Knowledge, Attitudes and Practices of Health Care Professionals towards Adverse Drug Reaction Reporting in Public Sector Primary Health Care Facilities in the Tshwane District

A mini-dissertation submitted by

Michelle Haines

In partial fulfilment of the requirements for the degree

Master of Pharmacy

in the

Faculty of Health Sciences

(School of Health Care Sciences)

of

Sefako Makgatho Health Sciences University

Department of Pharmacy

Supervisor: Prof JC Meyer

Co-supervisor: Prof RS Summers

2016
DECLARATION

I declare that the mini-dissertation hereby submitted to the Sefako Makgatho Health Sciences University, for the degree of Master of Pharmacy, in the Faculty of Health Sciences, School of Health Care Sciences, Department of Pharmacy, has not previously been submitted by me for a degree at this or any other university; that it is my work in design and execution, and that all material contained herein has been duly acknowledged.

Surname, Initials (Title)  Date
# TABLE OF CONTENTS

ACKNOWLEDGEMENTS

LIST OF FIGURES

LIST OF TABLES

LIST OF APPENDICES

ABBREVIATIONS AND ACRONYMS

ABSTRACT

## CHAPTER 1 INTRODUCTION

1.1 INTRODUCTION

1.2 BACKGROUND AND RATIONALE FOR THE STUDY

1.3 RESEARCH QUESTION

1.4 AIM OF THE STUDY

1.5 OBJECTIVES OF THE STUDY

1.6 IMPORTANCE OF THE STUDY

1.7 OUTLINE OF THE DISSERTATION

## CHAPTER 2 LITERATURE REVIEW

2.1 INTRODUCTION

2.2 ADVERSE DRUG REACTIONS

2.2.1 Importance of adverse drug reactions

2.2.2 Types of adverse drug reactions

2.2.3 Reporting of adverse drug reactions

2.3 PHARMACOVIGILANCE

2.3.1 The pharmacovigilance framework

2.3.2 Patient safety

2.4 POST-MARKETING SURVEILLANCE

2.4.1 Spontaneous reporting of adverse drug reactions

2.4.2 Advantages of spontaneous reporting of adverse drug reactions

2.4.3 Limitations of spontaneous reporting of adverse drug reactions

2.5 METHODS THAT COMPLEMENT SPONTANEOUS REPORTING SYSTEMS

2.5.1 Cohort Event Monitoring (CEM)

2.5.2 Targeted Spontaneous Reporting (TSR)

2.6 FACTORS ASSOCIATED WITH NON-REPORTING OF ADVERSE REACTIONS

2.7 SUMMARY
CHAPTER 3 METHODOLOGY ................................................................................. 19
  3.1 INTRODUCTION ............................................................................................ 19
  3.2 STUDY DESIGN ............................................................................................. 19
  3.3 STUDY SITE ................................................................................................ 19
  3.4 STUDY POPULATION AND SAMPLE ............................................................ 20
    3.4.1 Study population .................................................................................... 20
    3.4.2 Sample selection ................................................................................... 20
  3.5 DATA COLLECTION INSTRUMENT ............................................................... 23
  3.6 PILOT STUDY ................................................................................................ 23
  3.7 DATA COLLECTION ..................................................................................... 23
    3.7.1 Data collection period ........................................................................... 23
    3.7.2 Data collectors and training ................................................................... 24
    3.7.3 Data collection process ......................................................................... 24
  3.8 DATA ENTRY AND ANALYSIS .................................................................... 24
  3.9 RELIABILITY AND VALIDITY ..................................................................... 25
  3.10 BIAS ........................................................................................................... 26
  3.11 ETHICAL CONSIDERATIONS .................................................................... 26
  3.12 SUMMARY ................................................................................................ 27

CHAPTER 4 RESULTS AND DISCUSSION ................................................................. 28
  4.1 INTRODUCTION ......................................................................................... 28
  4.2 MANUSCRIPT ............................................................................................ 29
  4.3 LETTER TO THE EDITOR ......................................................................... 49

CHAPTER 5 LIMITATIONS, RECOMMENDATIONS AND CONCLUSIONS .......... 51
  5.1 INTRODUCTION ......................................................................................... 51
  5.2 LIMITATIONS OF THE STUDY ................................................................. 51
  5.3 RECOMMENDATIONS .............................................................................. 51
  5.4 CONCLUSIONS .......................................................................................... 52

REFERENCES ...................................................................................................... 53

APPENDICES ....................................................................................................... 60
ACKNOWLEDGEMENTS

I would like to express my sincere gratitude and acknowledgement to the following people for their contributions to my study:

- My supervisor, Prof Hannelie Meyer, for all her guidance and support throughout the course and for never giving up on me.

