COMMUNITY PHARMACISTS' KNOWLEDGE, ATTITUDE AND PRACTICES ON ADVERSE DRUG REACTION REPORTING IN SOUTH AFRICA

Rensche Mayne

A mini-thesis in partial fulfilment of the requirements for the degree M.Sc. in Pharmacy Administration and Policy Regulation in the School of Pharmacy, Faculty of Natural Sciences

School of Pharmacy, University of the Western Cape

Supervisor: Prof. Angeni Bheekie

Co-supervisor: Mr Rafik Bapoo

September 2018

ABSTRACT

Pharmacovigilance involves the management of sub-standard drugs, medication errors, “off-licence” drugs, abuse and misuse, lack of efficacy, poisoning, adverse drug reactions (ADRs), drug interactions, expired stock destruction and drug-related mortality.

Regulators and the pharmaceutical industry rely on healthcare professionals, including pharmacists, to report ADRs. The majority of pharmacists work in retail community pharmacies and they are often the first point of contact when ADRs are experienced, since self-medication, misuse of over-the-counter (OTC) medicines, vitamins and traditional medicines, increase the probability of ADRs. In South Africa (SA) ADRs have been known to cause adult deaths and hospital admissions.

In first-world communities, pharmacovigilance is more common among pharmacists, however in South Africa, ADR reporting compares poorly. Studies in the public sector have found that pharmacists lack pharmacovigilance knowledge and underreport ADRs. In comparison the pharmacovigilance knowledge and practice patterns among retail community pharmacists is poorly documented.

This study aimed to determine the knowledge, attitude and practice pattern of South African retail community pharmacists in adverse drug reporting. The study objectives were to:

- Measure the extent of ADR reporting among retail community pharmacists, and
- Compare ADR reporting with regard to knowledge, attitude and practices among retail community pharmacists.

A quantitative, anonymous online survey was conducted among 1460 community pharmacies. Quantitative data was collected measuring the knowledge of community pharmacists. Contact details for community pharmacies were obtained from websites and pharmacists were invited to participate in the survey.

Overall, pharmacists had low pharmacovigilance knowledge, with just over half of the participants (58%) identifying all the correct ADRs which qualify for reporting. Almost three quarters (72.13%, N=44) of pharmacists had never received any training in pharmacovigilance after registration as a pharmacist. Even so almost all participants (90%) agreed that filling in the ADR report form was essential and 73.66% stated that it formed part of their practice. However less than half of participating pharmacists (40%) could name drugs they had reported in the course of their career. Over half of the participants (54.55%) believed that clinical trials provided adequate information in determining the safety of registered medicinal products. Almost three quarters of participants (70.91%) acknowledged that they would fill in the ADR report form if they knew of its significance. Several barriers existed to ADR reporting with lack of training listed as the most (87.27%).

Patients rely on pharmacists' expertise to alert them to medicine-related concerns. South Africa needs a robust, transparent, national pharmacovigilance system to enable pharmacists to report adverse drug reactions encountered in their practice environment.

Key Words:

Pharmacovigilance, community pharmacists, knowledge, attitude and practices, South Africa, adverse drug reaction reporting.

DECLARATION

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

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

Signed at East London on this the 25th day of September, 2018

Rensche Mayne

ACKNOWLEDGEMENTS

My sincere gratitude to all who assisted me in the research. I would like to thank

- My supervisor, Professor Angeni Bheekie for her expert guidance and unwavering support.
- Mr Rafik Bapoo for managing the course.
- Mr Edward Upton for technical assistance.
- My family and friends for their constant encouragement and belief.
- My husband for his support, love and sponsorship.
- All the participants in this research.
- Almighty God, for making all things possible.

TABLE OF CONTENTS

FIGURES

LIST OF TABLES

LIST OF ABBREVIATIONS

ADR	Adverse Drug Reaction
AIDS	Acquired Immunodeficiency Syndrome
AEFI	Adverse Events Following Immunisation
ADRI	South Africa's Adverse Drug Reaction Database
APP	Application Software Program
ARV	Anti-Retroviral
CME	Continuing Medical Education
EC	Eastern Cape Province
EDL	Essential Drug List
EML	Essential Medicines List
EPI	Expanded Programme for Immunisation
EU	European Union
FS	Free State Province
GPhC	General Pharmaceutical Council in Great Britain
GP	Gauteng Province
HCP	Healthcare Professional
HIV	Human Immunodeficiency Virus
ICH	International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use
ICSR	Individual Case Safety Report

LP	Limpopo Province
MCC	Medicines Control Council
MHRA	Medicines and Healthcare Products Regulatory Agency UK
MIC	Medicines Information Centre
MP	Mpumalanga Province
NADEMC	National Adverse Drug Event Monitoring Centre
NC	Northern Cape Province
n.d.	no date
NGO	Non-Profit Organisation
NHI	National Health Insurance
KZN	KwaZulu-Natal Province
NW	North West Province
PBRER	Periodic Benefit-Risk Evaluation Reports
PIDM	WHO Programme for International Drug Monitoring
PIL	Patient Information Leaflet
PMR	Patient Medication Record
PSSA	Pharmaceutical Society of South Africa
PSUR	Periodic Safety Update Reports
PV	Pharmacovigilance
RPS	United Kingdom's Royal Pharmaceutical Society
SA	South Africa
SAAHIP	South African Association of Hospital and Institutional Pharmacists
SAHPRA	South African Health Products Regulatory Authority
SAMF	South African Medicines Formulary

SAPC	South African Pharmacy Council
SMS	Short Message Service
SOPs	Standard Operating Procedures
TB	Tuberculosis
TSR	Targeted Spontaneous Reporting
UK	United Kingdom
UMC	Uppsala Monitoring Centre in Sweden
UWC	University of the Western Cape
USA	United States of America
WC	Western Cape Province
WHO	World Health Organisation

CHAPTER 1

INTRODUCTION

Regulators and the pharmaceutical industry rely on healthcare professionals (HCPs) to report Adverse Drug Reactions (ADRs). In South Africa (SA), ADRs have been known to cause adult deaths and hospital admissions (Mehta, et al., 2017). The majority of pharmacists work in community pharmacies and they are often the first point of contact when ADRs are experienced (South African Pharmacy Council (SAPC), 2017). The focus of this study was primarily gaining insight into the practices of retail community pharmacy.

1.1 THE DEFINITION OF PHARMACOVIGILANCE

Pharmacovigilance is "the science and activities relating to the detection, assessment, understanding and prevention of adverse effects of a drug or any other drug-related problem" (World Health Organisation (WHO), 2018). This includes sub-standard drugs, medication errors, use of drugs off-label, abuse and misuse, lack of efficacy, poisoning, ADRs, adverse interactions with other drugs, and drug-related mortality (Jobson, 2003; World Health Organisation (WHO), 2015). In essence, pharmacovigilance covers the complete product life-cycle from medicine development to destruction of expired stock (Joubert and Naidoo, 2016). The World Health Organisation (WHO) collects pharmacovigilance data and processes this data to aid in the surveillance of the safety of drugs post-market (Maigetter, et al., 2015).

The WHO defines an ADR as "any response to a drug which is noxious and unintended, and occurs at doses normally used in man for prophylaxis, diagnosis, or therapy of disease, or for the modification of physiological function" (International Conference on Harmonisation (ICH) E2A, 1994). ADR reporting is a pharmacovigilance obligation.

An adverse drug event is any unpleasant medical event that might or might not be associated with the treatment (South African Health Products Regulatory Authority (SAHPRA), 2016).

Spontaneous reporting refers to the reporting of ADRs by any HCP as it is observed "spontaneously" (Joubert and Naidoo, 2016). It is also known as individual case safety reports (ICSRs) and is the most commonly used method of post-market surveillance worldwide (World Health Organisation (WHO), 2015).

1.2 THE PURPOSE OF THIS STUDY

The study aims to examine pharmacovigilance awareness among South African retail community pharmacists.

1.3 RESEARCH OBJECTIVES

The study objectives are to:

- Measure the extent of ADR reporting among retail community pharmacists, and
- Compare their pharmacovigilance knowledge, attitude and practices in ADR reporting in the practice environment.

1.4 THE IMPORTANCE OF THE STUDY

Patients rely on pharmacists to alert them about medicine-related concerns. These findings would provide pharmacy and health care planners, researchers and the pharmaceutical industry with insight into the retail community pharmacists' knowledge, attitude and practices in ADR reporting.

CHAPTER 2

LITERATURE REVIEW

Pharmacists are regarded as the authority on medicines and are accountable to health authorities in the practice of pharmacovigilance (Suleman, 2010).

2.1 INTRODUCTION

Medical catastrophes have catalysed the development of pharmacovigilance (Mehta, et al., 2017). The thalidomide disaster (1962) epitomised incorrect prescribing as an anti-emetic and sedative in pregnancy resulting in severe birth defects.

The safety of medicines remains one of the primary goals of pre-clinical studies and clinical trials (Suleman, 2010). Medication is only registered with a regulatory authority once the benefits outweigh the risks associated with the particular medication (Mehta, et al., 2017). This is the basis of the ethical principle of non-maleficence or “do not harm” (Jobson, 2003). The goal of pharmacovigilance is to optimise benefits and minimise risks; and the pharmaceutical industry, drug regulators, HCPs such as pharmacists, patients and the public are all responsible for upholding pharmacovigilance (Mehta, et al., 2017).

Periodic Safety Update Reports (PSURs) or Periodic Benefit-Risk Evaluation Reports (PBRERs) are global updates of the safety experience of a medicine at specific times after registration (South African Health Products Regulatory Authority (SAHPRA), 2016). These reports are compiled in accordance with the ICH Guideline on Periodic Benefit-Risk Evaluation Reports (PBRERs) E2C(R2) (International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) E2C(R2), 2012).

Spontaneous reports or ICSR reports are the reporting of ADRs as they are observed in practice.

2.2 THE IMPORTANCE OF PHARMACOVIGILANCE

Pharmacovigilance data is vital for the safety and effectiveness of medicine post-market and for providing information regarding regulatory actions, such as changes in labelling or withdrawal of products (Maigetter, et al., 2015). Post-market research identifies risk factors and quantifies adverse effect incidences (Mehta, et al., 2017). Pharmacovigilance identifies risks associated with drugs in a short time and the information generated has the potential of preventing further harm to patients (Maigetter, et al., 2015).

WHO (2002) states that ADRs cause increased mortality and morbidity throughout the world, contributing as a major public health problem (Cheema et.al. 2017), and misclassification of ADRs are partly to blame for the lack of focus on ADRs by stakeholders (Mehta, 2011).

Ioannidis (2009) argues that the monitoring of ADRs during clinical trials is inadequate since it does not mimic “real-life” situations and is often under-reported. All ADRs cannot be identified during clinical trials because of the small number of patients exposed, lack of long-term use data, co-morbid conditions, patient population diversity and the simultaneous use of other medication, food and herbs. Animal testing is not sufficient to predict safety in humans, and because the conditions are controlled during clinical trials, only the common ADRs are discovered (Mehta, 2011). Conflicts of interest and marketing often influence these results and give preference to effectiveness in the hope that any adverse effects will become apparent during case reports (Ioannidis, 2009).

An international data-based study (1950-2014) revealed that 462 medicinal products were withdrawn due to ADRs, concluding that harmful drugs were less likely to be withdrawn in African countries (Onakpoya, Heneghan and Aronson, 2016). Drugs

which were withdrawn included cisapride, rofecoxib, and cerivastatin (Lexchin, 2014); and product label changes following post-marketing pharmacovigilance data included among others aspirin, gamelonic acid, isotretinoin and kava kava (Jobson, 2003). Spontaneous reporting of ADRs in South Africa is not controlled and underreporting of ADRs is a major limitation (Joubert and Naidoo, 2016). Drug therapy is crucial to the health care of the population and one aspect linked to care provision is the response to such therapy. When people respond adversely to medicine therapy, imminent intervention from pharmacists to report ADRs is required. The key question that arises is: how are community pharmacists meeting their professional obligation in reporting ADRs in the practice setting?

2.3 PHARMACOVIGILANCE IN SOUTH AFRICA

This sections outlines the importance and history of pharmacovigilance in South Africa.

In SA, one in twelve hospital admittances are related to an ADR and it accounts for 16% of adult deaths (Mehta et. al., 2017).

The country has one of the biggest disease burdens worldwide with 19% of people living with Human Immunodeficiency Virus (HIV) (UNAIDS, 2018). Over and above this malaria and tuberculosis (TB) are added to this disease burden. In 2017, 9 478 malaria cases were reported (National Institute for Communicable Diseases (NICD), 2017) and 8.8% of reported deaths in 2013, were due to TB (Statistics SA, 2013). Since treatment regimes for such diseases are complicated, pharmacovigilance is crucial in protecting patient safety (Mehta et. al., 2017). Antiretroviral ADR reporting schemes have now been launched nationally in all provinces, but ADRs involving non-communicable diseases such as diabetes, hypertension, inflammatory conditions and strokes, have not been reported to the same extent (Mehta et.al, 2017).

Since the majority of South African pharmacists (70%) work in private sector community pharmacies, they are in direct contact with the population (South African Pharmacy Council (SAPC), 2017), and therefore pivotal in identifying and reporting ADRs to national health authorities. Community pharmacies are either independent or part of a pharmacy chain and most pharmacies are located in the urban areas where they service the insured population or those with medical aids (Gray, Ridden and Jugathpal, 2016).

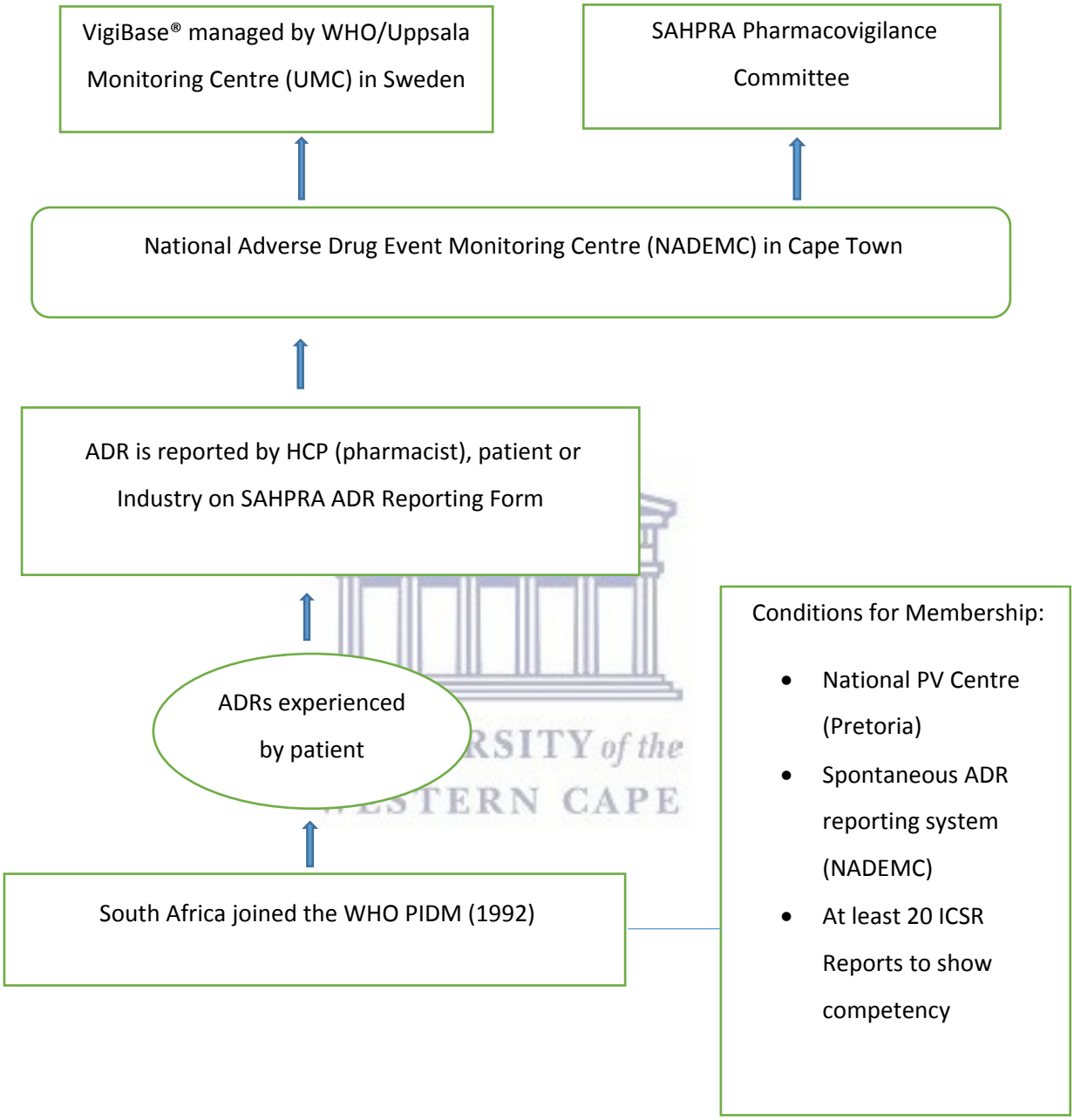
SA joined the WHO Programme for International Drug Monitoring (PIDM) in 1992 (Ampadu et. al, 2016). The conditions for membership include a designated national pharmacovigilance centre which is in Pretoria, a spontaneous ADR reporting system and the submission of at least 20 ICSRs to VigiBase® to show competence in completing ICSRs (Ampadu et. al., 2016). The Uppsala Monitoring Centre (UMC) in Sweden manages VigiBase® for WHO. VigiAccess® allows for easy access to VigiBase® and encourages ADR reporting (World Health Organisation (WHO), 2015). VigiFlow® is the web-based ICSR management system for PIDM. National pharmacovigilance centres receive feedback from UMC findings and make the necessary regulatory changes to labelling or initiate withdrawal of the product (World Health Organisation (WHO), 2015). Ampadu et. al. (2016) found that ICSR forms from Africa, spanning 35 countries with full PIDM membership, made up less than 1% of submissions to VigiBase® in 2015.

The Medicine Control Council (MCC) transitioned into the South African Health Products Regulatory Authority (SAHPRA) in 2017. All documents reflecting MCC pertains to SAHPRA (South African Health Products Regulatory Authority (SAHPRA), n.d.). The SAHPRA National Adverse Drug Event Monitoring Centre (NADEMC) at the University of Cape Town, is responsible for managing the national ADR Database (ADRI), which is subsequently submitted to UMC in Sweden (Figure 1). The flow diagram indicates that NADEMC is a subunit of SAHPRA. NADEMC liaises with SAHPRA and WHO (Jobson, 2003). Other institutions, parallel systems for public health programmes and NGOs also assess signals regarding ADRs, but they work independently and data is not always supplied to the national system

(Maigetter et. al, 2015). Most ICSR forms from Africa submitted to VigiBase ® are for antibiotics and antiretrovirals (Ampadu, et al., 2016). Databases used by the public health programmes, NGOs and NADEMC are not always compatible and data is difficult to analyse (Maigetter, et al., 2015).

In 1998, the Adverse Events Following Immunisation's (AEFI) Targeted Spontaneous Reporting (TSR) system of the Expanded Programme for Immunisation (EPI) was established with strong links to NADEMC (Mehta, et al., 2017). TSRs are reports of specific, pre-defined serious events for a group of medicines or patients (Mehta, et al., 2017). In 2003, the MCC issued ADR reporting guidelines for industry and the MCC pharmacovigilance expert committee was formed to advise the MCC on post-market safety issues (Mehta, et al., 2017). The national anti-retroviral (ARV) treatment programme was started in 2003 and TSR systems for ARVs were incorporated within provincial ARV programmes (Mehta, et al., 2017). Nevertheless, the SA regulatory and programmatic pharmacovigilance programmes have functioned in parallel, causing confusion and failing to benefit from each other's knowledge (Mehta, et al., 2017).

Figure 1 Schematic representation of ADR reporting structures from within South Africa, which is transmitted to the WHO international database Vigibase®



The South African Department of Health mandates that all ADRs which patients experience must be reported on the SAHPRA ADR Reporting Form in terms of section 33(o) of the Pharmacy Act, 53 of 1974 (The South African Pharmacy Council (SAPC) (2018a). The SAHPRA Guideline, "Post-marketing Reporting of Adverse Drug Reactions to Human Medicines in South Africa," pertains to Regulation 37

issued in terms of the Medicines and Related Substances Act, 1965 (Act 101 of 1965) as amended (South African Health Products Regulatory Authority (SAHPRA), 2016).

Pharmacists are required to report as a minimum the identifiable reporter of the ADR, including their qualification, an identifiable patient, the suspected medicine and the suspected reaction (South African Health Products Regulatory Authority (SAHPRA), 2016). See Appendix C for the SAHPRA ADR reporting form. The Bradford-Hill Criteria is useful in determining if an ADR is significant. This has become the most used framework when determining causal inference in epidemiological studies (Fedak, et al., 2015).

Pharmaceutical companies are required to inform SAHPRA, within the determined time frame, of suspected ADRs reported to them as per Regulation 37 in the Medicine and Related Substances Act, 1965 (Act 101 of 1965) as amended (South African Health Products Regulatory Authority (SAHPRA), 2003). SAHPRA is the legal body that ensures safety, efficacy and quality of medicines (Mehta, 2011). When an ADR is experienced in SA, the Holder of the Certificate of Registration (or applicant) of the drug, must advise consumers to report adverse drug reactions through their HCP (South African Health Products Regulatory Authority (SAHPRA), 2016). HCPs, including pharmacists, are therefore ethically obliged to report ADRs.

SAHPRA's Pharmacovigilance Committee reviews complaints and makes recommendations to SAHPRA which could include withdrawal of the particular drug or a call for changes to the product information by the pharmaceutical company (Mehta, 2011). Most interventions in SA are due to international warnings (Maigetter et. al., 2015), therefore SA community pharmacists could play a pivotal role in ADR reporting. SAHPRA may convey recommendations to HCPs, pharmaceutical companies, the Essential Drugs Programme, other public health institutions, the media and the public (Mehta, 2011). Medicine safety issues are communicated to HCPs via "Dear Healthcare Professional" letters or medical safety alerts in journals

(Maigetter, et al., 2015). In a South African Association of Hospital and Institutional Pharmacists (SAAHIP) conference (2013), findings from a pharmacovigilance workshop concluded that the pharmacovigilance system is in need of reform, and that pharmacists had poor pharmacovigilance knowledge and understanding of its purpose in the safety of patients (Summers, Dube and Meyer, 2013). Even though pharmacists are the custodians of medication, they seem to be failing in their duty to report ADRs. Pharmacists need to realise that the safety profile of any drug evolves throughout its lifespan (Mehta, 2011).

South African pharmacovigilance studies have mainly focused on the public health sector and on specific regions (Table 1). An Eastern Cape study conducted at a regional training centre attested that underreporting of ADRs was a big problem (Ruud, Srinivas and Toverud, 2010). A North West Province pharmacovigilance study conducted among hospital and community pharmacists, found that knowledge was low (Joubert and Naidoo, 2016). The findings from a Western Cape study conducted in the rural winelands found that pharmacists realised the importance of pharmacovigilance, but rarely reported ADRs themselves (Williams, 2015). The study also noted that some pharmacists viewed some ADRs as outside their legal or clinical scope of practice and preferred to refer the patient to the prescriber. Generally, the pharmacovigilance knowledge of pharmacists in the private sector is considered to be lower than that of those in the public sector (Maigetter, et al., 2015).

Table 1 Summary findings of pharmacovigilance studies conducted among South African pharmacists

	Eastern Cape Province	North West Province	Western Cape Province
Sector	Public	Public and Private	Public
Participants	HCP (n=12) pharmacists (n=3)	Pharmacists (n=102)	Pharmacists (n=18)
Pharmacovigilance (PV) knowledge among pharmacists	They were familiar with the concept.	Knowledge was low.	They realised importance of PV.
ADR Reporting	Low	Low (44.1%)	Low
Reason/Barriers	Lack of training, filling in the form, high workload, lack of feedback, fear of not being taken seriously.	Time (50%), did not know how to report (38%), did not know where to report (35%).	Some viewed ADR reporting as outside their legal and clinical scope. Lack of feedback, heavy workload, time, uncertainty in identifying ADR, reporting process.
Willingness to participate in training	Yes	High (80%)	High
Reference	Ruud, 2009	Joubert and Naidoo, 2016	Williams, 2015

Overall, research on the reporting of ADRs by South African pharmacists is limited (Suleman, 2010). Studies have reported that, in general, pharmacovigilance knowledge is low amongst pharmacists, which precludes them from actively reporting on ADRs, contributing to a public health problem (Mehta, 2011). Furthermore pharmacists seemed unsure about their exact role in adverse drug reaction reporting (Joubert and Naidoo, 2016).

In SA, pharmaceutical companies are a vital resource in educating HCPs on the importance of pharmacovigilance (Roux, 2014). This is true, especially since they are held accountable. Industry-sponsored Continuing Medical Education (CME) is, however, associated with less rational prescribing by doctors (Lieb and Scheurich, 2014). Pharmaceutial companies often sponsor meetings designed to allocate CME points to HCPs with product merchandise on display (Clarke, 2011). HCPs must be

resistant to aggressive marketing of new drugs by industry in order to recover drug development costs (Mehta, 2011). Due to lack of understanding about the safety of new medicines in SA and low ADR reporting, a large percentage of the population can potentially be exposed to the unknown side-effects of a new medicine. In other more vigilant countries these medicines are more likely to be withdrawn due to uncertain safety data (Mehta, 2011). The relationship between HCPs and the pharmaceutical industry needs to be regulated to ensure HCPs have the patient's best interest at heart (Clarke, 2011).

Barriers to ADR reporting in SA include lack of time, lack of knowledge, lack of feedback and lack of understanding (Suleman, 2010). Lack of feedback on submitted ADR reports and SAHPRA's reluctance to disclose information on ADR reporting rates are cited as HCPs' main barrier to ADR reporting (Maigetter, et al., 2015). Lack of communication and feedback from regulatory authorities were listed as the most critical shortcoming in national pharmacovigilance programmes in SA (Maigetter, et al., 2015), as feedback gives relevance and meaning to the ADR reporting process. Difficulty in communicating ADRs, poverty (Ruud, et al., 2010) and illiteracy in some communities affects ADR reporting (Mehta, 2011). In under-resourced provinces the likelihood of patients reporting ADRs may be lower compared to those reported in affluent provinces (Ruud, Srinivas and Toverud, 2012). Weak general national health infrastructure and systems, poor understanding, lack of pharmacovigilance education, low interest among HCPs (Ampadu, et al., 2016), and lack of HCP commitment were identified as reasons for poor ADR reporting (Maigetter, et al., 2015). Lack of manpower, skills and budgetary constraints at NADEMC led to a three-year backlog for ADRs analysis (Maigetter, et al., 2015). Even though a national pharmacovigilance system is in place, SA lacks the capacity to monitor it (Maigetter, et al., 2015). Therefore, the community pharmacist's proactivity in ADR reporting is crucial to minimising barriers to patient care and well-being.

Pharmacovigilance is seen as a vital practice as SAHPRA proposes to regulate complementary medicine in the near future (Gray, Riddin and Jugathpal, 2016).

Self-medication, misuse of over-the-counter (OTC) medicines, vitamins and traditional medicines increase the risk of ADRs in SA (Mehta, 2011). SAHPRA therefore underpins pharmacovigilance as a key professional obligation in protecting patient safety (Mehta et. al., 2017).

2.4 PHARMACOVIGILANCE IN THE REST OF THE WORLD

ADRs are responsible for 5% of all hospital admissions in Europe, and in the USA ADRs are among the top ten causes of death (Montanari-Vergallo, 2013). Various studies have shown that ADRs place a considerable burden on health care budgets around the world (Mehta, 2011).

Australia (30%), Netherlands (29.3%), Spain (24.5%) and Canada (28.4%), took the lead for pharmacist-led ADR reporting, while low reporting rates were noted from the United Kingdom (UK) (11.9%) and South Africa (2.8%) (Van Grootheest, et al., 2003). Community pharmacists in the Netherlands, Japan, Cuba and Portugal contribute considerably to ADR reports (Van Grootheest and de Jong-van den Berg, 2009).

In the UK, fewer community pharmacists report ADRs compared to hospital pharmacists even though community pharmacists are more accessible (Cheema, et al., 2017). This could be due to hospital pharmacists having a better understanding of ADRs due to regular clinical exposure compared to community pharmacists. Cheema et. al. (2017) concluded that UK pharmacists cited lack of time and adverse reactions not regarded as serious, as perceived hindrances to adverse drug reaction reporting. They added that even though an increase in pharmacist adverse drug reaction reporting was evident in recent years, further education and training was needed. Canadian pharmacists, who saw themselves as contributing to the safety data of health products, were more likely to report ADRs (Walji, 2008). A Jordanian study showed that pharmacists prefer to refer patients to the prescribing doctor or emergency ward, rather than report the ADR themselves (Suyagh, Farah and Abu Farha, 2014).

