Pharmacovigilance: The responsibility of Pharmaceutical Companies to protect patients from drug-related harms

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Abstract

Objective

Healthcare professionals (HCPs) have a primary role to play in the detection, assessment and spontaneous reporting of adverse drug reactions (ADRs). An improvement of their related knowledge, attitude and practice concerning pharmacovigilance and ADR reporting is vital. The objective of the study was to determine whether or not pharmacovigilance training, provided by a Pharmaceutical Company, would improve HCP's perceptions and adherence to pharmacovigilance and ADR reporting.

Method

A quasi-experimental research design was used. A total of 44 HCPs participated in the study. Participants were divided into two groups: an experimental group that received pharmaceutical training intervention; and a control group that did not receive any training. Using a self-administered questionnaire before and after the training intervention assessed the knowledge, attitudes, and practice of pharmacovigilance and ADR reporting displayed amongst the HCPs.

Results

A significant improvement in HCP knowledge, attitudes and practice towards pharmacovigilance was observed in the experimental group after the training intervention provided by the Pharmaceutical Company.

Conclusion

Pharmaceutical Companies have a vital role to play in enhancing a culture of responsible and consistent ADR reporting and pharmacovigilance adherence amongst HCPs, and can fulfil this role by providing continuous pharmacovigilance training and education to HCPs. Such a system will lead to

improved public health and safety in relation to the use of medicines, ultimately ensuring that Pharmaceutical Companies fulfil their ethical obligation and responsibility to protect patients from drug-related harms.

Keywords

Pharmacovigilance, healthcare professionals, adverse drug reaction, ADR reporting, Pharmaceutical Companies, pharmacovigilance training, knowledge, attitude, practice, South Africa

Declaration

I declare that this thesis that I now submit for assessment on the programme of study leading to the award of Master of Science Pharmacy Administration and Pharmacy Policy specialising in Regulatory Sciences has not been submitted as an exercise for a degree at this or any other college. It is entirely my own work and has not been taken form the work of others, save the extent that such work has been cited and acknowledge within the text of my work.

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Leanne Roux 12 May 2014

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List of Abbreviations

ADE	Adverse Drug Event
ADR	Adverse Drug Reaction
ADRI	South Africa's National Adverse Drug Reaction database
AIDS	Acquired Immunodeficiency Syndrome
CPD	Continuous Professional Development
HCP	Healthcare Professionals
HIV	Human Immunodeficiency Virus
MCC	Medicine Control Council
NADEMC	National Adverse Drug Event Monitoring Centre
NPC	National Pharmacovigilance Centre
OTC	Over the counter
SA	South Africa
TB	Tuberculosis
WHO	World Health Organisation

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Chapter 1: Introduction

The safe use of medicines, and the safety of patients are high priorities in the modern world (Mishra and Kumar, 2013). The introduction of new medicines has changed the way in which diseases are managed and controlled, and in many cases this has been a greatly beneficial evolution. However, this progress has not come without its share of risk, and despite all the benefits, evidence continues to mount that adverse reactions to medicines are a common, yet often preventable, cause of illness, disability and even death (WHO, 2004; Desai et al., 2011). Adverse drug reactions (ADRs) are one of the major drug related problems associated with pharmacotherapy (John et al., 2012), causing high incidences of morbidity and mortality around the world (Khalili et al., 2012). Available evidence suggest that ADRs have become a major global health problem, imposing considerable economic burdens on healthcare systems and society as a whole.

Epidemic diseases such as Human Immunodeficiency Virus/ Acquired Immunodeficiency Syndrome (HIV/AIDS), Tuberculosis (TB) and malnutrition, which are prevalent in South Africa (SA), are widely known to increase the risk of certain ADRs in patients. Self-medication and the misuse of over-the-counter (OTC) medicines, traditional and complementary medicines are widespread, adding to the potential risk of ADRs and drug-drug interactions. These and other factors are likely to increase the burden of drug-related morbidity and mortality in SA (Metha, 2011).

Literature clearly indicates that ADRs have become a major health problem, which needs to be addressed at all levels of health care. The lack of awareness and appreciation of the size and severity of the problem, as well as misclassification of ADRs as other diseases or the underlying condition, are partially to blame for this silent epidemic. More than half of the ADRs that occur in patients are considered to be preventable with improved prescribing, administration, monitoring and adherence. Therefore, in order to prevent or reduce harm to patients and thus improve public health,

mechanisms for evaluating and monitoring the safety of medicines in clinical use are vital. In practice, this means having a well-organised pharmacovigilance system in place as a matter of common process (Metha, 2011; WHO, 2004; Dheda et al., 2013).

The success or failure of any pharmacovigilance activity depends on the reporting of ADRs (Dheda et al; 2013). Spontaneous and voluntary reporting is an integral component of the pharmacovigilance program and is also the most effective methods of acquiring ADR information especially new and serious ADRs, relying mainly on healthcare professionals (HCP) to identify and report suspected ADRs to their National Pharmacovigilance Centre (NPC) or to the Pharmaceutical Company manufacturing the medicine. Thus, HCPs are the principal contributors of ADR reports and play an important role in the detection, assessment and spontaneous reporting of ADRs (Khalili et al., 2012; John et al., 2012; Fadara et al., 2011).

The spontaneous reporting system of the pharmacovigilance program has contributed significantly to improve the ADR reporting rates worldwide. Nevertheless, under-reporting is the major shortcoming of the spontaneous reporting system. Under-reporting delays the early detection of ADRs and can increase associated morbidity and mortality in the patient. Similarly to developed countries, reports of ADRs by HCPs in SA are extremely low. Thus, in SA, the understanding of the safety profile of medicines is often delayed, resulting in large populations of patients being exposed to medicines which may have an uncertain safety profile (Metha, 2011). Studies conducted into reasons for under-reporting mostly indicate that HCPs demonstrate a lack of knowledge and understanding regarding pharmacovigilance and ADR reporting (Metha, 2011; Suleman, 2010). In order to improve the participation of HCPs in spontaneous ADR reporting, it is necessary to increase their knowledge and attitude toward the practice of pharmacovigilance and the ADR reporting system (Desai et al., 2011).

Pharmaceutical companies have a vital role to play in increasing HCPs knowledge, attitudes and practises regarding pharmacovigilance and ADR reporting. The main responsibility of any Pharmaceutical Company is to ensure the quality, efficacy and safety of all their marketed products. All Pharmaceutical Companies are legally required to have an appropriate pharmacovigilance system in place to monitor the use and effect of their registered medication and to detect, assess, understand and prevent or report any ADR or medicine-related problem (EGMA, 2014). If Pharmaceutical Companies promote HCP's understanding of pharmacovigilance, and provide education and clinical training regarding pharmacovigilance and the ADR reporting systems, it may result in an improvement of their knowledge, attitudes and practice of pharmacovigilance, which is likely to result in significantly increased ADR reporting. Institutionalised recognition and endorsement of pharmacovigilance by Pharmaceutical Companies will increase the perceived validity of pharmacovigilance, and go a long way in shifting HCPs attitudes and behaviours as a result of increased awareness created by Pharmaceutical Companies.

The aim of this study is to create awareness around pharmacovigilance among HCPs, through an intervention in the form of pharmacovigilance training provided by a Pharmaceutical Company that considers pharmacovigilance an essential part of their business. The study further aims to identify the role that Pharmaceutical Companies can play in increasing HCPs knowledge, attitudes and practices regarding the benefits of pharmacovigilance and ADR reporting. Since there are considerable social and economic consequences stemming from ADRs, there is a clear need to engage HCPs in a well-structured programme to build synergies for monitoring ADRs (Mishra and Kumar, 2013). The current widespread ignorance surrounding the methods and importance of pharmacovigilance must be eradicated, to uphold patient safety, and ensure that avoidable deaths and dangers are prevented.

Chapter 2: Literature review

Where no counsel is, the people fall; but in the multitude of counsellors there is safety

(Proverbs 11:14, KJV)

2.1 Introduction to pharmacovigilance

Modern medicines have changed the way in which diseases are managed and controlled. However, despite all their benefits, evidence continues to mount that adverse reactions to medicines are a common, yet often preventable cause of illness, disability and even death (WHO, 2004).

A prime example of this problem is the Thalidomide tragedy of the 1960's, which led to congenital deformity in neonates born to mothers who used Thalidomide to treat morning sickness during pregnancy. Due to a lack of timely reporting of adverse reactions, the linkage between the effects of Thalidomide and the resulting congenital birth defects was difficult to draw – and likely responsible for the delayed conclusion of Thalidomide's adverse effects. Many cases could have been prevented if reporting followed a clear, approachable system whereby mothers, and doctors treating the mothers, knew to report their medicine usage along with the congenital birth defects of the affected infants.

The Thalidomide case became the modern starting point of a science focused on patient problems caused by the use of medicines. This science, and activities associated with it, is commonly termed pharmacovigilance (Chinenye and Michael, 2012; Mishra and Kumar, 2013).

Pharmacovigilance is defined by the World Health Organisation (WHO) as the science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other

drug-related problem. The aims of pharmacovigilance are to enhance patient care and patient safety in relation to the use of medicines; and to support public health programmes by providing reliable, balanced information for the effective assessment of the risk-benefit profile of medicines (WHO, 2004).

The safety of patients and the safe use of medicines are paramount priorities in the modern world (Mishra and Kumar, 2013). The main responsibility of any Drug Regulatory Authority and Pharmaceutical Company is to ensure the quality, efficacy, and safety of all marketed products. The first two criteria can be established through data obtained from *in vitro* testing to ensure compliance with acceptable standards and data obtained from animal studies, preclinical and clinical trials involving humans (Yadav, 2008).

It is a well-established fact, however, that pre-marketing clinical trials do not have the statistical power to detect rare ADR's nor do they have significant follow-up to identify delayed adverse drug reactions or effects from long-term exposure. In view of this, pharmacovigilance plays a prominent role in establishing the safety profile of marketed drugs, as pre-marketing clinical trials are often not enough to fully establish these criteria (Yadav, 2008).

Originally a modest appendix of drug regulation, pharmacovigilance has since become a major activity, and adherence to this system will ensure greater patient safety and stand to minimise preventable ADRs if it is properly followed and implemented on a large scale (Yadav, 2008; Rohilla et al., 2012). However, the problem remains a lack of reporting and knowledge about the importance of pharmacovigilance.

2.2 Adverse Drug Reactions (ADRs): A silent epidemic

Pharmacovigilance is particularly concerned with the reporting of ADRs. An ADR is defined by the WHO as a response to a medicine in humans or animals, which is noxious and unintended, including lack of efficacy, and which occurs at any dosage and can also result from overdose, misuse or abuse of medicine (Yadav, 2008; Zolezzi and Parsotam, 2005; Mishra and Kumar, 2013). An adverse drug event (ADE) is any undesirable experience associated with the use of a medical product in a patient. This broad definition includes ADRs and other events (including medication errors) related to the prescribing, preparation, dispensing, or administration of medications (Zolezzi and Parsotam, 2005).

ADRs are one of the major drug related problems associated with pharmacotherapy (John et al., 2012), and are a major cause of morbidity and mortality around the world (Khalili et al., 2012). In some countries, ADRs are ranked among the top ten leading causes of mortality (WHO, 2004). A meta-analysis of 69 prospective and retrospective studies conducted in various regions of the world involving 419 000 patients found that approximately 6.7 % of all hospitalisations were as a result of ADRs (Metha, 2011). Adverse events account for a large percentage of hospital admissions, from 3.2 % in France, to 6,7 % in the United States, to 12 % in Sweden, and 6,5 % in the UK (Suleman, 2010).

Several studies, such as those conducted by Metha (2008) and John et al. (2012) have also found that the cost of managing ADRs place a significant burden on health care budgets. Some countries reportedly spend up to 15 - 20 % of their hospital budget dealing with drug complications (Metha, 2011; John et al., 2012; Metha et al., 2008; Hema and Bhuvana, 2012). Therefore, in addition to the obvious morbidity and mortality cases that are caused by these largely preventable complications, ADRs pose a significant economic burden to global health care systems, as they prolong hospital stays and increase the overall cost of treatment (Hema and Bhuvana, 2012). Meta-analyses and

reviews of these studies have contributed to the recognition of drug safety as a major public health priority (Metha et al., 2008).

2.2.1 ADRs in South Africa (SA)

Most of the above-mentioned studies have been conducted in developed countries, where disease prevalence, access to medicines, drug use patterns and drug management systems differ markedly from those of developing countries. Studies to determine the frequency and nature of ADRs in SA during the HIV/AIDS pandemic have not been commonly reported (Metha et al., 2008).

Epidemic diseases such as HIV/AIDS, TB and malnutrition are well known to increase the risk of certain ADRs in patients. Reliable, independent drug information sources are not widely available and illiteracy is widespread in SA communities, preventing the comprehension of what ADRs are, and why they are necessary to report. Due to this problem alone, it is likely that ADRs go widely unreported in SA. Self-medication and the misuse of OTC medicines, traditional and complementary medicines are widespread, adding to the potential risk of ADRs and drug-drug interactions. These and other factors are likely to increase the burden of drug-related morbidity and mortality in SA (Metha et al., 2008).

In SA, approximately 11.6 % of the total population is infected with HIV, one of the highest burdens in the world (Metha et al., 2008). As a result of the HIV pandemic the incidence of TB has also risen sharply to an incidence of 600 cases per 100 000 of the total population per year. As both HIV/AIDS and TB are managed with long-term combination treatment regimens, the likelihood of drug-drug and drug-disease interactions is increased. The frequency, nature and population at risk of drug-related harm could thus be different from that seen in developed countries, where the burden of these diseases is comparatively low (Metha et al., 2008).