- My co-supervisor, Prof Robert Summers for his guidance and support.

- All the health care professionals’ in Tshwane District who participated in this study.

- Tshwane Health District for permission to use their facilities for the study.

- The statistician, Prof Schoeman for his advice and contributions to data analysis.

- Department of Pharmacy, Sefako Makgatho Health Sciences University for logistical and financial assistance.

- My husband and family for their love and support.
LIST OF FIGURES

Figure 2.1: Supporting Pharmacovigilance in Developing Countries: The Systems Perspective ................................................................. 9

Figure 3.1: Map of study facilities in the Tshwane District ............................................. 20

Manuscript:

Figure 1 Percentage of HCPs with knowledge of the type of events that should be reported ............................................................................. 39

Figure 2 Health care professionals’ role in ADR reporting ............................................. 42
LIST OF TABLES

Table 3.1: Health care professionals employed at PHC facilities in the Tshwane District .......................................................... 22

Manuscript:

Table 1 Demographic characteristics of participants ......................................................... 36
Table 2 Percentage of health care professionals’ with knowledge on adverse drug reactions ........................................................................................................ 38
Table 3 Mean and median (%) knowledge levels on ADRs by profession .............. 39
Table 4 Health care professionals’ attitudes towards the reporting of adverse drug reactions ........................................................................................................ 41
Table 5 Major factors which discourage reporting of ADRs ............................................. 42
Table 6 Mean and median (%) attitude levels on ADRs by profession .................. 43
Table 7 Practice of HCPs in adverse drug reaction reporting .................................. 44
Table 8 Mean and median (%) practice levels on ADRs by profession ............ 45
# LIST OF APPENDICES

<table>
<thead>
<tr>
<th>Appendix</th>
<th>Title</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Appendix 1:</td>
<td>Study information leaflet</td>
<td>60</td>
</tr>
<tr>
<td>Appendix 2:</td>
<td>Written Consent Form</td>
<td>61</td>
</tr>
<tr>
<td>Appendix 3:</td>
<td>Questionnaire</td>
<td>62</td>
</tr>
<tr>
<td>Appendix 4:</td>
<td>Permission to conduct pilot study</td>
<td>65</td>
</tr>
<tr>
<td>Appendix 5:</td>
<td>Permission to conduct study in the Tshwane District</td>
<td>66</td>
</tr>
<tr>
<td>Appendix 6:</td>
<td>MREC Clearance Certificate</td>
<td>67</td>
</tr>
<tr>
<td>Appendix 7:</td>
<td>Approval from Tshwane Research Committee</td>
<td>68</td>
</tr>
<tr>
<td>Appendix 8:</td>
<td>Author Guidelines</td>
<td>69</td>
</tr>
<tr>
<td>Abbreviation</td>
<td>Description</td>
<td></td>
</tr>
<tr>
<td>--------------</td>
<td>-------------</td>
<td></td>
</tr>
<tr>
<td>ADR</td>
<td>Adverse Drug Reaction</td>
<td></td>
</tr>
<tr>
<td>AE</td>
<td>Adverse Event</td>
<td></td>
</tr>
<tr>
<td>AIDS</td>
<td>Acquired Immunodeficiency Syndrome</td>
<td></td>
</tr>
<tr>
<td>ACT</td>
<td>Artemisinin-based combination therapy</td>
<td></td>
</tr>
<tr>
<td>ARV</td>
<td>Antiretroviral</td>
<td></td>
</tr>
<tr>
<td>ART</td>
<td>Antiretroviral Therapy</td>
<td></td>
</tr>
<tr>
<td>CEM</td>
<td>Cohort Event Monitoring</td>
<td></td>
</tr>
<tr>
<td>CHC</td>
<td>Community Health Centre</td>
<td></td>
</tr>
<tr>
<td>CSP</td>
<td>Community Service Pharmacist</td>
<td></td>
</tr>
<tr>
<td>DOH</td>
<td>Department of Health</td>
<td></td>
</tr>
<tr>
<td>HCP</td>
<td>Health Care Professional</td>
<td></td>
</tr>
<tr>
<td>HIV</td>
<td>Human Immunodeficiency Virus</td>
<td></td>
</tr>
<tr>
<td>MCC</td>
<td>Medicines Control Council</td>
<td></td>
</tr>
<tr>
<td>NADEMC</td>
<td>National Adverse Drug Event Monitoring Centre</td>
<td></td>
</tr>
<tr>
<td>NPC</td>
<td>National Pharmacovigilance Centre</td>
<td></td>
</tr>
<tr>
<td>PHC</td>
<td>Primary Health Care</td>
<td></td>
</tr>
<tr>
<td>PV</td>
<td>Pharmacovigilance</td>
<td></td>
</tr>
<tr>
<td>SPS</td>
<td>Strengthening Pharmaceutical Services</td>
<td></td>
</tr>
<tr>
<td>SRS</td>
<td>Spontaneous Reporting Systems</td>
<td></td>
</tr>
<tr>
<td>TB</td>
<td>Tuberculosis</td>
<td></td>
</tr>
<tr>
<td>TSR</td>
<td>Targeted Spontaneous Reporting</td>
<td></td>
</tr>
<tr>
<td>WHO</td>
<td>World Health Organization</td>
<td></td>
</tr>
</tbody>
</table>
ABSTRACT