Pharmacovigilance legislation in the EU and USA evolved to increase harmonisation and efficiency of their pharmacovigilance systems (Montanari-Vergallo, 2013). A global pharmacogivilance system is still a distant goal as even the basic definition of an adverse drug reaction differs between the EU and USA. In the EU, an adverse drug reaction needs to have a reasonable possibility of occurrence with the medicinal product, whereas in the USA any adverse drug event (whether related or not) is regarded as reportable (Montanari-Vergallo, 2013). In SA, a causal relationship between the adverse event and the medicine must at least be a possibility (South African Health Products Regulatory Authority (SAHPRA), 2016).

2.5 CONCLUSION

Pharmacists, as custodians of medication, are essential in recording and submitting ADRs to national health authorities in order to fulfil their professional obligations. Pharmaceutical companies and regulatory authorities rely on pharmacists to assist in the continuous surveillance of drugs to improve patient safety. Pharmacists are obliged to apply their expert knowledge protecting the safety of the population they are required to serve.

South Africa is in need of a robust, united, national pharmacovigilance system (Mehta et. al., 2017). Lack of manpower and a three-year backlog at NADEMC does little for encouraging ADR reporting (Maigetter et. al., 2015). Discrepancies across the provinces could indicate the lack of support community pharmacists have in pursuing pharmacovigilance. Strengthening of the current pharmacovigilance system (Joubert and Naidoo, 2016), requires strong political will and leadership by major stakeholders (Mehta, et al., 2017).

CHAPTER 3

METHODOLODY

3.1 INTRODUCTION

The study aimed to determine the knowledge, attitude and practice patterns of South African community pharmacists in ADR reporting, since it is regarded as a macro-level public health pharmacy activity (Bradley, Bheekie, and Sanders, 2011). The retail community pharmacists' role in pharmacovigilance is explored from community pharmacists' perspective working in small and large chain pharmacies. This chapter provides a brief summary of the research design, the data collection and data analysis processes that were undertaken for the study.

The section outlines the participant recruitment process and description of the questionnaire in the survey.

3.2 RESEARCH DESIGN

A quasi-experimental design, without any random pre-selection process, was selected for this quantitative study. Community pharmacists for the study were recruited from the public domain using electronic media. Pharmacists working in retail community pharmacies whose email addresses were obtained from websites were eligible to participate in the study.

Pharmacy details (telephone numbers and email addresses) were obtained via the telephone directory and electronically from websites. The following search terms were used to find community pharmacists working in community pharmacy:

- Pharmacies Eastern Cape
- Pharmacies Free State

- Pharmacies Gauteng
- Pharmacies Kwa-Zulu Natal
- Pharmacies Limpopo
- Pharmacies Mpumalanga
- Pharmacies Northern Cape
- Pharmacies North West Province
- Pharmacies Western Cape
- Pharmacies Yellow pages

This quantitative study consisted of a survey questionnaire. It is common practice to use surveys when researching health services and surveys are useful in exploring the characteristics of a situation or data for testing hypothesis (Kelly, et al., 2003).

3.3 QUANTITATIVE RESEARCH

Surveys usually refer to the selection of a rather large sample of people from a pre-determined population (or population of interest) and collect a relatively small amount of data from them (Kelly, et al., 2003). The information from the smaller group of individuals is then used to make inference about the wider population (Kelly, et al., 2003).

Survey research was chosen for this study because it provided a snapshot of the realities in community pharmacy regarding pharmacovigilance at a specific time (Kelly, et al., 2003). Survey research provides real time information, can cover a large population and produces a large amount of data in a short time (Kelly, et al., 2003). Disadvantages of survey research are that it can lack depth or detail, and it is difficult to secure a high response rate (Kelly, et al., 2003).

SurveyMonkey® (SurveyMonkey, 2018(d)), was considered the most accessible, because it allows for a range of data collection methods and gives easy access to the survey by clicking on a link.

Contents of study questionnaire

Quantitative data was obtained by asking pharmacists working in community pharmacies in each province, closed, fixed questions with a view of evaluating their knowledge, attitude and practice pattern of ADR reporting.

The study questionnaire consisted of 40 questions. Section one had seven questions which explored the demographic information from the participants. Section two aimed to measure the knowledge of community pharmacists regarding ADR reporting and pharmacovigilance, and was comprised of twelve questions. Section three aimed to determine community pharmacists actual practice behaviour in pharmacovigilance on a daily basis, and consisted of five questions. The opinion and feeling of community pharmacists concerning ADR reporting and pharmacovigilance was explored in the last section containing sixteen questions.

The questions were compiled based on literature reviewed (locally and internationally), and from anecdotal conversations with pharmacists, patients and HCPs.

3.3.1 Study Population

The total population of this study consisted of community pharmacists working in community pharmacies which could be contacted electronically via website addresses.

Inclusion and exclusion criteria

The study included community pharmacists male or female, of all ages, in all provinces, newly qualified or experienced, working in retail community pharmacies including small independent pharmacies and large chain-type pharmacies. The study did not include pharmacists working in hospitals, academia, primary care or

industry. Pharmacist registration numbers or P numbers further served as an inclusion criterion for verification purposes. These P numbers were verified on the SAPC website (South African Pharmacy Coucil (SAPC), 2018).

3.3.2 Sampling Strategy

The success of the sample representing the population depends on how well the sample frame corresponds to it. Sample frame examples include phone directories (Adwok, 2015). Community pharmacies listed on websites supplying email addresses were selected, and this included independent pharmacies and chain pharmacies. The email addresses were obtained in the order they were originally found on the relevant websites consulted and were saved to a spreadsheet. It was reasonable to assume that the pharmacy contact details in the telephone directories and on websites are current. The sample frame is the number of community pharmacists with access to electronic mail in the pharmacy.

Purposive sampling is a type of non-random sampling that depends on data collection from members within a specific population (Kelly, et al., 2003). The contact details of community pharmacies which were accessible in the public domain, initiated the process to engage with the practising pharmacists. In this way pharmacists working in public health or hospitals were excluded from the study. The personal contact details of community pharmacists from the SAPC register were not originally requested to avoid delaying the data collection process. It is difficult to accurately determine where pharmacists are working at any given time in SA because of their high mobility, a large locum work force, and an unknown number of pharmacists who keep their registration but leave the workplace or immigrate (Gray, Ridden and Jugathpal, 2016).

The advantages of using non-random sampling are that it is simple and can provide data in a short period of time (Research Methodology, n.d). The disadvantages are that it is vulnerable to bias and sampling error (Research Methodology, n.d).

Sampling error is the deviation of the sample data from the true population data and this is decreased as the size of the sample increases (eMathZone, n.d.).

Small study samples decrease the internal and external validity of the research (Faber and Fonseca, 2014). Response rates for postal questionnaires are usually 20% on average, because the survey is received by the respondents without any previous contact with the researcher (Kelly, et al., 2003). These same circumstances exist for online surveys. Large study samples are more representative of the population and provide a large enough data set to examine (Kelly, et al., 2003), whereas a small study sample may lead to false assumptions (Faber and Fonseca, 2014). In this study the sample population was increased in anticipation of low survey response rates.

Electronic data collection process

Due to the low response rate using the email addresses found on websites and the high number of erroneous email addresses, a list of community pharmacy contact details were requested from the SAPC on 26 June 2018. The SAPC community pharmacist list was unavailable to the researcher at the time of this dissertation submission. Due to the high number of erroneous electronic mail addresses on the websites identified from returned and undelivered emails, several attempts were made to increase the study sample, including phoning pharmacies to obtain email addresses.

This study was performed using electronic surveys with reminders via SurveyMonkey® inquiring from pharmacists their knowledge, practice and opinion of pharmacovigilance (APPENDIX B).

The inclusion criterion for study participants was the provision of the pharmacist's SAPC registration number to verify registration as a pharmacist with the SAPC. Registration numbers were verified on the SAPC website (South African Pharmacy Coucil (SAPC), 2018(b)). The final proposal for the research was submitted to the

University of the Western Cape (UWC) on 23 April 2018 (APPENDIX E). Ethical clearance for the study was obtained from UWC on 8 June 2018 (APPENDIX F). The questionnaire was piloted on the 9th of June 2018 with pharmacists who were not involved in the study.

The questionnaire consisted of 40 questions with multiple choice answers (APPENDIX B). It was developed in June 2018, using the SurveyMonkey® online survey tool. Responses were coded to facilitate categorisation of responses. Internal validity was maintained by asking "check questions". Participants were requested to answer the survey within ten minutes as a means to achieve authentic responses.

The first method of collection used was sending an Information Sheet (APPENDIX A) and the web link to the survey from two Gmail email accounts. The Information Sheet provided the background to the study, the objectives, and benefits to participants and potential risks related to participation. Confidentiality and voluntary participation were emphasised with the ethics clearance reference number from UWC included in the Information Sheet. The Information Sheet further stated that participants who clicked on the web link, were in agreement to voluntary participate in the study.

A second method of collection, namely the SurveyMonkey® email collector, was used due to the high rate of emails from the Gmail accounts being blocked or returned. The Information Sheet (APPENDIX A) was included in the message in the SurveyMonkey® email collector providing the background to the study, voluntary participation details and the ethical clearance from UWC.

See Table 2 for details of the data collection process.

Reminder emails using the SurveyMonkey® email collector for partial responses were sent out on 3 occasions, while reminder emails from SurveyMonkey® were sent out to all email addresses that were unresponsive on a weekly basis from the 29th of June 2018 to the 6th of August 2018. The survey was closed on the 8th of August 2018.

The average time the respondents had spent on the survey was 15 minutes.

20 responses were obtained using the weblink on the Gmail email addresses.

62 responses were obtained using the MonkeySurvey® email collector.

3.3.3 Data Analysis

The total number of email invitations sent via SurveyMonkey® email collector was 1677 emails. 145 emails bounced and 11 opted out. Nine participants emailed the Gmail email account directly to request removal of email addresses or to inform the researcher that the link was dysfunctional, probably due to a computer firewall on their computer system.

Of the 1677 emails that were originally sent out, only 1460 email addresses could be reached and only 82 responded. This left the population at 1460.

Twenty responses were obtained using the weblink on the Gmail email addresses and 62 responses were obtained using the MonkeySurvey® email collector. The study sample was therefore 82, resulting in a response rate of 5.62%.

SurveyMonkey® provides data collection methods and basic data analysis. Responses to each question were expressed as a percentage. Trends were observed in the knowledge, attitude and practice pattern of adverse drug reaction reporting in the sample. This data was analysed at face value.

Statistical manipulation was inconclusive due to the small study sample and descriptive statistics (percentage) was used to interpret findings.

3.4 ETHICAL CONSIDERATIONS

An Information Sheet outlining the study's purpose, objective, significance and dissemination of the findings was sent electronically to prospective participants. The benefits and risks of participating in the study were outlined (APPENDIX A).

The participants were informed by the Information Sheet that participation was entirely voluntary and that they could withdraw from the study at any time. Informed consent was obtained from the pharmacists by clicking on the link provided before the questionnaire was uploaded. The inclusion criterion for the study participants was the provision of the pharmacist's SAPC registration number or P-number and this was only known to the researcher. Study participants were completely anonymised; they were not identifiable by name and their responses were not linked to them personally. The survey was completed online. There was no direct, physical contact with the participants for the study. Participants were not exposed to any risks in the study.

Ethical approval for the study was obtained from the University of the Western Cape Biomedical Research Ethics Committee on the 8th of June 2018, before the study was conducted. Ethical clearance reference number: BM18/4/4 (APPENDIX F).

3.5 CONCLUSION

This chapter outlined the methodology used in the study. The research design, qualitative research approach, population, sampling strategy and data analysis were discussed. The many obstacles when using online surveys in quantitative research were identified. The web search route for obtaining contact details is not recommended. Finally, the ethical considerations were examined. The next chapter examines the results obtained followed by the discussion.

CHAPTER 4

RESULTS

4.1 INTRODUCTION

This chapter presents the results and discussion from this quantitative study, which used a survey questionnaire from the 16th of June 2018 to and including the 8th of August 2018.

The results are presented under a title which was extracted from the questionnaire, tabulated and discussed thereafter. Therefore the table does not have an individual title.

The survey questionnaire was sent out via two Gmail account email addresses, providing the weblink for the survey from SurveyMonkey®, and it was also sent via the SurveyMonkey® own email collector. Regular electronic reminders were sent out to recruit participants.

The complete list of questions of the survey can be found in Appendix B.

4.2 RESULTS OF SURVEY QUESTIONNAIRE

Study sample:

For a 95% confidence level with a margin of error of 5%, a study sample of 305 responses is required from a population of 1460 (SurveyMonkey, 2018(c)). A margin of error of 5% proves that the survey was effective. The research aimed for a study sample of 305. After removing the unknown email addresses, bounced email addresses and opted out email addresses, 1460 emails were delivered using the two methods of data collection.

Of the 82 responses which were obtained, only 70 of the participants were registered pharmacists as confirmed by the SAPC register and therefore comprised the study sample (South African Pharmacy Coucil (SAPC), 2018(b)). The study sample was therefore 70 out of a population of 1460; representing a response rate of 4.79% to the survey. The 12 invalid participants' answers were removed from the results. Although 82 responses were collected, only 55 participants answered all 40 questions. There was a completion rate of 70%.

The study sample of 305 was therefore not obtained. The study sample of 82 responses gave a 95% confidence level with a larger margin of error of 11%. This larger margin of error would give less confidence in the results.

The survey consisted of 40 questions and was divided into 4 sections, namely Demographics, Knowledge, Practice and Opinion. The results are tabulated below.

Demographics (1-7)

4.2.1 Age range of the participants.

In the study all participants answered this question.

Answer choices	**Responses**	
	%	**N**
24-30 years	25.71	18
31-40 years	30.00	21
41-50 years	20.00	14
51-60 years	21.43	15
Above 60	2.86	2
Total respondents	**100**	**70**
Non-respondents	**0**	**0**

One third of the participants (30.00%, N=21) were in the age range of 31-40 years of age, which indicates that they are economically active and tend to have an interest in the topic as part of professional practice. Participants above the age of 60 years were least represented (2.86%, N=2) which indicates retirement. One fifth of the participants (20.00%, N=14) were in the 41-50 age range.

4.2.2 Gender of the participants.

All participants answered this question.

Answer choices	**Responses**	
	%	**N**
Male	45.71	32
Female	54.29	38
Total respondents	**100**	**70**
Non-respondents		

Just over half (54.29%, N=38) of the participants were female and 45.71% (N=32) were male. This indicates an almost even split between the genders in participating in the survey.

4.2.3 SAPC registration number of P-number as verification of registration as a pharmacist in South Africa.

All participants answered this question. Unfortunately 11 participants did not provide a valid registration or P number. One participant did the survey twice. Registration and P numbers were verified on the SAPC website (South African Pharmacy Coucil (SAPC), 2018(b)).

Registration numbers were only known to the researcher and all answers to survey questions were completely anonymised.

	Responses	
	%	**N**
Total respondents	100	70
Non-respondents	0	0

4.2.4 Title or position in the pharmacy.

Participants were invited to tick as many options as applicable. All participants answered this question.

Answer choices	**Responses**	
	%	**N**
Pharmacy Manager in a Chain of Pharmacy	54.29	38
Pharmacy Manager in an Independent Pharmacy	4.29	3
Responsible Pharmacist	25.71	18
Pharmacist Owner of an Independent Pharmacy	18.57	13
Locum	0	0
Junior Pharmacist	10	7
Total respondents	**100**	**70**
Non-respondents	**0**	**0**

Most of the respondents (54.29%, N=38)) were pharmacy managers in a chain-type of pharmacy. Only 3 respondents (4.29%) were pharmacy managers in an independent-type of pharmacy, while 13 participants (18.57%) indicated that they are the pharmacist owner of an independent pharmacy. A quarter (25.71%, N=18) of the respondents regarded themselves as the responsible pharmacist.

4.2.5 Degree or qualification held.

All participants answered this question. Participants could only tick one option.

Answer choices	Responses	
	%	N
B.Pharm	82.86	58
Dip.Pharm	1.43	1
M.Pharm	7.14	5
Other	8.57	6
Total respondents	**100**	**70**
Non-respondents	**0**	**0**

Six participants (8.57%) provided information on other degrees obtained in addition to their pharmacy degree (B.Pharm). These were PhD degrees, MBL and BSc degrees amongst others. A total of 5 participants (7.14%) held Master of Pharmacy degrees.

4.2.6 Years of experience as a community pharmacist.

All participants answered this question.

Answer choices	Responses	
	%	N
Less than 2 Years	14.29	10
2-5 Years	22.86	16
5-10 Years	14.29	10
10-20 Years	24.29	17
More than 20 Years	24.29	17
Total respondents	**100**	**70**
Non-respondents	**0**	**0**

The participant experience categorised less than 2 years can be regarded as newly registered pharmacists (14.29%, N=10) and the group of more than 10 years can be regarded as the most experienced of participants (24.29% + 24.29% = 48.58%). The lowest respondents (14.29%, N=10) were newly qualified or had 5-10 years of experience in community pharmacy (14.29%, N=10). There was an almost even split between all the years of experience in community pharmacy.

4.2.7 Province of employment as a community pharmacist.

In this question all participants selected to answer the question.

Answer Choices	Results	
	%	N
Western Cape Province	15.71	11
Eastern Cape Province	11.43	8
KwaZulu-Natal Province	14.29	10
Gauteng Province	32.86	23
North West Province	4.29	3
Limpopo Province	2.86	2
Free State Province	8.57	6
Northern Cape Province	2.86	2
Mpumalanga Province	7.14	5
Total Respondents	**100**	**70**
Non-respondents	**0**	**0**

A third (32.86%, N=23) of the respondents was located in Gauteng province, followed by an equal distribution in the Western Cape Province (15.71%, N=11) and KwaZulu-Natal Province (14.29%, N=10). Respondents from Limpopo Province (2.86%) and Northern Cape Province (2.86%) were the least represented in the study sample (N=2). The participant distribution is reflective of the country's economically developed areas (Statistics SA, 2011).

Knowledge (8-19)

4.2.8 Pharmacists' first encounter with pharmacovigilance.

Sixty-one participants answered this question and 9 did not. This question related to the pharmacist's first encounter with pharmacovigilance and further inquired where they had first encountered "pharmacovigilance".

Answer Choices	Results	
	%	N
From the South African Pharmacy Council (SAPC)	13.11	8
From the South African Health Products Regulatory Authority (SAHPRA)	3.28	2
From a Pharmaceutical Company	4.92	3
From your CPD (Continuing Professional Development)	8.20	5
From an academic institution	50.82	31
I can't remember	13.11	8
Other	6.56	4
Total Respondents		**61**
Non-Respondents		**9**

Half of the participants (50.82%, N=31) first heard of pharmacovigilance from an academic institution as would be expected from a pharmacy degree level course. It is interesting that 2 participants (3.28%) selected SAHPRA and 8 (13.11%) selected the SAPC. It is encouraging that 5 (8.20%) participants encountered pharmacovigilance during their CPD. Those participants who selected the "other" option elaborated on their university course and one respondent listed the Standard Operating Procedures (SOPs) of the company for which he worked.

4.2.9 Pharmacovigilance training after qualifying as a pharmacist.

Sixty-one participants answered this question and 9 selected not to answer. This question was asked to ascertain whether any pharmacovigilance training was available and which pharmacists had used it after qualifying as a pharmacist.

Answer Choices	Responses	
	%	N
Yes	19.67	12
No	72.13	44
I am not sure	8.20	5
Total Respondents		**61**

Non-Respondents		**9**

Almost three quarters of the respondents (72.13%, N=44) had not received any pharmacovigilance training after qualifying as a pharmacist. Such a high proportion is concerning as pharmacists have a professional and ethical obligation to ensure medicine safety in the public. One could speculate that the community pharmacists might not have been aware of training opportunities available to them, or there may not have been pharmacovigilance-specific training available to them. Other reasons for lack of training may have been cost of training and/or lack of time. Personal preference of training, i.e. online or workshops may also have contributed to the high number of pharmacists that had not received training.

4.2.10 Training facilitator.

Sixty-one participants answered this question and 9 selected not to answer. This follow-up question inquired who provided the training. Participants were invited to select as many options as applicable.

Answer Choices	**Response**	
	%	**N**
South African Pharmacy Council representative	0.00	0
A Pharmaceutical Company representative	9.84	6
A higher education representative	11.48	7
Pharmaceutical Society of South Africa representative	3.28	2
I have not received any training	70.49	43
Other	6.56	4
Total Respondents		**61**
Non-Respondents		**9**

This question also served as a check question. Since 72.13 % of participants stated in question 4.2.9 that they had not received any training it is logical to assume that the same option in question 4.2.10 would have the same results. An equally high proportion (70.49%, N=43) of participants indicated that they had not received any post-qualification training in question 4.2.10.

None of the participants selected SAPC, which is interesting since 8 participants selected the SAPC as the first institute where they heard about pharmacovigilance in a previous question (question 4.2.8). Six participants (9.84%) selected a pharmaceutical company, 7 (11.48%) selected a higher education representative and 2 (3.28%) selected the PSSA. One participant under the option of "other" listed the Pharmacovigilance Unit at Groote Schuur Hospital. Other facilitators included the Northern Cape Department of Health, public sector hospitals and the CDP program: Positive Impact Programme, which is offered by a chain pharmacy to their pharmacists for CPD.

4.2.11 What ADR reporting entails according to community pharmacists.

In this study 61 of participants answered the question and 9 did not answer. Participants were invited to select as many options as applicable. This question aimed to determine how many participants regard filling in the ADR report form in their practice.

Answer Choices	**Response**	
	%	**N**
Contacting the prescriber	68.85	42
Referring the patient to the prescriber	62.30	38
Filling in an ADR reporting form and sending it	91.80	56
Making a note on the patient's medication record	77.05	47
Total Respondents		**61**
Non-Respondents		**9**

Almost all (91.08%, N= 56) of participants selected filling in an ADR form and claimed that they had sent it as part of ADR reporting. Two thirds of the participants (68.85%, N=42) also opted to contact the prescriber, and a similar proportion (62.30%, N=38) would also refer the patient back to the prescriber. This is consistent with a study done in the Western Cape, where pharmacists associated an ADR with an intervention that needed to take place and would therefore prefer to refer the patient to the prescriber (Williams, 2015). In a UK study, 94.9% of pharmacists, were familiar with the appropriate form for ADR reporting (Cheema, et al., 2017).

4.2.12 ADRs that qualify for reporting.

In this study 61 participants answered the question and 9 did not. Participants were invited to select as many options as applicable. This question tested whether community pharmacists knew what adverse drug reactions are reportable.

Answer Choices	**Response**	
	%	**N**
All ADRs to new marketed drugs or drugs added to the Essential Drugs List (EDL)	70.49	43
All ADRs listed in the package insert experienced by the patient	37.70	23
All serious interactions and reactions	85.25	52
Ambiguous adverse reactions listed in the package insert	39.34	24
Unusual or interesting drug reactions	83.61	51
Product quality problems like contamination, stability and defective compounds	57.38	35
Product quality problems like poor packaging and labelling	37.70	23
Treatment failures	27.87	17
ADRs due to herbal preparations	62.30	38
Total Respondents		**61**
Non-Respondents		**9**

Even though almost all (91.80%) of the participants indicated that ADR reporting entailed filling in an ADR report form, (question 4.2.11) few of the participants (11.43%, N=8) identified correctly all the ADRs which qualify for reporting. These results are consistent with a UK study, where most participants selected to report ADRs that are serious and ADRs experienced by new drugs (Cheema, et al., 2017). The results are also reflected by a study done in the Western Cape, where there was confusion over what ADRs qualified for reporting (Williams, 2015). Over a third (37.70%, N=23) selected the incorrect option that all ADRs in the package insert should be reported. All the above mentioned options qualified for ADR reporting with the exception of one of them namely “all ADRs in the package information leaflet that

the patient may experience". All ADRs in the package leaflet experienced by the patient should not be reported on the ADR report form as this will cause a considerable workload if all ADRs experienced by patients were reported.

4.2.13 Serious Adverse Events.

Sixty-one participants answered this question and 9 participants did not. Participants were invited to select as many options as deemed applicable. The question tested whether pharmacists knew what adverse reactions were regarded as serious.

Answer Choices	**Results**	
	%	**N**
Life-threatening	100	61
Disability	72.13	44
Death	83.61	51
Hospitalization	81.97	50
Sick leave at home	26.23	16
Total Respondents		**61**
Non-Respondents		**9**

A quarter (26.23%, N=16) of participants selected sick leave at home as a serious adverse event which is incorrect. All participants (100%) agreed that life-threating events are regarded as serious adverse events. Interestingly a similar high proportion (83.61%, N=51) regarded death as a serious event, hospitalisation (81.97%, N=50) and disability (72.13%, N=44). Serious adverse events need to be reported within 15 calendar days to regulatory authorities (South African Health Products Regulatory Authority (SAHPRA), 2016).

4.2.14 Pharmacovigilance responsibilities.

Sixty-one participants answered this question and 9 did not. This answer related to the pharmacovigilance knowledge of pharmacists and whether they regarded these options listed below as part of their pharmacovigilance responsibilities. Pharmacists were invited to select as many options as relevant.

Answer Choices	Results	
	%	N
Adverse drug reactions	95.08	58
Substandard drugs	47.54	29
Medication errors	49.18	30
Use of drugs off-licence without adequate scientific research	50.82	31
Abuse and misuse	62.30	38
Lack of efficacy	32.79	20
Poisoning	57.38	35
Adverse interactions with other drugs, herbs, food and chemicals	77.05	47
Drug-related mortality	73.77	45
Destruction of expired stock	24.59	15
Total Respondents		**61**
Non-Respondents		**9**

All the options related to the pharmacovigilance responsibilities of pharmacists and therefore all options should have been selected by all participants. Almost all (95.08%, N=58) participants identified adverse drug reactions, but only three quarters (77.05%, N=47) selected adverse interactions with other drugs, food and chemicals as the pharmacist's pharmacovigilance responsibilities. Three quarters (73.77%, N=45) of the participants selected drug-related mortality and a third (32.79%, N=20) of them selected lack of efficacy, while a quarter (24.59%, N=15) selected the destruction of expired stock as an option.

4.2.15 Pharmacovigilance as a legal obligation.

In this question 61 participants selected to answer and 9 did not. The question aimed to establish whether pharmacists viewed pharmacovigilance as a legal obligation. The question did however ask if it was a legal obligation *in their opinion.*

Answer Choices	Results	
	%	N
Yes	78.69	48
No	3.28	2
I am not sure	18.03	11
Total Respondents		**61**
Non-Respondents		**9**

Over three quarters (78.69%, N=48) of the participants regarded pharmacovigilance as a legal requirement. Two participants (3.28%) did not regard pharmacovigilance as a legal requirement. Eleven participants (18.03%) were unsure if pharmacovigilance was a legal requirement. Pharmacovigilance is in fact an ethical obligation.

4.2.16 The fate of the ADR report form.

Sixty-one respondents answered this question and 9 participants did not.

This question aimed to establish if pharmacists knew what happened to the ADR report form once it was sent to the relevant authorities and who used the data which they had submitted. Participants were required to select as many options as applicable.

Answer Choices	Results	
	%	N
They are reviewed by NADEMC	54.10	33
They are reviewed by they WHO UMC in Sweden	24.59	15
They are assessed by SAHPRA	60.66	37
They are assessed by the Medicine Information Centre in Cape Town	55.74	34
Total Respondents		**61**
Non-Respondents		**9**

More than half of the number of pharmacists (55.74%, N=34) selected that ADRs are assessed by the Medicine Information Centre (MIC) in Cape Town, which is only correct for ADRs submitted from the Western Cape Province. The MIC does

however provide information on ADRs for all provinces. Only a quarter (24.59%, N=15) of the respondents knew that ADR data is reviewed by the WHO Uppsala Monitoring Centre (UMC) in Sweden. ICSR forms received from Africa by WHO UMC account for less than 1% of the total ICSR forms received globally (Ampadu et. al., 2016). Over half (54.10%, N=33) of the respondents selected NADEMC and 60.66% (N=37) selected SAHPRA, which is correct (South African Health Products Regulatory Authority (SAHPRA), 2016). NADEMC is a subunit of SAHPRA.

4.2.17 WHO definition of pharmacovigilance.

Sixty-one participants answered the question and 9 did not. This question aimed to establish whether pharmacists were familiar with the WHO definition of pharmacovigilance. Participants could only select one option.