A recent observational study conducted in the medical wards of a secondary hospital in the Western Cape estimated that 6.3 % of hospitalised patients were admitted as a direct result of an ADR, while a further 6.3 % of patients developed a significant ADR while in hospital. These results are comparable to the results reported in the meta-analysis study involving 419 000 patients in developed countries (Metha, 2011; Metha et al., 2008). More than half of the ADRs that occurred in patients in the community were considered to be preventable with improved prescribing, administration, monitoring and adherence to pharmacovigilance principles. Patients with HIV/AIDS were found to have an increased risk of ADRs, due to the effect of the disease on the immune system as well as the safety profile of the complex drug regimens that patients with HIV/Aids are often receiving (Metha, 2011). The study found that ADRs contribute substantially to patient morbidity and hospitalisation in SA, further increasing the burden and cost of managing adult patients in an already over-extended healthcare system (Metha et al., 2008).

Owing to the aforementioned evidence, available literature suggests that ADRs have become a major global public health problem.

2.3 ADR reporting

The success or failure of any pharmacovigilance system depends on the reporting of suspected ADRs (Dheda et al., 2013). The monitoring of ADRs is carried out by various methods, of which voluntary or spontaneous reporting is most commonly practised (Kulkarni et al., 2013), and is considered the cornerstone of any pharmacovigilance system (Bawazir, 2006).

Spontaneous and voluntary reporting systems are integral components of drug safety surveillance programs, and also present the most effective methods of acquiring ADR information, particularly in

the case of new and serious ADRs (John et al., 2012). This method of reporting relies on HCPs to identify and report any suspected ADRs to their NPC or to the Pharmaceutical Company that manufactures the drug (Mishra and Kumar, 2013).

Despite the vital importance of this form of reporting, under-reporting is the major shortcoming of the spontaneous reporting system (John et al., 2012). The rate of under-reporting in this category is estimated at figures exceeding 90 – 95 % of cases (Santosh et al., 2013). Reporting rarely exceeds 10 % of cases – proving that this instance of reporting is woefully underutilised (Mishra and Kumar, 2013). Under-reporting directly delays the early detection of ADRs and can increase associated morbidity and mortality in the patient (John et al., 2012). Overall, under-reporting of ADRs is the most common and significant problem facing effective pharmacovigilance programs (Mishra and Kumar, 2013).

2.4 Under-reporting by HCPs

Several studies have established the crucial role that HCPs play in the detection, assessment and spontaneous reporting of ADRs. To gain insight into the underlying reasons for under-reporting, numerous global studies were conducted to assess the attitudes and behaviour that HCPs exhibited towards their national ADR reporting programs; with the aim of identifying reasons for under-reporting, and determining the steps that could be adapted to increase reporting rates (Bawazir, 2006; Zolezzi and Parsotam, 2005; John et al., 2012).

The key barriers deterring the improved monitoring and reporting of ADRs have been analysed in various studies and can be summarised as follows:

- Fear of personal and organisational liability
- Lack of resources for surveillance and reporting

- Labour-intensive, complex, and time-consuming reporting processes
- Ambiguity in interpreting whether the medication was the cause of the AE
- HCPs being ignorant of the official procedures and protocols of reporting
- ADRs are mistakenly considered too trivial or insignificant to report
- ADRs are mistakenly considered too commonplace to report
- HCPs incorrectly assume that the serious ADRs of the drug are well documented and that further reporting of incidences is unnecessary.
- Minimal feedback is provided to reporters once reports are submitted – this may be a deterrent to potential reporters as they feel the reports go unseen or unappreciated.
- No incentives, rewards, or motivation to report
- Lack of knowledge and confidence to distinguish between significant ADRs and minor ones

(Bawazir, 2006; Zolezzi and Parsotam, 2005; John et al., 2012).

Similarly, in SA, reports of ADRs by HCPs are extremely low: One of the few studies conducted in SA on barriers to ADR reporting by HCPs indicated that most HCPs demonstrated a lack of understanding as to what should be reported, in combination with a lack of sufficient skills and knowledge to identify ADRs (Metha, 2011; Suleman, 2010).

Identifying the factors influencing reporting is an essential step in determining measures to enhance reporting. Several studies carried out to assess the knowledge, attitude, and practice among HCPs have documented that the knowledge of ADR reporting procedures are inadequate among HCPs (John et al., 2012). The New Zealand report by Zolezzi and Parsotam (2005) found that knowledge appeared to be a greater influence on ADR reporting than attitudes and beliefs. In order to improve the reporting rate, it is important to improve the knowledge, attitudes and practices of the HCP regarding ADR reporting and pharmacovigilance (Subish et al., 2007).

2.5 Problem statement

The literature clearly identifies that ADRs have become a major global health problem, which needs to be seriously addressed at all levels of healthcare. The lack of awareness and appreciation of the scope and severity of the problem, as well as the misclassification of ADRs as other, non drug-related diseases or symptoms of the underlying condition, are partially to blame for the rise and spread of this silent epidemic.

The current widespread ignorance surrounding the methods and importance of pharmacovigilance must be addressed. More than half of the ADRs that occurred in patients were considered to be preventable with improved prescribing, administration, monitoring and adherence (Metha, 2011).

Increased knowledge and awareness around the benefits of pharmacovigilance could serve to alter this current perception and see pharmacovigilance take the prevalent position it deserves. Pharmacovigilance provides one of the best opportunities to achieve a reduction in preventable AEs and ADRs, and to increase patient well being and drug safety.

2.6 Goals and objectives of the study

HCPs occupy a critical role in the detection, assessment and spontaneous reporting of ADRs. As such, the improvement of their knowledge, attitudes and practice regarding pharmacovigilance is essential (Khalili et al., 2012). The main objective of the study was to determine whether or not pharmacovigilance training (Intervention), provided by a Pharmaceutical company would improve HCP's perceptions of pharmacovigilance and ADR reporting. The study further aimed to identify the significant role that Pharmaceutical Companies can play in increasing HCP's awareness around the importance of pharmacovigilance and drug safety.

2.7 Improving HCP's pharmacovigilance awareness

Ensuring that patients are protected from the harmful effects of medicines is a shared responsibility. Pharmaceutical Companies, drug regulators, HCPs and patients all need to understand the potential risks of medicines and their responsibility in minimising and managing those risks (Metha, 2011).

Developing awareness of the potential risks of medicines, both direct and indirect, while also understanding the extent of their benefits, is critical in addressing the problem of drug-induced diseases. Failing to maintain a sense of constant vigilance when using medicines in patients can have devastating and even potentially fatal consequences, particularly given the local SA context, as discussed (Metha, 2011).

HCPs have a central role to play in drug safety by contributing to the prevention, identification, documentation, and reporting of ADRs. All HCPs have roles to play in maintaining a balance between a medicine's benefits and risks (Zolezzi and Parsotam, 2005). HCPs in particular need to gain a broader understanding of pharmacovigilance, and increase ADR reporting to effectively prevent avoidable, harmful drug interactions. HCPs need to understand their role and responsibility in the detection, management, documentation and reporting of ADRs, all of which are essential activities for optimising patient safety (Zolezzi and Parsotam, 2005).

If Pharmaceutical Companies commit themselves to following a set pharmacovigilance system, whereby the reporting and monitoring of ADRs, AEs and side-effects are clearly marked as vital components to their operation, attitudes and behaviours displayed towards this system could shift as a result of increased awareness, institutionalised recognition and endorsement by Pharmaceutical Companies. Drug safety is, after all, an integral part of the Pharmaceutical Company's responsibility. Pharmaceutical Companies have an ethical obligation to ensure that, to the greatest extent of their

knowledge, their drugs will not cause death or harmful interactions. Pharmaceutical Companies can occupy a vital perception-shifting role in the greater establishment of pharmacovigilance, and in so doing, more clearly meet their key responsibility.

2.8 The role that Pharmaceutical Companies play in increasing HCP's pharmacovigilance awareness

The current perception of pharmacovigilance sees this crucial act categorised into a mere administrative obligation – seen as a chore rather than a potentially life-saving endeavour. Increased awareness around the benefits of pharmacovigilance could serve to alter this perception and see pharmacovigilance take the fundamental position it deserves.

If Pharmaceutical Companies can be made to implement and normalise pharmacovigilance systems while raising awareness around the benefits resulting from such systems, it may lead to HCPs effectively upholding patient safety and ensuring that patients can safely negate the harmful effects of medicines or combinations of medicines.

2.8.1 Role and responsibility of Pharmaceutical Companies

The main responsibility of any Pharmaceutical Company is to ensure the quality, efficacy, and safety of all their marketed products (Yadav, 2008; Rohilla et al., 2012).

All Pharmaceutical Companies are legally required to monitor the use and effect of their registered medication and to detect, assess, understand and prevent any ADRs or other medicine-related problems that may arise. It is important to assess on a permanent basis that the risk-benefit of a

given medicine remains positive during its entire life cycle. Therefore, monitoring the use and effect of medicines is an essential part of the activities of a Pharmaceutical Company (EGMA, 2014).

In order to achieve the goal of maintaining the highest safety standards, the newly adopted legal framework for pharmacovigilance clearly sets out the roles and the responsibilities of Pharmaceutical Companies in this area. Companies must ensure that (MCC, 2012):

- An appropriate system of pharmacovigilance is in place in order to assume the responsibility and liability for their medicines;
- appropriate action can be taken when and where necessary;
- all information impacting the risk-benefit balance of a medicine is reported to the authorities;
- a person responsible for pharmacovigilance is permanently and continuously at their disposal.

Pharmaceutical Companies, together with all other stakeholders must work together to meet all these requirements and ensure that patients only receive safe and effective medicines (EGMA, 2014; MCC, 2012).

2.9 Hypothesis to be tested

The development of a robust pharmacovigilance intervention program by a Pharmaceutical Company will improve HCP's knowledge, attitude and practice towards pharmacovigilance and ADR reporting.

It is assumed that improved knowledge and attitudes towards pharmacovigilance will result in more instances of ADR reporting.

2.10 A robust pharmacovigilance system

What Pharmaceutical Companies should ultimately develop is a comprehensive pharmacovigilance system, which is firmly integrated into clinical care, and is effective in identifying and addressing ADRs that pose the greatest threats to the SA population.

The pharmacovigilance system must:

- Improve patient care and safety in relation to the use of the Pharmaceutical Company's medicines and medical interventions
- Improve public health and safety in relation to the use of medicines
- Contribute to the assessment of benefit, harm, effectiveness and risk of medicine
- Encourage the safe, rational and more effective (including cost-effective) use of medicines.

Furthermore, this system should:

- Promote understanding, education and clinical training in pharmacovigilance and its effective communication to HCPs and the public (WHO, 2002);
- while ensuring that health workers and patients are confident of the pharmacovigilance system and the medicines they use.

The Pharmaceutical Company should further encourage HCPs to exercise caution and vigilance when prescribing, administering and monitoring the use of medicines in their patients. Moreover, the reporting of unusual problems and reactions encountered with the use of these medicines to the National Adverse Drug Event Monitoring Centre (NADEMC) or Pharmaceutical Company contributes to making these medicines safer for patients, both in SA and globally (Metha, 2011).

A robust pharmacovigilance system is crucial in quantifying previously recognised ADRs, identifying unrecognised ADEs, evaluating the effectiveness of medicines in real-world situations, as well as decreasing the mortality and morbidity associated with adverse events (Dheda et al., 2013).

This system may result in the increased reporting of ADRs, which in turn will lead to an effective pharmacovigilance system and overall increase in patient safety, as patients will be protected from the harmful effects of medicines. This approach permits pharmacovigilance to contribute to a safe and rational use of drugs for the benefit and well-being of those patients that are dependent on pharmacotherapy (Suleman, 2010).

Chapter 3: Methodology

3.1 Introduction

Available literature and evidence shows that ADRs have become a major global health problem. ADRs impose a considerable economic burden on society and health-care systems (John et al., 2012). Exacerbating this problem is the fact that the reporting of ADRs to Health Care Authorities or Pharmaceutical Companies responsible for the drug rarely exceeds 10 % of cases (Bawazir, 2006). The lack of awareness and appreciation of the size and severity of the problem, as well as the misclassification of ADRs as other non drug-related disease or symptoms of the underlying condition, are partially to blame for rise and spread of this silent epidemic.

HCPs occupy a critical role in the detection, assessment and spontaneous reporting of ADRs. As such, the improvement of their related knowledge, attitude and perception towards pharmacovigilance is essential (Khalili et al., 2012).

3.2 Objectives of the study

The main objective of the study is to determine whether or not pharmacovigilance training provided by a Pharmaceutical Company would improve HCP's knowledge, attitudes and practice of pharmacovigilance and ADR reporting. The study further aims to identify the significant role that Pharmaceutical Companies can play in increasing HCP's awareness around the importance of pharmacovigilance and drug safety. Prior approval from the University of the Western Cape Ethical committee was obtained before the initiation of the study.