**Background:** In Tshwane District, reports on adverse drug reactions (ADRs) should be submitted to the Tshwane Metsweding Regional Pharmacy and then discussed at the Tshwane District Pharmacy and Therapeutics Committee meeting on a quarterly basis. Over the 18 month period before this study, very few ADRs were discussed at the committee. It would therefore be important to determine the knowledge, attitude and practices of health care professionals (HCPs) in an attempt to understand why ADRs are not being reported. The results of this study could be used to design and initiate a programme to promote ADR reporting in the Tshwane District.

**Aim:** The aim of the study was to determine the knowledge, attitudes and practices of HCPs towards ADR reporting in public sector primary health care (PHC) facilities in the Tshwane District.

**Methods:** This study followed a descriptive, cross-sectional design using a quantitative methodology. The study was conducted in eight public sector Community Health Care Centres (CHCs) and 40 Primary Health Care (PHC) facilities in the Tshwane Health District. A self-administered questionnaire was distributed to a sample of 218 HCPs, which included medical practitioners, professional nurses, pharmacists and pharmacist assistants. Data were captured using Microsoft Excel™, proof-read for accuracy and cleaned for statistical analysis with SAS, release 9.2, running under Microsoft Windows. Responses were categorised according to knowledge, attitudes and practices based on the questions included on the questionnaire. For knowledge, attitudes and practices, correct or preferred responses were summarised by frequency counts and percentages for each item as well as for medical practitioners, professional nurses, pharmacists and pharmacist assistants separately. An overall score (%) with 95% confidence interval based on responses from all participants was calculated for knowledge, attitudes and practices.

An individual overall score (%) was calculated for each participant, for knowledge, for attitudes and for practices, based on positive or preferred responses. A mean (%) for knowledge, attitudes and practices was calculated for each profession (medical practitioners, professional nurses, pharmacists and pharmacist assistants). Mean knowledge, attitude and practice levels (%) of the different professions were compared by an analysis of variance (ANOVA), followed by pair wise comparisons by t-test.

Ethical clearance for the study was obtained from the Medunsa Research Ethics Committee (MREC) of the University of Limpopo, now Sefako Makgatho Health Sciences University, prior
to the commencement of the study (MREC/H/270/2013). Ethical approval was also obtained from the Gauteng Health Ethics Committee and permission to conduct the study in the PHC facilities in Tshwane District was obtained from the Chief Director of the Tshwane District.