Answer Choices	**Results**	
	%	**N**
The science and activities relating to the detection and assessment of adverse effects or any other drug-related problem	22.95	14
The science and activities relating to the understanding and prevention of adverse effects or any other drug-related problem	18.03	11
All of the above	59.02	36
Total Respondents		**61**
Non-Respondents		**9**

Only 59.02% of pharmacists (N=36) knew that both statements related to the WHO definition of pharmacovigilance. This result was slightly better than the result from the pharmacovigilance study done in the North West Province in 2015, where just under half of the participants (46.1%) selected the correct WHO definition (Joubert and Naidoo, 2016).

4.2.18 Drugs withdrawn from the market for safety reasons.

Sixty-one participants answered this question and 9 did not. This question was included to establish whether pharmacists knew of drugs that had previously been withdrawn in order to highlight post-market surveillance as a real concern for the safety of drugs. The question however inquired whether if occurred, "from their practice experience".

	Results	
	%	**N**
Drug Example	70.49	43
None	30.00	18
Total Responses		**61**
Non-responses		**9**

Forty-three participants (70.49%) could name a drug that had been withdrawn post-market. Responses from participants also included thalidomide which was withdrawn in 1962 (Mehta, et al., 2017), indicating therefore that it would not have occurred during their practice experience. Thalidomide is however used today in certain types of cancers and leprosy. Almost a third (30%, N=18) of respondents stated "none" or "can't remember". One participant stated warfarin and another tetracycline, as drugs that were withdrawn, which are incorrect.

4.2.19 Authorities monitoring ADR reporting.

Sixty-one participants responded and 9 did not. This question was asked to establish whether pharmacists knew where the ADR report form was sent to. Participants could only select one option. This question is linked to question 4.2.16 which aimed to establish whether participants knew who assessed the data they submitted.

Answer Choices	**Responses**	
	%	**N**
SAHPRA	8.20	5
NADEMC	24.59	15
All of the above	40.98	25
I am not sure	26.23	16
Total Respondents		**61**

Non-Respondents		**9**

The correct answer is all of the above. Less than half (40.98%, N=25) of the participants knew the correct answer, while a quarter (26.23%, N=16) of them were not sure.

Practice (20-24)

4.2.20 ADR management.

Fifty-seven participants answered the question and 13 did not. This question was asked to determine how pharmacists generally managed ADRs in community pharmacy. Participants could select as many options as possible.

Answer Choices	**Responses**	
	%	**N**
Phoning the prescriber	77.19	44
Referring the patient to the prescriber	71.93	41
Referring the patient to the hospital emergency ward	36.84	21
Counselling the patient and leaving it up to the patient to decide what is best	22.81	13
Filling in an ADR report form	73.68	42
Total Respondents		**57**
Non-Respondents		**13**

Even though almost all (91.80%) of the participants agreed in question 4.2.11 that ADR reporting entailed filling in the ADR report form, only three quarters (73.68%, N=42) of them claimed that they had filled in an ADR report form in their practice. This could indicate that most pharmacists did indeed endeavour to fill in the ADR report form once faced with an ADR, which might indicate lack of knowledge regarding what ADRs need to be reported. Three quarters of pharmacists (71.93%, N=41) referred the patient back to the prescriber, which coincides with a Western Cape study, where pharmacists would rather refer the patient to the prescriber than fill in an ADR report form, even though ADRs are often discussed during counselling sessions (Williams, 2015). One fifth (22.81%, N=13) of the participants indicated that they left it up to the patient to decide what was best.

4.2.21 Drugs the pharmacist have reported on the ADR report form.

Only 57 participants answered this question and 13 did not. In this question participants were asked to name the drugs they have reported on, using the ADR report form, in the course of their career up to date.

	Results	
	%	**N**
Drug example	40.00	23
None	59.65	34
Total Respondents		**57**
Non-Respondents		**13**

More than half (59.65%, N=34) of the participants reported “none” to this question which meant that they had never reported an ADR on the ADR report form. This figure is higher than the UK, where just less than half (45%) of pharmacists in a similar UK study, had reported an ADR (Cheema, et al., 2017). This result is also reflected in a study done in the North West Province, where just over 40% of respondents had ever reported an ADR (Joubert and Naidoo, 2016). In the previous question (4.2.20) more than 70% of pharmacists stated that they did report ADRs on the ADR report form in their ADR management in their practice. This could indicate that even though they have never reported an ADR on an ADR report form, some pharmacists do endeavour to do so once they are faced with an ADR. Participants from across all age ranges provided examples with most examples supplied from those above 30 year age range. Examples included rofecoxib, Vioxx®, aspirin, lansoprazole and salbutamol amongst others.

4.2.22 Location of the ADR report form.

Fifty-seven participants answered this question and 13 did not. This question aimed to establish if pharmacists knew where to locate the ADR report form. Participants were invited to select as a many options as applicable.

Answer Choices	Results	
	%	N
SAHPRA	42.11	24
SAPC	54.39	31
SAMF back page	68.42	39
Other	21.05	12
Total Respondents		**57**
Non-Respondents		**13**

Over half (54.39%, N=31) of the participants erroneously selected the SAPC. The ADR report form is not accessible from the SAPC. Twelve participants (21.05%) selected "other". Answers ranged from the company's intranet, the company the pharmacist worked for, yellow forms in hospital pharmacy, the Essential Medicines List (EML) or Essential Drug List (EDL). Two participants (3.50%) stated the MCC under "other". This could indicate that they were not aware that the MCC changed into SAHPRA in 2017.

4.2.23 Preferred method of submitting the ADR report form.

Fifty-seven participants selected to answer this question and 13 did not. This question was asked to establish the preferred method of submitting the ADR form based on participants' experience. Only one option was available for selection.

Answer Choices	Results	
	%	N
Telephone	8.77	5
Fax	3.51	2
Email	84.21	48
Post/Courier	1.75	1
Other	1.75	1
Total Respondents		**57**
Non-Respondents		**13**

Most of the participants (84.21%, N=48) selected the option to send the ADR form via email. On the ADR form itself an email and telephone number are available.

One selected to do so via post. NADEMC's address can be found in Appendix 1 of the SAHPRA "Post-Marketing Reporting of ADRs in SA" guideline (South African Health Products Regulatory Authority (SAHPRA), 2016). Other methods included telephonically reporting (8.77%, N=5) and fax (3.51%, N=2), while email was deemed the other the option.

4.2.24 ADRs reported on the ADR form this past year.

Fifty-seven participants answered this question and 13 did not. This question aimed to determine how many ADRs participants have reported on the ADR report form this year. Participants could only select one option.

Answer Choices	**Responses**	
	%	**N**
At least one	17.54	10
At least two	0.00	0
At least three	1.75	1
Four and more	1.75	1
None	78.95	45
Total Respondents		**57**
Non-Respondents		**13**

Over three quarters (78.95%, N=45) of the participants stated that they had not reported any ADRs this past year. Surprisingly less than a fifth (17.54%, N=10) stated that they had reported at least one ADR on the ADR report form this year, one participant had reported at least 3 ADRs. This participant was from the 41-50 years age group and with 10-20 years of community pharmacy experience. One participant had reported four and more ADRs on the ADR report form this year. This participant was from the 31-40 years age group with 2-5 years of community pharmacy experience. In question 4.2.21 pharmacists could name drugs on which they have reported ADRs in their career and only 23 could name any such drugs. These results coincide with other studies that described South Africa's ADR reporting as poor (Maigetter, et al., 2015).

Opinion (25-40)

4.2.25 Role of the SAPC in pharmacovigilance.

Fifty-five participants answered this question and 15 did not. This question refers to the opinion of community pharmacists regarding the role of the SAPC, as the regulator, in promoting pharmacovigilance. Participants could only select one option.

Answer Choices	**Response**	
	%	N
Very prominent	10.91	6
Somewhat prominent	14.55	8
Hardly prominent	43.64	24
I am not sure	30.91	17
Total Respondents		**55**
Non-Respondents		**15**

Less than half (43.64%, N=24) of the participants believed that the SAPC's role has been hardly prominent, while less than a third (30.91%, N=17) claimed to be unsure. Six participants (10.91%) thought the SAPC's role had been very prominent. The SAPC, as the regulator, must ensure safe, quality pharmaceutical service to all South Africans (South African Pharmacy Council, n.d.(b)).

4.2.26 Support from employer in fulfilling pharmacovigilance responsibilities.

Fifty-five participants answered the question and 15 did not. Participants could only select one option.

Answer Choices	**Response**	
	%	**N**
Yes	58.18	32
No	21.82	12
I am not sure	20.00	11
Total Respondents		**55**
Non-Respondents		**15**

Over half (58.18%, N=32) of participants felt that they received enough support from their employer to fulfil their pharmacovigilance responsibilities. One fifth of the participants felt that they did not (21.82%, N=12) while another was not sure (20.00%, N=11). Even so, 40% of participants (N=22) cited in survey question 4.2.36 lack of support as one of the barriers to ADR reporting.

4.2.27 Pharmacovigilance education responsibility.

Fifty-five participants answered this question and 15 did not. This question was to determine, in the opinion of community pharmacists, who should be responsible for pharmacovigilance education and training. Participants could select as many options as applicable.

Answer Choices	**Response**	
	%	**N**
SAPC	76.36	42
Pharmaceutical Industry	49.09	27
Academia	54.55	30
SAHPRA	47.27	26
PSSA	52.73	29
Pharmacists through CPD	70.91	39
Total Respondents		**55**
Non-Respondents		**15**

Three quarters (76.36%, N=42) of the participants selected the SAPC, while a similar proportion opted for pharmacists themselves through CPD (70.91%, N=39). The SAPC, as the regulator established in terms of the Pharmacy Act, 1974 (Act 53 of 1974) has a mandate to promote the health, safety and wellbeing of patients and the public ensuring quality pharmaceutical service for South Africans (South African Pharmacy Council, n.d.(b)). Half of the participants identified the pharmaceutical industry (49.09%, N=27) and SAHPRA (47.27%, 26) as the least responsible provider to offer pharmacovigilance education and training.

4.2.28 Clinical Trial information as adequate safety information.

Fifty-five participants answered this question and 15 did not. This question was to determine if community pharmacists regarded clinical trials as adequate in determining the safety profile of registered medicinal products. Participants could only select one option.

Answer Choices	**Response**	
	%	N
Yes	54.55	30
No	30.91	17
I am not sure	14.55	8
Total Respondents		55
Non-Respondents		15

More than half of pharmacists (54.55%, N=30) believed that clinical trials provided adequate safety data for medicinal products. Less than a fifth (14.55%, N=8) of the participants were not sure. Clinical trials do not provide adequate information regarding the safety of medicines (World Health Organisation (WHO), 2002). This may indicate a lack of understanding of the process of drug development.

4.2.29 ADR reporting on the ADR report form as part of the clinical and legal competence of pharmacists.

Fifty-five participants answered this question and 15 did not. This question was to determine if pharmacists regarded ADR reporting as outside their clinical and legal competence. Only one option could be selected.

Answer Choices	**Results**	
	%	**N**
Yes	10.91	6
No	72.73	40
I am not sure	16.36	9
Total Respondents		**55**
Non-Respondents		**15**

Almost three quarters (72.73%, N=40) of the participants were of the opinion that ADR reporting on the ADR report form was not outside their scope of clinical and legal competence, with 10.91% (N=6) of them indicating that it was so. Less than a fifth (16.36%, N=9) of the participants were not sure. The study by Williams (2015) in the Western Cape also identified participants that were of the opinion that it was outside the scope of practice as pharmacists.

4.2.30 ADR reporting by public health sector pharmacists versus community pharmacists.

Fifty-five pharmacists answered this question and 15 did not. This question was to determine if community pharmacists regarded ADR reporting to be more relevant to pharmacists working in public health sectors. Only one option could be selected.

Answer Choices	**Results**	
	%	N
Yes	16.36	9
No	76.36	42
I am not sure	7.27	4
Total Respondents		**55**
Non-Respondents		**15**

Over three quarters (76.36%, N=42) of the participants did not regard ADR reporting to be more relevant to pharmacists working in the public health sector.

4.2.31 Pharmaceutical companies and regulators rely on ADR reporting by pharmacists.

Fifty-five participants answered this question and 15 did not. Pharmacists could select as many options as applicable. This question was asked to determine if pharmacists were aware of the importance of ADR reporting. The options which provided aimed to reveal what pharmacists would do if they knew the importance of ADRs.

Answer Choices	Results	
	%	N
Become more aware of ADRs	67.27	37
Ensure that I received the required training	74.55	41
Be proactive in filling in the ADR report form	70.91	39
Other	3.64	2
Total Respondents		**55**
Non-Respondents		**15**

Most participants (74.55%, N=41) indicated that they would ensure that they received the required training if they knew that regulators and the industry relied on this information to guarantee the safety of medicinal products. A high proportion (70.91%, N=39) of participants selected that they would fill in the ADR report form. This result reflects the conclusion of similar studies done in the Western Cape Province, where pharmacists indicated that they are willing to cooperate in order to improve pharmacovigilance systems (Williams, 2015), and are prepared to participate in further pharmacovigilance training (Joubert and Naidoo, 2016). Participants who selected "other" (3.64%, N=2) also listed being proactive in monitoring pharmacovigilance. One participant under "other" displayed his frustration at none of the above options reflecting the reality of working in community pharmacy, and added that pharmaceutical representatives are only interested in marketing their product and are not interested in any feedback regarding ADRs.

4.2.32 Number of ADRs reported on ADR report form in career.

Fifty-five participants answered this question and 15 did not. This question was to determine if participants have used the ADR report form in their career and asked how many ADR report forms they have submitted in their career. Participants could only select one option.

Answer Choices	Results	
	%	N
Less than 3	87.27	48
Between 3 and 5	9.09	5
Between 5 and 10	0.00	0
More than 10	3.64	2
Total Respondents		**55**
Non-Respondents		**15**

This question relates to question 4.2.24, where participants had to state how many ADRs they have reported on the ADR report form in this year, and to question 4.2.21, where they had to name a few examples of drugs on which they have reported ADRs. Most participants (87.27%, N=48) stated that they have filled in less than 3 ADRs report forms in their career. Only 2 participants (3.64%) selected more than 10 and they were in the age group 31-50 years with one participant having had 2-5 years and the other having had 10-20 years of community pharmacy experience.

4.2.33 ADR reporting burdens.

Fifty-five participants answered this question and 15 did not. This question was asked to determine what the biggest deterrent for pharmacists in the reporting of ADRs was. Pharmacists were asked to only choose one deterrent to ADR reporting.

Answer Choices	Results	
	%	**N**
It may overburden the PSSA	3.64	2
It may overburden SAHPRA	1.82	1
It may overburden the pharmaceutical company	3.64	2
The company I work for	3.64	2
My work load	34.55	19
I have no concerns	52.73	29
Total Respondents		**55**
Non-Respondents		**15**

About half of the participants (52.73%, N=29) selected that they had no concerns. A third (34.55%, N=19) of them acknowledged that their workload was a concern when it came to ADR reporting.

4.2.34 Feelings towards ADR reporting as part of pharmacovigilance responsibilities.

Fifty-five pharmacists answered this question and 15 did not. This question related to the concerns pharmacists had with regard to ADR reporting. Participants could select as many options as applicable.

Answer Choices	**Results**	
	%	**N**
I do not have enough time	16.36	9
I am not confident in filling in the ADR report form	29.09	16
ADRs are not a common occurrence, therefore I tend to overlook it	40.00	22
The report is not an immediate concern therefore I tend to neglect it	14.55	8
It is not my responsibility	1.82	1
None of the above	32.73	18
Total Respondents		**55**
Non-Respondents		**15**

Less than a third (29.09%, N=16) of participants selected that they were not confident in filling in the ADR report form, which relates to the need for further training. In question 4.2.9, almost three quarters (72.13%) of participants indicated that they had never received training in pharmacovigilance after graduation. Less than a fifth (16.36%, N=9) of the participants indicated that they did not have enough time, which further relates to the previous question (4.2.33), where a third (34.55%) of participants indicated that it would overburden their workload. Less than half (40%, N=22) of pharmacists admitted that they tended to overlook it as it was not a common occurrence. One participant indicated that they did not consider it their responsibility. The participants who selected “none of the above” (32.73%, N=18)

could either have other concerns or no concerns. This question could have provided more information if the option “other” had been given.

4.2.35 The shortage of pharmacists as a factor influencing ADR reporting.

Fifty-five participants answered this question and 15 did not. Participants were asked if they thought the shortage of pharmacists affected pharmacovigilance. Participants could select more than one option.

Answer Choices	**Results**	
	%	N
Is partly to blame for the lack of time and support provided by employers to maintain pharmacovigilance	27.27	15
Is one of the reasons pharmacists are reluctant in taking on pharmacovigilance responsibilities	36.36	20
Does not affect pharmacovigilance	50.91	28
Total Respondents		**55**
Non-Respondents		**15**

Over a quarter (27.27%, N=15) of the participants regarded the shortage of pharmacists as partly to blame for employers not supporting pharmacovigilance and over a third (36.36%, N=20) of them regarded the shortage of pharmacists as one of the reasons employees did not pursue pharmacovigilance. About half (50.91%, N=28) of the respondents did not think that the shortage of pharmacists affected pharmacovigilance.

4.2.36 Main obstacles to pharmacovigilance.

Fifty-five participants answered the question and 15 did not. Participants were asked to select the main obstacles to pharmacovigilance in their opinion. Participants could select as many options as possible.

Answer Choices	Results	
	%	N
Lack of training	87.27	48
Lack of pharmacists	25.45	14
Lack of time	34.55	19
Lack of incentive	16.36	9
Lack of feedback	58.18	32
Lack of support	40.00	22
Other	7.27	4
Total Respondents		**55**
Non-Respondents		**15**

The majority (87.27%, N= 48) of participants selected lack of training, which is higher than the percentage responses received to question 4.2.9, where almost three quarter (72.13%) indicated that they had never received pharmacovigilance training, which was lower than the percentage responses received to question 4.2.34, where over a quarter (29.09%) of participants claimed that they were not confident in filling in the ADR report from. A quarter (25.45%, N=14) of the participants selected lack of pharmacists as an obstacle to pharmacovigilance training. However in question 4.2.35, half (50.91%) of participants selected that the shortage of pharmacists did not affect pharmacovigilance. These results are not consistent with one another. Participants could be referring to the lack of pharmacists in the pharmacy they work in and not necessarily to the shortage of pharmacists nationally. Over a quarter (27.27%, N=15) of participants alluded to the shortage of pharmacists as a factor contributing to employers lacking the time and support for pharmacovigilance, while over a third (36.36%, N=20) further added that such human resource shortage led to pharmacists being reluctant in undertaking pharmacovigilance responsibilities in question 4.2.35.

A third (34.55%, N=19) of the participants selected lack of time which correlated with question 4.2.34, where less than a fifth (16.36%) of participants selected that they did not have the time. In question 4.2.33, a third (34.55%) of the participants

selected that their extreme workload was one of the reasons they had for not reporting ADRs.

Four (7.27%) participants noted that the form was not easy to fill in, that it required data that pharmacists did not have i.e. laboratory results, that there was a lack of a standardised unbiased database of products to check ADRs, and that patients did not report back to the pharmacist when they experienced ADRs. These results were consistent with other UK studies, where almost half of the participants (46.6%) stated that lack of time prevented them from reporting ADRs (Cheema, et al., 2017), and in Jordan, where similar barriers to ADR reporting were found (Suyagh, Farah and Abu Farha, 2014). These barriers were also listed by South African studies conducted in the Western Cape (Williams, 2015), the North West Province (Joubert and Naidoo, 2016) and in the Eastern Cape (Ruud, Srinivas and Toverud, 2010).

4.2.37 Pharmacist access to ADRs experienced by patients.

Fifty-five participants answered this question and 15 did not. Participants were asked whether they feel patients trust them enough to discuss ADRs with them. Participants could only select one option.

Answer Choices	**Results**	
	%	**N**
Yes	83.64	46
No	9.09	5
I am not sure	7.27	4
Total Respondents		**55**
Non-Respondents		**15**

The majority (83.64%, N=46) indicated that patients trusted them enough to talk to them about ADRs, 9.09% (N=5) of them noted that they did not feel patients trusted them enough, and 7.27% (N=4) were not sure. Community pharmacists are often the first point of call for patients when ADRs arise.

4.2.38 Patient expectations of pharmacists regarding ADRs.

Fifty-five answered this question and 15 did not. This question was asked to ascertain whether pharmacists thought patients expect them to manage the ADRs they were experiencing. Participants could only select one option.

Answer Choices	**Results**	
	%	N
Yes	96.36	53
No	1.82	1
I am not sure	1.82	1
Total Respondents		55
Non-Respondents		15

Almost all (96.36%, N=53) of the participants stated that they thought patients expected them to be proactive when it came to ADRs management, indicating the desire and need for ongoing training and support from stakeholders.

4.2.39 Location of the ADR report form on the internet.

Fifty-five participants answered this question and 15 did not. This question was asked to determine if pharmacists knew where to find the ADR report form on the SAHPRA website. Participants could only select one option.

Answer Choices	**Results**	
	%	N
Yes	69.09	38
No	12.73	7
I am not sure	18.18	10
Total Respondents		**55**
Non-Respondents		**15**

Over two thirds (69.09%, N=38) of the participants believed the ADR report form could be easily found on the internet. Almost one fifth (18.18%, N=10) was not sure. The form is not easily found on the SAHPRA website, as it can only be accessed under the “Application Forms” menu, under “Publications” (South African Health Products Regulatory Authority (SAHPRA), n.d.).

4.2.40 Responsibility for reporting ADRs on the ADR reporting form and assisting with the identification of problems with drugs post-market.

Fifty-five participants answered this question and 15 did not. Participants could only select one option. This question was asked to determine if pharmacists regarded ADR reporting on the ADR report form more of the prescriber's responsibility.

Answer choices	**Results**	
	%	**N**
Yes	34.55	19
No	50.91	28
I am not sure	14.55	8
Total Respondents		**55**
Non-Respondents		**15**

Half (50.91%, N=28) the number of participants selected that it was not the prescriber's responsibility, while a third (34.55%, N=19) believed that it was the prescriber's responsibility to complete ADR report forms. Such responses indicated that pharmacists are passing the responsibility to report ADRs to the prescribers. In another study in the Western Cape, a participant also considered that pharmacists should keep the forms and make sure they are filled in, but the relevant doctor or nurse should complete the form (Williams, 2015). It is not clear if pharmacovigilance is part of the medical doctor degree's curriculum.

4.3. COMPARISON OF LEVEL OF KNOWLEDGE BETWEEN PROVINCES

This section aimed to test the knowledge of community pharmacists regarding ADR reporting, using the ADR report form. The aim was to compare the knowledge level between provinces statistically. Unfortunately, due to the low response rate overall and from the individual provinces, data was inadequate to make statistical comparisons. Question 4.2.7, was used to ascertain the knowledge among participants across the nine provinces.

4.3.1 Pharmacists' first encounter with pharmacovigilance (survey question 8).

Sixty-one participants answered this question and 9 did not. This question related to

the pharmacist's first encounter with pharmacovigilance. Participants could only select one option.

	Answer Choices							
Province	**SAPC**	**SAHPRA**	**Industry**	**CPD**	**Academia**	**Can't remember**	**Other**	**Total N**
WC	33.33% N=3	0.00% N=0	0.00% N=0	11.11% N=1	33.33% N=3	22.22% N=2	0.00% N=0	**9**
EC	33.33% N=2	0.00% N=0	0.00% N=0	16.67% N=1	33.33% N=2	0.00% N=0	16.67% N=1	**6**
KZN	0.00% N=0	0.00% N=0	11.11% N=1	22.22% N=2	44.44% N=4	11.11% N=1	11.11% N=1	**9**
GP	10.00% N=2	10.00% N=2	5.00% N=1	0.00% N=0	65.00% N=13	10.00% N=2	0.00% N=0	**20**
NW	0.00% N=0	0.00% N=0	0.00% N=0	0.00% N=0	66.67% N=2	33.33% N=1	0.00% N=0	**3**
LP	0.00% N=0	0.00% N=0	0.00% N=0	0.00% N=0	100.00% N=2	0.00% N=0	0.00% N=0	**2**
FS	0.00% N=0	0.00% N=0	0.00% N=0	16.67% N=1	50.00% N=3	33.33% N=2	0.00% N=0	**6**
NC	0.00% N=0	0.00% N=0	0.00% N=0	0.00% N=0	100.00% N=1	0.00% N=0	0.00% N=0	**1**
MP	20.00% N=1	0.00% N=0	20.00% N=1	0.00% N=0	60.00% N=3	0.00% N=0	0.00% N=0	**5**
Total N	**8**	**2**	**3**	**5**	**31**	**8**	**4**	**61**

Participants in most provinces listed academia as the first institution where they had heard mention of pharmacovigilance, whereas those located in the Western Cape (33.33%, N=3), the Eastern Cape (33.33%, N=2), Gauteng (10.00%, N=2) and Mpumalanga (20.00%, N=1) province had also identified with the SAPC. Other institutions which the participants had referred to included company Standard Operating Procedures (SOPs) for the Eastern Cape and Groote Schuur hospital in the Western Cape.

4.3.2 Pharmacovigilance training after qualifying as a pharmacist (survey question 9).

Sixty-one participants answered this question and 9 selected not to answer. This question was asked to ascertain whether any training existed for pharmacists after qualifying as a pharmacist.

	Answer Choices			
Province	**Yes**	**No**	**I am not sure**	**Total N**
WC	33.33% N=3	55.56% N=5	11.11% N=1	**9**
EC	0.00% N=0	100.00% N=6	0.00% N=0	**6**
KZN	11.11% N=1	88.89% N=8	0.00% N=0	**9**
GP	20.00% N=4	60.00% N=12	20.00% N=4	**20**
NW	33.33% N=1	66.67% N=2	0.00% N=0	**3**
LP	0.00% N=0	100.00% N=2	0.00% N=0	**2**
FS	33.33% N=2	66.67% N=4	0.00% N=0	**6**
NC	0.00% N=0	100.00% N=1	0.00% N=0	**1**
MP	20.00% N=1	80.00% N=4	0.00% N=0	**5**
Total N Respondents	**12**	**44**	**5**	**61**

Most of the participants across the provinces indicated that they had not received any training. Notably a higher percentage of responses were obtained from participants located in the Western Cape (33.33%, N=3), North West (33.33%, N=1) and Free State (33.33%, N=1) compared to those from Gauteng (20.00%, N=4), Mpumalanga (20.00%, N=1) and KwaZulu-Natal (11.11%, N=1).

The Eastern Cape, Limpopo and Northern Cape Province participants had not received any training in pharmacovigilance after qualifying. These figures coincide

with the low number of pharmacists in some these provinces and therefore training opportunities. With only 65 pharmacists registered community pharmacists, who are located in the Northern Cape (South African Pharmacy Council (SAPC), 2017), such a limited human resource could explain poor exposure to pharmacovigilance training opportunities.

A census in 2011 indicated that the Western Cape had the highest percentage of schooling and employment, while Limpopo and the Eastern Cape had the lowest percentage (Statistics SA, 2011). All the provinces except the Western Cape (22.22%) listed academia as the institution where participants had first encountered pharmacovigilance, further indicating poor exposure to pharmacovigilance training opportunities.

4.3.3 Training facilitator (survey question 10).

Sixty-one participants answered this question and 9 selected not to answer. This question inquired who provided the training from the previous question. Participants were invited to select as many options as applicable.

	Answer Choices						
Province	**SAPC**	**Industry**	**Higher Education**	**PSSA**	**No training**	**Other**	**Total N**
WC	0.00% N=0	11.11% N=1	11.11% N=1	0.00% N=0	66.67% N=6	11.11% N=1	**9**
EC	0.00% N=0	0.00% N=0	0.00% N=0	0.00% N=0	100.00% N=6	0.00% N=0	**6**
KZN	0.00% N=0	11.11% N=1	0.00% N=0	0.00% N=0	77.78% N=7	11.11% N=1	**9**
GP	0.00% N=0	10.00% N=2	15.00% N=3	10.00% N=2	65.00% N=13	5.00% N=1	**21**
NW	0.00% N=0	0.00% N=0	33.33% N=1	0.00% N=0	66.67% N=2	0.00% N=0	**3**
LP	0.00% N=0	0.00% N=0	0.00% N=0	0.00% N=0	100.00% N=2	0.00% N=0	**2**
FS	0.00% N=0	0.00% N=0	33.33% N=2	0.00% N=0	50.00% N=3	16.67% N=1	**6**
NC	0.00% N=0	0.00% N=0	0.00% N=0	0.00% N=0	100.00% N=1	0.00% N=0	**1**
MP	0.00% N=0	40.00% N=2	0.00% N=0	0.00% N=0	60.00% N=3	0.00% N=0	**5**
Total N Responses	**0**	**6**	**7**	**2**	**43**	**4**	**61**

Participants from the Western Cape (11.11%, N=1), KwaZulu-Natal (11.11%, N=1) and Gauteng (10%, N=2) seemed to have minimal training from industry compared to those located in the Mpumalanga Province (40%, N=2).