3.3 Experimental design

In order to determine if the pharmacovigilance training would be successful in bringing about more positive attitudes towards pharmacovigilance, increase pharmacovigilance knowledge and ultimately result in increased ADR reporting, a simple pre-test / post-test design was considered:

Observation point 1 (pre-test) → Intervention (pharmacovigilance training) → Observation point 2 (post-test)

If there were differences in outcomes at Observation point 2, then one would hope to attribute those differences to the pharmacovigilance training intervention. The main problem with this approach is the lack of a control group. Without a control group it is not possible to conclude that the observed differences in outcomes are directly due to the pharmacovigilance training intervention, as differences may arise from memory bias and/or various other factors. It was therefore imperative to have a control group and thus utilise a quasi-experimental research design:

Non-random experimental group: Observation point 1 (pre-test) → Intervention (pharmacovigilance training) → Observation point 2 (post-test)

Non-random control group: Observation point 1 (pre-test) → No intervention → Observation point 2 (post-test)

At Observation point 1 (pre-test), both groups where given a questionnaire to complete. After completing the questionnaire the experimental group received pharmacovigilance training (the intervention), while the control group did not receive any training. Two weeks after the

pharmacovigilance training intervention both groups were asked to complete the same questionnaire again, Observation point 2 (post-test).

This approach was not a purely experimental design, as the experimental and control groups were not randomly selected (please refer section 3.7 for the discussion on the selection of research participants). Given the non-random selection of participants, a concern was that there may have been inherent differences between the groups to start off with, and so differences at Observation point 2 may be due to pre-existing group differences and not due to the pharmacovigilance training (intervention). Statistical tests were performed to assess the equivalence of the groups (please refer to section 3.8).

Table 1: Interventional Quasi-experiment study design			
Groups	**Observation point 1**	**Intervention**	**Observation point 2**
Non-random Experimental Group	Pre-test (Questionnaire)	Pharmacovigilance training	Post-test (Questionnaire)
Non-random Control group	Pre-test (Questionnaire)	No pharmacovigilance training	Post-test (Questionnaire)

3.4 Questionnaire design

The knowledge, attitudes, and practice of pharmacovigilance and ADR reporting among the HCPs were assessed by using a self-administered pen-and-paper questionnaire (please refer to Appendix 1). The same questionnaire was used for Observation point 1 (pre-test) and Observation point 2 (post-test) to ensure test-retest reliability.

The questionnaire consisted of the following sections:

1. Demographic information of participant
2. Questions about knowledge of HCPs regarding ADRs, pharmacovigilance, the importance of ADR reporting, an ADR monitoring centre, and ADR reporting system
3. A pharmacovigilance attitudinal scale
4. Practice of reporting of ADRs; the questions on practice in the questionnaire included whether HCPs have previously reported an ADR, and the number of times they have reported ADRs to the NPC or Pharmaceutical Company responsible for manufacturing the drug in question.
5. Factors encouraging and discouraging the reporting of ADRs.

The questionnaire was designed based on similar previous studies that measured the knowledge, attitudes and practice of HCPs and ADRs (Khalili et al., 2012; Santosh et al., 2013; John et al., 2012; Ramesh and Parthasarathi, 2009; Subish et al., 2007). The questionnaire consisted of 36 questions that were structured to obtain the demographics of the HCPs, establish the extent of their knowledge and attitudes regarding pharmacovigilance and ADR reporting, and shed light on their personal experience of reporting, if any existed. Questions to establish knowledge mainly centred on general concepts of pharmacovigilance and ADR reporting systems. Attitude questions focused on the HCP viewpoint regarding different aspects of ADR reporting. The HCP's responses were measured on a Likert scale, with response options ranging from "strongly agree", "strongly disagree" and "not sure" for the attitude questions (Khalili et al., 2012; John et al., 2012). The questionnaire was tested for content validity by pharmacovigilance experts Dr Jaco van Zyl and Dr Carine Paige.

A covering letter providing information about the research, and instructions to complete the questionnaire were attached to the questionnaire. Informed consent was obtained from each participant, and confidentiality ensured (Santosh et al., 2012).

3.5 Pilot study

To develop and test the adequacy of the questionnaire, several pilot studies were conducted in preparation for the principal study. The pilot studies assisted in designing the research instrument and research protocol, uncovering and identifying potential problems that might occur during the study and assessing the likely success of the proposed study, therefore improving the internal validity of the questionnaire.

The questionnaire was distributed to volunteers who were similar to the target population. Several of the principal investigator's HCP colleagues, instructors of the Pharmaceutical Company and randomly selected HCPs participated in the pilot studies. Pilot study participants were not included in the principal study. Participants of the pilot study were asked to record the time it took to complete the questionnaire, identify ambiguities and difficult questions, and provide any feedback or comments on the questionnaire.

The pilot study identified two difficult questions, four questions that were too long and three double-barrelled questions (i.e. a double –barrelled question asked about more than one thing in a single question). The pilot study further identified that questions in section B of the questionnaire were leading the participant towards the correct answer.

The questionnaire was amended to discard all unnecessary and difficult questions. Double-barrelled questions were re-worded, shortened and revised. Questions were re-assessed to ensure each

question provided an adequate range of responses, and that replies could be interpreted in terms of the information that was required. The pilot study provided valuable insights and improved the chances of a successful study outcome (Van Teijlingen and Hundley, 2001).

3.6 Pharmacovigilance Training (Intervention)

HCPs occupy a critical role in the detection, assessment and spontaneous reporting of ADRs. As such, the improvement of their related knowledge, attitude and practice regarding pharmacovigilance is essential (Khalili et al. 2012). An integral part of Pharmaceutical Company X's (the Pharmaceutical Company wishes to remain anonymous) pharmacovigilance system is to promote understanding, education and clinical training in pharmacovigilance and its effective communication to HCPs and the public. By providing pharmacovigilance training, Pharmaceutical Company X hopes to ensure that HCPs and patients are confident of the pharmacovigilance system and the medicines they use.

The pharmacovigilance training included the following sections:

- History and background of pharmacovigilance
- What pharmacovigilance is and why it is so important
- International pharmacovigilance
- South African pharmacovigilance
- The role of the Pharmaceutical Company in pharmacovigilance
- Pharmaceutical Company X's pharmacovigilance vision
- Pharmaceutical Company X's pharmacovigilance system
- HCP's roles and responsibilities to ensure patient safety
- Reporting ADRs
- Modern technology: Making ADR reporting easy

- Pharmacovigilance systems ensuring patient safety in relation to drug use

The pharmacovigilance training illustrated the importance, seriousness, preventability and necessity of pharmacovigilance and ADR reporting. Pharmaceutical Company X committed to continuously encouraging HCPs to exercise caution and vigilance when prescribing, administering and monitoring the use of medicines in their patients. Moreover, Pharmaceutical Company X will unremittingly motivate HCP's to report unusual problems and reactions encountered with the use of these medicines to the Company, NADEMC (National Adverse Drug Event Monitoring Centre) or the MCC (Medicines Control Council of South Africa). The constant motivation and encouragement provided to HCPs by Pharmaceutical Company X will cultivate a drug safety culture nationwide, and by doing so, play a perception-shifting role in the greater establishment of pharmacovigilance, leading to improvement of public health and safety in relation to the use of medicines.

3.7 Research participants

The interventional study was conducted amongst HCPs, specifically doctors and pharmacists working in hospitals and pharmacies in the Western Cape, South Africa. A total of 44 HCPs participated in the study, 22 in the experimental group that received the pharmacovigilance training and 22 in the control group that did not receive the pharmacovigilance training.

Regarding experimental group participants, Pharmaceutical Company X presented a training day event for HCPs in the Western Cape, South Africa for Continuous Professional Development (CPD). Pharmacovigilance training was one of the topics presented at the training day. Before the researcher presented the pharmacovigilance training, she invited HCPs to participate in the study. Regarding the control group, the researcher randomly invited HCPs working in hospitals and pharmacies situated in the Western Cape to participate in the study. The researcher attempted to

match the control group and experimental group participants on age, gender and profession, and ensured that group sizes were equivalent. Participants did not have an equal probability of falling into either the experimental group or the control group. Participants were non-randomly assigned by the researcher to either the experimental group or the control group on a non-random basis by virtue of some participants attending the CPD while others did not. Therefore, the study design is quasi-experimental and is not a true experimental design.

Informed consent was attained from each participant. Participant's anonymity and confidentiality were maintained throughout the study, ensuring participant protection. Participants were adequately informed about the objectives and aims of the study. HCPs that were not willing to participate were excluded from the study.

3.8 Statistical analysis

The effect of the pharmacovigilance intervention program in improving knowledge, attitudes and practice of pharmacovigilance and ADR reporting was evaluated by comparing responses pre- and post-test between the experimental and control groups. The researcher hypothesised that more positive attitudes and greater knowledge of pharmacovigilance would result from the pharmacovigilance training. All data was analysed using the SPSS statistical software package. A statistician, Dr Dylan Fincham, was consulted to ensure that the data was analysed properly. Descriptive statistics were computed to describe the sample, and a frequency analysis was conducted to assess differences in pharmacovigilance knowledge pre-test and post-test. An analysis of variance (ANOVA) was performed to assess group differences in attitudes towards pharmacovigilance.

While parametric procedures assume that certain assumptions are met (e.g. normally distributed residuals, equality of variances and homoscedasticity), several studies have shown that the F-statistic in particular is robust with small samples if the group sizes and variances are roughly equal (Norman, 2010; Brown and Forsythe, 1974). The latter requirements were met, so it was deemed appropriate to perform an ANOVA on the data to assess group mean differences in attitudes towards pharmacovigilance.

The results and findings of the study will be discussed in the chapter to follow.

Chapter 4: Results

4.1 Demographics

A total of 44 HCPs participated in the study, of which 21 were female and 23 were male. As explained in the methodology section, HCPs participating in the study were divided into two groups, an experimental group that received pharmacovigilance training (intervention) and a control group that did not receive pharmacovigilance training. Both groups consisted of 22 HCPs all working within the private healthcare sector.

The control group and the experimental group were well matched, each group consisted of 9 doctors and 13 pharmacists. Half of the participants were between 31 – 40 years of age and most had around 6 – 10 years of experience in their respective fields. Table 2 below summarises the demographic characteristics of the participants.

Table 2: Demographic characteristics of study participants

	Control group		Experimental group	
	Pre-test n (%)	Post-test n (%)	Pre-test n (%)	Post-test n (%)
Gender				
Male	11 (50)	11 (50)	10 (46)	10 (46)
Female	11 (50)	11 (50)	12 (54)	12 (54)
Age				
24-30	4 (18)	4 (18)	3 (14)	3 (14)
31-40	11 (50)	11 (50)	12 (55)	12 (55)
41-50	5 (23)	5 (23)	4 (18)	4 (18)
51-60	2 (9)	2 (9)	3 (14)	3 (14)
>60	0 (0)	0 (0)	0 (0)	0 (0)

Table 2: Demographic characteristics of study participants				
	Control group		Experimental group	
	Pre-test n (%)	Post-test n (%)	Pre-test n (%)	Post-test n (%)
Profession				
Doctor	9 (41)	9 (41)	9 (41)	9 (41)
Pharmacist	13 (59)	13 (59)	13 (59)	13 (59)
Experience				
1-5 years	2 (9)	2 (9)	1 (5)	1 (5)
6-10 years	9 (41)	9 (41)	4 (18)	4 (18)
11-15 years	5 (23)	5 (23)	9 (41)	9 (41)
16-20 years	4 (18)	4 (18)	5 (23)	5 (23)
>20 years	2 (9)	2 (9)	3 (14)	3 (14)
Internet access				
Yes	22 (100)	22 (100)	22 (100)	22 (100)
No	0 (0)	0 (0)	0 (0)	0 (0)

4.2 Knowledge of pharmacovigilance

Below are the responses of participants to the questions surrounding knowledge of pharmacovigilance; they are consistent with trends reported in literature.

4.2.1 HCP awareness of pharmacovigilance scores

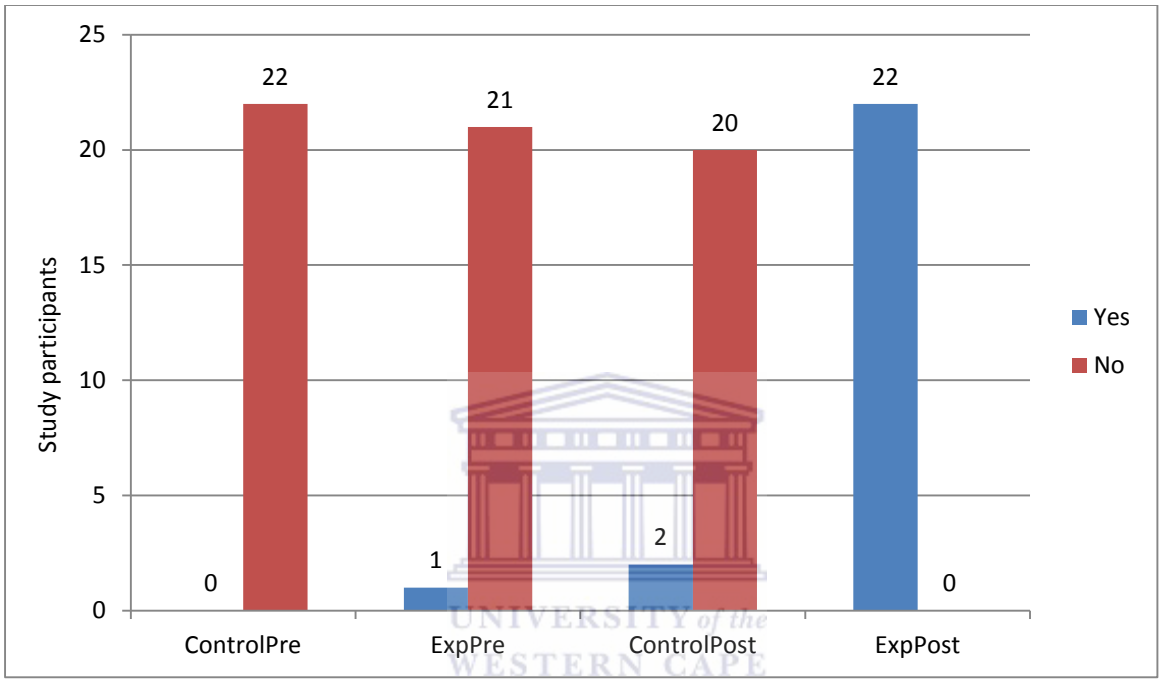
According to Figure 1, before the pharmacovigilance training intervention (Observation point 1: pre-test) 43 HCPs (98% of all the HCP participating in the study) were not aware of the term pharmacovigilance. This finding is similar to results reported in literature where numerous studies have revealed that HCPs were unaware of the pharmacovigilance and ADR reporting systems which existed in their country (Hema and Bhuvana, 2012; Zolezzi and Parsotam, 2005; Khalili et al., 2012).

