY PROBLEM:

Trade Name	Batch No	Registration No	Dosage form & strength	Expiry Date	Size/Type of container

Product available for evaluation?: Y N

REPORTING DOCTOR/PHARMACIST Etc:

NAME: ..... **QUALIFICATIONS:**.....
ADDRESS: ....
Signature
Date .....
TEL: (.....).....

This report does not constitute an admission that medical personnel or the product caused or contributed to the event.

9. Are ADR reporting forms easily available to you in practice?

Yes		No	

10. To whom should you report ADRs? You may tick/cross more than one box.			
The National Adverse Event Monitoring Centre (NADEMC)		Pharmaceutical and Therapeutics Committee (PTC)	
The Medicines Control Council (MCC)		Medical Supply Depot (MSD)	
The Safety and Quality Subcommittee		Other	

If you selected "other", please specify:

---

11. Have you ever encountered an ADR in practice?			
Yes		No	

12. Have you ever reported an ADR that you encountered?			
Yes		No	

13. How many ADR reports have you submitted on average?			
<1/ year		1-10/ year	
<1/month		1-10/ month	

14. Why is it important to report ADRs? Please rate on a scale from 1 to 5, 1 being not important and 5 being very important.					
Reason	**1**	**2**	**3**	**4**	**5**
To identify new ADRs					
To improve patient safety					
To measure the incidence of ADRs					
To share information about ADRs with colleagues					
To identify relatively safe drugs					
It is a requirement					

15. In which of the following cases, are you most likely to report an ADR? You may tick/cross more than one box.				
Seriousness of the ADR			Unusualness of the reaction	
Involvement of a new drug			Level of certainty that it is an ADR	
None of the above				

16. What are the factors that discourage you from reporting ADRs? You may tick/cross more than one box.			
Do not know how to report		Not knowing where to report	
Did not think it was important to report		Managing the patient was more important than reporting ADRs	
Lack of access to ADR reporting form		Patient confidentiality	
It is time-consuming		There is a lack of feedback after forms have been submitted	
Other			

If you selected "other", please specify:

---

17. In your view, which ADRs should be reported? You may tick/cross more than one box.			
None		All ADRs	
All serious ADRs		ADRs to new drugs	
Unknown ADRs to old drugs		ADRs to herbal and non-allopathic drugs	
ADRs to vaccinations		Other	

If you selected "other", please specify:

---

18. In your opinion, which of these professionals should report ADRs? You may tick/cross more than one box.

Medical practitioners			Nurses	
Pharmacists			Other	

If you selected "other", please specify:

_____

19. If you think a patient is experiencing an ADR, how would you check the information? You may tick/cross more than one box.

Textbook			Colleague	
Internet			Package Insert	
Other				

20. Do you agree or disagree with the following statements? Please rate on a scale from 1 to 5, 1 being strongly disagree and 5 being strongly agree.

Statement	**1**	**2**	**3**	**4**	**5**
ADR reporting is a professional obligation					
I know how to report an ADR					
I have received sufficient ADR reporting training					
I know how to fill out a NADEMC form					
ADR reporting adds up to unnecessary workload					
An allergic reaction to a medicine is an ADR					

I always check the patient's allergies before I give them any medicine					
I would like to receive more training on ADR reporting					
I have seen a patient experience an ADR					
Nobody really benefits if I report an ADR					

21. Do you have any suggestions about how reporting can be improved? You may tick/cross more than one box.	
ADR reporting made mandatory	
Workshops and seminars	
Pharmacovigilance teaching programmes for undergraduates, interns and postgraduates.	
Education for nurses and paramedicals	
Monthly meetings of rare ADRs	
Bring out bulletins on ADRs	
Other	

If you selected "other", please specify:

We thank you for your co-operation!

Appendix C: Focus Group Question Guide

1. What is your understanding of the term ‘pharmacovigilance’?
2. What do you understand by the term ‘adverse drug reaction’?
    - Expand on what you believe to be the differences between side effects and adverse effects, if any.
3. What are your thoughts on the reporting of Adverse Drug Reactions?
    - Why is it important/ not important.
4. Can you describe your previous experiences of reporting Adverse Drug Reactions, if any?
    - Witnessing them/ reporting them.
5. What do you understand about how and where to report ADR’s?
6. Under what circumstances would you report an ADR?
    - Is it based on how serious the reaction is?
    - Should mild ADR’s be reported?
7. What are some of the factors that have discouraged you from reporting ADR’s in the past?
    - How can these be changed?
    - What would make reporting ADR’s easier for you?
    - In your opinion, would using a mobile application to report ADR’s be helpful?
8. Is receiving feedback after submitting forms important?
9. Do you believe ADR reporting should be made mandatory?
10. How do you believe hospital staff can be made more aware of the existence of the ‘Adverse Drug Reaction and Product Quality Problem Report Form’?