Participants from the Western Cape (11.11%, N=1), Gauteng (15.00%, N=3), North West (33.33%, N=1) and Free State Province (33.33%, N=2) indicated that they had received training from academia. Participants from Gauteng (10.00%, N=2) had also selected PSSA as a training provider. Other training facilitators mentioned under the option "other" included the Northern Cape Department of Health for the Western Cape, Groote Schuur Hospital for KwaZulu-Natal, public sector hospitals for Gauteng Province and the Positive Impact CPD Programme which is linked to some chain

pharmacies for the Free State Province. The varied bodies offering pharmacovigilance training may be reflective of the lack of standardisation in pharmacovigilance understanding and practice among community pharmacists.

4.3.4 What ADR reporting entailed according to community pharmacists (survey question 11).

In this study 61 of the participants answered the question and 9 did not answer. Participants were invited to select as many options as applicable. This question refers to the number of participants who actually filled in an ADR report form.

	Answer Choices				
Provinces	**Contact the prescriber**	**Referring patient to prescriber**	**Filling in the ADR report form**	**Making a note on the PMR**	**Total N**
WC	55.56% N=5	66.67% N=6	100.00% N=9	77.78% N=7	**27**
EC	100.00% N=6	50.00% N=3	83.33% N=5	83.33% N=5	**19**
KZN	88.89% N=8	88.89% N=8	88.89% N=8	88.89% N=8	**32**
GP	60.00% N=12	60.00% N=12	95.00% N=19	75.00% N=15	**58**
NW	66.67% N=2	66.67% N=2	66.67% N=2	100.00% N=3	**9**
LP	0.00% N=0	0.00% N=0	100.00% N=2	0.00% N=0	**2**
FS	83.33% N=5	66.67% N=4	83.33% N=5	66.67% N=4	**18**
NC	100.00% N=1	100.00% N=1	100.00% N=1	100.00% N=1	**4**
MP	60.00% N=3	40.00% N=2	100.00% N=5	80.00% N=4	**14**
Total Responses	**42**	**38**	**56**	**47**	**61**

Participants from the Western Cape (100.00%, N=9), Mpumalanga Province (100%, N=5), Limpopo (100.00%, N=2) and Northern Cape (100.00%, N=1) all indicated that

ADR reporting entailed filling in an ADR report form. The province with the lowest ADR report form use was the North West Province at 66.67% (N=2).

4.3.5 ADRs that qualify for reporting (survey question 12).

In this study 61 of the participants answered the question and 9 did not answer. Participants were invited to select as many options as applicable. This question asked whether community pharmacists knew what adverse drug reactions were reportable.

	Answer Choices									
Province	**New drugs ADRs**	**All ADRs in PIL**	**Serious ADRs**	**Ambiguous ADRs**	**Unusual ADRs**	**Product Quality problems**	**Package Quality problems**	**Treatment failures**	**Herbal**	**Total N**
WC	77.78% N=7	33.33% N=3	88.89% N=8	33.33% N=3	88.89% N=8	55.56% N=5	22.22% N=2	11.11% N=1	66.67% N=6	**43**
EC	83.33% N=5	50.00% N=3	83.33% N=5	66.67% N=4	100.00 % N=6	33.33% N=2	33.33% N=2	50.00% N=3	66.67% N=4	**34**
KZN	77.78% N=7	33.33% N=3	88.89% N=8	22.22% N=2	88.89% N=8	77.78% N=7	44.44% N=4	55.56% N=5	66.67% N=6	**50**
GP	65.00% N=13	40.00% N=8	85.00% N=17	35.00% N=7	80.00% N=16	70.00% N=14	45.00% N=9	30.00% N=6	60.00% N=12	**102**
NW	33.33% N=1	0.00% N=0	66.67% N=2	33.33% N=1	100.00 % N=3	66.67% N=2	33.33% N=1	33.33% N=1	33.33% N=1	**12**
LP	50.00% N=1	50.00% N=1	100.00% N=2	50.00% N=1	100.00 % N=2	50.00% N=1	100.00 % N=2	50.00% N=1	100.00 % N=2	**13**
FS	66.67% N=4	16.67% N=1	83.33% N=5	50.00% N=3	50.00% N=3	33.33% N=2	16.67% N=1	0.00% N=0	66.67% N=4	**23**
NC	100.00 % N=1	100.00 % N=1	100.00% N=1	0.00% N=0	100.00 % N=1	0.00% N=0	0.00% N=0	0.00% N=0	0.00% N=0	**4**
MP	80.00% N=4	60.00% N=3	80.00% N=4	60.00% N=3	80.00% N=4	40.00% N=2	40.00% N=2	0.00% N=0	60.00% N=3	**25**
Total Responses	**43**	**23**	**52**	**24**	**51**	**35**	**23**	**17**	**38**	**61**

All the above options are true, except the option “All ADRs in the PIL experienced by the patient”. All ADRs in the PIL experienced by the patient should not be reported on the ADR report form and this would lead to a considerable increase in workload if they were. The North West Province was the only province where the participants did not select the incorrect option, even though a census in 2011 showed that the North West Province had the lowest number of people with a higher education (Statistics SA, 2011).

4.3.6 Serious Adverse Events (survey question 13).

Sixty-one participants answered this question and 9 did not. The question aimed to establish whether pharmacists knew what adverse reactions were regarded as serious. Participants were invited to select as many as deemed applicable.

	Answer Choices					
Provinces	**Life-threatening**	**Disability**	**Death**	**Hospitali-sation**	**Sick leave at home**	**Total N**
WC	100.00% N=9	77.78% N=7	100.00 % N=9	77.78% N=7	22.22% N=2	**34**
EC	100.00% N=6	50.00% N=3	66.67% N=4	66.67% N=4	16.67% N=1	**18**
KZN	100.00% N=9	77.78% N=7	100.00 % N=9	88.89% N=8	11.11% N=1	**34**
GP	100.00% N=20	75.00% N=15	80.00% N=16	85.00% N=17	40.00% N=8	**76**
NW	100.00% N=3	100.00% N=3	100.00 % N=3	100.00% N=3	0.00% N=0	**12**
LP	100.00% N=2	0.00% N=0	0.00% N=0	0.00% N=0	0.00% N=0	**2**
FS	100.00% N=6	83.33% N=5	100.00 % N=6	100.00% N=6	33.33% N=2	**25**
NC	100.00% N=1	100.00% N=1	100.00 % N=1	100.00% N=1	0.00% N=0	**4**
MP	100.00% N=5	60.00% N=3	60.00% N=3	80.00% N=4	40.00% N=2	**17**
Total Responses	**61**	**44**	**51**	**50**	**16**	**61**

All the above options are true, except for sick leave at home. Participants from the provinces who had selected all the correct options were those from the North West, Limpopo and Northern Cape Province. The incorrect option was mostly selected by Gauteng (40%, N=8) and Mpumalanga Province (40%, N=2) participants.

4.3.7 Pharmacovigilance responsibilities (survey question 14).

Sixty-one pharmacists answered this question and 9 did not. This question related to the pharmacovigilance knowledge of pharmacists as to whether they regarded the options given as part of their pharmacovigilance responsibilities. Pharmacists were invited to select as many options as deemed relevant.

	Answer Choices										
Provinces	**ADRs**	**Substandard drugs**	**Medication Errors**	**Unsubstantiated off-licence use**	**Abuse and misuse**	**Lack of efficacy**	**Poisoning**	**D/I with drugs, herbs, food and chemicals**	**Drug related mortality**	**Expired stock**	**Total N**
WC	100.00 % N=9	44.44% N=4	44.44% N=4	44.44% N=4	77.78% N=7	33.33% N=3	66.67 % N=6	77.78 % N=7	77.78 % N=7	22.22 % N=2	**53**
EC	100.00 % N=6	33.33% N=2	50.00% N=3	33.33% N=2	83.33% N=5	33.33% N=2	50.00 % N=3	66.67 % N=4	66.67 % N=4	0.00 % N=0	**31**
KZN	100.00 % N=9	44.44% N=4	66.67% N=6	66.67% N=6	66.67% N=6	22.22% N=2	66.67 % N=6	77.78 % N=7	66.67 % N=6	22.22 % N=2	**54**
GP	95.00% N=19	60.00% N=12	55.00% N=11	55.00% N=11	50.00% N=10	45.00% N=9	50.00 % N=10	75.00 % N=15	80.00 % N=16	35.00 % N=7	**120**
NW	100.00 % N=3	33.33% N=1	66.67% N=2	0.00% N=0	33.33% N=1	0.00% N=0	66.67 % N=2	100.00 % N=3	66.67 % N=2	0.00 % N=0	**14**
LP	50.00% N=1	0.00% N=0	0.00% N=0	0.00% N=0	100.00 % N=2	0.00% N=0	100.00 % N=2	100.00 % N=2	50.00 % N=1	50.00 % N=1	**9**
FS	83.33% N=5	33.33% N=2	16.67% N=1	66.67% N=4	66.67% N=4	33.33 % N=2	50.00 % N=3	66.67% N=4	66.67 % N=4	16.67 % N=1	**30**
NC	100.00 % N=1	100.00 % N=1	100.00 % N=1	100.00 % N=1	100.00 % N=1	0.00 % N=0	100.00 % N=1	100.00 % N=1	100.00 % N=1	100.00 % N=1	**9**
MP	100.00 % N=5	60.00% N=3	40.00% N=2	60.00% N=3	40.00% N=2	40.00 % N=2	40.00 % N=2	80.00 % N=4	80.00 % N=4	20.00 % N=1	**28**
Total N Responses	**58**	**29**	**30**	**31**	**38**	**20**	**35**	**47**	**45**	**15**	**61**

All the options relate to the pharmacovigilance responsibilities of pharmacists and therefore all options should have been selected. Most of the correct answers were obtained from a Northern Cape Province participant (100%, N=1).

4.3.8 Pharmacovigilance as a legal obligation (survey question 15).

In this question 61 participants selected to answer and 9 did not. The purpose of the question was to establish whether pharmacists realised that pharmacovigilance was a legal obligation. The question however asked if it was a legal obligation in *their opinion*. Participants could only select one option.

	Answer Choices			
Provinces	**Yes**	**No**	**I am not sure**	**Total N**
WC	66.67% N=6	0.00% N=0	33.33% N=3	**9**
EC	66.67% N=4	0.00% N=0	33.33% N=2	**6**
KZN	77.78% N=7	0.00% N=0	22.22% N=2	**9**
GP	85.00% N=17	5.00% N=1	10.00% N=2	**20**
NW	100.00% N=3	0.00% N=0	0.00% N=0	**3**
LP	100.0% N=2	0.00% N=0	0.00% N=0	**2**
FS	66.67% N=4	0.00% N=0	33.33% N=2	**6**
NC	100.00% N=1	0.00% N=0	0.00% N=0	**1**
MP	80.00% N=4	20.00% N=1	0.00% N=0	**5**
Total Respondents	**48**	**2**	**11**	**61**

Most respondents came from Gauteng with 85% of them (N=17) regarding pharmacovigilance as a legal obligation and 5% (N=1) not. All respondents from North West (N=3), Limpopo (N=2) and Northern Cape Province (N=1) regarded

pharmacovigilance as a legal obligation. One participant from Mpumalanga Province did not regard pharmacovigilance as a legal obligation.

4.3.9 The fate of ADRs once reported on the ADR report form (survey question 16).

Sixty-one participants answered this question and 9 did not. This question aimed to establish if pharmacists knew what happened to the ADR report form once it was sent to the relevant authorities. Participants were required to select as many options as applicable.

	Answer Choices				
Provinces	**Reviewed by NADEMC**	**Reported to UMC**	**Assessed by SAHPRA**	**Assessed by MIC**	**Total N**
WC	55.56% N=5	11.11% N=1	55.56% N=5	55.56% N=5	**16**
EC	16.67% N=1	16.67% N=1	83.33% N=5	50.00% N=3	**10**
KZN	55.56% N=5	33.33% N=3	33.33% N=3	55.56% N=5	**16**
GP	60.00% N=12	25.00% N=5	65.00% N=13	60.00% N=12	**42**
NW	66.67% N=2	33.33% N=1	66.67% N=2	66.67% N=2	**7**
LP	50.00% N=1	50.00% N=1	100.00% N=2	0.00% N=0	**4**
FS	66.67% N=4	16.67% N=1	50.00% N=3	83.33% N=5	**13**
NC	0.00% N=0	0.00% N=0	100.00% N=1	100.00% N=1	**2**
MP	60.00% N=3	40.00% N=2	60.00% N=3	20.00% N=1	**9**
Total Responses	**33**	**15**	**37**	**34**	**61**

Only the first three options are correct. Participants from the Limpopo Province were represented as the only province that did not select the wrong option. Less than 50% of participants knew that the WHO UMC in Sweden reviewed ADRs.

4.3.10 WHO definition of pharmacovigilance (survey question 17).

Sixty-one answered the question and 9 did not. This question established whether pharmacists were familiar with the WHO definition of pharmacovigilance. Participants could only select one option.

	Answer Choices			
Provinces	**Science and activities related to detection and assessment of ADRs**	**Science and activities related to understanding and prevention of ADRs**	**All of the Above**	**Total N**
WC	22.22% N=2	22.22% N=2	55.56% N=5	**9**
EC	16.67% N=1	16.67% N=1	66.67% N=4	**6**
KZN	0.00% N=0	33.33% N=3	66.67% N=6	**9**
GP	25.00% N=5	10.00% N=2	65.00% N=13	**20**
NW	0.00% N=0	0.00% N=0	100.00% N=3	**3**
LP	0.00% N=0	50.00% N=1	50.00% N=1	**2**
FS	50.00% N=3	16.67% N=1	33.33% N=2	**6**
NC	0.00% N=0	0.00% N=0	100.00% N=1	**1**
MP	60.00% N=3	20.00% N=1	20.00% N=1	**5**
Total N Respondents	**14**	**11**	**36**	**61**

Both statements related to the WHO definition of pharmacovigilance. Participants from the North West (N=3) and Northern Cape Province (N=1) selected the correct options.

4.3.11 Drugs withdrawn from the market for safety reasons (survey question 18).

Sixty-one participants answered the question and 9 did not. This question was asked in order to establish whether pharmacists knew of drugs that had previously been withdrawn with the aim of highlighting the serious need for post-market surveillance in maintaining drug safety. The question was however to be answered "from their practice experience".

Provinces	Number of drug examples given	None or unknown	Total N
WC	77.7% N=7	22.22% N=2	**9**
EC	83.33% N=5	16.67% N=1	**6**
KZN	88.89% N=8	11.11% N=1	**9**
GP	90.00% N=18	10.00% N=2	**20**
NW	100.00% N=3	0.00% N=0	**3**
LP	100.00% N=2	0.00% N=0	**2**
FS	66.67% N=4	33.33% N=2	**6**
NC	100.00% N=1	0.00% N=0	**1**
MP	100.00% N=5	0.00% N=0	**5**
Total Respondents	**53**	**8**	**61**

Participants from the North West (100%, N=3), Limpopo (100%, N=2), Northern Cape (100%, N=1) and Mpumalanga Province (100%, N=5) provided the most examples. Responses from other provinces included rofecoxib, Vioxx® and Locabiotal®. In addition, responses from participants also included thalidomide, a drug which was withdrawn in 1962, therefore ADR reporting would not have occurred during their practice experience. One participant stated warfarin and another tetracycline which were both incorrect.

4.3.12 Authorities to which the ADR report form is sent (survey question 19).

Sixty-one participants responded and 9 did not. This question was asked to establish whether pharmacists knew where to send the ADR report form for assessment. Participants could only select one option.

	Answer Choices				
	SAHPRA	**NADEMC**	**All of the above**	**I am not sure**	**Total N**
WC	0.00% N=0	33.33% N=3	44.44% N=4	22.22% N=2	**9**
EC	16.67% N=1	0.00% N=0	16.67% N=1	66.67% N=4	**6**
KZN	11.11% N=1	44.44% N=4	22.22% N=2	22.22% N=2	**9**
GP	5.00% N=1	20.00% N=4	55.00% N=11	20.00% N=4	**20**
NW	0.00% N=0	0.00% N=0	66.67% N=2	33.33% N=1	**3**
LP	50.00% N=1	0.00% N=0	50.00% N=1	0.00% N=0	**2**
FS	0.00% N=0	16.67% N=1	50.00% N=3	33.33% N=2	**6**
NC	0.00% N=0	0.00% N=0	0.00% N=0	100.00% N=1	**1**
MP	20.00% N=1	60.00% N=3	20.00% N=1	0.00% N=0	**5**
Total Respondents	**5**	**15**	**25**	**16**	**61**

The correct answer is all of the above. Most of the correct answers came from Gauteng (55.00%, N=11), North West (66.67%, N=2), Limpopo (50%, N=1) and Free State Province (50%, N=3) participants.

4.3.13 ADRs reported on the ADR form this past year (survey question 24).

Fifty-seven participants answered this question and 13 did not. Participants could only select one option.

	Answer Choices					
Provinces	**At least one**	**At least two**	**At least three**	**Four and more**	**None**	**Total N**
WC	33.33% N=3	0.00% N=0	0.00% N=0	0.00% N=0	66.67% N=6	**9**
EC	0.00% N=0	0.00% N=0	0.00% N=0	0.00% N=0	100.00% N=5	**5**
KZN	12.50% N=1	0.00% N=0	12.50% N=1	0.00% N=0	75.00% N=6	**8**
GP	5.26% N=1	0.00% N=0	0.00% N=0	5.26% N=1	89.47% N=17	**19**
NW	0.00% N=0	0.00% N=0	0.00% N=0	0.00% N=0	100.00% N=3	**3**
LP	0.00% N=0	0.00% N=0	0.00% N=0	0.00% N=0	100.00% N=2	**2**
FS	50.00% N=3	0.00% N=0	0.00% N=0	0.00% N=0	50.00% N=3	**6**
NC	0.00% N=0	0.00% N=0	0.00% N=0	0.00% N=0	100.00% N=1	**1**
MP	50.00% N=2	0.00% N=0	0.00% N=0	0.00% N=0	50.00% N=2	**4**
Total Respondents	**10**	**0**	**1**	**1**	**45**	**57**

One participant in Gauteng Province (5.26%) indicated that they had reported four or more ADRs this year. One participant in KwaZulu-Natal (12.50%) indicated that they had reported at least three ADRs this year. In addition, Western Cape (33.33%, N=3), KwaZulu-Natal (12.50%, N=1), Gauteng (5.26%, N=1), Free State (50.00%, N=3) and Mpumalanga Province (50.00%, N=2) respondents indicated that they had reported at least one ADR this year. The Eastern Cape, North West, Limpopo and Northern Cape Province respondents had not reported ADRs this past year.

4.3.14 Number of ADRs reported on ADR report form in career (survey question 32).

Fifty-five participants answered this question and 15 did not. This question was to determine if participants have ever used the ADR report form. Participants could only select one option.

	Answer Choices				
Provinces	**Less than 3**	**Between 3 and 5**	**Between 5 and 10**	**More than 10**	**Total N**
WC	88.89% N=8	11.11% N=1	0.00% N=0	0.00% N=0	**9**
EC	80.00% N=4	20.00% N=1	0.00% N=0	0.00% N=0	**5**
KZN	87.50% N=7	0.00% N=0	0.00% N=0	12.50% N=1	**8**
GP	88.89% N=16	5.56% N=1	0.00% N=0	5.56% N=1	**18**
NW	100.00% N=3	0.00% N=0	0.00% N=0	0.00% N=0	**3**
LP	50.00% N=1	50.00% N=1	0.00% N=0	0.00% N=0	**2**
FS	100.00% N=5	0.00% N=0	0.00% N=0	0.00% N=0	**5**
NC	0.00% N=0	100.00% N=1	0.00% N=0	0.00% N=0	**1**
MP	100.00% N=4	0.00% N=0	0.00% N=0	0.00% N=0	**4**
Total Respondents	**48**	**5**	**0**	**2**	**55**

Participants in KwaZulu-Natal (12.50%, N=1) and Gauteng Province (5.56%, N=1) had reported more than 10 ADRs on an ADR report form during their career. Most participants had reported less than 3 ADRs, with North West and Mpumalanga Province reporting the fewest. KwaZulu-Natal had the highest Human Immunodeficiency Virus (HIV) infection figures in 2014, but HIV infection was currently increasing in the Western Cape (Zuma, Manzin and Mohlabane, 2014). A higher number of ADR reports can be associated with more complicated drug regimens as can be found in HIV. Life expectancy in KwaZulu-Natal and Mpumalanga was about a decade lower than the Western Cape (Bradshaw et. al., 2006) and diseases (e.g. tuberculosis, diarrhoea) due to poverty are more prevalent in the rural provinces. This could indicate that ADR reporting is more prevalent in provinces with a high percentage of communicable diseases regardless of training available from academia or pharmaceutical industries in these areas. It could also indicate that community pharmacists have a more pivotal role in poorer provinces.

4.4 CONCLUSIONS

This chapter delivered the results for this quantitative research study. The results of the survey, including the collection methods and data analysis were examined.

Data was analysed using descriptive statistics.

The findings indicated that community pharmacists were more likely to report ADRs when their pharmacovigilance knowledge was high, however it also showed that good pharmacovigilance knowledge did not necessarily mean that participants are more likely to report ADRs. Poorer provinces had a higher rate of ADR reporting regardless of training available.

CHAPTER 5

DISCUSSION AND CONCLUSION

This study aimed to determine the knowledge, attitude and practice pattern of South African community pharmacists in ADR reporting. The study primarily focused on whether pharmacists use the ADR report form to manage ADRs as part of their pharmacovigilance responsibilities and whether they feel they have adequate support and training to do so.

Results from this quantitative study indicated that the knowledge of South African retail community pharmacists was low on pharmacovigilance. The study showed that very few participants (19.67%) had ever received any training in pharmacovigilance after qualifying. Most participants (91.80%) indicated that they regarded filling in the ADR report form as part of their pharmacovigilance responsibilities, however about three quarters (73.68%) of participants indicated that they would consider filling in the ADR report form in their practice. Only 40% of participants provided examples of drugs for which they had claimed to have filled in the ADR report form during the course of their career.

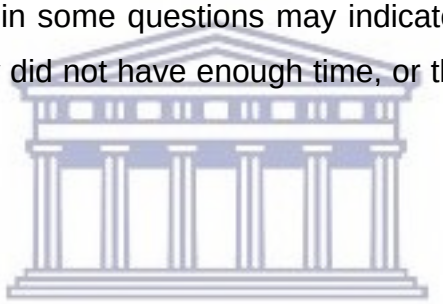
5.1 INTERPRETATION OF QUANTITATIVE RESULTS OF SURVEY QUESTIONNAIRE

5.1.1 Study sample and survey response rate

Response rates to surveys are notoriously low with internal company surveys aiming for a response rate of 30% and external surveys aiming for 10% (SurveyMonkey, 2018). Since the community pharmacist population is 1460 and only 82 responses were received, the response rate was only 5% (SurveyMonkey, 2018 (d)). The study therefore did not meet its target study sample. It was therefore not feasible to relate the results to all community pharmacists in South Africa. The lack of participants in this study may indicate the lack of time pharmacists have in pursuing administrative tasks, and the low average completion rate (70%) further supports this notion. A

census in 2011, showed that Gauteng had the greatest population size and the Northern Cape the smallest (Statistics SA, 2011). A third of the survey responses came from Gauteng (32.86%).

Only 82 participants responded to the survey out of a population of 1460 and of these respondents only 71 were pharmacists as confirmed by the SAPC (South African Pharmacy Coucil (SAPC), 2018(b)). It is hoped that pharmacists did not delegate the responsibility of completing the survey to non-pharmacist personnel. If this has been the case the results could explain the low and erratic knowledge scores, but would also elucidate another problem. A culture of apathy may be growing amongst South African community pharmacists. One participant did the survey twice leaving the study sample at 70. The high number of participants that selected the unsure option in some questions may indicate that the questions were either not clear, or that they did not have enough time, or they were not interested in the survey.



5.1.2 Demographics

The results show the approximate even split between the ages of participants, years of experience as a community pharmacist and gender.

Eleven participants were not in fact pharmacists. It is not clear why some non-pharmacists participants answered the survey. They either took it upon themselves to answer the survey, or the task of answering the questionnaire was delegated to them and this could indicate lack of time, or lack of interest. In the questions relating to position in the pharmacy and qualification held, some of the respondents selected that they were pharmacists but had the qualification of post-basic pharmacist assistant, or were in management and development. The registration numbers they provided confirmed that they were not registered with the SAPC as pharmacists.

Half of the participants (54.29%) indicated that they occupied the position of manager in chain-type pharmacies and only a minority (4.29%) were pharmacist owners. It is therefore reasonable to assume that the participants in the study sample were experienced, qualified community pharmacists. Most of the respondents (82.86%) had a B.Pharm qualification and the majority were from Gauteng (32.86%). The lowest response rates were obtained from Limpopo (N=2) and Northern Cape Province (N=2).

Non-response bias occurs when the demographic of the population is not participating in the survey for various reasons (SurveyMonkey, 2018(a)). The approximate even split between ages, years of service, position in the pharmacy and gender indicates that the results in this small sample can be reflective of the general community pharmacist population.

5.1.3 Knowledge

It is obvious from the answers in the knowledge section that community pharmacists did not have good pharmacovigilance knowledge. These results are consistent with other studies done in South Africa (Joubert and Naidoo, 2016; Williams, 2015).

The main area of concern seemed to be training with only a fifth (19.67%) of the participants having ever received any pharmacovigilance training after qualifying. It seemed the first and the last institution participants identified in providing pharmacovigilance training was a university.

CPD is a legal obligation in South Africa (Government Gazette Republic of South Africa (RSA), 2011). Registered pharmacists are required to participate in CPD and make an annual declaration to the Council that they will comply with all the requirements relating to CPD as determined by the Council (Government Gazette Republic of South Africa (RSA), 2011). The SAPC states that CPD is a professional obligation, and that patients have a right to be confident that pharmacists and

pharmacy support personnel should stay informed about the profession in order to maintain this level of confidence (South African Pharmacy Council (SAPC), n.d.(a)). In the UK the current CPD requirements for pharmacists are being replaced by a system of revalidation, which means pharmacists must submit four CPD records before their annual registration due date in order to register (Pharmacy Magazine, 2018).

Almost all participants (91.80%) were in agreement that ADR reporting consisted of filling in an ADR report form and two thirds (68.85%) would have also considered contacting the prescriber. The SAPC states that ADRs must be reported to the medical practitioner as well as the regulatory authority (South African Pharmacy Council (SAPC), 2010). When asked what ADRs needed to be reported, over a third (37.70%) incorrectly selected all ADRs experienced by the patient as listed in the patient information leaflet. To report all ADRs as listed in the patient information leaflet would cause a considerable burden on regulatory authorities and pharmacist workload. Nevertheless in some instances reporting all the ADRs may be required to determine if there is an increase in common ADRs of a medicinal product. The pharmacist needs to use his knowledge and discretion to ascertain if this is required. The WHO (2002) states that any adverse reaction that is regarded as clinically significant needs to be reported as soon as possible (World Health Organisation (WHO), 2002). Only adverse drug reactions to newly marketed drugs or new drugs in the Essential Drug List, serious interactions and reactions, ambiguous ADRs in the package insert, unusual or interesting ADRs, product quality problems like contamination and poor packaging, treatment failures and herbal ADRs should be reported (South African Health Products Regulatory Authority (SAHPRA), 2016; Government Gazette Republic of South Africa (RSA), 2003; Jobson, 2003). Two thirds of the participants (62.30%) would report herbal drug ADRs.

These results indicated that participants did not know what ADRs qualified for reporting. Guidance on voluntary reporting can be found in the Government Gazette No. 7659 of 2 May 2003 (Government Gazette Republic of South Africa (RSA), 2003). Even though almost all of the participants (95.08%) agreed that ADR

reporting was part of pharmacovigilance, only three quarters (73.68%) would likely fill in an ADR report form in their practice.

Pharmacovigilance responsibilities include the management of ADRs, substandard drugs, medication errors, use of drugs off-licence without substantiated scientific basis, abuse and misuse, lack of efficacy, poisoning, adverse interactions with other drugs, drug-related mortality and the destruction of expired stock (Jobson, 2003, World Health Organisation (WHO), 2015).