At Observation point 2 (post-test) no significant changes were observed in the awareness of pharmacovigilance amongst the control group, but the experimental group after receiving the pharmacovigilance training intervention showed a major increase in pharmacovigilance awareness. This finding strongly suggests that there is a great need to create awareness of pharmacovigilance amongst HCPs (Kulkarni et al., 2013), and also emphasises the urgent need to educate and inform HCPs about pharmacovigilance and ADR reporting (Zolezzi and Parsotam, 2005).

To optimise patient safety, HCPs need to understand their role and responsibility in the detection, management, documentation and reporting of ADRs. Research into ADR reporting has shown that HCPs who undergo training are more likely to participate in pharmacovigilance activities and report ADRs (Zolezzi and Parsotam, 2005). It is imperative for Pharmaceutical Companies to create pharmacovigilance and ADR reporting awareness programs to increase HCP's knowledge of the

benefits of such a system. Continued educational initiatives are required for the multidisciplinary health care team to sustain a successful ADR monitoring and reporting program (Zolezzi and Parsotam, 2005).

Figure 1: HCP awareness of pharmacovigilance scores

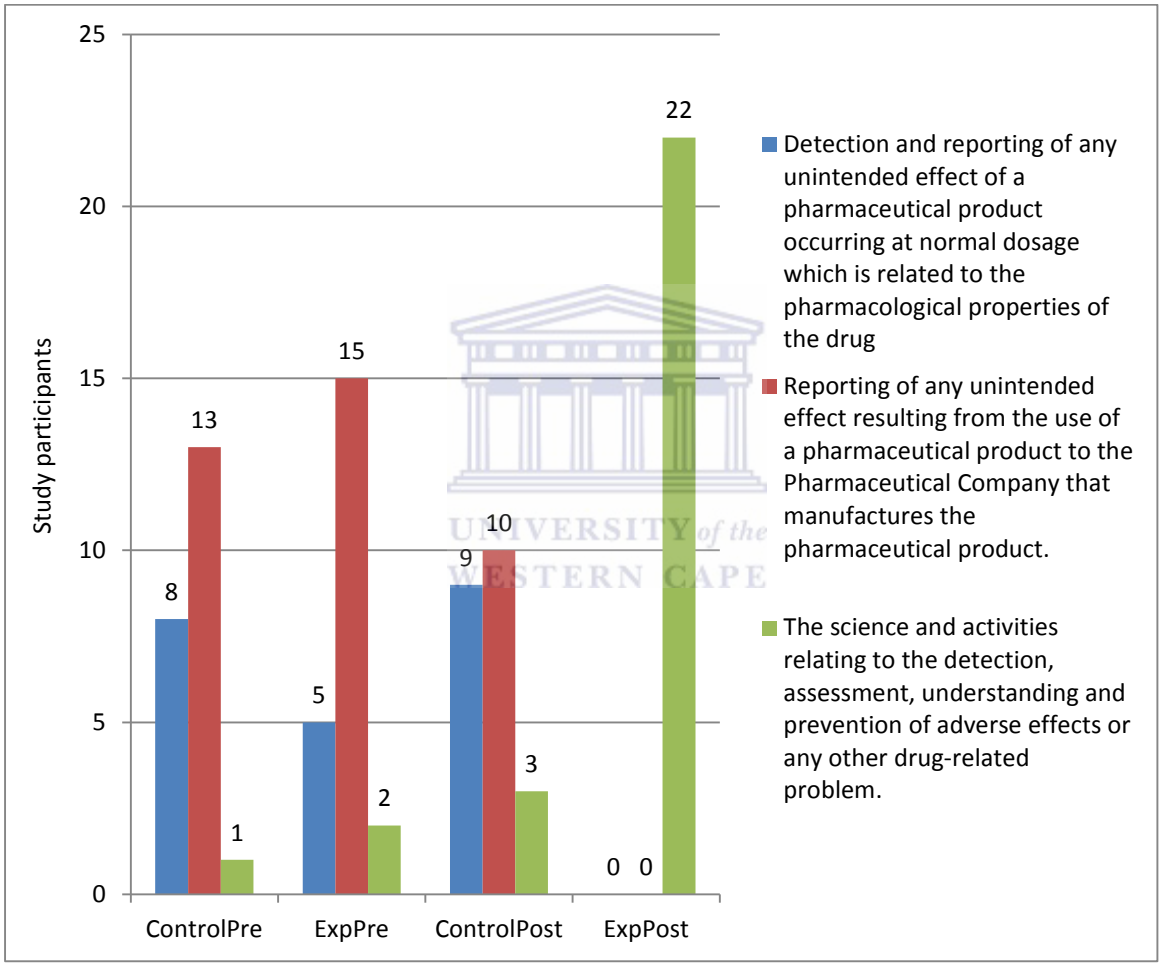


4.2.2 Definition of pharmacovigilance

Pharmacovigilance is defined by the WHO as the science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other drug-related problem (Correct definition is indicated in green in Figure 2 below), (WHO,2000; Mishra and Kumar, 2013). According to Figure 2, at Observation point 1 (pre-test) 21 (95 %) of the control group participants and 20 (91 %) of the experimental group participants were not able to correctly define pharmacovigilance.

At Observation point 2 (post-test), 19 (86 %) of the control group participants that did not receive the training intervention still did not have the knowledge to define pharmacovigilance, but the experimental group showed a significant increase in awareness after the intervention and the entire experimental group could correctly defined the term pharmacovigilance.

Figure 2: Pharmacovigilance definition

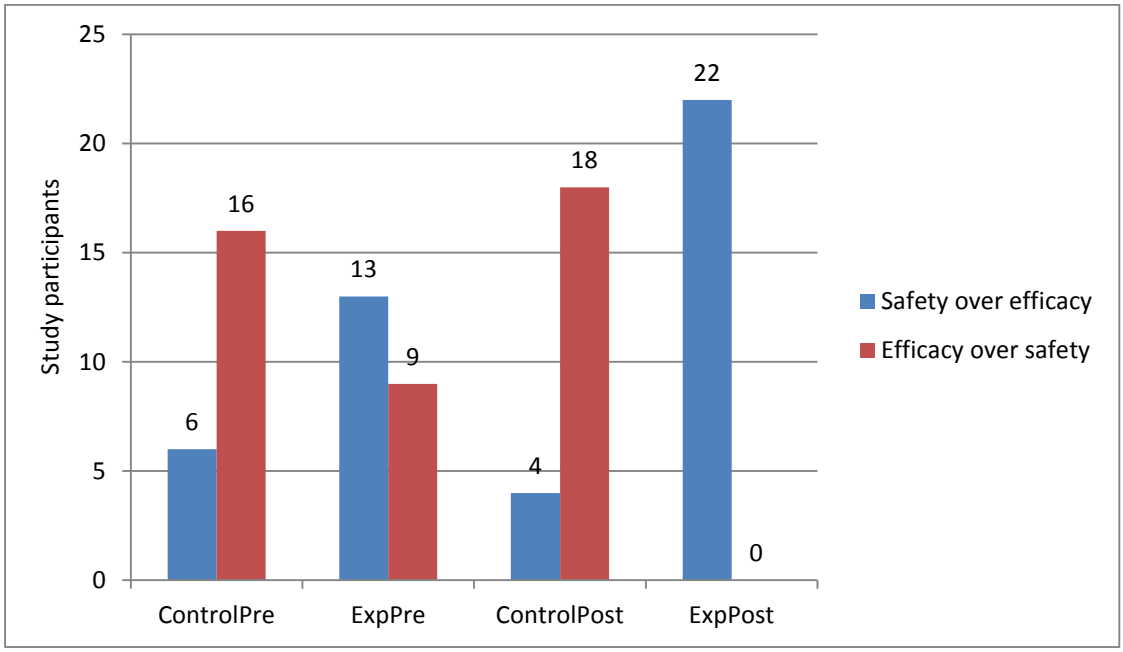


4.2.3 The aims of pharmacovigilance

The aims of pharmacovigilance are to enhance patient care and patient safety in relation to the use of medicines, and to support public health programmes by providing reliable, balanced information for the effective assessment of the risk-benefit profile of medicines (WHO). Therefore, pharmacovigilance aims to assess safety over efficacy. According to Figure 3, 16 (73 %) of the control group participants and 9 (41 %) of the experimental group participants at Observation point 1 (pre-test) assumed that pharmacovigilance aimed to assess the efficacy of a drug over the safety of a drug.

At Observation 2 (post-test), an increase was seen as 18 (82 %) of the control group participants wrongly stated the aim of pharmacovigilance as assessing efficacy over safety, but the experimental group showed a vast improvement in knowledge as all HCP in the experimental group indicated that pharmacovigilance aims to access safety over efficacy, indicating a positive response to the pharmacovigilance training and in increase in knowledge.

Figure 3: The aim of pharmacovigilance

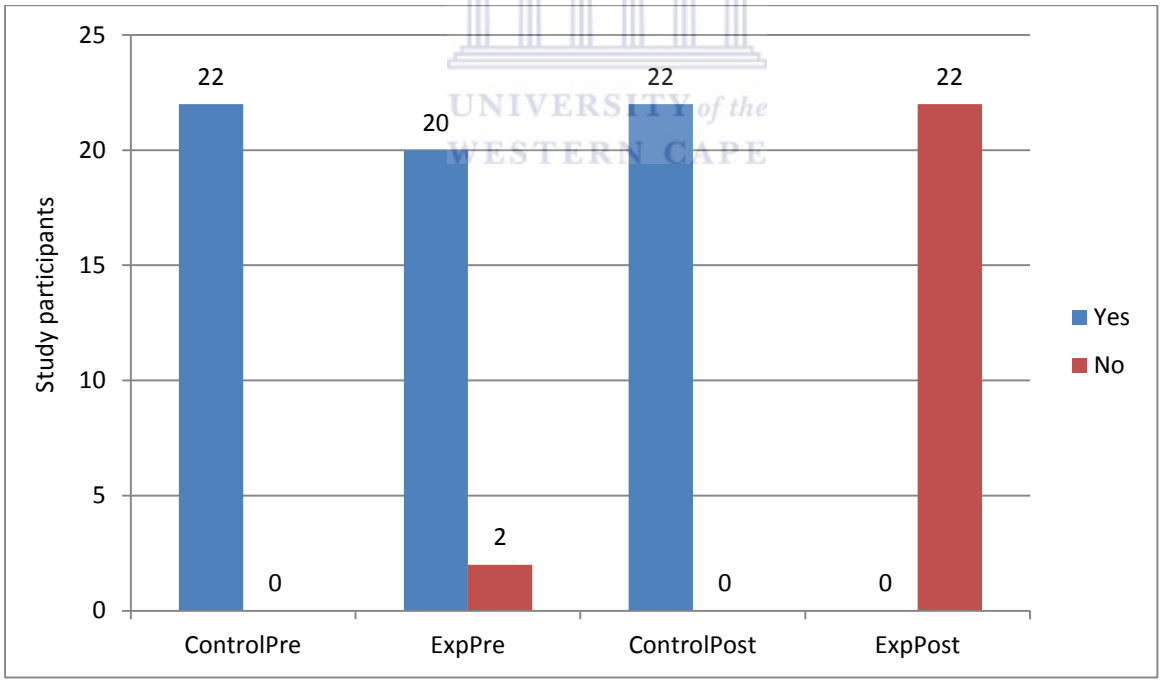


4.2.4 Definition of an ADR

An ADR is defined by the WHO as a response to a medicine in humans or animals, which is noxious and unintended, including lack of efficacy, and which occurs at any dosage and can also result from overdose, misuse or abuse of medicine (WHO, 2000; Yadav, 2008).

According to Figure 4, at Observation point 1 (pre-test) 42 HCP (95 %) of the participants wrongly defined an ADR. At Observation point 2 (post-test) the control group did not show any improvement in their knowledge as the entire group incorrectly defined ADR, but a significant difference was seen in the experimental group after the training as the entire group correctly defined an ADR.