Appendix D: Participant Information Document for Questionnaire

Study Title:

Evaluating and Improving Frameworks for Adverse Drug Reaction Reporting

Dear Participant

We are conducting a study to determine the current perceptions of doctors, nurses and pharmacists with regards to the pharmacovigilance activity of adverse drug reaction reporting at [redacted]. The purpose of the study is to gain an understanding of the knowledge, attitude and practices of health care professionals with regards to Adverse Drug Reaction (ADR) reporting.

Participants (doctors, nurses and pharmacists) will be asked to complete a questionnaire about ADR reporting, consisting of close-ended questions.

We would like you to consider participating in this study. The pages to follow contain all the relevant information relating to the study. Should you require any further information, please feel free to contact the study researcher or supervisors.

Neelaveni Padayachee	Neelaveni.Padayachee@wits.ac.za	011 717 2269
Belinda Strydom	Belinda.Strydom@righttocare.org	072 369 5430
Yashmay Gordhon	yashmayg@yahoo.com	079 135 6785

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

Prof. Cleaton Jones	011 717 2100

Thank you for taking time to consider participation.

INTRODUCTION

You are invited to consider participating in a research study. Your participation in this study is entirely voluntary.

1. 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.
2. You should not agree to take part unless you are satisfied about all the procedures involved.
3. 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.

Some of the most frequently asked questions you may have are answered below:

WHAT IS THE PURPOSE OF THE STUDY?

The purpose of the study is to gain an understanding of the knowledge, attitude and practices of nurses, doctors and pharmacists at [redacted] with regards to their involvement of ADR reporting.

WHO IS INVOLVED IN THE STUDY?

The questionnaire will be open to all doctors, nurses and pharmacists at [redacted] who are interested in participating. Only the researchers involved will see the questionnaire responses.

WHAT DO I HAVE TO DO?

You are requested to answer the questions contained in two questionnaires, and to attend a training session on the importance of ADR reporting.

DO I HAVE TO TAKE PART?

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

ARE THERE ANY BENEFITS IF I TAKE PART?

ARE THERE ANY DISADVANTAGES TO TAKING PART?

None we are aware of.

WHO HAS REVIEWED AND GIVEN ETHICAL APPROVAL FOR THE STUDY?

- This study protocol has been submitted to the University of the Witwatersrand, **Human Research Ethics Committee (HREC)**

HOW WILL MY PARTICIPATION IN THE STUDY AND QUESTIONAIRE RESPONSES BE KEPT CONFIDENTIAL?

- No information regarding your participation or responses will be used for any purpose other than to gain an understanding of the perception of ADR reporting.
- At no point in the study will you be asked to divulge any personal or identifiable information.

WHO WILL HAVE ACCESS TO THE RESULTS OF THE STUDY?

- The researchers and supervisors
- The results obtained may be presented to peers

Participant Name: Signature:

Appendix E: Consent Form and Participant Information Sheet for Focus Groups



Consent Form and Participant Information Sheet for Focus Groups

Study Title: Evaluating and Improving Frameworks for ADR Reporting

Study Number: M160246

INFORMED CONSENT

Dear Participant,

We are conducting a study to determine the current perceptions of doctors, nurses and pharmacists with regards to the pharmacovigilance activity of adverse drug reaction (ADR) reporting at [redacted]. The purpose of the study is to gain an understanding of the knowledge, attitude and practices of health care professionals with regards to ADR reporting, and to use this information to implement an effective system of reporting.

Each focus group will contain approximately 8-10 participants (2 groups of nurses and 2 groups of pharmacists). 2 groups (1 group of nurses and 1 group of pharmacists) will be chosen at random to be involved in a brief training seminar. The focus groups will be based on a broad set of questions dealing with ADR reporting. The focus group will take approximately 1 hour and will be recorded for purposes of the study. Information gathered during the focus groups will not disclose any personal or identifiable information.

We would like you to consider participating in this study. The pages to follow contain all the relevant information relating to the study. Should you require any further information, please feel free to contact the study researcher or supervisors.

Neelaveni Padayachee	Neelaveni.Padayachee@wits.ac.za	011 717 2269
Belinda Strydom	Belinda.Strydom@righttocare.org	072 369 5430
Yashmay Gordhon	yashmayg@yahoo.com	079 135 6785

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

Prof. Cleaton Jones	011 717 2100

Consent for Focus Group: Name: Signature: Date:

RECORDING CONSENT FORM

Study Title: Evaluating and Improving Frameworks for ADR Reporting

Study Number: M160246

Researcher: Yashmay Gordhon

Wits University, Department of Pharmacy and Pharmacology

This study involves the audio recording of the focus group. Neither your name nor any other personal or identifiable information will be associated with the recording or the transcript. Only the researcher, supervisors and ethics committee, if necessary, may listen to the recordings.

The recordings taken will be transcribed by the researcher and erased after the retention time frame. HSPCA Standards recommends that recordings be destroyed after 2 years if the research is published or 6 years if unpublished. Transcripts of responses during focus groups may be reproduced in whole or in part for use in presentations or written products that result from this study. No identifying information will be used in said presentations or written products.