Most participants (59.02%) seemed to know the WHO definition of pharmacovigilance, namely “the science and activities relating to the detection and assessment of adverse effects or any other drug-related problem, and the science and activities relating to the understanding and prevention of adverse effects or any other drug-related problem” (International Conference on Harmonisation (ICH) E2A, 1994). Pharmacovigilance therefore seemed to be a topic of confusion for most pharmacists. Pharmacovigilance is one of the competency standards for pharmacists in South Africa. It is covered in Domain 2 under the “Safe and Rational Use of Medicine and Medical Devices” (South African Pharmacy Council (SAPC), 2018(a)). Domain 2 relates to the WHO concept that promotes medicines and medical devices to be appropriate to the needs of patients, in doses to meet individual needs, for the correct period of time and in a cost-effective way for the patient and the community (see Table 3) (South African Pharmacy Council (SAPC), 2018(a)). Pharmacovigilance requirements at pharmacist entry level into practice are to “monitor, receive, record and report quality defects, adverse drug reactions and events, and perform post-marketing surveillance studies” (South African Pharmacy Council (SAPC), 2018(a)). The majority of respondents (80%) considered pharmacovigilance as a legal obligation. It is in fact an ethical obligation. Guidelines for ADR reporting were published in the Government Gazette no 7659 of 2 May 2003, pertaining to Regulation 34 and 37 of Act 90 of 1997 and the Medicines and Related Substances Control Act (Act 101, 1965) (Government Gazette Republic of South Africa (RSA), 2003). This may indicate a gap in the undergraduate pharmacy syllabus.

Under half of the participants (40%) knew that the ADR form was sent to SAHPRA and NADEMC. More than a quarter of participants were not sure to whom it should be sent. In fact it is stated on the ADR report form (APPENDIX C) that the form can either be submitted to the MCC (now called SAHPRA) or NADEMC. More than half of participants (55.74%) selected that the MIC in Cape Town assessed ADRs. The MIC manages information and provides publications and research on ADRs, but they only assess and review ADRs from the Western Cape Province, as confirmed by the MIC (personal communication, January 2019). A quarter of participants (24.59%) knew ADRs were reviewed by the WHO UMC in Sweden. NADEMC is a subunit of SAHPRA.

Almost three quarters of participants (70%) were aware of drugs that had been withdrawn due to safety issues post-market during their practice experience. A number of participants mentioned thalidomide, which was surprising since there have been numerous recalls since then (Jobson, 2003; Onakpoya, Heneghan and Aronson, 2016). One participant mentioned warfarin and another tetracycline, which is incorrect.

Overall the study results indicated confusion among the community pharmacists about what ADRs needed to be reported, what adverse events were regarded as serious, where to obtain the ADR report form, who assessed the form and what pharmacovigilance was. There was no significant association between knowledge scores and years of service in community pharmacy. A similar finding from a North West Province study, also showed no significant association between experience and pharmacovigilance knowledge (Joubert and Naidoo, 2016).

5.1.4 Practice

This section describes the practices of South African community pharmacists concerning pharmacovigilance. In the knowledge section, almost all (91.80%) of the participants agreed that ADR reporting was part of pharmacovigilance, but only three quarters (73.68%) mentioned that they actually undertook ADR reporting in practice.

This indicated that even though pharmacists regarded ADR reporting as important, in practise they would tend to refrain from reporting them. The study showed that pharmacists from the age group of 31-40 years reported the most ADRs during their career.

On the whole, most pharmacists followed the SAPC guidelines (South African Pharmacy Council (SAPC), 2010), in that they would contact the prescriber (77.19%) and complete the ADR report form (73.68%). Only 40% of participants could name drugs they had previously reported on an ADR report form. This could indicate that some participants had not yet been faced with an ADR to report, but would endeavour to do so when the situation arose and this in turn indicated a lack of knowledge as to what an ADR was. The differing scores in the knowledge section, where almost all (91.80%) of participants agreed that filling in the ADR report form was part of ADR reporting, but fewer actually did it in practice, further supported this notion.

It is significant that 2 respondents chose to mention the MCC in favour of SAHPRA as an institution which could provide the ADR report form. This could indicate that there were still a number of pharmacists that did not know that the MCC had changed to SAHPRA in 2017. Over 50% of participants seemed to think the form could be obtained from the SAPC. The researcher contacted the SAPC on the 7th of August 2018 via email to ascertain whether an ADR report form was available from them as no mention of the form could be found on the SAPC website. To date, no reply has been received, hereby concluding that the form could not be obtained from the SAPC. The ADR report form can however be found at the back of the South African Medicines Formulary (SAMF) and on the SAHPRA website under the heading: “Application forms” in the “Publications” menu. It can also be obtained from hospitals, the Department of Health and some chain-pharmacy intranets and their SOPs.

Most participants (84.21%) indicated that they preferred to email the form. This indicated the need for faster and easier submission of ADR report forms using technology. A standard APP on a smartphone or dedicated website for ADRs of all drugs would facilitate easier ADR reporting in South Africa. Reports sent electronically do in fact overload the system and NADEMC prefers ADR report forms

to be faxed (Maigetter, et al., 2015). Data is captured manually and processed slowly which causes delays, because forms from public health programmes, NGOs and NADEMC are not always compatible (Maigetter, et al., 2015). A standardised, more user-friendly ADR reporting form would improve the process of reporting (Maigetter, et al., 2015). NADEMC should however be able to accommodate ADRs that are emailed in this present age.

5.1.5 Opinion

This section aimed to elucidate the attitude and feeling of community pharmacists towards pharmacovigilance and in particular ADR reporting. A general level of frustration was apparent from most participants due to lack of training and lack of support from the SAPC. One participant also expressed their frustration at the pharmaceutical industry in South Africa and its lack of concern about ADRs. Most interventions in SA are due to safety data which is circulated from international warnings (Maigetter, et al., 2015).

Most pharmacists (58.18%) felt they received enough support from their employer to pursue pharmacovigilance, even though 40% cited lack of support as one of the barriers to ADR reporting. This could indicate a lack of support from regulatory authorities. It is the responsibility of employers, by supplying SOPs for ADRs and training, to ensure that their pharmacists are maintaining pharmacovigilance, which is an ethical obligation. Less than half of the participants (43.64%) felt that the SAPC had not been very proactive in pharmacovigilance and three quarters of participants (76.36%) felt the SAPC should take responsibility for pharmacovigilance education.

Other bodies selected as responsible for pharmacovigilance education were academic institutions, the PSSA, and pharmacists themselves through CPD. Competence standards have indeed been developed by the SAPC to assess pharmacists' CPD needs, which are based on the seven unit standards for entry-level pharmacists and have been accepted by the SAPC as the minimum

competencies required for registration (South African Pharmacy Council (SAPC), n.d.(a)). The pharmaceutical industry and SAHPRA were listed as below 50% by participants as responsible for pharmacovigilance training. Pharmaceutical company representatives, who frequent medical practitioners during drug detailing visits, have proven to be associated with more items being prescribed on prescriptions (Lieb and Scheurich, 2014) and this could perhaps explain pharmacists' reluctance to obtain training from the pharmaceutical industry due to its bias. Most pharmacists regard pharmacovigilance centres, such as at SAHPRA, as remote entities maintaining little contact with pharmacists (Joubert and Naidoo, 2016). In the pharmacovigilance study done in the North West Province in 2015, more than half of the respondents expressed their dissatisfaction with the current pharmacovigilance system in South Africa (Joubert and Naidoo, 2016). Still, the results indicated that all stakeholders were responsible for pharmacovigilance training.

Over half (54.55%) of the participants felt that clinical trials provided adequate protection for patients in determining the safety of registered medicinal products. Clinical trials are insufficient because animal testing is insufficient, and patients in clinical trials are pre-selected and limited in number. Only the more common ADRs are detected during clinical trials and some ADRs only have an incidence of 1 in 10 000, making it even more difficult to predict ADRs in special groups such as children, pregnant women and the elderly (World Health Organisation (WHO), 2002). This could further indicate the lack of pharmacists' knowledge, not just with regard to pharmacovigilance, but also with regard to the process of drug development. It may also explain pharmacists' reluctance in filling in ADR report forms, since if they were of the opinion that clinical trials were adequate, they therefore might not regard post-market surveillance of drugs as important. Less than a fifth of the participants regarded ADR reporting as outside their clinical and legal competence (10.91%), and regarded it more relevant to pharmacists working in the public sector (16.36%). Most ADR report forms which public sector pharmacists complete, are linked to ARV report submissions (Maigetter, et al., 2015).

Even so, most participants indicated that they would have ensured that they received the correct training and would have reported ADRs, if they had known that

pharmaceutical companies and regulators relied on such information. This indicated a positive attitude towards pharmacovigilance and further training. There seems to be a distinct knowledge gap between community pharmacists, regulators, academia and the pharmaceutical industry with most pharmacists reporting less than 3 ADRs in the course of their career.

A third of the pharmacists (34.55%) were concerned that ADR reporting would create an excess workload. Less than half of them (40%) admitted that they tended to overlook ADRs since it was not a common occurrence and a quarter (29.09%) seemed to admit that they were not confident in filling in the ADR report form. Such a situation could easily motivate pharmacists to rather refer the patient back to the doctor (Williams, 2015). Further it points to either participants' lack of knowledge concerning the significance and importance of post-market surveillance, or a lack of available resources (training support and the tools) required to identify and assess ADRs.

In SA, a shortage of approximately 12 000 pharmacists (2017) was reported (Ndenze, 2017; Gray, Ridden.and Jugathpal., 2016), but such a pharmacy workforce shortage was not seen by most participants (80.91%, N=28) to affect a pharmacist's active involvement in pharmacovigilance. The biggest barriers to ADR reporting cited were lack of training (87.27%), lack of support (40.00%), lack of time (34.55%) and lack of incentive (16.36%). Other reasons listed were lack of an unbiased, standardised database. Lack of training, lack of support, lack of time and lack of incentive are consistent with barriers found in other studies and literature, and need to be addressed (Cheema, et al., 2017; Joubert and Naidoo, 2016; Suyagh, Farah and Abu Farha, 2014; Williams, 2015).

Over half (58.18%) of the participants cited lack of feedback as a barrier to ADR reporting. Similar studies also identified lack of feedback and communication from regulators as a barrier to ADR reporting (Mehta, et al., 2017), and similarly noted in a Western Cape study, where a participant stated that she had not received a

reference number from the regulatory authorities in five years (Williams, 2015). NADEMC receives ADR forms, thereafter a unique identification number is assigned to the ADR report form and the reporter is notified with an acknowledgement letter and the unique identification number (Government Gazette Republic of South Africa (RSA), 2003). ADR reporting is likely to improve if reporters knew the report resulted in an action or outcome (Williams, 2015).

A drugs or therapeutics bulletin via email to HCPs from SAHPRA identifying risks and changes to labelling of products would ensure that pharmacists had adequate unbiased knowledge on suspected ADRs (Maigetter, et al., 2015), and would also remind them of their duty to assist regulatory authorities in the post-market surveillance of medicinal products. The Royal Pharmaceutical Society (RPS) through the Medicines and Healthcare Products Regulatory Agency (MHRA) in the UK sends electronic mail Drug Alerts to individual registered pharmacists on a regular basis. In SA drug alerts are usually communicated through pharmaceutical companies or as medical safety alerts in local journals (Maigetter, et al., 2015). Most pharmacovigilance notifications come from industry and this was also demonstrated in a similar study in the North West Province, where more than three quarters (73.5%) of participants received notifications from manufacturers (Joubert and Naidoo, 2016).

A recent SAHPRA press release (July 2018) urged the withdrawal of some valsartan containing products due to the presence of a carcinogen, and asked all HCPs to record all ADRs to the drug in the ADR report form (South African Health Products Regulatory Authority (SAHPRA), 2018). An email or SMS from regulatory authorities to all registered HCPs would have created a more harmonised and effective operation, but instead it was mainly communicated through the pharmaceutical industry representatives.

Pharmacists are in the unique position of being the only HCP patients have access to on a regular basis, when they collect either monthly repeat prescriptions, or need

advice on self-medication for minor ailments (Cheema, et al., 2017; Williams, 2015). ADRs should not be difficult to identify in a community pharmacy setting, since ADR reporting occur in many medical consultations (Cheema, et al., 2017). The local community pharmacy easily becomes a pillar of trust and support in a population and therefore it is fair to assume that community pharmacists generally develop a relationship with customers, and that customers or patients would discuss the problems they experience with medication with their community pharmacists. Over three quarters of participants (83.64%) felt that their patients trusted them enough to discuss ADRs. Patients, trusting their pharmacists, would expect pharmacists to look after their welfare and promote the safety of medicine. Almost all participants (96.36%) agreed that patients would indeed expect them to be proactive when it came to ADR management. According to SAPC competence standard 9, pharmacists have an obligation to work professionally in pharmacy practice (South African Pharmacy Council (SAPC), n.d.(a)). A person who achieved this standard is capable of developing a trusting relationship with patients (South African Pharmacy Council (SAPC), n.d.(a)). Since most of the participants were from chain-type pharmacies and not independent pharmacies, it would be interesting to explore whether large chain-type pharmacies (with a larger turn-over of pharmacists and generally busier) were less trusted by patients.

Daily activities in a pharmacy typically consist of dispensing of medicine and stock control (Gray, Ridden and Jugathpal, 2016). Since 2000, dispensing of medicine has already been mastered by robots in some developed countries (Goundrey-Smith, 2008), but despite this being the case, pharmacovigilance is one of the tasks technology cannot replace since it requires communication and judgement (Chemist and Druggist, 2018). Pharmacists need to demonstrate their worth in this respect.

The ADR report form is not easily found on the SAHPRA website, even though over two thirds (69.09%) of participants selected that it was. A conspicuous menu for ADRs on the Home page of the SAHPRA website is therefore recommended. The UK Yellow Card Scheme has a website dedicated to the reporting of ADRs and includes an APP for use on a smartphone or tablet for easy reporting, and easy access to these Yellow Forms is provided (YellowCard, n.d.). The Yellow Card

Scheme is administered by the MHRA. The MHRA defines an ADR as “any unwanted or harmful reaction experienced following the administration of a drug or combination of drugs under normal conditions of use and which is expected to be related to the drug” (Medicines and Healthcare products Regulatory Agency (MHRA), n.d.).

It is concerning that a third of the participants (34.55%) regarded the filling in of the ADR report form as more the prescribers’ responsibility, and that almost a fifth (14.55%) of the participants were unsure. This figure correlated with the high number of participants (62.30%) who regarded ADR reporting as referring the patient to the prescriber. Regulation Gazette No. 7659 of 2 May 2003 invites all HCPs to report ADRs even if they are not certain that the product caused the event (Government Gazette Republic of South Africa (RSA), 2003). Pharmacovigilance evaluations take precedence over any other cumulative ADR reporting requirements and consumers must be advised to report the reaction through their HCP (South African Health Products Regulatory Authority (SAHPRA), 2016). HCPs, including pharmacists, are therefore responsible for submitting ADR report forms, and the information needed to complete the form should be obtained from the medical practitioner responsible for the patient if possible (South African Health Products Regulatory Authority (SAHPRA), 2016). The WHO stipulates that all suspected ADRs must be reported by all HCPs as part of their professional responsibility, even if they are doubtful regarding the relationship between the drug and the reaction, or are concerned about duplicate reporting (World Health Organisation (WHO), 2002). It seems pharmacists are shifting the responsibility of ADR reporting to the prescribers, which does not necessarily guarantee that the ADR would in fact be reported. Such a situation could be due to the barriers to ADR reporting listed in this study and the literature (Cheema, et al., 2017; Joubert and Naidoo, 2016; Suyagh, Farah and Abu Farha, 2014; Williams, 2015).

Pharmacists, however, agreed that they would ensure they received the correct training on ADR reporting if they were made aware of its significance. All stakeholders, i.e. employers, universities, regulatory authorities, the pharmaceutical industry and pharmacists themselves, need to take responsibility for

pharmacovigilance training and promote filling in the ADR report form, so as to support post-market surveillance of drugs. Pharmacists need encouragement and regular CPD programmes in pharmacovigilance to improve knowledge about adverse drug reactions and on adverse drug reaction reporting. Since the SAPC is responsible for the registration of pharmacists, as a regulatory authority it should also include the responsibility of providing pharmacists with the necessary guidance to become competent in pharmacovigilance.

The South African government endeavours to implement the National Health Insurance (NHI), which aims to improve patient satisfaction, quality of life and health outcomes across all socioeconomic groups (Department of Health Republic of South Africa (RSA), 2017). A competent pharmacovigilance system promotes harmonisation and expansion of active and passive surveillance, and in doing so prioritises post-marketing monitoring within the regulatory authority and installs a culture of active risk management in clinical practice with communication (Mehta, 2011). Therefore a more systematic approach to instituting pharmacovigilance and its practices (Maigetter, et al., 2015), is crucial for SA. Increased funding and separate budgets are required to achieve these goals, as post-marketing surveillance does not generate any direct income for stakeholders (Mehta, et al., 2017). Strong political will is required to put patient safety first and to support this critical service.

5.1.6 Responses from participants who had received pharmacovigilance training

The participants who indicated that they had received pharmacovigilance training after qualifying, demonstrated a better completion rate (91.67%) with only one incomplete submission in the survey. Twelve participants (16.67%) indicated that they had received training post-qualifying.

Even though the trained participant group had a better understanding of ADR reporting and pharmacovigilance, there were still vital knowledge gaps observed. It is clear that training is not enough to improve ADR reporting, and concerted efforts are required from different pharmacy sectors to facilitate a change in professional practice.

It is concerning that more than half of the trained participants believed that clinical trials were adequate in protecting the safety of patients from medicinal products. This shows a clear gap in pharmacists' knowledge concerning safety aspects during drug development. Still, most agreed that if they had known that the information they provided on ADR report forms was vital for the safety of patients, and that the pharmaceutical industry and regulators relied on the information, they would have used the ADR report form. Pharmacists are willing to comply if they are given the correct information.

5.2 LIMITATIONS OF THE STUDY AND SUGGESTIONS FOR FURTHER RESEARCH

Constraints of the research were that not all community pharmacists in SA participated in the survey. Pharmacists are dealing with a considerable workload on a daily basis and regular follow-ups to complete surveys were sent in order to get enough statistical power. Some pharmacists however, requested removal of their details from the contact list, possibly due to high workload.

The survey was conducted over a period of less than 8 weeks, an extension by 3 to 4 weeks might have resulted in a different outcome, since the emails could only be initiated once ethical clearance was obtained from UWC. Therefore the response rate of the survey was only 5%, which is below the accepted figure of 20% for survey questionnaires sent via the internet or post without any previous contact (Kelly, et al., 2003). Internal company surveys aim for a response rate of 30% while external surveys aim for 10% (SurveyMonkey, 2018). The survey questionnaire consisted of forty questions which should only take 10 minutes to complete. The average completion time was however 15 minutes with a completion rate of 70%. Ambiguous questions and limited investigation into the value of ADR reporting would require attention in future studies.

Descriptive statistics were used due the limited number of completed surveys received but Chi-square analysis could also have shown some interesting trends after accommodating the high number of incomplete surveys received.

Pharmacists might not have been able to remember the exact number of adverse drug reactions they had reported within the specified time. Electronic access to pharmacists might have been limited if pharmacies did not display their email address on the internet and some email addresses were not current. The web search route for retail pharmacies were time-consuming and a different route of obtaining contact details is recommended. Some pharmacists may have used the internet to assess the correct answers and so false positive results may have been obtained. It was assumed that pharmacists would not discuss the survey or google the answers.

The survey did not ask participants which ADRs caused them to fill in the ADR report, but they were only required to identify the drugs they had reported. This might have given a clearer indication on what ADRs pharmacists regarded as reportable. The questionnaire relied on self-reported responses, so the actual number of pharmacists that report ADRs could in fact be higher or lower than the recorded number. The survey also did not explore the outcome, e.g. if the patient was hospitalised or not.

The study specifically focused on pharmacists working in a community retail pharmacy at the time of receiving the survey. Assumptions were that measuring the knowledge, attitude and practice of ADR reporting would give an indication of one aspect of pharmacovigilance awareness among community pharmacists. Other areas of pharmacovigilance, such as medication errors, abuse and misuse, poisoning, use of drugs off-label, lack of efficacy, destruction of expired stock, drug-interactions and substandard drugs were not assessed in this study.

Some pharmacies that are part of large chain stores could not complete the survey due to technical difficulties experienced with companies' IT firewalls. For example, the options could not be clicked on or the survey did not want to scroll down.

Other limitations related to the survey itself included using a Gmail account as a survey collector. Gmail accounts list “conversations” compared to “inbox” and “outbox” style accounts, which made blocked or returned emails very difficult to count and some emails were returned over a couple of days as “undeliverable”. Sending out emails in small batches to avoid being returned as blocked or “undeliverable” was time consuming.

Despite these limitations significant data was collected with an almost even split between ages, gender and years of experience in community pharmacy indicating a trend from a small sample representative of the demographics of the population.

5.3 CONCLUSION

The findings of the research generally confirmed the documentary analysis of the literature and no major contradictions were identified. Despite all the limitations and problems with conveying the research, valuable insights were gained into the practice and opinions of retail community pharmacists held regarding pharmacovigilance.

The results showed that pharmacists with sound pharmacovigilance knowledge are more likely to report ADRs. However, even though some pharmacists had pharmacovigilance knowledge that may be regarded as sufficient, some of these pharmacists were still failing in their effort to report ADRs. Despite the results pharmacists showed a positive attitude towards pharmacovigilance and ADR reporting, provided they were supplied with the knowledge to demonstrate its significance.

Most participants did not know the significance of ADR reporting even though the WHO regard it as a moral and professional obligation (World Health Organisation (WHO), 2002). A guide by SAHPRA and the SAPC, such as the MHRA guide for

pharmacists in the UK, emphasising the importance of ADR reporting, the background, how to report and how the data is used to improve patient safety, is recommended (Medicines and Healthcare products Regulatory Agency (MHRA), n.d.). The low knowledge scores in addition to the low completion rate, in combination with non-pharmacists attempting to complete the survey, might indicate a feeling of discouragement amongst South African community pharmacists. Still the results showed that pharmacists would participate in pharmacovigilance activities and training if given the correct information, and if guided by medicine and pharmacist regulatory authorities.

Currently pharmacists are left to include pharmacovigilance training in their own CPD. If filling in the ADR report form was given the same urgency and importance as keeping the prescription register for example, then ICSR forms from Africa to the WHO Uppsala Monitoring Centre in Sweden would be considerably more than the current 1% (Ampadu, et al., 2016). Therefore the provision of structured pharmacovigilance training and support for South African community pharmacists and a culture of ADR reporting need to be nurtured (Cheema, et al., 2017).

Revalidation in the UK, is a process by which the regulatory authority guarantees that pharmacists are fit to practice by keeping their knowledge up-to-date and by maintaining the correct attitude and practices to protect the safety of patients (Pharmacy Magazine, 2018). A program similar to that of the UK may be suitable in South Africa to ensure community pharmacists maintain their knowledge by pursuing the training they need. A website dedicated to ADRs, as the case in the UK, providing drug alerts and feedback would place the focus back on ADRs. The availability of an APP on a smart device for all ADRs would make the reporting of ADRs more user-friendly.

Public education and feedback are required to enhance the reporting of ADRs and the media needs to be educated about the risk versus benefit of medicines (Mehta, et al., 2017). Reporting systems need to focus more on active surveillance

(Maigetter, et al., 2015), which in turn can only materialise if pharmacists have the necessary knowledge, and if the ADR form is easily obtained, relatively easy to complete and convenient to send.

It is vital that SAHPRA preserves its independence in providing non-biased and current medical product information and there is an opportunity to strengthen its pharmacovigilance systems as it completes its transformation from the MCC (Mehta, et al., 2017). The SAPC, as the regulator established in terms of the Pharmacy Act, 1974 (Act 53 of 1974) has a mandate to promote the health, safety and wellbeing of patients and the public ensuring quality pharmaceutical service for South Africans (South African Pharmacy Council, n.d.(b)). By working closely with SAHPRA, the SAPC could strengthen efforts to improve ownership among retail community pharmacists to be proactive in pharmacovigilance. The success of pharmacovigilance programmes depends on the collaboration of all HCPs, and regulatory harmonisation would improve ADR reporting and assessing.

There is no doubt that further research is required into the knowledge, attitude and practice of South African community pharmacists when it comes to ADR reporting. A pharmacovigilance education programme directed to ADR reporting by community pharmacists could be assessed from a randomised controlled trial with a control group receiving pharmacovigilance training from a regulatory body in order to standardise pharmacovigilance knowledge and measure ADR report rates (Cheema, et al., 2017). Further studies with a larger sample and initiated by a regulatory body would be recommended to confirm the data collected. Pharmacists, in general, are prepared to undergo the necessary training.

Overall the results have shown that retail community pharmacists in South Africa are inexperienced and unaware of the required measures needed to safeguard the public from registered medicinal products. This is further based on their reliance on clinical trials and their belief that they provide adequate safety information on registered products. These gaps in knowledge could be due to lack of training

and/or lack of guidance from regulatory authorities. This might indicate South Africa had become careless in guaranteeing the safety of medicines. This notion may already have been identified by the Department of Health, the SAPC and the PSSA, as the focus in pharmacy month in 2018 (September) was the wise use of medicine with one of the aims of the initiative being to improve communication between pharmacists and patients (South African Pharmacy Council (SAPC), 2018(c)).

Community pharmacists have a history of participating in public health services at a primary level (Bradley, Bheekie, and Sanders, 2011). At the very least this survey has made participants more aware of ADRs and the need for completing ADR report forms. Community pharmacists remain the most accessible HCP, especially to patients taking new drugs, as these are usually launched in community pharmacies with the associated dynamic marketing. They are therefore well-placed to identify ADRs resulting from the use of newer pharmaceutical agents.

REFERENCES

Adwok, J. (2015) 'Probability Sampling - A Guideline for Quantitative Health Care Research', *The Annals of African Surgery,* July 2015, Vol. 12, Issue 2 pp.95-99 [Online]. Available at: https://webcache.googleusercontent.com/search?q=cache:IzhpiGAHMAgJ:https://www.ajol.info/index.php/aas/article/download/126349/115865+&cd=13&hl=en&ct=clnk&gl=za (Accessed: 23 August 2018).

Ampadu, H.H., Hoekman, J., De Bruin, M.L., Pal, S.N., Olsson, S., Sartori, D., Leufkens, H.G.M. and Dodoo, A.N.O. (2016) 'Adverse Drug Reaction Reporting in Africa and a Comparison of Individual Case Safety Report Characteristics between Africa and the Rest of the World', *Drug Safety,* January 2016 39: 335-345 [Online]. Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4796322/ (Accessed: 23 August 2018).

Anderson, P. (2012(a)) *Standard Deviation.* [Online]. Available at: https://www.youtube.com/watch?v=09kiX3p5Vek (Accessed: 16 August 2018).

Anderson, P. (2012(b)) *Statistics for Science.* [Online]. Available at: https://www.youtube.com/watch?v=jf9VT4V4aRI (Accessed: 16 August 2018).

Anderson, P. (2016) *Student's t-test.* [Online]. Available at: https://www.youtube.com/watch?v=pTmLQvMM-1M (Accessed: 23 August 2018).

Bradley, H., Bheekie, A. and Sanders, D. (2011) 'Public Health: Every Pharmacist's Business', *SA Pharmaceutical Journal,* Vol 78, No 10 [Online]. Available at:

http://www.sapj.co.za/index.php/SAPJ/article/view/1193 (Accessed: 23 August 2018).

Bradshaw, D., Nannan, N., Laubscher, R., Groenewald, P., Joubert, J., Nojilana, B., Norman, R., Pieterse, D. and Schneider, M. (2006) 'South African National Burden of Disease Study 2000 Estimates of Provincial Mortality', *MRC South Africa* [Online]. Available at: http://www.samrc.ac.za/sites/default/files/files/2017-07-03/estimate.pdf (Accessed: 23 August 2018).

Cheema, E., Haseeb, A., Khan, T.M., Sutcliffe, P. and Singer, D.R. (2017) 'Barriers to Reporting of Adverse Drug Reactions: a Cross Sectional Study among Community Pharmacists in the United Kingdom', *Pharmacy Practice (Granda),* Jul-Sep; 15(3):931 [Online]. Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5597805/ (Accessed: 23 August 2018).

Chemist and Druggist (2018) *Xrayser: What Can a Pharmacist Do That a Robot Can't.* C&D [Online]. Available at: https://www.chemistanddruggist.co.uk/opinion/xrayser-what-can-pharmacist-do-robot-cant (Accessed: 22 August 2018).

Clarke, D. (2011) 'The Ethical Issues around Pharmaceutical Company Marketing', *The South African Journal of Bioethics and Law,* Vol4, No1 [Online]. Available at: http://www.sajbl.org.za/index.php/sajbl/article/view/131/99 (Accessed: 10 July 2018).