Figure 4: Definition of an ADR

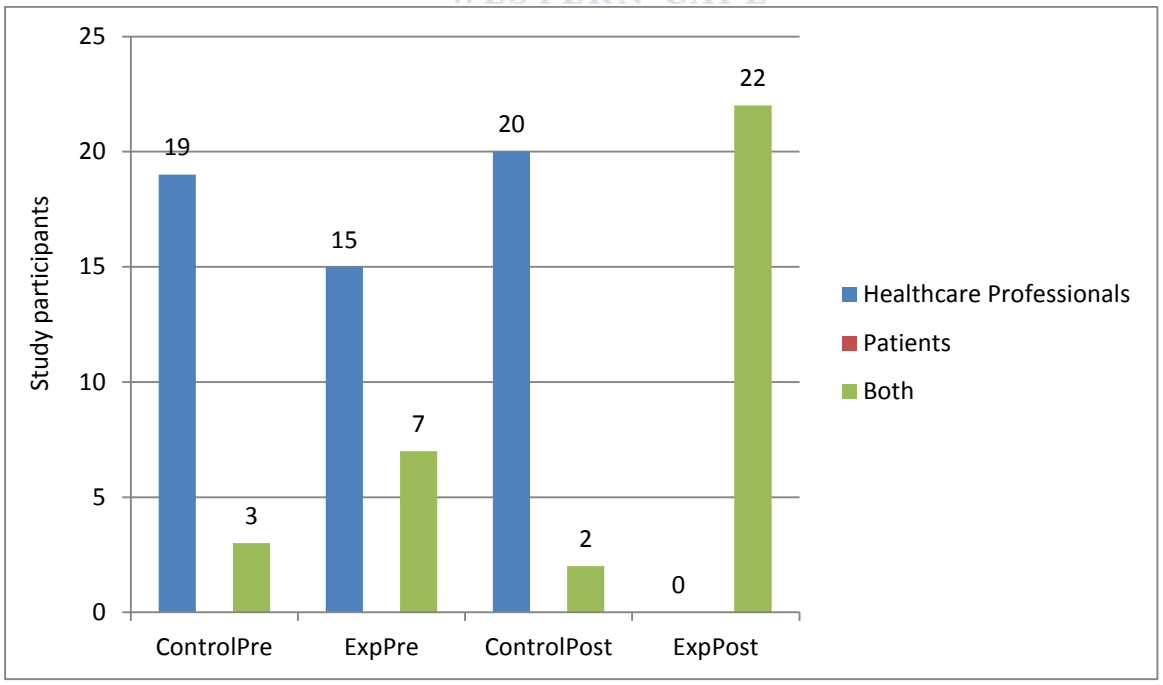


4.2.5 Reporting of ADRs

The success or failure of any pharmacovigilance system depends on the reporting of suspected ADRs (Dheda et al., 2013). HCPs are the principal contributors of ADR reports (Khalili et al., 2012), however in attempts to increase reporting in many countries, including SA, patients are also allowed to report ADRs. Therefore, both HCPs and patients can report ADRs to NADEMC, MCC or the Pharmaceutical Company in SA.

According to Figure 5, at Observational point 1 (pre-test), 19 (86 %) of the control group participants and 15 (68 %) of the experimental group participants believed that only HCPs could report ADRs. At Observational point 2 (post-test), 20 (91 %) of the control group participants still believed that only HCPs can report ADRs, whereas the entire experimental group that received the pharmacovigilance training indicated that both HCPs and patients can report ADRs.

Figure 5: Reporting of ADRs



4.2.6 Serious Adverse Event

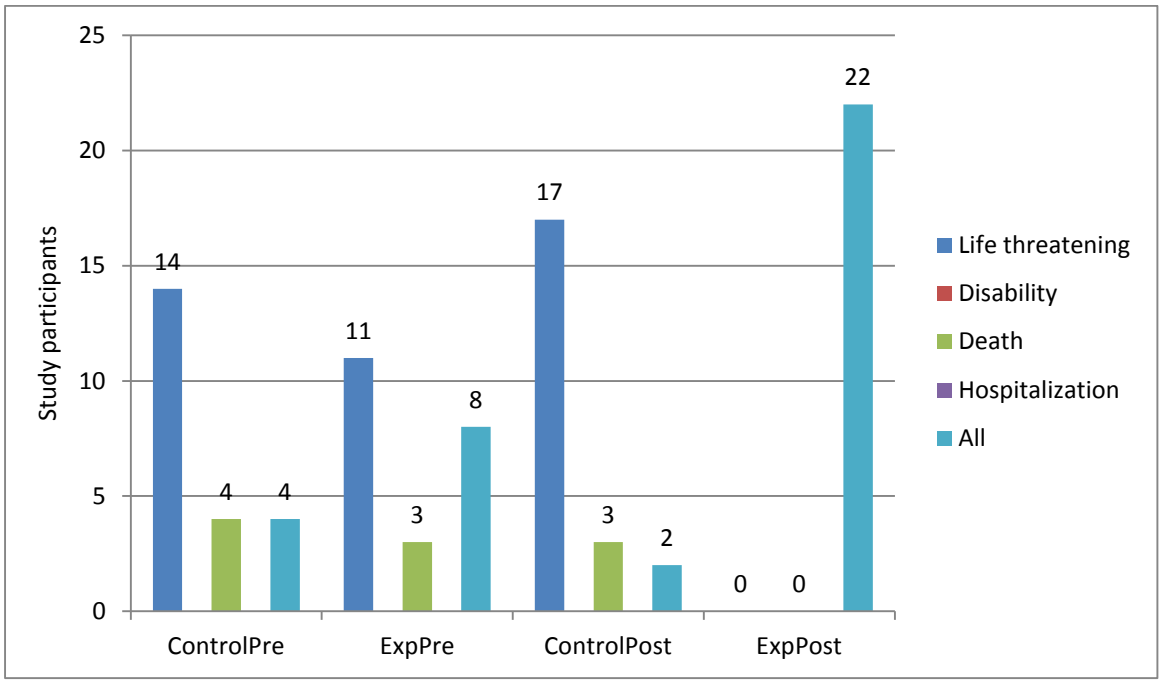
A serious adverse event is defined by the WHO as any untoward medical occurrence that at any dose:

- Results in death
- Requires inpatient hospitalisation or the prolonging of existing hospitalisation
- Results in persistent or significant disability/incapacity
- Is life-threatening (WHO, 2000; Uppsala Monitoring Centre, 2011)

According to Figure 6, results for the control group at Observation point 1 (pre-test) were as follows: 14 HCPs (64 %) believed that when an AE was life threatening it was classified as serious, 4 HCPs (18 %) stated that when and AE results in death it was defined as serious and 4 HCPs (18 %) correctly answered the questions that all of the available options could classify and AE as serious. Similarly, results for the experimental group at Observation point 1 (pre-test) indicated that 11 HCPs (50 %) believed that when an AE was life threatening it was classified as serious, 3 HCPs (14 %) stated that when an AE results in death it was defined as serious and 8 HCPs (36 %) correctly answered the question that all the options provided could classify and AE as serious.

Results at Observation point 2 (post-test) for the control group showed an increased belief that an AE is serious when it is life threatening, 17 HCPs (77 %) compared to the 14 (64%) pre-test, and a slight decrease in the belief that an AE is classified as serious only when it results in death, selected by 3 HCPs (14 %). Only 2 HCPs (9 %) correctly answered this question at Observational point 2, compared to 4 HCPs (18 %) at Observational point 1. A noteworthy change in the results was observed at Observational point 2 (post-test) for the experimental group as the complete group correctly answered the question.

Figure 6: Serious Adverse Event



4.2.7 HCP awareness of South Africa's dedicated ADR reporting centre

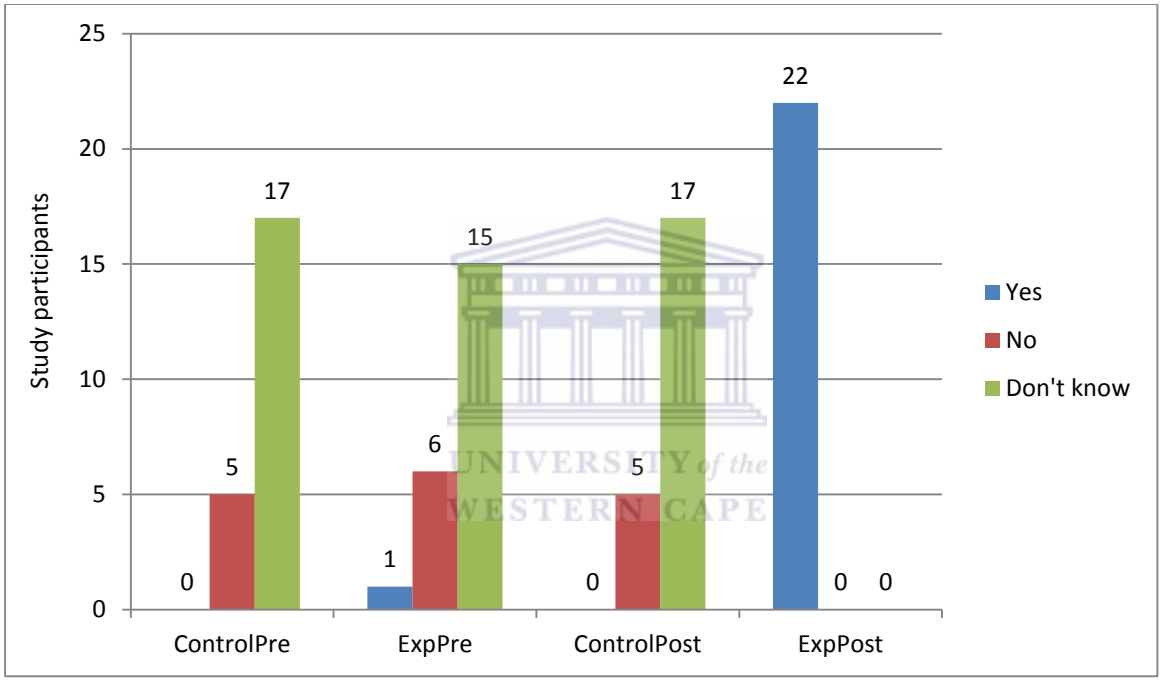
The MCC is the statutory body that has the responsibility to ensure the safety, efficacy and quality of all medicines used by the South African public. The MCC's national pharmacovigilance programme is co-ordinated by the NPC in Pretoria. One of the units functioning under the NPC is the NADEMC in Cape Town. This is the unit of the MCC responsible for managing the national ADR database (ADRI) which houses all spontaneous reports of ADRs submitted by local HCPs, Pharmaceutical Companies and patients. The data from the ADR database is routinely fed into an international database of these reports housed in Sweden at the Uppsala Monitoring Centre (The WHO Collaborating Centre for International Drug Monitoring), (Metha, 2011).

As evident from the data presented in Figure 7 below, at Observation point 1 (pre-test), 17 (77 %) of the control group participants and 15 (68 %) of the experimental group participants did not know if

SA had a dedicated reporting centre, 5 (23 %) control group participants and 6 (27 %) of the experimental group participants said that SA does not have a dedicated ADR reporting centre.

No changes were observed in the results of the control group at Observation point 2 (post-test), but a significant difference was noted in the response received from the experimental group.

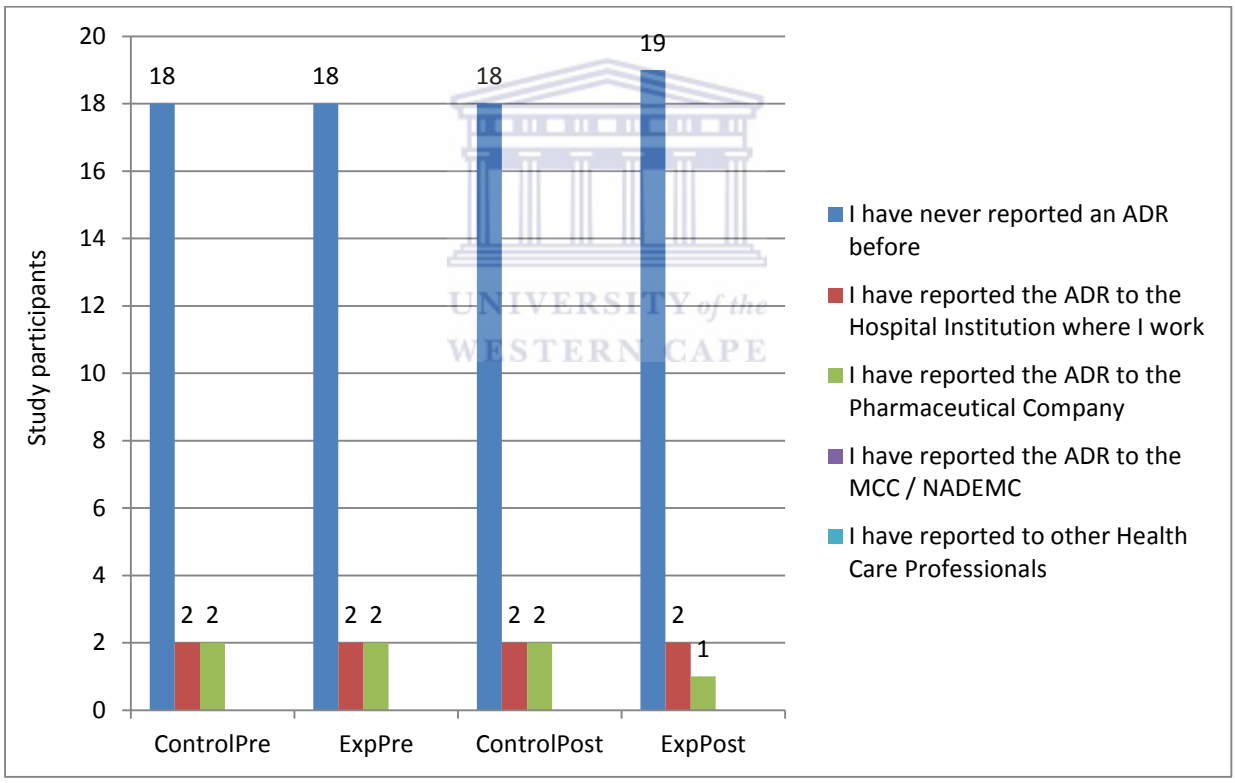
Figure 7: HCP awareness of South Africa's dedicated ADR reporting centre



4.2.8 HCP reporting of ADR experience

Most of the HCPs in both the control and experimental group at Observational point 1 (pre-test) and Observational point 2 (post-test) had never reported an ADR before (see Figure 8). Numerous studies have been conducted to assess the underreporting of ADRs by HCPs, and most have indicated a lack of sufficient skills and knowledge to identify ADRs. The lack of knowledge of where and how ADR's should be reported would automatically affect reporting. Therefore, awareness programmes are necessary to improve ADR reporting among HCPs (Mishra and Kumar, 2013).