By signing this form, I am allowing the researcher to record the interview as part of this research.

Participant Name: Signature:

Researcher Yashmay Gordhon   Signature:

Thank you for taking time to consider participation.

PARTICIPANT INFORMATION SHEET

INTRODUCTION

You are invited to consider participating in a research study. Your participation in this study is entirely voluntary.

4. 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.
5. You should not agree to take part unless you are satisfied about all the procedures involved.
6. 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.

Some of the most frequently asked questions you may have are answered below:

WHAT IS THE PURPOSE OF THE STUDY?

The purpose of the study is to gain an understanding of the knowledge, attitude and practices of nurses, doctors and pharmacists at [redacted] with regards to their involvement of ADR reporting, and to implement an effective system of reporting.

WHO IS INVOLVED IN THE STUDY?

The study involves a questionnaire and 4 focus groups. The questionnaire will be open to all doctors, nurses and pharmacists at [redacted] who are interested in participating. The questionnaire responses will be seen only by the researchers involved.

The focus group will involve a small group of nurses and pharmacists at [redacted] who are interested in participating. The focus group recordings will be heard only by the researchers involved.

WHAT DO I HAVE TO DO?

You are requested to attend a focus group, in which the reporting of ADRs will be discussed.

DO I HAVE TO TAKE PART?

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

ARE THERE ANY BENEFITS IF I TAKE PART?

No.

ARE THERE ANY DISADVANTAGES TO TAKING PART?

None we are aware of.

WHO HAS REVIEWED AND GIVEN ETHICAL APPROVAL FOR THE STUDY?

- This study protocol has been submitted to the University of the Witwatersrand, **Human Research Ethics Committee (HREC)**

HOW WILL MY PARTICIPATION IN THE STUDY AND QUESTIONAIRE RESPONSES BE KEPT CONFIDENTIAL?

- No information regarding your participation or responses will be used for any purpose other than to gain an understanding of the perception of ADR reporting.
- Any personal or identifiable information included in the audio recording or transcripts will not be used in presentations or in written products resulting from the study and will only be known to the researcher.

WHO WILL HAVE ACCESS TO THE RESULTS OF THE STUDY?

- The researchers and supervisors
- The results obtained may be presented to peers

Appendix F: Ethical Clearance Certificate

R14/49 Miss Yashmay Gordhon

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)

CLEARANCE CERTIFICATE NO. M160246

NAME: (Principal Investigator)	Miss Yashmay Gordhon
DEPARTMENT:	Pharmacy and Pharmacology Charlotte Maxeke Johannesburg Academic Hospital
PROJECT TITLE:	Evaluation and Improving the Frameworks of Adverse Drug Reaction Reporting
DATE CONSIDERED:	26/02/2016
DECISION:	Approved unconditionally
CONDITIONS:	
SUPERVISOR:	Neelaveni Padayachee
APPROVED BY:	Professor P. Cleaton-Jones,Chairperson, HREC (Medical)
DATE OF APPROVAL:	25/04/2016

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 February and will therefore be due in the month of February each year.

Principal Investigator Signature Date

PLEASE QUOTE THE PROTOCOL NUMBER IN ALL ENQUIRIES

Appendix G: Approval of Change of Title

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG

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15 August 2017
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Dear Miss Gordhon

Master of Pharmacy: Change of title of research

I am pleased to inform you that the following change in the title of your Dissertation for the degree of **Master of Pharmacy** has been approved:

From:	**Evaluating and improving the frameworks for adverse drug reaction reporting**
To:	**Evaluating the knowledge, attitudes and practices of healthcare workers towards adverse drug reaction reporting in a Public Tertiary Hospital**

Yours sincerely

Mrs Sandra Benn
Faculty Registrar
Faculty of Health Sciences

Appendix H: Plagiarism Detection Report (Turnitin)

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Evaluating the Knowledge, Attitudes and Practices of Healthcare Workers towards Adverse Drug Reaction Reporting in a Public Tertiary Hospital

Researcher: Yashmay Gordhon

Supervisors: Neelaveni Padayachee & Belinda Strydom

A dissertation submitted to the School of Therapeutic Sciences, Faculty of Health Sciences, University of the Witwatersrand in fulfillment of the requirements for the degree of Master of Pharmacy

Signed on 17 October 2017 in Johannesburg

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Date: 24 October 2017

Note to Examiners:

Please note that my student, Yashmay Gordhon (student number 604159) received a similarity report of 23% from Turnitin. This was due to the fact that Turnitin found an 8% similarity to a paper submitted to the University of Witwatersrand, which is the student's (Yashmay Gordhon's) protocol from the 24rd of March 2016. Please excuse this from the report.

SINCERELY,
NEELAVENI PADAYACHEE



FACULTY OF HEALTH SCIENCE,
UNIVERSITY OF WITWATERSRAND.

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