Department of Health Republic of South Africa (RSA) (2017) *National Health Insurance (NHI) for South Africa.* DoH [Online]. Available at: http://www.health.gov.za/index.php/nhi (Accessed: 31 July 2018).

eMathZone (n.d) *Sampling Errors.* [Online]. Available at: https://www.emathzone.com/tutorials/basic-statistics/sampling-errors.html (Accessed: 4 July 2018).

Etikan, I., Musa, S. & Alkassim, S. (2016) 'Comparison of Convenience Sampling and Purposive', *Amercian Journal of Theoretical and Applied Statistics,* 5(1): 1-4 [Online]. Available at: http://article.sciencepublishinggroup.com/pdf/10.11648.j.ajtas.20160501.11.pdf (Accessed: 23 August 2018).

Faber, J. and Fonseca, L.M. (2014) 'How Sample Size Influences Research Outcomes', *Dental Press Journal of Orthodontics,* Jul-Aug; 19(4): 27-29 [Online]. Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4296634/ (Accessed: 1 July 2018).

Fedak, K.M., Bernal, A., Capshaw, Z. A. and Gross, S. (2015) 'Applying the Bradford Hill Criteria in the 21st Century: How Data Integration has Changed Causal Inference in Molecular Epidemiology', *Emerging Themes in Epidemiology,* 12:14 [Online]. Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4589117/ (Accessed: 5 July 2018).

Google Mail (2018) *Fix bounced or rejected emails.* Gmail [Online]. Available at: https://support.google.com/mail/answer/6596?visit_id=1-636675850177826585-363259239&rd=1 (Accessed: 19 July 2018).

Goundrey-Smith, S. (2008) 'Pharmacy Robots in UK Hospitals: The Benefits and Implementation Issues*', Pharmacy Journal,* Vol. 280, pp 599-602 [Online]. Available at: https://www.pharmaceutical-journal.com/download?ac=1065210&firstPass=false (Accessed: 22 August 2018).

Government Gazette Republic of South Africa (RSA) (2003) *Regulation Gazette No. 7659, Adverse Drug Reaction Forms, 2 May 2003, No. 24785* [Online]. Available at: https://www.gov.za/sites/default/files/24785a.pdf (Accessed: 31 July 2018).

Government Gazette Republic of South Africa (RSA) (2011) *Regulation Gazette No. 9528, Regulations Relating to Continuing Professional Development (CPD), 6 May 2011, No 34254.* [Online]. Available at: https://www.mm3admin.co.za/documents/docmanager/0C43CA52-121E-4F58-B8F6-81F656F2FD17/00012727.pdf (Accessed: 2 August 2018).

Gray, A., Ridden, J.and Jugathpal, J. (2016) 'Health Care and Pharmacy Practice in South Africa', *The Canadian Journal of Hospital Pharmacy,* Jan-Feb; 69(1): 36-41 [Online]. Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4777579/ (Accessed: 23 August 2018).

Hedt, B. L. and Pagano, M. (2011) 'Health Indicators: Eliminating Bias From Convenience Sampling Estimators', *Stat Med,* Feb 28; 30(5):560-568 [Online]. Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3951147/ (Accessed: 4 July 2018).

International Conference on Harmonisation (ICH) E2A (1994) *Clinical Safety Data Management: Definitions and Standards for Expedited Reporting E2A.* ICH [Online]. Available at: https://www.ich.org/fileadmin/Public_Web_Site/ICH_Products/Guidelines/Efficacy/E2A/Step4/E2A_Guideline.pdf (Accessed: 6 February 2018).

International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) E2C(R2) (2012) *Periodic Benefit-Risk Evaluation Report (PBRER) E2C (R2).* ICH [Online]. Available at:

http://www.ich.org/fileadmin/Public_Web_Site/ICH_Products/Guidelines/Efficacy/E2C/E2C_R2_Step4.pdf (Accessed: 9 July 2018).

Ioannidis, J. (2009) 'Adverse Events in Randomised Trials- Neglected, Restricted, Distorted and Silenced', *Arch Intern Med*, Vol 169(no19) [Online]. Available at: http://olympias.lib.uoi.gr/jspui/bitstream/123456789/24017/1/Ioannidis-2009-Adverse%20events%20in%20ra.pdf (Accessed: 23 August 2018).

Jobson, R. (2003) 'Pharmacovigilance: A Brief Glimpse', *SA Family Practice,* 45(2) pp 53-57 [Online]. Available at: http://www.safpj.co.za/index.php/safpj/article/download/1989/2537 (Accessed: 23 August 2018).

Joubert, M.C. and Naidoo, P. (2016) 'Knowledge, Perceptions and Practices of Pharmacovigilance amongst Community and Hospital Pharmacits in a Selected District of North West Province, South Africa', *Health SA,* Vol. 24, Dec, pp. 238-244 [Online]. Available at: https://ac.els-cdn.com/S1025984816300084/1-s2.0-S1025984816300084-main.pdf?_tid=0bb77826-ff56-11e7-be9f-00000aab0f27&acdnat=1516613257_466461310392bba555866c1af5873b37 (Accessed: 23 August 2018).

Kelly, K., Clark, B., Brown, V. and Sitzia, J. (2003) 'Good Practice in the Conduct and Reporting of Survey Research', *International Journal for Quality in Health Care,* Vol. 15, Issue 3, 1 May, pp. 261-266 [Online]. Available at: https://academic.oup.com/intqhc/article/15/3/261/1856193 (Accessed: 1 July 2018).

Lexchin, J. (2014) 'How Safe are New drugs? Market Withdrawal of Drugs Approved in Canada between 1990 and 2009', *Open Medicine,* 8(1): e14-e19 [Online]. Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4085091/ (Accessed: 6 February 2018).

Lieb, K. and Scheurich, A. (2014) 'Contact between Doctors and the Pharmaceutical Industry, Their Perceptions, and the Effects on Prescribing Habits', *PLoS ONE,* 9(10): e110130 [Online]. Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4199668/ (Accessed: 23 August 2018).

Maigetter, K., Pollock, A.M., Kadam, A., Ward, K. and Weiss, M.G. (2015) 'Pharmacovigilance in India, Uganda and South Africa with Reference to WHO's Mimimum Requirements', *International Journal of Health Policy and Management,* May; 4(5): 295-305 [Online]. Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4417633/ (Accessed: 23 August 2018).

Medicines and Healthcare products Regulatory Agencey (MHRA) (n.d) *Reporting Adverse Drug Reactions with the Yellow Card Scheme - A Guide for Pharmacists.* MHRA [Online]. Available at: http://www.mhra.gov.uk/home/groups/comms-ic/documents/websiteresources/con036033.pdf (Accessed: 4 August 2018).

Medicines Information Centre (MIC) (n.d.) *Home.* MIC [Online]. Available at: http://www.mic.uct.ac.za/ (Accessed: 26 July 2018).

Mehta, U. (2011) 'Pharmacovigilance: The Devastating Consequences of Not Thinking about Adverse Drug Reactions', *CME Continuing Medical Education,* June. Vol.29, No.6 pp. 247-251 [Online]. Available at: http://www.cmej.org.za/index.php/cmej/article/view/2170/1827 (Accessed: 26 August 2018).

Mehta, U., Kalk, E., Boulle,A., Nkambule, P., Gouws, J., Rees, H. and Cohen, K. (2017) 'Pharmacovigilance: A Public Health Priority for South Africa', *South African Health Review,* pp. 125-133 [Online]. Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5708547/ (Accessed: 23 August 2018).

Montanari-Vergallo, G. (2013) 'Recent Developments in EU and US Pharmacovigilance Legislation', *Journal Pharmacovigilance,* Vol 1, Issue 2 [Online]. Available at: http://citeseerx.ist.psu.edu/viewdoc/download?doi=10.1.1.1033.5784&rep=rep1&type=pdf (Accessed: 23 August 2018).

Moodley, K. and Myer, L. (2007) 'Health Research Ethics Committees in South Africa 12 Years into Democracy', *BMC Medical Ethics,* 8:1 [Online]. Available at: https://bmcmedethics.biomedcentral.com/articles/10.1186/1472-6939-8-1 (Accessed: 25 August 2018).

National Institute for Communicable Diseases (NICD) (2017) *Malaria in South Africa 2017: an update.* NICD [Online]. Available at: http://www.nicd.ac.za/wp-content/uploads/2017/05/Malaria-update.pdf (Accessed: 19 March 2018).

Ndenze, B. (2017) 'SA has Huge Pharmaceutical Skills Shortage', *Times Live,* 28 June [Online]. Available at: https://www.timeslive.co.za/news/south-africa/2017-06-28-sa-has-huge-pharmaceutical-skills-shortage/ (Accessed: 20 August 2018).

Onakpoya, I.J., Heneghan, C.J. and Aronson, J.K. (2016) 'Post-marketing Withdrawal of 462 Medicinal Products Because of Adverse Drug Reactions: a Systematic Review of the World Literature*', BMC Medicine,* 14:10 [Online]. Available

at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4740994/ (Accessed: 25 August 2018).

Pharmacy Magazine (2018) *Getting to Grips with Revalidation – an Essential Guide.* [Online]. Available at: https://www.pharmacymagazine.co.uk/getting-to-grips-with-revalidation (Accessed: 30 July 2018).

Rajanandh, M.G, Praveen, K.V and Yuvasakthi, S. (2016) 'Roles of Pharmacist in Pharmacovigilance: A Need of the Hour', *Journal of Pharmacovigilance,* 2 Dec [Online]. Available at: https://www.omicsonline.org/open-access/roles-of-pharmacist-in-pharmacovigilance-a-need-of-the-hour-2329-6887-1000221.php?aid=83551 (Accessed: 25 August 2018).

Research Methodology (n.d.) *Convenience Sampling.* [Online]. Available at: https://research-methodology.net/sampling-in-primary-data-collection/convenience-sampling/ (Accessed: 4 July 2018).

Roux, L. (2014) 'Pharmacovigilance: The Responsibility of Pharmaceutical Companies to Protect Patients From Drug-Related Harms', *Hibernia College in patnership with the University of the Western Cape* [Online]. Available at: http://etd.uwc.ac.za/xmlui/bitstream/handle/11394/4234/Roux_MSc_2014.pdf;sequence=1 (Accessed: 27 August 2018).

Ruud, K., Srinivas, S.C. and Toverud, E.L. (2010) 'Addressing Gaps in Pharmacovigilance Practices in the Antiretroviral Therapy Program in the Eastern Cape Province, South Africa [Abstract]', *Research in Social and Administrative Pharmacy,* Dec; 6(4): 345-53 [Online]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/21111391 (Accessed: 27 August 2018).

Sivo, S.A., Saunders, C., Chang, Q. and Jiang, J.J. (2006) 'How Low Should You Go? Low Response Rates and the Validity of Inference in IS Questionnaire Research', *Journal of the Association for Information Systems,* Vol.7 No. 6 pp. 351-414 [Online]. Available at: https://business.ucf.edu/wp-content/uploads/2014/11/How-Low-Should-You-Go..Low-Response-Rates-and-the-Validity-of-Inference-in-IS-Questionnaire-Research.pdf (Accessed: 5 July 2018).

South African Health Products Regulatory Authority (SAHPRA) (n.d.) *Guidelines.* SAHPRA [Online]. Available at: http://www.sahpra.org.za/publications/index/1 (Accessed: 14 February 2018).

South African Health Products Regulatory Authority (SAHPRA) (2003) *General Regulations Made in terms of the Medicine and Related Substances Act, 1965 (Act No. 101 of 1965) as amended.* SAHPRA [Online]. Available at: http://www.sahpra.org.za/documents/f6cae0ccRegulations_to_Act_101_published_2003.pdf (Accessed: 27 August 2018).

South African Health Products Regulatory Authority (SAHPRA) (2016) *Post-Marketing Reporting of Adverse Drug Reactions to Human Medicines in South Africa.* SAHPRA [Online]. Available at: http://www.sahpra.org.za/documents/f39361792.33_ADR_reporting_post-marketing_Jul16_v4.1_showing_changes.pdf (Accessed: 27 August 2018).

South African Health Products Regulatory Authority (SAHPRA) (2018) *Medicines Safety Communition: Recommendations About the Urgent Recall of Valsartan in Reponse to the Potential Risk of Cancer.* SAHPRA [Online]. Available at: http://www.sahpra.org.za/documents/dd0da3fd10.18_Media_Release_Valsartan_Jul18_v1.pdf (Accessed: 1 August 2018).

South African Pharmacy Council (SAPC) (n.d.(a)) *Guidance Document for Continuing Professional Development (CPD) for Persons Registered with the South African Pharmacy Council (SAPC).* SAPC [Online]. Available at: https://www.mm3admin.co.za/documents/docmanager/0C43CA52-121E-4F58-B8F6-81F656F2FD17/00010994.pdf (Accessed: 2 August 2018).

South African Pharmacy Council (n.d.(b)) *Welcome.* SAPC [Online]. Available at: https://www.pharmcouncil.co.za/ (Accessed: 7 August 2018).

South African Pharmacy Council (SAPC) (2010) *Good Pharmacy Practice in South Africa.* SAPC [Online]. Available at: https://www.mm3admin.co.za/documents/docmanager/0C43CA52-121E-4F58-B8F6-81F656F2FD17/00052829.pdf (Accessed: 31 July 2018).

South African Pharmacy Council (SAPC) (2017) *Statistics for Registered Persons and Organisations.* SAPC [Online]. Available at: https://www.sapc.za.org/B_statistics.asp (Accessed: 27 August 2018).

The South African Pharmacy Council (SAPC) (2018a) *Board Notice 59 of 2018, 2018 Competency Standards for Pharmacists in South Africa*. SAPC [Online]. Available at: https://www.mm3admin.co.za/documents/docmanager/0c43ca52-121e-4f58-b8f6-81f656f2fd17/00126360.pdf (Accessed: 23 August 2018).

South African Pharmacy Coucil (SAPC) (2018b) *Registrations.* SAPC [Online]. Available at: https://www.pharmcouncil.co.za/B_Regs_Search.asp (Accessed: 1 August 2018).

South African Pharmacy Council (SAPC), (2018c) *September is Pharmacy Month - Use Medicines Wisely.* SAPC [Online]. Available at: http://pharmaciae.org.za/september-is-pharmacy-month-use-medicines-wisely/ (Accessed: 22 August 2018).

Statistics SA (2011) *Census 2011 Provinces at a Glance.* [Online]. Available at: http://www.statssa.gov.za/census/census_2011/census_products/Provinces%20at%20a%20glance%2016%20Nov%202012%20corrected.pdf (Accessed: 7 February 2018).

Statistics SA (2013) *Causes of Death 2013*. [Online]. Available at: http://www.statssa.gov.za/?page_id=737&id=3 (Accessed: 19 March 2018

statslectures (2010) *Hypothesis Testing with Pearson's r.* [Online]. Available at: https://www.youtube.com/watch?v=rR-jptLvhFw (Accessed: 19 August 2018).

Suleman, F. (2010) 'Pharmacovigilance - Who is Responsible and Why Should We Care?*', SA Association of Hospital and Institutional Pharmacists,* Oct, pp. 56-58 [Online]. Available at: https://www.sapj.co.za/index.php/SAPJ/article/viewFile/892/822 (Accessed: 30 January 2018).

Summers, R., Dube, N. and Meyer, H. (2013) 'Pharmacovigilance: a Vital Tool or a Wasted Effort?', *SA Pharmaceutical Journal, Vol. 80, No 7* [Online]. Available at: http://www.sapj.co.za/index.php/SAPJ/article/view/1621/2621 (Accessed: 30 January 2018).

SurveyMonkey (2018a) *Completion Rates.* [Online]. Available at: https://www.surveymonkey.com/mp/what-is-the-difference-between-a-response-rate-and-a-completion-rate/ (Accessed: 24 July 2018).

SurveyMonkey (2018b) *Help Centre.* [Online]. Available at: https://help.surveymonkey.com/results?stq=firewall (Accessed: 19 July 2018).

SurveyMonkey (2018c) *Sample Size Calculator.* [Online]. Available at: https://www.surveymonkey.com/mp/sample-size-calculator/ (Accessed: 19 July 2018).

Surveymonkey (2018d). *Survey Sample Size.* [Online]. Available at: https://www.surveymonkey.com/mp/sample-size/ (Accessed: 24 July 2018).

Suyagh, M., Farah, D. and Abu Farha, R. (2014) 'Pharmacist's Knowledge, Practice and Attitudes toward Pharmacovigilance and Adverse Drug Reactions Reporting Process', *Saudi Pharmaceutical Journal,* Vol. 23, Issue 2, April, pp. 147-153 [Online]. Available at: https://www.sciencedirect.com/science/article/pii/S1319016414000681 (Accessed: 27 August 2018).

Torjesen, I. (2014) 'UK Regulator Removes Need to Report all Adverse Drug Reactions in Children', *The Pharmaceutical Journal,* 30 Sept [Online]. Available at: https://www.pharmaceutical-journal.com/news-and-analysis/uk-regulator-removes-need-to-report-all-adverse-drug-reactions-in-children/20066676.article (Accessed: 30 Janaury 2018).

UNAIDS (2018) *Country South Africa.* [Online]. Available at: http://www.unaids.org/en/regionscountries/countries/southafrica (Accessed: 6 February 2018).

University of the Western Cape (UWC) (n.d.) *Policy on Research Ethics.* UWC [Online]. Available at: https://www.google.co.za/url?sa=t&rct=j&q=&esrc=s&source=web&cd=1&cad=rja&uact=8&ved=0ahUKEwiomO7V1bPVAhUKJcAKHZGHCMAQFggkMAA&url=http%3A%2F%2Flib.uwc.ac.za%2Fresearch%2Fimages%2FResearch%2520Ethics%2520Policy.pdf&usg=AFQjCNEGsBqvel_wyXcWQ-jCDysDNwv6Iw (Accessed: 30 Janaury 2018).

University of the Western Cape (UWC) (2014) *Research Proposal Guide.* UWC [Online]. Available at: https://www.google.co.za/url?sa=t&rct=j&q=&esrc=s&source=web&cd=2&cad=rja&uact=8&ved=0ahUKEwj3tLSt1bPVAhWHHsAKHZ9NBjoQFggqMAE&url=https%3A%2F%2Fwww.uwc.ac.za%2FStudents%2FPostgraduate%2FDocuments%2FRESEARCH_PROPOSAL.pdf&usg=AFQjCNGSX8u9-nywsOEgwEeL69InlLN (Accessed: 30 Janaury 2018).

Van Grootheest, A. C. and De Jong-van den Berg, L.T.W. (2009) 'The Role of Hospital and Community Pharmacists in Pharmacovigilance [Abstract]', *Research in Scoial and Administrative Pharmacy,* Vol 1, Issue 1, March, pp. 126-133 [Online]. Available at: http://www.rsap.org/article/S1551-7411(04)00010-5/abstract (Accessed: 5 February 2018).

Van Grootheest, K., Olsson S., Couper, M. and De Jong-van den Berg, L. (2003) 'Pharmacists' Role in Reporting Adverse Drug Reactions in an International Prespective', *Pharmacoepidemiology and Drug Safety, John Wiley & Sons, Ltd* [Online]. Available at: http://www.academia.edu/22109223/Pharmacists_role_in_reporting_adverse_drug_reactions_in_an_international_perspectiv (Accessed: 8 February 2018).

Walji, R. (2008) 'Reporting Adverse Drug Reactions Associated with Herbal Products: Consumer, Health Food Store Personnel and Pharmacist Perspectives', *University of Toronto* [Online]. Available at: https://tspace.library.utoronto.ca/bitstream/1807/17295/1/Walji_Rishma_200811_PhD_Thesis.pdf (Accessed: 7 February 2018).

Williams, C. (2015) 'Perceptions and Experiences of Reporting of Adverse Drug Reactions by Public Sector Pharmacists in a Rural District in the Western Cape', *University of the Western Cape (UWC)* [Online]. Available at: https://webcache.googleusercontent.com/search?q=cache:VKEeGktJ1SEJ:https://etd.uwc.ac.za/bitstream/handle/11394/4915/Williams_cj_mph_chs_2015.pdf%3Fsequence%3D1%26isAllowed%3Dy+&cd=5&hl=en&ct=clnk&gl=za (Accessed: 30 January 2018).

World Health Organisation (WHO) (2002) *Safety of Medicine - A Guide to Detecting and Reporting Adverse Drug Reactions - Why Health Professionals Need to Take Action.*WHO [Online]. Available at: http://apps.who.int/medicinedocs/en/d/Jh2992e/12.html (Accessed: 5 February 2018).

World Health Organisation (WHO) (2015) *WHO Pharmacovigilance Indicators: A Practical Manual for the Assessment of Pharmacovigilance Systems.* WHO [Online]. Available at: http://www.who.int/medicines/areas/quality_safety/safety_efficacy/EMP_PV_Indicators_web_ready_v2.pdf?ua=1 (Accessed: 5 July 2018).

World Health Organisation (WHO) (2018) *Pharmacovigilance.* WHO [Online]. Available at: http://www.who.int/medicines/areas/quality_safety/safety_efficacy/pharmvigi/en/ (Accessed 3 February 2018).

YellowCard (n.d.) *Home.* [Online]. Available at: https://yellowcard.mhra.gov.uk/ (Accessed: 30 July 2018).

Zuma, K., Manzini, K. and Mohlabane, N. (2014) 'HIV Epidemic in South Africa: A Comparison of HIV Epidemic Patterns of Two Extreme Provinces in South Africa', *Health SA Gesondheid,* Vol 19, No. 1 [Online]. Available at: https://hsag.co.za/index.php/HSAG/article/view/716 (Accessed: 6 February 2018).

APPENDIX A

Information Sheet

Faculty of Natural Science
University of the Western Cape
Private Bag X17, Bellville 7535, Cape Town
South Africa
Tel: 021-9593666; Fax: 021-9593407
E-mail:
rmpharmacovigilance@gmail.com
15 June 2018

Dear Community Pharmacist

I am a pharmacy master's student at UWC with over 10 years' experience in South Africa and in the United Kingdom. **This masters is delivered in association with Healthcare Learning in the UK as a Master's of Science in Pharmacy Administration and Policy Regulation.**

I have identified an area of concern among community pharmacists with regards to **pharmacovigilance** and specifically in the **reporting of adverse drug reactions** (ADRs). I am hoping that my research will focus attention on this vital responsibility and create an awareness of the need for ongoing support and training. One in twelve hospital admissions in South Africa is related to an ADR and it accounts for 16% of adult deaths (Mehta et. al., 2017).

As part of my Master's degree, I am conducting research entitled: **Community Pharmacists' Knowledge, Attitude and Practices on Adverse Drug Reaction Reporting in South Africa: A Comparative Study.**

The **objective** of the study is to compare the pharmacovigilance knowledge, attitude and practices among South African pharmacists. Research will comprise of an anonymous questionnaire to determine the level of pharmacovigilance knowledge, their attitude, and practice pattern in fulfilling these responsibilities.

Benefits to Participants: The study will indicate the status of pharmacovigilance among community pharmacists. This study may create an awareness among academic institutions, regulatory authorities and community pharmacy employers of gaps in pharmacists' pharmacovigilance knowledge.

Potential Risks to Participants: The questionnaire will present no risk as it is completely confidential.

Confidentiality: All information provided in the questionnaire will be kept strictly confidential. SAPC numbers are only necessary to verify that you are a registered pharmacist with the SAPC and will only be available to the researcher. Ethics clearance has been obtained from UWC.

Ethics Reference Number: BM18/4/4

Voluntary Participation: Participation is entirely voluntary. You are under no obligation to answer questions and you are free to withdraw from the study at any time.

Publication of Results: Completed questionnaires from you and other participants will be used in writing a Masters dissertation which will be available after the examination process. Results may also be published in academic journals. The research report, as well as any publication arising from the research can be made available to you upon request after completion of the review process.

The survey will take approximately 10 minutes to complete. The questions should be completed with responses that come to mind immediately. Responses obtained from the survey will be coded and not be linked personally to any participant.

By clicking on the link (below), it implies that you have consented to participate voluntarily in the study.

Please click on the link below or paste it in your browser:

https://www.surveymonkey.com/r/BZRTWS7

Thank you in advance.

Rensche Mayne

rmpharmacovigilance@gmail.com

Ethics Contact details as follows:
BMREC: Research Development
Private Bag X17, Bellville, 7535
Tel: + 27 21 959 4111
Email: research-ethics@uwc.ac.za

REFERENCES

Mehta, U.C., Kalk, E., Boulle,A., Nkambule, P., Gouws, J., Rees, H. and Cohen, K. (2017) 'Pharmacovigilance: A Public Health Priority for South Africa', *South African Health Review,* Pg.125-133 [Online]. Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5708547/ (Accessed: 18 March 2018)

APPENDIX B

Questionnaire for Community Pharmacists

Demographics

1. Indicate your age from one of the options mentioned below (tick only one option):

a) 24-30 years

b) 31-40 years

c) 41-50 years

d) 51-60 years

e) Above 60

2. Gender (tick only one option):

a) Male

b) Female

3. Please provide your SAPC registration number or P number. This information is required to verify that you are a registered pharmacist in South Africa:

_____

4. Please indicate your title/position in the pharmacy (tick as many as applicable):

a) Pharmacy Manager in a Chain of pharmacy

b) Pharmacy Manager in an Independent Pharmacy

c) Responsible Pharmacist

d) Pharmacist Owner of an Independent Pharmacy

e) Locum

f) Junior Pharmacist

5. What is your highest qualification? (tick only one option):

a) B.Pharm

b) Dip.Pharm

c) M.Pharm

d) Other: Please specify_____

6. How long have you been working in community pharmacy? (tick only one option):

a) Less than 2 years

b) 2-5 years

c) 5-10 years

d) 10-20 years

e) More than 20 years

7. In which province are you currently practising as a community pharmacist? (tick only one option)?

a) Western Cape

b) Eastern Cape

c) KwaZulu-Natal

e) Gauteng

f) North West

g) Limpopo

h) Free State

i) Northern Cape

j) Mpumalanga

Knowledge

8. Where did you first hear about or encounter pharmacovigilance? (tick only one option):

a) From the South African Pharmacy Council (SAPC)

b) From a pharmaceutical company

c) From your CPD (Continuing Professional Development)

d) From an academic institution

e) Other (please specify) _____

f) I can't remember.

g) From the South African Health Products Regulatory Authority (SAHPRA)

9. Have you ever received training in pharmacovigilance?

a) Yes

b) No

c) I am not sure

10. Who offered the pharmacovigilance training to you? (tick as many as applicable):

a) South African Pharmacy Council representative

b) A pharmaceutical company representative

c) A higher education representative

d) Pharmaceutical Society of South Africa representative

e) Other_____

f) I have not received any training

11. In your opinion, Adverse Drug Reaction (ADR) reporting entails (tick as many as applicable):

a) Contacting the prescriber

b) Referring the patient to the prescriber

c) Filling in the Adverse Drug Reactions Reporting Form

d) Making a note on the patient's medication record

12. Which of the following adverse drug reactions qualify for reporting? Select as many options which are deemed applicable:

a) All adverse drug reactions to new marketed drugs or drugs added to the Essential Drugs List

b) All serious interactions and reactions

c) Ambiguous adverse reactions in the package insert

d) Unusual or interesting drug reactions

e) Product quality problems like contamination, stability and defective compounds

f) Product quality problems like poor packaging and labelling

g) Treatment failures

h) All adverse reactions experienced by the patient

i) Herbal adverse reactions experienced by the patient

13. From your experience, which of the following is most likely identified as a serious adverse event and therefore should be reported within 15 calendar days? Select as many options which are deemed applicable:

a) Life-threatening

b) Disability

c) Death

d) Hospitalisation

e) Sick leave at home

14. Which of the following should be reported or managed as part of the pharmacovigilance responsibilities of a pharmacist? Select as many options which are deemed applicable:

a) Adverse drug reactions

b) Substandard drugs

c) Medication errors

d) Use of drugs off-licence with inadequate scientific basis

e) Abuse and misuse

f) Lack of efficacy

g) Poisoning

h) Adverse interactions with other drugs, herbs, food and chemicals

i) Drug-related mortality

j) Destruction of expired stock

15. In your view, is pharmacovigilance a legal requirement for pharmacists?

a) Yes

b) No

c) I am not sure

16. In your opinion, once adverse drug reactions are reported on the ADR report form (tick as many as applicable):

a) They are reviewed by the National Drug Event Monitoring Centre (NADEMC) in Cape Town

b) They are reported to VigiBase managed by the World Health Organisation (WHO) Uppsala Monitoring Centre in Sweden

c) They are assessed by the South African Health Products Regulatory Authority (SAHPRA) Pharmacovigilance Committee

d) They are assessed by the Medicine Information Centre in Cape Town.