Figure 8: HCP reporting of ADR experience

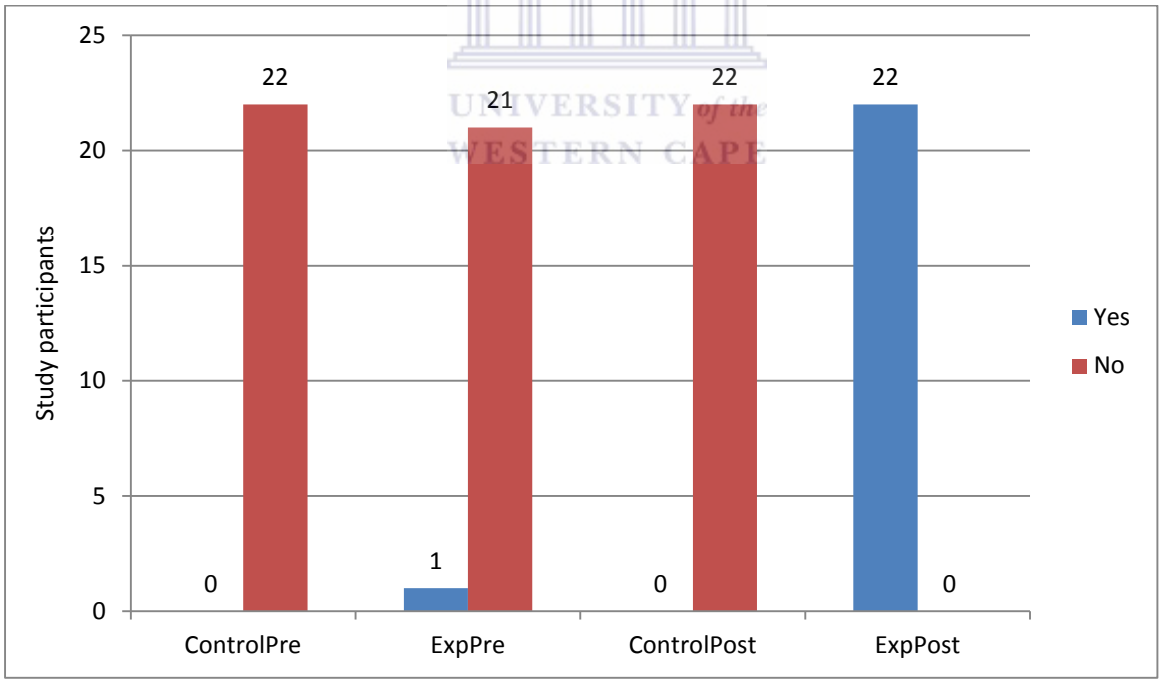


4.2.9 HCP awareness of MCC and NADEMC statutory bodies

Similar to the results discussed above, HCPs were not aware that SA has a dedicated ADR reporting centre, and that one could submit ADR reports to these statutory bodies.

According to Figure 9, at Observation point 1 (pre-test), 43 HCPs (98 % of all HCPs participating in this study) were not aware that they could report ADRs to the SA national bodies. At Observation point 2 (post-test) no changes to the results of the control group were observed, but results from the experimental group indicated a 100 % improvement in HCP knowledge about SA reporting systems.

Figure 9: HCP awareness of MCC and NADEMC statutory bodies

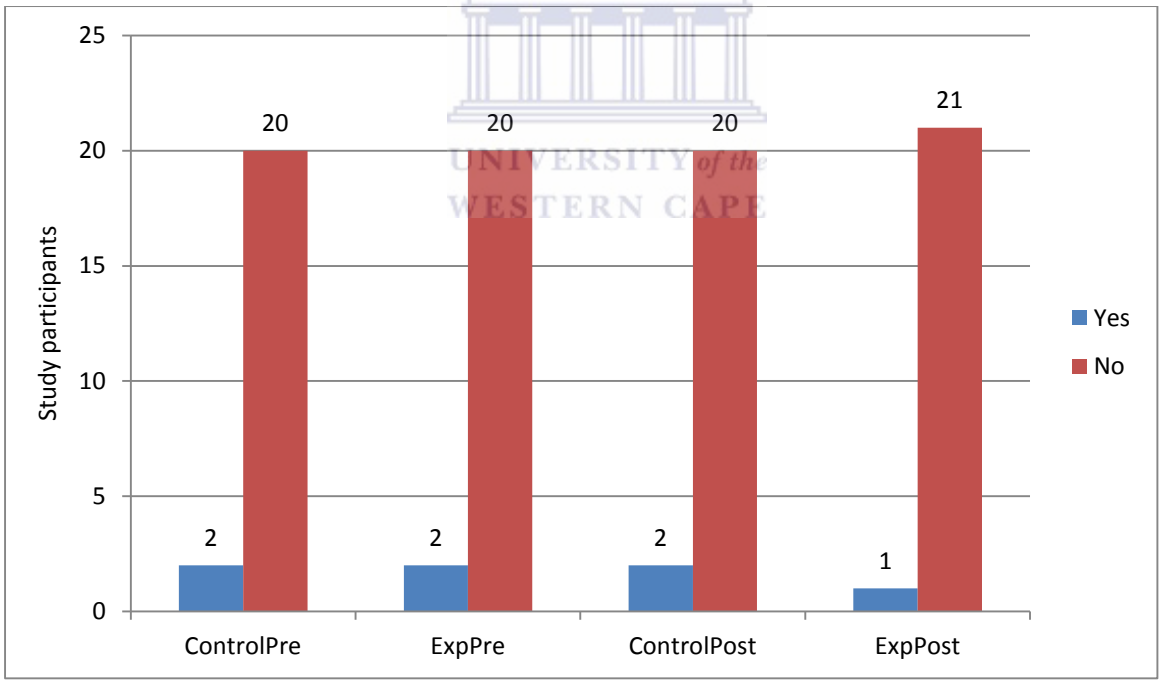


4.2.10 HCP reporting to a Pharmaceutical Company

Ensuring that patients are protected from the harmful effects of medicines is a shared responsibility. HCPs can report ADRs to the Pharmaceutical Company manufacturing the drug, and the Pharmaceutical Company will be responsible to submit the ADR report to the Regulatory Authority.

As indicated in Figure 10 below, 92 % of all participating HCP pre- and post-test (40 HCP pre-test and 41 HCP's post-test), have never reported an ADR to a Pharmaceutical Company. This finding emphasises the crucial role that Pharmaceutical Companies play in increasing HCP awareness of pharmacovigilance and simplifying the ADR reporting procedure through training and education.

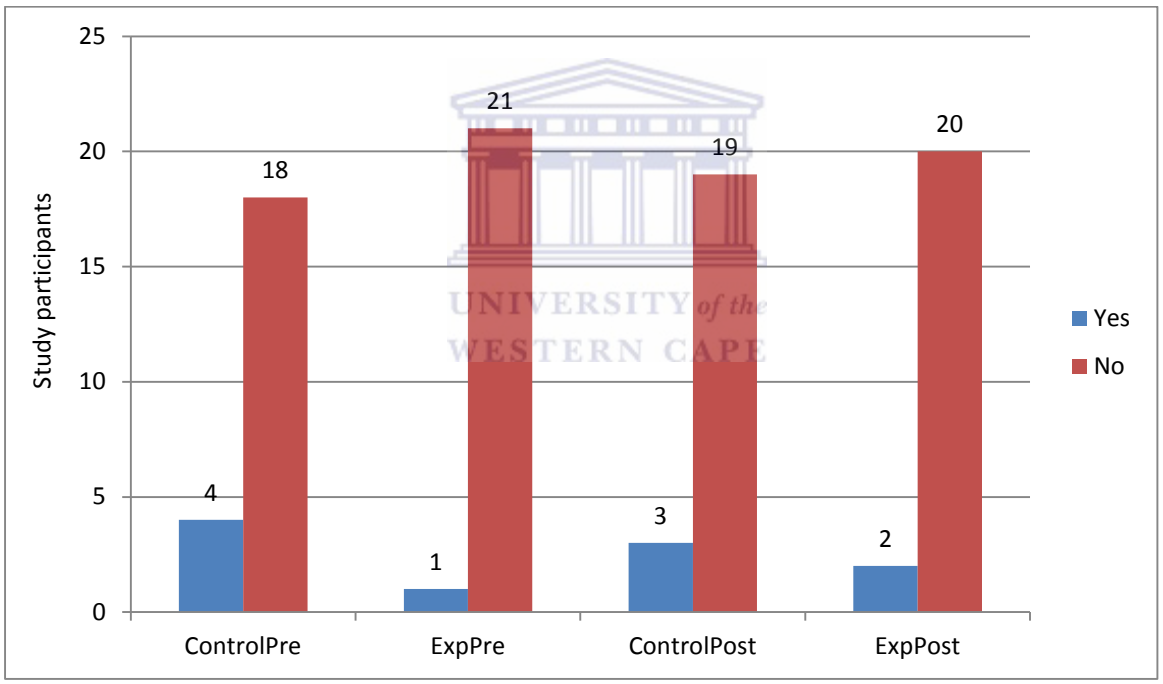
Figure 10: HCP reporting to a Pharmaceutical Company



4.2.11 Reporting new/strange side-effects to a Pharmaceutical Company

As presented in Figure 11 below, 39 HCP (89 % of HCP participating in this study), at both Observation points (pre and post-test), have never come across a strange/new/serious side effect of a drug and felt the urge to report it to the Pharmaceutical Company manufacturing the drug. This may be due to a lack of adequate experience and knowledge to identify potential risk of a medication, and once again highlights the important role that a Pharmaceutical Company plays in creating awareness about drug safety throughout the lifespan of a medication.

Figure 11: Reporting new/strange side-effects to a Pharmaceutical Company



4.3 Internal reliability of the attitudinal scale

As discussed previously, items that informed the attitudinal scale (please refer to table 3 below) were based on similar previous studies. To develop and test adequacy of the questionnaire, several pilot studies were conducted in preparation for the principal study. The pilot studies identified ambiguities, double-barrelled and difficult questions, which were subsequently removed. The questionnaire was amended and revised to ensure replies that could be interpreted in terms of the information that was required. The questionnaire was tested for content validity by pharmacovigilance experts Dr. Jaco van Zyl and Dr. Carine Paige.

Several scale items needed to be reverse-coded, given that they were phrased negatively. Cronbach's alpha coefficients were computed to assess the internal reliability of the attitudinal scale. Results indicated excellent reliability with alpha=0.94. Furthermore, there were no poorly performing items as deletion of any items would not significantly improve upon the internal consistency of the scale.

Table 3: Internal reliability

Scale item	Corrected Item-Total Correlation	Cronbach's Alpha if Item Deleted
I don't know how to report an ADR	.857	.944
I am aware of the procedure to report an ADR	.844	.944
One ADR report will make no difference to the wellbeing of patients	.843	.944
Managing the patient is more important than reporting ADR's	.816	.944
I don't have time to report ADR's	.839	.944

Table 3: Internal reliability		
Scale item	Corrected Item-Total Correlation	Cronbach's Alpha if Item Deleted
ADR reporting will create more work for me	.830	.944
Pharmacovigilance is unnecessary as most ADR's are already understood	.883	.943
If I receive training and assistance I will be more willing to report ADR's	-.438	.959
I am aware of the benefits of a good pharmacovigilance system	.853	.943
Reporting of ADRs is part of my professional duty	.782	.945
Currently there is widespread ignorance surrounding the importance of pharmacovigilance in South Africa	.710	.947
pharmacovigilance is an overrated system and won't improve public health and safety	.856	.945
A large proportion of ADRs can be prevented through more judicious medicine use	.453	.949
Healthcare professionals need to gain a broader understanding of pharmacovigilance	.415	.950
Healthcare professionals need to increase ADR reporting to effectively prevent avoidable, harmful drug reactions	.559	.948
The success or failure of any pharmacovigilance activity depends on the reporting of suspected adverse reactions	.695	.947
Reporting ADRs is not an integral part of my professionals duties to uphold patient safety	.820	.944
Pharmacovigilance won't lead to fewer ADR's	.795	.945

Table 3: Internal reliability		
Scale item	Corrected Item-Total Correlation	Cronbach's Alpha if Item Deleted
Pharmacovigilance is not enough to negate the harmful effects of medicines or combinations of medicines	.835	.944
Pharmaceutical companies do enough to raise awareness about pharmacovigilance and ADR reporting	.275	.952

4.4 Differences in attitudes between the experimental and control groups

The mean scores of the control group pre- and post-test, as well as the experimental group pre-test were very similar. The mean score of the experimental group post-test were much lower, the lower mean score indicating an increase in HCP's attitudes towards pharmacovigilance. Lower attitudinal scores reflect more positive attitudes towards pharmacovigilance.