17. The World Health Organisation (WHO) defines pharmacovigilance as (tick only one option):

a) …the science and activities relating to the detection and assessment of adverse effects or any other drug-related problem.

b) … the science and activities relating to the understanding and prevention of adverse effects or any other drug-related problem.

c) All of the above

18. From your practice experience, a drug which was identified as having a high risk for patient safety and subsequently discontinued from the market is:

Name of drug: _____

19. Adverse drug reactions are usually reported to the (tick only one option):

a) South African Health Products Regulatory Authority (SAHPRA)

b) National Adverse Drug Event Monitoring Centre (NADEMC)

c) All of the above

d) I am not sure

Practice

20. In my practice, I generally manage adverse drug reactions by (tick as many as applicable): Check question

a) Phoning the prescriber

b) Referring the patient to the prescriber

c) Referring the patient to the hospital emergency ward

d) Counselling the patient and leaving it up to the patient to decide what is best

e) Filling in a ADR reporting form

21. Please specify the name(s) of the drug(s) for which you have reported adverse drug reactions on the ADR reporting form: Check question_____

22. The adverse drug reaction (ADR) report form is accessible from (tick as many as applicable):

a) The South African Health Product Regulatory Authority (SAHPRA)

b) The South African Pharmacy Council (SAPC)

c) The back page of the South African Medicines Formulary (SAMF)

d) Other

23. Based on my experience, I prefer reporting an adverse drug reaction on the ADR report form by (tick only one option):

a) Telephone

b) Fax

c) Email

d) Post / Courier

e) Other_____

24. Over this last year I was able to report the following number of adverse drug reactions on an ADR form (tick only one option):

a) At least one

b) At least two

c) At least three

d) Four and more

e) None

Opinion

25. In your opinion, the role of the South African Pharmacy Council (SAPC) in supporting the practice of pharmacovigilance among pharmacists has been (tick only one option):

a) Very Prominent

b) Somewhat Prominent

c) Hardly Prominent

d) I am not sure

26. I feel that I receive enough support from my employer to fulfil my pharmacovigilance responsibilities (tick only one option):

a) Yes

b) No

c) I am not sure

27. Who do you think should take responsibility for pharmacovigilance education? (tick as many as applicable):

a) The South African Pharmacy Council (SAPC)

b) The Pharmaceutical Industry

c) Academia

d) The South African Health Products Regulatory Authority (SAHPRA)

e) The Pharmaceutical Society of South Africa

f) Pharmacists through CPD

28. In my view, clinical trials offer adequate information in determining the safety of registered medicinal products (tick only one option):

a) Yes

b) No

c) I am not sure

29. In my view, adverse drug reporting on the ADR reporting form lies outside of the scope of the clinical and legal competence of pharmacists (tick only one option):

a) Yes

b) No

c) I am not sure

30. I think that completing the Adverse Drug Reaction (ADR) report form is more relevant to pharmacists working in the public health sector (tick only one option):

a) Yes

b) No

c) I am not sure

31. If I knew that pharmaceutical companies and regulators relied on information obtained from pharmacists' written reports on adverse drug reactions to guarantee the safety of patients, I feel that I would (tick as many as applicable):

a) Become more aware of adverse drug reactions

b) Ensure that I received the required training

c) Be proactive in filling in the ADR reporting form

d) Other

32. Based on my experience as a pharmacist, the number of adverse drug reactions which I have reported on the ADR report form in my career could be estimated at (tick only one option):

a) Less than 3

b) Between 3 and 5

c) Between 5 and 10

d) More than 10

33. One of my concerns about adverse drug reporting is that it may overburden the (tick only one option):

a) Pharmaceutical Society of South Africa

b) South African Health Products Regulatory Authority (SAHPRA)

c) Pharmaceutical company

d) The company I work for

e) My workload

f) I have no concerns

34. In my practice, I feel that when it comes to fulfilling my pharmacovigilance responsibilities regarding adverse drug reactions (tick as many as applicable):

a) I do not have enough time

b) I am not confident in filling in the adverse drug reaction form

c) ADRs are not a common occurrence, therefore I tend to overlook it

d) The report is not an immediate concern, therefore I tend to neglect it

e) It is not my responsibility

f) None of the above

35. In my opinion, the shortage of pharmacists (tick as many as applicable):

a) Is partly to blame for the lack of time and support provided by employers to maintain pharmacovigilance

b) Is one of the reasons for pharmacists becoming reluctant in taking on pharmacovigilance responsibilities

c) Does not affect pharmacovigilance

36. In my view, the main obstacles to pharmacovigilance are (tick as many as applicable):

a) Lack of training

b) Lack of pharmacists

c) Lack of time

d) Lack of incentive

e) Lack of feedback

f) Lack of support

g) Other

37. I feel that in my practice, patients trust me enough to talk about adverse drug reactions (tick only one option):

a) Yes

b) No

c) I am not sure

38. I think that patients would expect me to be proactive when adverse drug reactions cause distress to their health (tick only one option):

a) Yes

b) No

c) I am not sure

39. I think the adverse drug reaction form is easily accessible from the relevant websites:

a) Yes

b) No

c) I am not sure

40. I think it is more the prescribers' responsibility to report adverse drug reactions on the adverse drug reaction (ADR) report form and so assist post-market surveillance of drugs:

a) Yes

b) No

c) I am not sure

Thank you for participating in the study.

APPENDIX C

Adverse Drug Reactions Reporting Form

health
Department:
Health
REPUBLIC OF SOUTH AFRICA

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

(Including Herbal Products)

mcc
MEDICINES CONTROL COUNCIL

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

Reporting Health Care Facility/Practice

Tel: 012 395 8197 (MCC) 021 447 1618 (NADEMC) Fax: 086 620 7253 E-mail: adr@health.gov.za	Facility/Practice				
	District		Tel		
	Province		Fax		

Patient Details

Patient Initials		File/Reference Number		Date of Birth/Age			
Sex	☐ M ☐ F ☐ Unk	Race		Weight (kg)		Height (cm)		Pregnant?	☐ N ☐ Y
Allergies				Estimated Gestational Age at time of reaction			

Suspect Medicine(s) [Medicines suspected to have caused the ADR]

Trade Name [Generic Name if Trade Name is unknown]	Route	Dose (mg) and Interval	Date Started/Given	Date Stopped	Reason for use	Batch Number	Expiry Date

All other Medicines Patient was taking at time of reaction [including over-the-counter and herbal products]

Trade Name [Generic Name if Trade Name is unknown]	Route	Dose (mg) and Interval	Date Started/Given	Date Stopped	Reason for use	Batch Number	Expiry Date

Adverse Drug Reaction/Product Quality Problem

Date and time of onset of reaction		Date reaction resolved/duration	

Please describe Adverse Reaction/Product Quality Problem: (kindly add as much clinical information as possible)

Intervention(tick all that apply)

- ☐ No intervention
- ☐ Intervention unknown
- ☐ Patient Counselled/non-medical treatment
- ☐ Discontinued Suspect Drug; **Replaced with:**_____
- ☐ Decreased Suspect Drug Dosage; **New Dose:**_____
- ☐ Treated ADR - with:_____
- ☐ Referred to Hospital: **Hospital Name**_____
- ☐ Other Intervention (e.g. dialysis):_____

Patient Outcomes (tick all that apply)

- ☐ ADR recovered/resolved☐ recovering/resolving
- ☐ not recovered/not resolved
- ☐ Patient Died: Date of death:_____
- ☐ Impairment/Disability ☐ Congenital Anomaly
- ☐ Patient Hospitalised or Hospitalisation prolonged
- ☐ Life Threatening ☐ Other:_____
- ☐ ADR reappeared after restarting suspect drug/similar drug (rechallenge)?: ☐ N ☐ Y ☐ Not done ☐ Unknown

Laboratory Results

Lab Test	Test Result	Test Date

Additional Laboratory Results

Lab Test	Test Result	Test Date

Co-morbidities/Other Medical Condition(s)

Reported by

Name		E-mail	
Designation	☐ Nurse ☐ Pharmacist ☐ Doctor ☐ Other:	Telephone	
Date reported:		Signature	

THIS ADR REPORT IS NOT A CONFIRMATION THAT THE REPORTER OR THE SUSPECT MEDICINE(S) CAUSED THE ADR v4.0 07/16

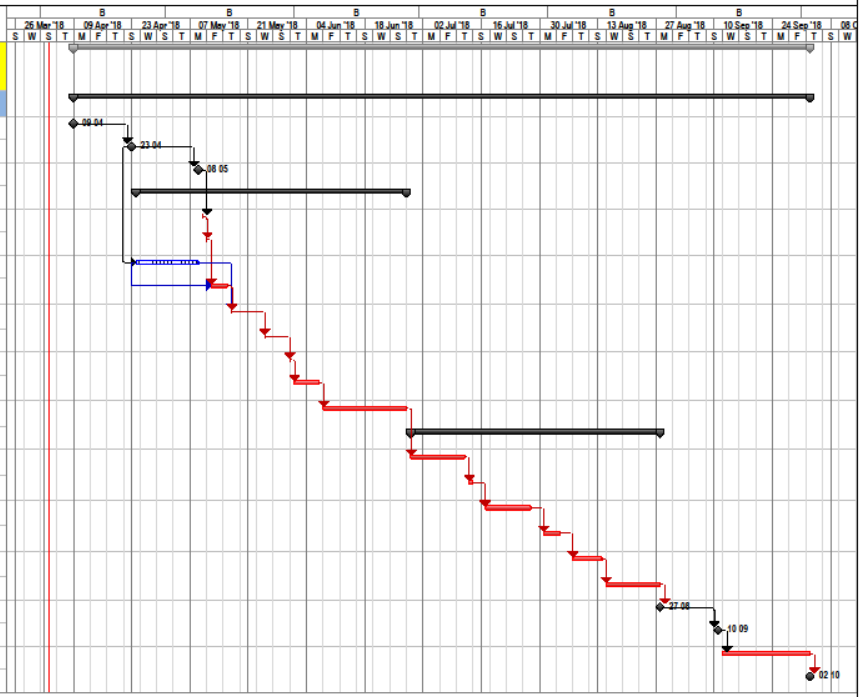
APPENDIX D

Timeline for Research

RESEARCH DISSERTATION
COMMUNITY PHARMACISTS' KNOWLEDGE OF ADR REPORTING IN SOUTH AFRICA

RENSCHE MAYNE

ID	Outline Number	Task Name	Dur	Start	Finish
0	0	COMMUNITY PHARMACISTS' KNOWLEDGE ON ADR REPORTING IN SOUTH AFRICA	123 d	09 04 18	02 10 18
1	1	RESEARCH & DISSERTATION SCHEDULE	123 d	09 04 18	02 10 18
2	1.1	Submit title registration form to UWC	0 d	09 04 18	09 04 18
3	1.2	Submit final proposal to supervisor	0 d	23 04 18	23 04 18
4	1.3	Receive acceptance of proposal from UWC	0 d	08 05 18	08 05 18
5	1.4	Conduct Survey / Data sourcing	46 d	23 04 18	27 06 18
6	1.4.1	Pilot survey questionaire	1 d	09 05 18	09 05 18
7	1.4.2	Revise questionaire incorporating feedback	1 d	10 05 18	10 05 18
8	1.4.3	Obtain community pharmacist contact details	10 d	23 04 18	08 05 18
9	1.4.4	Create MonkeySurvey Quantitative questionnaire	3 d	11 05 18	15 05 18
10	1.4.5	Send invitation for MonkeySurvey participation	1 d	16 05 18	16 05 18
11	1.4.6	Send out second reminders	1 d	24 05 18	24 05 18
12	1.4.7	Send out third reminders	1 d	30 05 18	30 05 18
13	1.4.8	Collect MonkeySurvey results	5 d	31 05 18	06 06 18
14	1.4.9	Code MonkeySurvey results	15 d	07 06 18	27 06 18
15	1.5	Write up thesis	42 d	28 06 18	27 08 18
16	1.5.1	Table results	10 d	28 06 18	11 07 18
17	1.5.2	Confirm hypothesis	2 d	12 07 18	13 07 18
18	1.5.3	Write up thesis	10 d	16 07 18	27 07 18
19	1.5.4	Write reference section and confirm references	5 d	30 07 18	03 08 18
20	1.5.5	Write abstract	5 d	06 08 18	13 08 18
21	1.5.6	Draft Dissertation	10 d	14 08 18	27 08 18
22	1.6	Submit Dissertation for preliminary review	0 d	27 08 18	27 08 18
23	1.7	Receive feedback on Preliminary submission	0 d	10 09 18	10 09 18
24	1.8	Revise Dissertation incorporating comments	15 d	11 09 18	02 10 18
25	1.9	Submit Final Dissertation	0 d	02 10 18	02 10 18



DISSERTATION PROPOSAL 18 04 02 Page 1 of 1 Print date: 02 04 18 6:48 PM

APPENDIX E

DISSERTATION PROPOSAL

UNIVERSITY OF WESTERN CAPE

RESEARCH PROPOSAL

Name of candidate:	**Rensche Mayne**
Student number:	**3774623**
Proposed degree:	**Masters of Science in Pharmacy Administration and Policy Regulation**
Programme / Department:	**School of Pharmacy**
Title of thesis:	**Community pharmacists' knowledge, attitude and practices on adverse drug reaction reporting in South Africa**
Supervisor:	**Professor Angeni Bheekie**
Date:	**28 March 2018**

Summary (Faculty)

Background

Pharmacovigilance involves the management of substandard drugs, medication errors, “off-licence” drugs, abuse and misuse, lack of efficacy, poisoning, adverse drug reactions (ADRs), drug-, food- and chemical interactions, expired stock destruction and drug-related mortality. Regulators and the pharmaceutical industry rely on pharmacists to report ADRs. In South Africa (SA) ADRs cause adult deaths and hospital admissions. The majority of pharmacists work in community pharmacies and they are often the first point of contact when ADRs are experienced.

Complicated treatments for communicable diseases, self-medication, misuse of over-the-counter (OTC) medicines, vitamins and traditional medicines, increase the probability of ADRs. In the developed world, pharmacovigilance is common among pharmacists. SA however compares poorly in terms of ADR reporting. Studies in the public sector have found that pharmacists lack pharmacovigilance knowledge and underreport ADRs, but studies have yet to explore the pharmacovigilance knowledge and practice patterns among community pharmacists.

Aim and objectives

This study aims to determine the knowledge, attitude and practice pattern of South African community pharmacists in ADR reporting. The study objectives are to:

- Measure the extent of ADR reporting among community pharmacists.
- Compare ADR reporting in knowledge, attitude and practices of community pharmacists across the nine South African provinces.

Method

A quantitative, online, anonymous survey will be conducted among community pharmacists across the nine SA Provinces. Contact details from community pharmacies will be obtained from websites to measure their knowledge, attitude and

practice patterns in ADR reporting. Differences among participants across the provinces will be compared.

Ethics

Participants will not be identifiable by name, therefore their responses will not be linked personally. An information sheet outlining the study's purpose, objective, significance and dissemination of the findings will be available electronically to prospective participants. The benefits and risks for participating in the study will be outlined. Written informed consent will be obtained from each survey participant and confidentiality will be assured throughout the study. Participants can withdraw from the study at any time.

Conclusion

Patients rely on pharmacists' expertise to guarantee their safety. SA needs a robust, united, national pharmacovigilance system and access to independent drug information.

Abstract

Pharmacovigilance involves the management of substandard drugs, medication errors, "off-licence" drugs, abuse and misuse, lack of efficacy, poisoning, adverse drug reactions (ADRs), drug-, food- and chemical interactions, expired stock destruction and drug-related mortality.

Regulators and the pharmaceutical industry rely on pharmacists to report ADRs. In South Africa (SA) ADRs cause adult deaths and hospital admissions. The majority of pharmacists work in community pharmacies and they are often the first point of contact when ADRs are experienced.

Complicated treatments for communicable diseases, self-medication, misuse of over-the-counter (OTC) medicines, vitamins and traditional medicines, increase the probability of ADRs. In the developed world, pharmacovigilance is common among

pharmacists. SA however compares poorly in terms of ADR reporting. Studies in the public sector have found that pharmacists lack pharmacovigilance knowledge and underreport ADRs, but studies have yet to explore the pharmacovigilance knowledge and practice patterns among community pharmacists.

This study aims to determine the knowledge, attitude and practice pattern of South African community pharmacists in adverse drug reporting.

A quantitative online, anonymous survey will be conducted among community pharmacists across the nine SA Provinces. Contact details from community pharmacies will be obtained from websites to measure their knowledge, attitude and practice patterns in ADR reporting. Differences among participants across the provinces will be compared. The study will also determine the measure of support community pharmacists receive in pursuing ADR reporting.

Patients rely on pharmacists' expertise to guarantee their safety. SA needs a robust, united, national pharmacovigilance system and access to independent drug information.

Title

Community pharmacists' knowledge, attitude and practices on adverse drug reaction reporting in South Africa: a comparative study.

Key Words

Pharmacovigilance, community pharmacists, knowledge, attitude and practices, South Africa (SA), adverse dug reaction (ADR) reporting

Aims and Objectives of the Research

Academic Aim: The study aims to determine the knowledge, attitude and practice pattern of South African community pharmacists in ADR reporting, since it is regarded as a macro-level public health pharmacy activity (Bradley, Sanders and Bheekie, 2011).

Strategic Aim: The study aims to examine pharmacovigilance awareness among South African community pharmacists. The findings would provide pharmacy and health care planners, researchers and the pharmaceutical industry potential deficiencies knowledge, attitude and practices in ADR reporting.

The study objectives are to:

- Measure the extent of ADR reporting among community pharmacists.
- Compare the pharmacovigilance knowledge, attitude and practices of community pharmacists across the nine South African provinces.

Research question

What is the knowledge, attitude and practice pattern among community pharmacists across South Africa in reporting adverse drug reactions?

Research Hypothesis

The hypothesis is: If community pharmacists have limited pharmacovigilance knowledge (independent variable), then they are less likely to report on adverse drug reactions (dependent variable).

The alternate hypothesis is: If community pharmacists have sound pharmacovigilance knowledge (independent variable), then they are more likely to report on adverse drug reactions (dependent variable).

Rationale /Background

The safety of medicines remains one of the primary goals of pre-clinical studies and clinical trials (Suleman, 2010). The World Health Organisation (WHO) (2002) states that adverse drug reactions (ADRs) cause increased mortality and morbidity throughout the world. One in twelve hospital admittances in South Africa (SA) are related to an ADR and it accounts for 16% of adult deaths (Mehta et. al., 2017). This amounts to a considerable financial burden for an already overstretched health system (Mayosi and Benatar, 2014).

SA has one of the biggest disease burdens worldwide with 19% of people living with HIV (UNAIDS, 2018) along with malaria and tuberculosis (TB). In 2017, 9 478 malaria cases were reported (National Institute for Communicable Diseases (NICD), 2017) and 8.8% of reported deaths (2013) were due to TB (Stats SA, 2013). Treatment regimes for such diseases are complicated and therefore pharmacovigilance is crucial to protect patient safety (Mehta et. al., 2017). Antiretroviral ADRs reporting schemes have now been launched nationally in all provinces, but ADRs involving non-communicable diseases also need to be reported (Mehta et.al, 2017).

In the developed world, pharmacovigilance is common practice among pharmacists (Van Grootheest, Olsson, Couper and de-Jong-van den Berg, 2003). Australia (30%), Netherlands (29.3%), Spain (24.5%) and Canada (28.4%), took the lead for pharmacist-led ADR reporting, while low reporting rates were noted from United Kingdom (UK,11.9%) and South Africa (2.8%). Community pharmacists in the

Netherlands, Japan, Cuba and Portugal contribute considerably to ADR reports (Van Grootheest and de Jong-van den Berg, 2009).

Literature Review / Framework of the Research

Pharmacists are regarded as the authority on medicines, who are accountable to health authorities in the practice of pharmacovigilance (Suleman, 2010).

The Importance of Pharmacovigilance

Ioannidis (2009) argues that the monitoring of ADRs during clinical trials is inadequate since it does not mimic “real-life” situations and is often under-reported. An international data-based study revealed that 462 medicinal products were withdrawn (1950 – 2014) due to ADRs (Onakpoya, Heneghan and Aronson, 2016). Drugs which were withdrawn included cisapride, rofecoxib, and cerivastatin (Lexchin, 2014); and product label changes following post-marketing pharmacovigilance included among others aspirin, gamelonic acid, isotretinoin and kava kava (Jobson, 2003).

Cheema et. al. (2017) concluded that pharmacists in the United Kingdom (UK) cited lack of time and adverse reactions not regarded as serious, were perceived hindrances to adverse drug reporting. They added that even though an increase in pharmacist adverse drug reporting was evident in recent years, further education and training is however needed. Pharmacists who saw themselves as contributing to the safety data of health products were more likely to report ADRs in Canada (Walji, 2008). A Jordanian study showed that pharmacists prefer to refer patients to the prescribing doctor or emergency ward, rather than report the ADR themselves (Suyagh, Farah and Abu Farha, 2014). Pharmacists, seem to overlook their responsibilities, when it comes to ADR reporting.

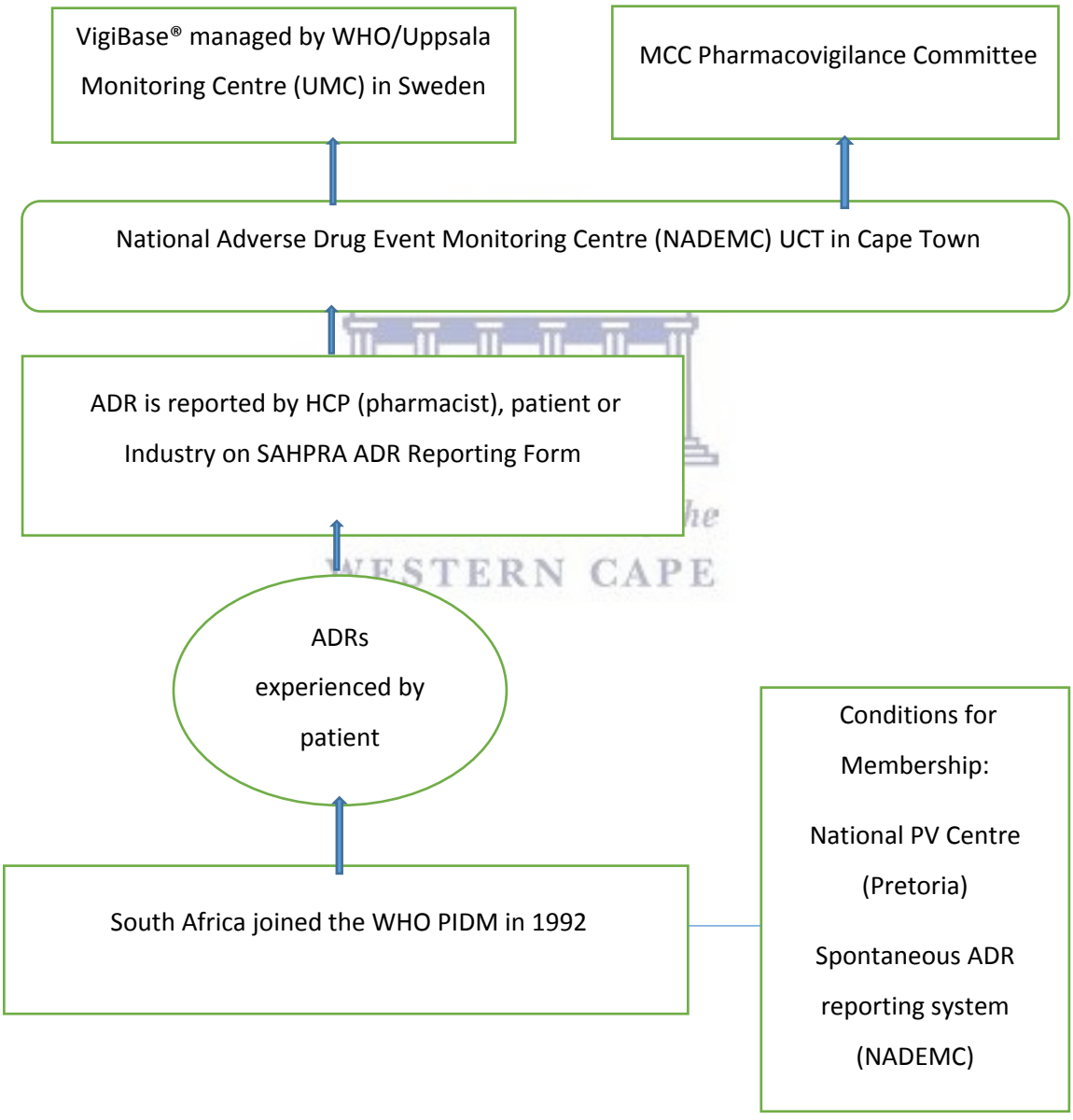
Pharmacovigilance in South Africa

Drug therapy is crucial to the health care of the population. One aspect linked to care provision is response to such therapy. When people respond adversely to medicine therapy, imminent intervention from pharmacists to report ADRs is required. Since the majority of South African pharmacists (70%) work in private sector community pharmacies, they are in direct contact with the population (South African Pharmacy

Council (SAPC), 2017), and therefore pivotal in identifying and reporting ADRs to national health authorities.

SA joined the WHO Programme for International Drug Monitoring (PIDM) in 1992 (Ampadu et. al, 2016). The conditions for membership include a designated national Pharmacovigilance centre (in Pretoria), a spontaneous ADR reporting system and the submission of at least 20 Individual Case Safety Reports (ICSR) to VigiBase ® to show competence in completing ICSRs (Ampadu et. al., 2016). The Uppsala Monitoring Centre (UMC) in Sweden manages VigiBase® for the WHO. Ampadu et. al. (2016) found that ICSR forms from Africa make up less than 1% of submission to VigiBase®. The Medicine Control Council (MCC) transitioned into the South African Health Products Regulatory Authority (SAHPRA) in 2017 and their website is in a transition phase (South African Health Products Regulatory Authority (SAHPRA), n.d.). The South African Health Products Regulatory Authority (SAHPRA) National Adverse Drug Event Monitoring Centre (NADEMC), at the University of Cape Town, is responsible for managing the national ADR Database (ADRI) which is fed into UMC in Sweden (Figure 1). NADEMC liaise with SAHPRA and WHO (Jobson, 2003). Other institutions, parallel systems for public health programmes and NGOs also assess signals from ADRs, but they work independently and data is not always supplied to the national system (Maigetter et. al, 2015). NADEMC is a subunit of SAHPRA.

Figure 1 Schematic representation of adverse drug reporting structures within South Africa and the WHO international database Vigibase ®



The South African Department of Health mandates that all ADRs which patients experienced, must be reported on the SAHPRA ADR Reporting Form in terms of section 33(o) of the Pharmacy Act, 53 of 1974 (Department of Health Notice 590 of 2017 - The South African Pharmacy Council, 2017).

Pharmacists are required to report as a minimum the identifiable reporter of the ADR including their qualification, an identifiable patient, the suspected medicine and the suspected reaction (South African Health Products Regulatory Authority (SAHPRA), 2016). See Appendix C for the SAHPRA ADR reporting form. Pharmaceutical companies are required to inform SAHPRA within the determined time frame of suspected ADRs reported to them as per Regulation 37 in the Medicine and Related Substances Act, 1965 (Act 101 of 1965) as amended (South African Health Products Regulatory Authority (SAHPRA), 2003). SAHPRA is the legal body that ensures safety, efficacy and quality of medicines (Mehta, 2011).

SAHPRA's Pharmacovigilance Committee reviews complaints and make recommendations to SAHPRA which could include withdrawal of the particular drug or a call for changes to the product information by the pharmaceutical company. Most interventions in SA are due to international warnings (Maigetter et. al., 2015), therefore SA community pharmacists could play a pivotal role in ADR reporting.

In a Pharmacovigilance workshop held at the South African Association of Hospital and Institutional Pharmacists (SAAHIP) conference 2013, it was determined that the pharmacovigilance system in SA is in need of reform (Summers, Dube and Meyer, 2013). The findings from the workshop were that pharmacists had poor pharmacovigilance knowledge and understanding of its purpose in the safety of patients (Summers, Dube and Meyer, 2013). Even though pharmacists are the custodians of medication, they seem to be failing in their duty to report ADRs.

South African pharmacovigilance studies have mainly focused on the public sector and on specific regions (Table 1). An Eastern Cape study conducted at a regional training centre attested that underreporting of ADRs was a big problem (Ruud, Srinivas and Toverud, 2009). A North West pharmacovigilance study conducted among hospital and community pharmacists found that knowledge was low (Joubert and Naidoo 2016). The findings from a Western Cape study conducted in the rural

winelands found that pharmacists realised the importance of pharmacovigilance, but rarely reported ADRs themselves (Williams (2015). The study also noted that some pharmacists viewed some ADRs as outside their legal or clinical scope of practice and preferred to refer the patient to the prescriber.

Table 1 Summary findings of pharmacovigilance studies conducted among South African pharmacists

	Eastern Cape	**North West province**	**Western Cape**
Sector	Public	Public and Private	Public
Participants	HCP (n=12) pharmacists (n=3	n=102	n=24
Pharmacovigilance (PV) knowledge among pharmacists	They were familiar with the concept	Low	They realised importance of PV
ADR Reporting	Low	Low (44.1%)	Low
Reason/Barriers	Lack of training, filling in the form, high workload, lack of feedback, fear of not being taken seriously	Time (50%) Did not know how to report (38%) Did not know where to report (35%)	Some viewed ADR reporting as outside their legal and clinical scope. Lack of feedback, heavy workload, time, uncertainty in identifying ADR, reporting process
Willingness to participate in training	Yes	High (80%)	High
Reference	Ruud, 2009	Joubert & Naidoo, 2016	Williams, 2015

Overall, research on the reporting of ADRs by South African pharmacists is limited (Suleman, 2010). Studies that have been done, found that generally pharmacovigilance knowledge is low amongst pharmacists. This could mean that pharmacists knowledge is limited, which is precluding them from actively reporting on ADRs which have become a public health problem (Mehta, 2011).

Pharmaceutical companies are vital in SA in educating healthcare professionals (HCP) on the importance of pharmacovigilance (Roux, 2014). This is true, especially since they are accountable. Industry-sponsored continuing medical education (CME) is, however, associated with less rational prescribing by doctors (Lieb and Scheurich, 2014). HCPs must be resistant to aggressive marketing of new drugs by industry (Mehta, 2011). It is interesting that the pharmaceutical industry in South Africa is rather unwilling to disclose payments for research and hospitality, compared to mandatory disclosure in the United States (US) and voluntary disclosure in the UK, as part of a move towards more transparency and trust (Kahn, 2016). Independent drug information is not readily available in SA and as a result of this there is a greater need for pharmacists to become more vigilant in reporting ADRs (Mehta, 2011).

Barriers to ADR reporting in SA includes lack of time, lack of knowledge, lack of feedback and lack of understanding (Suleman, 2010). Difficulty in communicating ADRs and poverty are also listed by Ruud, Srinivas and Toverud (2012) as obstacles. In poor provinces the likelihood of patients reporting ADRs may be less compared to those reported in affluent provinces (Ruud, Srinivas and Toverud, 2012).

Pharmacovigilance is seen as a vital practice as SAHPRA proposes to regulate complementary medicine in the near future (Gray, Riddin and Jugathpal, 2016). Self-medication, misuse of over-the-counter (OTC) medicines, vitamins and traditional medicines; increase the risk of ADRs in SA (Mehta, 2011). SAHPRA underpins pharmacovigilance to protect patient safety (Mehta et. al., 2017).

Conclusion

Pharmacists, as custodians of medication, are essential in recording and submitting ADRs to national health authorities to fulfil their professional obligation. Pharmaceutical companies and regulatory authorities rely on pharmacists to assist in the continuous surveillance of drugs to improve patient safety. Pharmacists must use their expert knowledge to protect the safety of those who trust them.

South Africa is in need of a robust, united, national pharmacovigilance system (Mehta et. al., 2017). Lack of manpower and a three-year backlog at NADEMC does little for encouraging ADR reporting (Maigetter et. al., 2015). Discrepancies across

the provinces could indicate the lack of support community pharmacists may have in pursuing pharmacovigilance.

Delimitation of Study Area/Assumptions on which the Research Project Rests

Limitations

Constraints of the research are that not all pharmacists in SA will participate in the survey. Pharmacists are dealing with a considerable workload on a daily basis and regular follow-up to complete surveys will have to be done in order to get enough statistical power. Pharmacists may not be able to remember the exact number of adverse drug reactions they have reported within the specified time. Electronic access to pharmacists may be limited if pharmacies do not display their email address on the internet. The survey results rely on self- reporting by pharmacists. Some pharmacists may access the internet to record the correct answers.

Assumptions are that measuring the knowledge, attitude and practice of ADR reporting will give an indication of one aspect of pharmacovigilance awareness among community pharmacists. Other areas of pharmacovigilance will not be assessed in this study. It is assumed that pharmacists will not discuss the survey or google the answers. The study specifically focuses on pharmacists working in a community retail pharmacy at the time of receiving the survey.

Interpretations of Key Terms

Pharmacovigilance is “the science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other drug-related problem” (World Health Organisation (WHO), 2018). This includes substandard drugs, medication errors, use of drugs “off-licence” with inadequate scientific basis, abuse and misuse, lack of efficacy, poisoning, ADRs, adverse interactions with other drugs, food and chemicals, and drug-related mortality

(Jobson, 2003). It covers the complete product life-cycle from medicine development to destruction of expired stock (Joubert and Naidoo, 2016).

The WHO defines an ADR as “any response to a drug which is noxious and unintended, and occurs at doses normally used in man for prophylaxis, diagnosis, or therapy of disease, or for the modification of physiological function” (International Conference on Harmonisation (ICH) E2A, 1994). ADR reporting is a pharmacovigilance obligation.

An adverse drug event is any unpleasant medical event that might not be associated with the treatment (South African Health Products Regulatory Authority (SAHPRA), 2016).

Research Design / Research Methodology

The quantitative study is a quasi-experimental design, without any random pre-selection process. Pharmacists for the study will be recruited from the public domain using paper and electronic media.

Pharmacist details (telephone numbers and email addresses) are obtained via the telephone directory and electronically from websites. The following search terms will be used to find community pharmacists:

- Pharmacies Eastern Cape
- Pharmacies Free State
- Pharmacies Gauteng
- Pharmacies Kwa-Zulu Natal
- Pharmacies Limpopo
- Pharmacies Mpumalanga
- Pharmacies Northern Cape
- Pharmacies North West Province
- Pharmacies Western Cape

Quantitative data will be obtained by asking pharmacists (N) closed, fixed questions in each province to elucidate their knowledge, attitude and practices of ADR reporting and to follow-up on how they reported such observations. The study sample (n) is the number of community pharmacists in practice in South Africa (currently at 3349) completing the survey (South African Pharmacy Council (SAPC), 2017). The sample frame is the number of community pharmacists with access to electronic mail.

This study will be performed using electronic surveys with reminders (Survey Monkey) asking questions to pharmacists regarding their knowledge, practice and opinion of pharmacovigilance. The inclusion criterion for the study participants is provision of the pharmacist's SAPC registration number. Responses will be coded to facilitate categorisation of responses. Reminder emails will be sent in response to the survey within specified time frames. The questionnaire will be piloted with pharmacists who would not be involved in the study. Internal validity will be maintained by asking a few "check questions". Participants would be requested to answer the survey within 10 minutes as a means to achieve authentic responses.

The means, range and median are calculated for each province. The standard deviation and variance are calculated to see how far the data is from the mean. Data is represented with a histogram and examined for skewness. A one-way Anova test determines if the difference between provinces is significant. We reject the null hypothesis if the p- value is less 0.05 (see above). Confounding variables are age of participants and years of experience.

Ethics Statement / Ethical Considerations

Ethical approval for the study will be obtained from the University of the Western Cape Biomedical Research Ethics Committee before the study is conducted. Informed consent will be obtained from the pharmacists before the questionnaire is uploaded and mailed electronically. Participants will be invited to participate in the study. The inclusion criterion for the study participants is provision of the pharmacist's SAPC registration number. Study participants will be completely anonymised; they will not be identifiable by name and their responses will not be linked to them personally. Written informed consent will be obtained from each

survey participant and confidentiality will be assured throughout the study (APPENDIX A). Participants can withdraw from the study at any time from the study.

An information sheet outlining the study's purpose, objective, significance and dissemination of the findings will be available electronically to prospective participants. The benefits and risks for participating in the study will be outlined (APPENDIX A).

There is no direct, physical contact with the participants for the study. Participants will not be exposed to any risks in the study.

_____

Rensche Mayne

Bibliography

Academy, J. (2012) *Excel - One-Way ANOVA Analysis Toolpack* [Online]. Available at: https://www.youtube.com/watch?v=nmHFFFpOVZs (Accessed: 7 February 2018).

Ampadu, H.H., Hoekman, J., De Bruin, M.L., Pal, S.N., Olsson, S., Sartori, D., Leufkens, H.G.M. and Dodoo, A.N.O. (2016) 'Adverse Drug Reaction Reporting in Africa and a Comparison of Individual Case Safety Report Characteristics Between Africa and the Rest of the World', *Drug Safety*, 39:335-345 [Online]. Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4796322/ (Accessed: 30 January 2018).

Bradley, H., Bheekie, A. and Sanders, D (2011) 'Public Health: Every Pharmacist's Business', *SA Pharmaceutical Journal*, Vol 78, No 10 [Online]. Available at: http://www.sapj.co.za/index.php/SAPJ/article/view/1193 (Accessed: 30 January 2018).

Bradshaw, D., Nanna, N., Laubscher, R., Groenewald, P., Joubert, J., Nojilana, B., Norman, R., Pieterse, D. and Schneider, M. (2006) 'South African National Burden of Disease Study 2000 Estimates of Provincial Mortality', *MRC South Africa* [Online]. Available at: http://www.mrc.ac.za/bod/estimate.pdf (Accessed: 6 February 2018).

Cheema, E., Haseeb, A., Khan, T.M., Sutcliffe, P. and Singer, D.R. (2017) 'Barriers to Reporting of Adverse Drug Reactions: a Cross Sectional Study among Community Pharmacists in the United Kingdom', *Pharmacy Practice (Granada)*, Jul-Sep; 15(3):931 [Online]. Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5597805/ (Accessed: 30 January 2018).

Department of Health Notice 590 of 2017 - *The South African Pharmacy Council (SAPC) (2017) Competency Standards for Pharmacists in South Africa*. SAPC [Online]. Available at: https://www.mm3admin.co.za/documents/docmanager/0c43ca52-121e-4f58-b8f6-81f656f2fd17/00126360.pdf (Accessed: 1 February 2018).

Gray, A., Ridden, J. and Jugathpal, J. (2016) 'Health Care and Pharmacy Practice in South Africa', *Canadian Journal of Hospital Pharmacy*, Jan-Feb; 69(1): 36-41 [Online]. Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4777579/

(Accessed: 30 January 2018).

International Conference on Harmonisation (ICH) E2A (1994) *Clinical Safety Data Management: Definitions and Standards for Expedited Reporting E2A*. ICH [Online]. Available at: https://www.ich.org/fileadmin/Public_Web_Site/ICH_Products/Guidelines/Efficacy/E2A/Step4/E2A_Guideline.pdf (Accessed: 6 February 2018).

International Conference on Harmonization (ICH) E9 (2017) *Guidance for Industry Statistical Principles for Clinical Trials E9.* ICH [Online]. Available at: http://www.ich.org/fileadmin/Public_Web_Site/ICH_Products/Guidelines/Efficacy/E9/Step4/E9_Guideline.pdf (Accessed: 30 January 2018).

Ioannidis, J. (2009) 'Adverse Events in Randomised Trials- Neglected, Restricted, Distorted and Silenced', *Arch Intern Med*, Vol 169(no19) [Online]. Available at: http://olympias.lib.uoi.gr/jspui/bitstream/123456789/24017/1/Ioannidis-2009-Adverse%20events%20in%20ra.pdf (Accessed: 5 February 2018).

Jobson, R. (2003) 'Pharmacovigilance: A Brief Glimpse', *SA Fam Pract*, 45(2) [Online]. Available at: http://www.safpj.co.za/index.php/safpj/article/download/1989/2537 (Accessed: 30 January 2018).

Joubert, M. and Naidoo, P. (2016) 'Knowledge, Perceptions and Practices of Pharmacovigilance amongst Community and Hospital Pharmacists in a Selected District of North West Province, South Africa', *Health SA Gesondheid*, Vol 21, Pg 238-244 [Online]. Available at: https://www.sciencedirect.com/science/article/pii/S1025984816300084 (Accessed: 30 January 2018).

Kahn, T. (2016) 'The Pharmaceutical Industry pays Millions to Healthcare Professionals Every Year - Without Having to Disclose Details', *BusinessDay* [Online]. Available at: https://www.businesslive.co.za/bd/national/health/2016-12-13-sas-closet-deals-between-doctors-and-drug-makers (Accessed: 6 February 2018).

Lexchin, J. (2014) 'How Safe are New drugs? Market Withdrawal of Drugs Approved in Canada between 1990 and 2009', *Open Medicine*, 8(1):e14-e19 [Online]. Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4085091/ (Accessed: 6 February 2018).

Lieb, K. and Scheurich, A. (2014) 'Contact Between Doctors and the Pharmaceutical Industry, Their Perceptions, and the Effects on Prescribing Habits', *PLos One*, 9(10):e11130 [Online]. Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4199668/ (Accessed: 6 February 2018).

Maigetter, K., Pollock, A.M., Kadam, A., Ward, K. and Weiss, M.G. (2015) 'Pharmacovigilance in India, Uganda and South Africa with Reference to WHO's Minimum Requirements', *International Journal of Health Policy and Management*, May;4(5):295-305 [Online]. Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4417633/ (Accessed: 30 Janaury 2018).

Mayosi, BM and Benatar, SR. (2014). 'Health and Health Care in South Africa — 20 Years after Mandela', *The New England Journal of Medicine*, 371:1344-1353 [Online]. Available at: http://www.nejm.org/doi/full/10.1056/NEJMsr1405012#t=article (Accessed: 9 March 2018).

Mehta, U.C. (2011) 'Pharmacovigilance: The Devastating Consequences of Not Thinking about Adverse Drug Reactions', *Continuing Medical Education*, Vol 29,No 6 [Online]. Available at: http://www.cmej.org.za/index.php/cmej/article/view/2170/1827 (Accessed: 6 February 2018).

Mehta, U.C., Kalk, E., Boulle,A., Nkambule, P., Gouws, J., Rees, H. and Cohen, K. (2017) 'Pharmacovigilance: A Public Health Priority for South Africa', *South African Health Review*, Pg.125-133 [Online]. Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5708547/ (Accessed: 30 January 2018).

Moodley, K. and Myer, L. (2007) 'Health Research Ethics Committees in South Africa 12 Years into Democracy', *BMC Medical Ethics*, 8:1 [Online]. Available at: https://bmcmedethics.biomedcentral.com/articles/10.1186/1472-6939-8-1 (Accessed: 30 January 2018).

National Institute of Communicable Diseases (NICD) (2017) *Malaria in South Africa 2017: an update.* NICD [Online]. Available at: http://www.nicd.ac.za/wp-content/uploads/2017/05/Malaria-update.pdf (Accessed: 19 March 2018).

Onakpoya, I.J., Heneghan, C.J., and Aronson, J.K., (2016) 'Post-marketing Withdrawal of 462 Medicinal Products Because of Adverse Drug Reactions: a Systematic Review of the World Literature', *BMC Medicine*, 14: 10 [Online]. Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4740994/ (Accessed: 6 February 2018).

Postgrad.com, (n.d.) *Writing a Dissertation Proposal*. [Online]. Available at: https://www.postgrad.com/advice/exams/dissertations_and_theses/dissertation_proposal/ (Accessed: 30 January 2018).

Rajanandh, M.G., Praveen, K.V. and Yuvasakthi, S. (2016) 'Roles of Pharmacist in Pharmacovigilance: A Need of the Hour', *Journal of Pharmacovigilance* [Online]. Available at: https://www.omicsonline.org/open-access/roles-of-pharmacist-in-pharmacovigilance-a-need-of-the-hour-2329-6887-1000221.php?aid=83551 (Accessed: 5 February 2018).

Roux, L. (2014) 'Pharmacovigilance: The Responsibility of Pharmaceutical Companies to Protect Patients From Drug-Related Harm', *University of the Western Cape* [Online]. Available at: http://etd.uwc.ac.za/xmlui/bitstream/handle/11394/4234/Roux_MSc_2014.pdf;sequence=1 (Accessed: 1 February 2018).

Rumsey, D. (2010) *Statistics Essentials for Dummies*. Indianapolis: Wiley Publishing Inc.

Ruud, K.W., Srinivas, S.C. and Toverud, E. (2010) ' Addressing Gaps in Pharmacovigilance Practices in the Antiretroviral Therapy Program in the Eastern Cape Province, South Africa [Abstract]', *Elsevier*, Vol 6, Issue 4, Pg. 345-353 [Online]. Available at: https://www.sciencedirect.com/science/article/pii/S1551741109001442 (Accessed: 30 January 2018).

Science, B. (2011) *Chi-squared Test*. [Online]. Available at: https://www.youtube.com/watch?v=WXPBoFDqNVk (Accessed: 30 January 2018).

Science, Bozeman (2012) *Statistics for Science*. [Online]. Available at: https://www.youtube.com/watch?v=jf9VT4V4aRI (Accessed: 7 February 2018).

Science, B. (2016) *Student's t-test*. [Online]. Available at: https://www.youtube.com/watch?v=pTmLQvMM-1M (Accessed: 30 January 2018).

South African Health Products Regulatory Authority (SAHPRA) (n.d.) *South African Health Products Regulatory Authority*. SAHPRA [Online]. Available at: http://www.sahpra.org.za/ (Accessed: 19 March 2018).

South African Health Products Regulatory Authority (SAHPRA) (2003) *General Regulations Made in Terms of the Medicine and Related Substances Act, 1965 (Act No. 101 of 1965) as amended*. SAHPRA [Online]. Available at: http://www.mccza.com/documents/f6cae0ccRegulations_to_Act_101_published_2003.pdf (Accessed: 1 February 2018).

South African Health Products Regulatory Authority (SAHPRA) (2016) *Post-Marketing Reporting of Adverse Drug Reactions to Human Medicines in South Africa.* SAHPRA [Online]. Available at: http://www.mccza.com/documents/f39361792.33_ADR_reporting_post-marketing_Jul16_v4.1_showing_changes.pdf (Accessed: 30 January 2018).

South African Pharmacy Council (SAPC) (2017) *Statistics for Registered Persons and Organisations*. SAPC [Online]. Available at: https://www.sapc.za.org/B_statistics.asp (Accessed: 3 February 2018).

Statistics SA (2011) *Census 2011 Provinces at a Glance*. [Online]. Available at: http://www.statssa.gov.za/census/census_2011/census_products/Provinces%20at%20a%20glance%2016%20Nov%202012%20corrected.pdf (Accessed: 7 February 2018).

Statistics SA (2013) *Causes of Death 2013*. [Online]. Available at: http://www.statssa.gov.za/?page_id=737&id=3 (Accessed: 19 March 2018).

Suleman, F. (2010) 'Pharmacovigilance - Who is Responsible and Why Should We Care?, *SA Association of Hospital and Institutional Pharmacists*, October, Pg56-58 [Online]. Available at: https://www.sapj.co.za/index.php/SAPJ/article/viewFile/892/822 (Accessed: 30 January 2018).

Summers, R., Dube, N. and Meyer, H. (2013) 'Pharmacovigilance: a Vital Tool or a Wasted Effort?', *SA Pharmaceutical Journal*, Vol 80, No 7 [Online]. Available at: http://www.sapj.co.za/index.php/SAPJ/article/view/1621/2621 (Accessed: 30 January 2018).

Suyagh, M., Farah, D. and Abu Farha, R. (2014) 'Pharmacist's Knowledge, Practice and Attitudes toward Pharmacovigilance and Adverse Drug Reactions Reporting Process', *Saudi Pharmaceutical Journal*, Vol 23, Issue 2, Pg. 147-153[Online]. Available at: https://www.sciencedirect.com/science/article/pii/S1319016414000681 (Accessed: 6 February 2018).

UNAIDS (2018) *Country South Africa*. [Online]. Available at: http://www.unaids.org/en/regionscountries/countries/southafrica (Accessed: 6 February 2018).

University of the Western Cape (UWC) (n.d.) *Policy on Research Ethics*. UWC [Online]. Available at: https://www.google.co.za/url?sa=t&rct=j&q=&esrc=s&source=web&cd=1&cad=rja&uact=8&ved=0ahUKEwiomO7V1bPVAhUKJcAKHZGHCMAQFggkMAA&url=http%3A%2F%2Flib.uwc.ac.za%2Fresearch%2Fimages%2FResearch%2520Ethics%2520Policy.pdf&usg=AFQjCNEGsBqvel_wyXcWQ-jCDysDNwv6Iw (Accessed: 30 January 2018).

University of the Western Cape (UWC) (2014) *Research Proposal Guide*. UWC [Online]. Available at: https://www.google.co.za/url?sa=t&rct=j&q=&esrc=s&source=web&cd=2&cad=rja&uact=8&ved=0ahUKEwj3tLSt1bPVAhWHHsAKHZ9NBjoQFggqMAE&url=https%3A%2F%2Fwww.uwc.ac.za%2FStudents%2FPostgraduate%2FDocuments%2FRESEARCH_PROPOSAL.pdf&usg=AFQjCNGSX8u9-nywsOEgwEeL69InlLN (Accessed: 30 January 2018).

Van Grootheest, A.C. and de Jong-van den Berg, L.T.W. (2009) 'The Role of Hospital and Community Pharmacists in Pharmacovigilance [Abstract]', *Research in Social and Administrative Pharmacy,* Vol 1, Issue 1, Pg. 126-166 [Online]. Available at: http://www.rsap.org/article/S1551-7411 (04)00010-5/abstract (Accessed: 5 February 2018).

Van Grootheest, K., Olsson, S., Couper, M. and De Jong-van den Berg, L. (2003) ' Pharmacists' Role in Reporting Adverse Drug Reactions in an International Perspective', *Wiley InterScience* [Online]. Available at: http://www.academia.edu/22109223/Pharmacists_role_in_reporting_adverse_drug_reactions_in_an_international_perspectiv (Accessed: 8 February 2018).

Walji, R. (2008) 'Reporting Adverse Drug Reactions Associated with Herbal Products: Consumer, Health Food Store Personnel and Pharmacist Perspectives', *University of Toronto* [Online]. Available at: https://tspace.library.utoronto.ca/bitstream/1807/17295/1/Walji_Rishma_200811_PhD_Thesis.pdf (Accessed: 7 February 2018).

Williams, C. (2015) 'Perceptions and Experiences of Reporting of Adverse Drug Reactions by Public Sector Pharmacists in a Rural District in the Western Cape', *University of the Western Cape (UWC)* [Online]. Available at: https://webcache.googleusercontent.com/search?q=cache:VKEeGktJ1SEJ:https://et

d.uwc.ac.za/bitstream/handle/11394/4915/Williams_cj_mph_chs_2015.pdf%3Fsequence%3D1%26isAllowed%3Dy+&cd=5&hl=en&ct=clnk&gl=za (Accessed: 30 January 2018).

World Health Organisation (WHO) (2002) *Safety of Medicine - A Guide to Detecting and Reporting Adverse Drug Reactions - Why Health Professionals Need to Take Action*. WHO [Online]. Available at: http://apps.who.int/medicinedocs/en/d/Jh2992e/12.html (Accessed: 5 February 2018).

World Health Organisation (WHO) (2018) *Pharmacovigilance*. WHO [Online]. Available at: http://www.who.int/medicines/areas/quality_safety/safety_efficacy/pharmvigi/en/ (Accessed: 3 February 2018).

World Medical Association (WMA) (2013) *WMA Declaration of Helsinki - Ethical Principles for Medical Research involving Human Subject*s. WMA [Online]. Available at: https://www.wma.net/policies-post/wma-declaration-of-helsinki-ethical-principles-for-medical-research-involving-human-subjects (Accessed: 30 January 2018).

Zuma, K., Manzini, K. and Mohlabane, N. (2014) 'HIV Epidemic in South Africa: A Comparison of HIV Epidemic Patterns of Two Extreme Provinces in South Africa', *Health SA Gesondheid*, Vol 19, No1 [Online]. Available at: https://hsag.co.za/index.php/HSAG/article/view/716 (Accessed: 6 February 2018).

APPENDIX F

Ethical Clearance

UNIVERSITY of the WESTERN CAPE

OFFICE OF THE DIRECTOR: RESEARCH
RESEARCH AND INNOVATION DIVISION

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

08 June 2018

Dr A Bheekie and Ms R Mayne
School of Pharmacy
Faculty of Natural Science

Ethics Reference Number: BM18/4/4

Project Title: Community pharmacist's knowledge, attitude and practice on adverse drug reaction reporting in South Africa: a comparative study.

Approval Period: 07 June 2018 – 07 June 2019

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

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

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

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

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

PROVISIONAL REC NUMBER -130416-050

FROM EVIDENCE TO ACTION THROUGH KNOWLEDGE

TABLES

Table 2 Summary of data collection process

Date	Collector	Emails sent	Emails returned	Reason
17/6/18	pvsurvey@gmail.com	190	119	Emails were sent in bulk using blind copy and flagged as spam.
18/6/18	rmpharmacovigilance @gmail.com	231	90	Addresses returned as undelivered or message blocked.
19/6/18	rmpharmacovigilance @gmail.com	67	12	Addresses returned as undelivered or message blocked.
19/6/18	MonkeySurvey® Email Collector	407	13	11 Bounced and 2 Opted out.
20/618	MonkeySurvey® Email Collector	494	46	44 Bounced and 2 Opted out.
21/6/18	MonkeySurvey® Email Collector	367	16	13 Bounced and 3 Opted Out.
22/6/18	rmpharmacovigilance @gmail.com	106	100	Emails were sent in bulk using blind copy and flagged as spam.
22/6/18	MonkeySurvey® Email Collector	267	37	36 Bounced and 1 Opted out.
23/6/18	rmpharmacovigilance @gmail.com	113	5	Addresses returned as undelivered or message blocked.
23/6/18	MonkeySurvey® Email Collector	142	39	39 Bounced.
24/6/18	rmpharmacovigilance @gmail.com	375	34	Addresses returned as undelivered or message blocked.
25/6/18	Sought assistance form a pharmacist with technological expertise to e-mail community pharmacists			
26/6/18	SAPC pharmacy list requested			Not received by Sept
27/6/18	rmpharmacovigilance @gmail.com reminder	880	98	Addresses returned as undelivered or message blocked.
27/6/18	pvsurvey@gmail.com	40	6	Addresses returned as undelivered or message blocked.
28/6/18	rmpharmacovigilance @gmail.com reminder	480	19	Addresses returned as undelivered or message blocked.
28/6/18	pvsurvey@gmail.com	360	53	Addresses returned as

	reminder			undelivered or message blocked.
29/6/18	MonkeySurvey® Email Collector reminder for partial responses	1	0	n/a
2/7/18	MonkeySurvey® Email Collector Reminder	1518	3	Participants requested removal of email address via the Gmail account.
6/7/18	MonkeySurvey® Email Collector reminder for partial responses	10	0	n/a
9/7/18	MonkeySurvey® Email Collector Reminder	1484	2	Participants informed the researcher via Gmail that the survey was not working.
16/7/18	MonkeySurvey® Email Collector Reminder	1482	2	Participants informed the researcher via Gmail that the survey was not working.
20/7/18	MonkeySurvey® Email Collector reminder for partial responses	13	0	n/a
23/7/18	MonkeySurvey® Email Collector Reminder	1462	1	Participants requested removal of email address via the Gmail account.
30/7/18	MonkeySurvey® Email Collector Reminder	1455	1	Participants requested removal of email address via the Gmail account.
6/8/18	MonkeySurvey® Email Collector Reminder	1447	0	n/a

Table 3 Table for Domain 2 Pharmacy Competency Standards

DOMAIN 2: SAFE AND RATIONAL USE OF MEDICINES AND MEDICAL DEVICES				
COMPETENCIES	BEHAVIOURAL STATEMENTS			
	Item no.	Entry Level into Practice	Intermediate Practice	Advanced Practice
2.7 Pharmacovigilance	2.7.1	2.7.1.1 Monitor, receive, record and report quality defects, adverse drug reactions and events.	2.7.1.2 Manage pharmacovigilance activities and classify the events accordingly.	2.7.1.3 Design and implement interventions to prevent and minimise adverse drug events.
	2.7.2	2.7.2.1 Perform post marketing surveillance studies.	2.7.2.2 Compile reports of the post marketing surveillance studies.	2.7.2.3 Review pharmacovigilance reports and report to regulatory authority.
2.8 Clinical trials	2.8.1	2.8.1.1 Apply master documents (e.g. SOPs) according to GxP.	2.8.1.2 Implement and monitor compliance in line with GxP.	2.8.1.3 Interpret guidelines, legislation and policies in line with GxP.
	2.8.2	2.8.2.1 Compile master documents.	2.8.2.2 Review master documents.	2.8.2.3 Approve master documents.