Table 4: Descriptive statistics								
	N	Mean	Std. Deviation	Std. Error	95% Confidence Interval for Mean		Minimum	Maximum
					Lower Bound	Upper Bound		
ControlPre	22	63.86	5.14	1.10	61.59	66.14	55	79
ControlPost	22	63.77	4.21	0.90	61.91	65.64	56	71
ExpPre	22	67.00	3.48	0.74	65.46	68.54	57	74
ExpPost	22	36.82	3.43	0.73	35.30	38.34	32	45
Total	88	57.86	12.94	1.38	55.12	60.61	32	79

4.4.1 Test of homogeneity of variances

The results show that the variances are roughly equal (i.e. they're not significantly different).

Table 5: Test of homogeneity of variances			
Levene Statistic	df1	df2	Sig.
1.32	3	84	0.27

4.4.2 ANOVA

The omnibus results show that there were indeed significant differences between group means. Post-hoc tests were then performed to identify which groups differed.

Table 6: ANOVA					
	Sum of Squares	df	Mean Square	F	Sig.
Between Groups	13140.64	3	4380.21	257.71	0.00
Within Groups	1427.73	84	17.00		
Total	14568.36	87			

4.4.3 Post-hoc tests

Post-hoc tests were Bonferroni-corrected for multiple comparisons.

Table 7: Bonferroni-corrected Post-hoc test

		Mean Difference (I-J)	Std. Error	Sig.	95% Confidence Interval	
					Lower Bound	Upper Bound
ControlPre	ControlPost	0.09	1.24	1.00	-3.27	3.45
	ExpPre	-3.14	1.24	0.08	-6.50	0.22
	ExpPost	27.05	1.24	0.00	23.69	30.40
ControlPost	ControlPre	-0.09	1.24	1.00	-3.45	3.27
	ExpPre	-3.23	1.24	0.07	-6.59	0.13
	ExpPost	26.95	1.24	0.00	23.60	30.31
ExpPre	ControlPre	3.14	1.24	0.08	-0.22	6.50
	ControlPost	3.23	1.24	0.07	-0.13	6.59
	ExpPost	30.18	1.24	0.00	26.82	33.54
ExpPost	ControlPre	-27.05	1.24	0.00	-30.40	-23.69
	ControlPost	-26.95	1.24	0.00	-30.31	-23.60
	ExpPre	-30.18	1.24	0.00	-33.54	-26.82

There was no significant difference in attitudes towards pharmacovigilance between the control group pre-test and the experimental group pre-test (mean difference=3.1, p=0.08). This suggests that there were no inherent differences between the groups before the initiation of the pharmacovigilance training. We can therefore assume that a significant difference in attitudes

towards pharmacovigilance between the groups post-test can attributed to the pharmacovigilance training.

There was no significant difference in attitudes towards pharmacovigilance in the control group pre-test and post-test (mean difference=0.09, p=1.0). In contrast, however, there was a significant difference in attitudes towards pharmacovigilance in the experimental group pre-test and post-test (mean difference=30.1, p=0.00) with more positive attitudes towards pharmacovigilance seen post-test. This finding suggests that the pharmacovigilance training was successful in bringing about more positive attitudes towards pharmacovigilance.

4.5 Conclusion

The data clearly indicates a positive response to the pharmacovigilance training presented by Pharmaceutical Company X. The experimental group showed a significant increase in their knowledge, attitudes and practise towards pharmacovigilance and ADR reporting post-test. The results of the data will be discussed in the next chapter.

Chapter 5: Discussion and recommendation

5.1 Discussion of the study findings

In this study the researcher evaluated the effectiveness of a Pharmaceutical Company's pharmacovigilance training program in the improvement of HCP's knowledge, attitudes and practices regarding pharmacovigilance and ADR reporting. There were two groups of HCPs: a control group and an experimental group, each group consisting of 22 participants who were matched on a demographical and professional basis. Both groups were asked to complete a questionnaire assessing their knowledge and attitudes at Observation point 1 (pre-test). After completing the questionnaire, an intervention in the form of pharmacovigilance training was provided to the HCPs in the experimental group. The control group did not receive the pharmacovigilance training intervention. The two groups were then asked to complete the same questionnaire at Observation point 2 (post-test) two weeks later.

At Observation point 1 (pre-test), there were no significant differences in knowledge, attitudes and practice towards pharmacovigilance and ADR reporting between the control group and the experimental group. This was an interesting pre-test finding as the control group and experimental group were well matched, both consisting of 22 HCPs, with 9 doctors and 13 pharmacists each. Other group similarities included age, gender and years of experience. In terms of outcomes, both groups exhibited inadequate knowledge regarding pharmacovigilance and ADR reporting. This finding is similar to results reported in several studies conducted around the world, indicating that HCPs had poor knowledge about pharmacovigilance and the ADR reporting procedure in their countries (Bawazir, 2006; Mishra and Kumar, 2013; Kulkarni et al., 2013; Chinenye and Michael 2012; Khalili et al., 2012; Hema and Bhuvana, 2012).

A significant number of participants (98 %) were not aware of the term pharmacovigilance, 93 % of participants could not define pharmacovigilance, and most did not know what pharmacovigilance aims to achieve. According to the results, 97 % of HCPs were unaware of the existence of a South African ADR reporting centre, and these findings were comparable to research conducted in the United Arab Emirates (John et al., 2012), Saudi Arabia (Bawazir, 2006), India (Mishra and Kumar, 2013) and Nigeria (Fadara et al., 2011).

A considerable number (95 %) of participants did not know what an ADR is, and 73 % did not know when an AE is classified as serious. The majority of participants did not know how to report an ADR and where or to whom to report the ADR to. Most of the participants reported that they had never come across an ADR. These findings indicate a lack of awareness of the principles and practice of pharmacovigilance and ADR reporting amongst HCPs, and are consistent with the findings reported by other researchers (Mishra and Kumar, 2013; Desai et al., 2011; Bawazir, 2006; Zolezzi and Parsotam, 2005; Vallano et al., 2005; John et al., 2013; Fadara et al., 2011 and Chinenye and Michael, 2012). Lack of knowledge of where and how ADRs should be reported has been shown to result in the under-reporting of ADRs.

The findings of this study regarding reporting behaviour indicate a very low participation rate in reporting ADRs, as well as a generally poor attitude towards ADR reporting. This finding is consistent with the low percentage of HCPs who were aware of the ADR reporting program in SA. The review provides evidence of the significant and widespread under-reporting of ADRs, due to a lack of knowledge and confidence regarding pharmacovigilance and the ADR reporting system. These findings are similar to those of ADR reporting amongst HCPs in Nigeria (Chinenye and Michael 2012), India (Mishra and Kumar, 2013) and Saudi Arabia (Bawazir, 2006). The considerable number of HCPs that have never reported an ADR is comparable with studies conducted by Khalili et al. (2013), Zolezzi and Parsotam (2005), Bawazir (2006) and Mishra and Kumar (2013) who found that the

majority of HCPs were not aware of the ADR reporting program in their country and have never reported an ADR. Under reporting of ADRs is a worldwide phenomenon that has been established through various previous studies (Fadara et al., 2011; Kulkarni et al., 2013). The common observation about lack of knowledge regarding pharmacovigilance and ADR reporting indicates that under-reporting of ADRs is a major problem in the Western Cape.

Factors influencing the under-reporting of ADRs by HCPs have been extensively investigated by many researchers around the world. The reasons for the under-reporting of ADRs have been summarised by Inman (1996), Desai et al. (2011), Mishra and Kumar (2013) as the "seven deadly sins". This includes a lack of financial incentives (rewards for reporting), fear of litigation, complacency (the belief that the serious ADRs are already documented when a drug is introduced in the market), diffidence (belief that reporting should be done only when there is certainty that the reaction is caused by the use of a particular drug), indifference (belief that a single report would make no difference), ignorance (that only serious ADRs are to be reported), and lethargy (excuses about lack of time or disinterest). In this study a major reason for the under-reporting of ADRs observed was complacency, diffidence, indifference, ignorance and lethargy, which was also seen in the studies conducted in India by Hema and Bhuvana (2012) and Mishra and Kumar (2013). Overcoming these barriers will require intensive training and workshops about the concept of ADR reporting and the structure of ADR reporting in SA.

An interesting observation was that 93% of the respondents did not think that reporting ADRs was important. The observations were similar to a study done by John et al. (2012) and Vallano et al. (2005) in teaching hospitals in the United Arab Emirates and Spain, where the potential obstacles to spontaneous reporting of ADRs were identified to be difficulty in drawing the diagnosis of ADRs, lack of knowledge regarding the ADR reporting system, clinical workload on the doctors, a concern for patient confidentiality, and possible legal implications of reporting. These results are similar to other

studies that describe major obstacles to ADR reporting (Khalili et al., 2012; Santosh et al., 2013 and Fadara et al., 2011). While it is important to note that this study was conducted among doctors and pharmacists only, several studies involving other HCPs such as nurses and paramedic staff have indeed confirmed that the under-reporting of ADRs is common amongst all HCPs (Fadara et al., 2011; Mishra and Kumar, 2013).

As discussed above, the most serious problem affecting ADR reporting was inadequate knowledge about pharmacovigilance and the ADR reporting procedure. Chinenye and Michael (2012), Khalili et al. (2012) and Hema and Bhuvana (2012) suggest that one of the better means of overcoming under-reporting is to increase knowledge, improve attitudes and practices of the HCP in question regarding ADR monitoring and pharmacovigilance programs. These findings suggest the need for interventions to improve the knowledge, attitude and practice of HCPs regarding pharmacoviglance and ADR reporting (Subish et al., 2007).

At Observation point 2 (post-test), there were significant differences in knowledge and attitudes towards pharmacovigilance between the experimental and control groups, with more positive attitudes towards pharmacovigilance seen in the experimental group that received the pharmacovigilance training.

At Observation point 1, 95 % of the experimental group were unaware of pharmacovigilance, and did not know what an ADR was. At Observational point 2, 100 % of participants in the experimental group could correctly define pharmacovigilance, correctly identify the aims of pharmacovigilance and knew the definition of ADRs, and whom to report these issues to. A significant improvement in HCP's attitudes towards pharmacovigilance were also observed post intervention. The intervention had a considerable impact in reducing reported causes of under-reporting, including "did not know how to report", "lack of time", and that "reporting will create more work" (John et al., 2012; Santosh

et al., 2013; Mishra and Kumar, 2013). After the intervention, all HCPs believed that reporting ADRs was part of their professional duty to uphold patient safety, and were aware of the benefits of a pharmacovigilance system. Patient safety is a prime responsibility of HCPs, and by active and voluntary participation in the pharmacovigilance program, they contribute toward their patient's safety and medical ethics in general (John et al., 2012).

This finding suggests that the pharmacovigilance training intervention was successful in bringing about more positive attitudes towards pharmacovigilance, and improving the knowledge and practice of pharmacovigilance and ADR reporting amongst HCPs. The findings of this study are similar to results reported in a study published by Khalili et al. (2012) in Iran who also found an improvement in knowledge, more positive attitudes and perception towards pharmacovigilance and ADR reporting amongst HCPs after a similar intervention. Similarly, a study by Santosh et al. (2013) conducted amongst HCPs in Nepal showed more positive attitudes towards ADR reporting post training.

Previous studies conducted by Ramesh and Parthasarathi (2009) in India and John et al. (2012) in the United Arab Emirates amongst doctors and nurses showed that enhancing HCP's knowledge and improving awareness can increase the number of ADR reports. One of the important findings in this study was the positive correlation between knowledge and attitudes towards ADR reporting. This finding suggests that if knowledge of ADR reporting is improved, then the HCP's attitude towards pharmacovigilance may also improve, which would likely result in a positive increase of ADR reports received by NADEMC in the future.

All participants reported that the ADR reporting and monitoring system presented by the Pharmaceutical Company was simple and very useful, and said they would be more willing to report ADRs if they received assistance and training from Pharmaceutical Companies. Several studies have

shown that not only improving knowledge and awareness of ADR reporting can increase the reporting rates, but also creating an easy and convenient ADR reporting system (Ramesh and Parthasarathi, 2009). Pharmaceutical Company X has created an electronic reporting system, which is easy and convenient, and would assist HCPs in reporting ADRs without difficulty. According to Bawazir (2009) the internet is an important tool that most HCPs have access to, and should be fully utilised by Pharmaceutical Companies.

Assessed together, the results suggest that increased focus on pharmacovigilance with adequate, continuous training on identification and management of ADRs, and the practical use of the ADR system is necessary to improve pharmacovigilance practice in the Western Cape. Training should be provided by Pharmaceutical companies as it is ultimately their ethical responsibility to ensure the safety of their medicinal products. This approach can greatly influence the improved reporting culture amongst HCPs, and may improve the reporting rates of ADRs in SA, Pharmaceutical Companies therefore have an important role to play in the area of pharmacovigilance.

5.2 Study limitations

The results of this study need to be interpreted against the backdrop of the study limitations, which included the use of the same questionnaire at Observation point 1 and 2. This may create memory bias as the respondents may remember the questions the second time around and subsequently answer them slightly differently and independently of the pharmacovigilance training. However, memory bias was controlled by including a control group in the study. Furthermore, using the same questionnaire ensured test-retest reliability. Another limitation to the study was that the sample population was very small and only included 44 participants. Findings could not be applied to a wider medical community, as the study was restricted to doctors and pharmacist practising in

hospitals and pharmacies in the Western Cape only. Other limitations of this study involved limitations inherent to interventional studies.

5.3 Recommendations

The study indicated that there is an urgent need to improve the awareness of pharmacovigilance and ADR reporting among HCPs. Results from the study suggest that an increased focus on pharmacovigilance with adequate continuous training on identification and management of ADRs and practical use of the ADR system is necessary to improve pharmacovigilance practice in the Western Cape.

Therefore the following recommendations are made:

1. The Regulatory Authority of SA must emphasise to Pharmaceutical Companies the importance of creating a robust pharmacovigilance system, and the role that they can play in increasing patient safety with regards to the use of medicinal products. The MCC and NADEMC should motivate Pharmaceutical Companies to provide training to HCPs as well as patients regarding the benefits of pharmacovigilance and ADR reporting.

2. Pharmaceutical Companies must utilise the opportunities presented by pharmacovigilance to provide training and educational interventions to HCPs to improve their knowledge, attitudes and practices regarding pharmacovigilance and ADR reporting, as it is an ethical responsibility of the Pharmaceutical Company to ensure the safety of their medicinal products.

3. It is recommended that similar studies are conducted to assess and document the knowledge, attitudes and practise of a broader range of HCPs including nurses and paramedic staff (Ramesh and Parthasarathi, 2009; Malangu, 2014).

4. Patients form the most important aspect of pharmacovigilance, as a patient has a right to know the actual benefits and harms of a medicine prescribed to him/her. Studies to assess the knowledge, attitude and practice of pharmacovigilance and ADR reporting among patients are also recommended as direct patient participation in the reporting of medicine-related problems can increase the efficacy of the pharmacovigilance system significantly (Rohilla et al., 2012).

5. It is recommended that the Regulatory Authority and Pharmaceutical Companies simplify the ADR reporting procedure, by creating an easy and convenient ADR reporting system that is compatible with technology available in the 21st century. Utilisation of the internet and social media, which is available to most HCPs and patients will be very beneficial in assisting HCPs and patients in reporting ADRs.

6. A culture of learning about pharmacovigilance should start early in the professional training of HCPs. Pharmacovigilance should be included in the present academic curriculum and should include the application of pharmacovigilance in medical practice, and emphasis should be made on the ADR detection and reporting system (Hema and Bhuvana, 2012). It is recommended that pharmacovigilance be intensively taught during undergraduate study, and should be reinforced at the start of internship and community service as well as periodically thereafter through continuous educational programmes (Mishra and Kumar, 2013).

Ensuring that patients are protected from the harmful effects of medicines is a shared responsibility. Pharmaceutical Companies, drug regulators, HCPs and patients all need to understand the potential risks of medicines and their responsibility in minimising and managing those risks (Metha, 2011).

Chapter 6: Conclusion

Mechanisms for evaluating and monitoring the safe use of medicine are vital in order to prevent and reduce harm to patients, and which could result in an overall improvement in public health. In practice, this means having a well-organised pharmacovigilance system in place (WHO, 2004). The success or failure of any pharmacovigilance system depends on the reporting of suspected ADRs (Dheda et al., 2013). HCPs are the principal contributors of ADR reports, and have a central role to play in pharmacovigilance by contributing to the prevention, identification, documentation and reporting of ADRs. For and effective pharmacovigilance system to be functional and efficient, all the stakeholders need to be alert and attentive throughout the lifecycle of a medicinal product in the market (Arora, 2008). The main task at hand is to foster a culture of consistent and responsible reporting amongst HCPs. Pharmaceutical Companies can play a tremendous contributing role in increasing HCP's awareness and simplifying the ADR reporting system to assist with the coordination of reporting between HCPs and the Regulatory Authority to ensure a successful pharmacovigilance programme, and ultimately fulfilling their responsibility to protect patients from drug related harms (Hema and Bhuvana, 2012).

The main objective of the study was to determine whether or not an intervention in the form of pharmacovigilance training presented by a Pharmaceutical Company would improve HCP's knowledge, attitudes and practice of pharmacovigilance and ADR reporting. Prior to carrying out the intervention, it was necessary to evaluate the baseline knowledge, attitudes and practice of HCPs regarding pharmacovigilance and ADR reporting. Pre-intervention results indicated poor knowledge, negative or indifferent attitudes and unestablished practises towards pharmacovigilance and ADR reporting among HCPs. A significant improvement in HCP knowledge, attitudes and practice towards pharmacovigilance was observed post intervention, therefore indicating that the pharmacovigilance training intervention was successful in fostering a greater respect for pharmacovigilance and ADR

reporting. These results served to prove the hypothesis that if Pharmaceutical Companies develop a robust pharmacovigilance intervention program, the knowledge, attitudes and practice of HCPs towards pharmacovigilance and ADR reporting will improve.

The study further aimed to identify the significant role that Pharmaceutical Companies play in increasing HCP's awareness around the importance of pharmacovigilance and drug safety. Results from the study clearly indicate that Pharmaceutical Companies have a vital role to play in enhancing the pharmacovigilance and ADR reporting culture amongst HCPs, which would motivate HCPs to report any ADR, especially one that is previously unknown, in a timeous and responsible manner. With endorsement and recognition from a Pharmaceutical Company, HCPs will realise that it is essential that ADRs are reported, analysed and their significance communicated effectively to an audience that has the knowledge to interpret the information and implement a system that could minimise harm (WHO, 2004; Tumwikirize et al., 2011; Hema and Bhuvana, 2012).

The overall results from the study indicate that the investment made by Pharmaceutical Company X to create a robust pharmacovigilance system, that can improve patient care and safety in relation to the use of the company's medicines and medical interventions, was successful. Such an approach can greatly influence the positive development of a reporting culture among HCPs, and may improve the reporting rates of ADRs in the country, thereby effectively identifying and addressing ADRs that pose the greatest threats to the SA population and improving public health and safety in relation to the use of medicines, ultimately ensuring that Pharmaceutical Companies fulfil their ethical obligation to protect patients from drug-related harms.

Pharmacovigilance and all drug safety issues are relevant to anyone who has had their life touched by medical interventions. In a country like SA with a vast ethnic variability, different disease prevalence patterns, practice of different systems of medicines and different socioeconomic

statuses, it is important to have a standardised, robust pharmacovigilance and drug safety monitoring system in place. Pharmacovigilance is an essential element for the effective use of medicines and to ensure high quality medical care. It has the potential to inspire confidence and trust among patients and HCPs and contribute to raising the overall standards of medical practise (WHO, 2002).

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Appendix 1: Consent form and questionnaire

CONSENT FORM

Protocol Title:

Pharmacovigilance: The responsibility of Pharmaceutical companies to protect patients from drug-related harms.

Please tick the appropriate answer.

I confirm that I have read and understood the nature of the research as explained to me, and that I have had ample opportunity to ask questions all of which have been satisfactorily answered. ☐**Yes** ☐**No**

I understand that my participation in this study is entirely **voluntary** and that I may withdraw at any time, without giving reason, and without this decision affecting my future participation in further research. ☐**Yes** ☐**No**

I understand that my records may be viewed by individuals with delegated authority from Hibernia College and/or the University of the Western Cape. ☐**Yes** ☐**No**

I understand that my identity will remain confidential at all times. ☐**Yes** ☐**No**

☐**Yes** ☐**No**

FUTURE USE OF ANONYMOUS DATA:

I agree that I will not restrict the use to which the results of this study may be applied. I give my approval that unidentifiable data concerning my person may be stored or electronically processed for the purpose of scientific research and may be used in related or other studies in the future. (This would be subject to approval by an independent body, which safeguards the welfare and rights of people in biomedical research studies)

☐**Yes** ☐**No**

Participant :_____ _____

Signature Name in block capitals

Date _____

Institution: University of the Western Cape and Hibernia College

v1 January 2014

To be completed by the Principal Investigator/Student Researcher (in the presence of the participant).

I the undersigned, have taken the time to fully explain to the above participant the nature and purpose of this study in a manner that he/she could understand. I have explained the risks involved, the reason for research, as well as the possible benefits and have invited him/here to ask questions on any aspect of the survey that concerns them.

_____	Leanne Roux	B.Pharm, MBA	_____
Signature:	**Name in Block Capitals:**	**Qualification:**	**Date:**

_____

Site name (if applicable)

2 copies to be completed: 1 for patient and 1 for Principal investigator/Student researcher.

Dear Healthcare Professional

We request your time and cooperation in completing this questionnaire to evaluate the knowledge and awareness about Pharmacovigilance and Adverse drug reactions amongst healthcare professionals.

The results from this questionnaire are for research purposes as partial fulfilment of the requirements for the Master of Science in Pharmacy Administration and Pharmacy Policy Specialising in Regulatory Sciences.

Please note that your participation in this study is entirely voluntary, and your identity will remain confidential at all times.

Instructions

- Please complete the consent form and the questionnaire.
- The questionnaire should take you approximately 10 minutes to complete.
- The questionnaire comprises of 36 questions.
- Please tick the most appropriate answer, and answer all the questions.

Section A

1. Please indicate your gender:
    a. Male
    b. Female

2. Please provide your age in years:
    a. 24 – 30
    b. 31 – 40
    c. 41 – 50
    d. 51 – 60
    e. Above 60

3. Professional qualification
    a. Doctor
    b. Pharmacist

4. Please state your years of experience in your field
    a. 1 – 5
    b. 6 – 10
    c. 11 – 15
    d. 16 – 20
    e. Above 20

5. Do you have internet access
    a. Yes
    b. No

6. Are you aware of the term Pharmacovigilance?
    a. Yes
    b. No

7. What do you think Pharmacovigilance is?
    a. Detection and reporting of any unintended effect of a pharmaceutical product occurring at normal dosage which is related to the pharmacological properties of the drug
    b. Reporting of any unintended effect resulting from the use of a pharmaceutical product to the Pharmaceutical Company that manufactures the pharmaceutical product.
    c. The science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other drug-related problem.

8. What do you think pharmacovigilance aims to assess?
    a. Safety over efficacy
    b. Efficacy over safety

9. An Adverse drug reaction is defined as: any untoward medical occurrence that may present during treatment with a pharmaceutical product but which does not necessarily have a causal relationship with this treatment
    a. True
    b. False

10. ADR reporting can be done by
    a. Healthcare Professionals
    b. Patients
    c. Both

11. Which of the following defines a serious adverse event?
    a. Life threatening
    b. Disability
    c. Death
    d. Hospitalization
    e. All

12. Does South Africa have a dedicated ADR reporting centre?
    a. Yes
    b. No
    c. Don’t know

13. With regards to ADR reporting, please mark the statement that best describes your reporting experience:
    a. I have never reported an ADR before
    b. I have reported the ADR to the Hospital Institution where I work
    c. I have reported the ADR to the Pharmaceutical Company
    d. I have reported the ADR to the MCC / NADEMC
    e. I have reported to other Health Care Professionals

14. Are you aware that you can report ADR's to the Medicine Control Council (MCC) and the National Adverse Drug Event Monitoring Centre (NADEMC)?
    a. Yes
    b. No

15. Have you ever reported and ADR or side effect to a Pharmaceutical company?
    a. Yes
    b. No

16. Have you recently come across a side effect that you felt was strange/new/serious and wished to report it to the Pharmaceutical company
    a. Yes
    b. No

Section B

Please indicate your level of agreement to the following statements by marking with a tick in the appropriate column.

	Statements	Level of agreement				
		Strongly agree	Agree	Not sure	Disagree	Strongly disagree
17	I don't know how to report an ADR					
18	I am aware of the procedure to report an ADR					
19	One ADR report will make no difference to the wellbeing of patients					
20	Managing the patient is more important than reporting ADR's					
21	I don't have time to report ADR's					
22	ADR reporting will create more work for me					
23	Pharmacovigilance is unnecessary as most ADR's are already understood					
24	If I receive training and assistance I will be more willing to report ADR's					
25	I am aware of the benefits of a good pharmacovigilance system					
26	Reporting of ADRs is part of my professional duty					
27	Currently there is widespread ignorance surrounding the importance of Pharmacovigilance in South Africa					
28	Pharmacovigilance is an overrated system and won't improve public health and safety					
29	A large proportion of ADRs can be prevented through more judicious medicine use					
30	Healthcare professionals need to gain a broader understanding of Pharmacovigilance					

	Statements	Level of agreement				
		Strongly agree	Agree	Not sure	Disagree	Strongly disagree
31	Healthcare professionals need to increase ADR reporting to effectively prevent avoidable, harmful drug reactions					
32	The success or failure of any pharmacovigilance activity depends on the reporting of suspected adverse reactions					
33	Reporting ADRs is not an integral part of my professionals duties to uphold patient safety					
34	Pharmacovigilance won't lead to fewer ADR's					
35	Pharmacovigilance is not enough to negate the harmful effects of medicines or combinations of medicines					
36	Pharmaceutical companies do enough to raise awareness about pharmacovigilance and ADR reporting					

~ Thank you for your co-operation ~