Results: The response rate was 91.7%, with 200 completed questionnaires returned. The study showed that while the right attitude for ADR reporting existed among HCPs, the actual practice of ADR reporting was lacking. The results reflected upon the lack of awareness (57.5%) of respondents about the existence of an ADR reporting system, which will ultimately affect the reporting. The majority of HCPs (89.0%) felt that ADR reporting is a professional obligation, they would be encouraged to report it if the reaction is serious (89.5%), linked to a new product (89.5%), and is unusual (78.0%). However, 11.0% of HCPs were unaware of the professional obligation to report ADRs, and furthermore, only 12.0% of HCPs knew where the ADR forms were kept in the facilities. When responses of all HCPs were combined, overall 79.6% (95% CI: 76.9% - 82.3%) of responses were positive or preferred in terms of knowledge of ADRs, overall positive attitude was 63.3% (95% CI 60.7%-65.8%) and 24.6% (95% CI 21.7%-27.4%) of responses were positive in terms of practice.

Conclusion: The results of this study strongly suggest that underreporting of ADRs is associated with gaps in knowledge, attitudes and practices of HCPs. These findings are of great concern and suggest that there is a serious and urgent need to promote the reporting of ADRs amongst HCPs in the Tshwane District. Health care professionals will benefit from education and training, from the identification of ADRs to the reporting of ADRs. Continuous monitoring of ADR reporting and follow-up training is recommended for future practice to improve the rate of spontaneous reporting.
1.1 INTRODUCTION

The first section of this chapter presents the rationale for this study, which focussed on the knowledge, attitude and practices of health care professionals (HCPs) towards adverse drug reaction (ADR) reporting in public sector primary health care (PHC) facilities in the Tshwane Health District. The research question, aim and objectives of the study are given. The chapter ends with an overview of the importance of the study and an outline of the dissertation.

1.2 BACKGROUND AND RATIONALE FOR THE STUDY

Adverse drug reactions (ADRs) are a major public health problem because they directly cause an increase in mortality, morbidity and costs (Pernas, Herdeiro, Lopez-Gonzalez, Silva & Figueras, 2012). According to the World Health Organization’s (WHO) definition, an ADR is any noxious, unintended and undesired effect of a drug, which occurs at doses used in humans for prophylaxis, diagnosis or therapy (WHO, 2002).

If HCPs took responsibility for identifying and reporting medication-associated adverse events as they happen, a situation could occur in which pharmaceutical manufacturers and regulators, health care providers, funders and patients would not have to worry about the safety of approved medicines, vaccines or devices. If all HCPs worked together to establish effective pharmacovigilance systems, it will produce confidence in the services to which patients entrust their lives. Safety signals would be detected early on, and better and quicker safety decisions would be made (Mkele, Tsepe, Mayayise, Summers, O’Connor, Gous, Oosthuizen, Badenhorst, Grab & Kredo, 2010).

Under reporting of ADRs is a worldwide phenomenon. The determinants of under-reporting include lack of knowledge of the forms for reporting, ignorance of the rules and procedures for reporting and not being sure of the type of reactions to be reported (O Fadare, O Enwere, Afolabi, Chedi & Musa, 2011).

Adverse drug reaction spontaneous reporting systems are the basic methods for the comprehensive post-marketing surveillance of drug-induced risks. Spontaneous reporting systems are inexpensive and simple to operate. However, their strength, or otherwise, is directly linked to the actual reporting rate by the HCPs, under-reporting being the main intrinsic
disadvantage (Vessel, Mardani & Molloi, 2009). Many factors are associated with ADR under-reporting among HCPs. These factors have been broadly classified as personal and professional characteristics of health carers, and their knowledge and attitudes to reporting – referred to as ‘the seven deadly sins’ (Gupta & Udupta, 2011; Inman, 1996).

The Medicines Control Council (MCC) is the statutory body that has the responsibility to ensure the safety, efficacy and quality of all medicines used by the South African public. It is therefore also the responsibility of the MCC to monitor the performance of these medicines once they are marketed. Essential medicines are particularly important as they are used by a large percentage of the population. The MCC’s national pharmacovigilance programme is intended to be co-ordinated by the National Pharmacovigilance Centre (NPC) in Pretoria. One of the units functioning under the NPC is the National Adverse Drug Event Monitoring Centre (NADEMC) in Cape Town. This centre manages the national ADR database (ADRI) which houses all spontaneous reports of ADRs submitted by local health professionals and pharmaceutical manufacturers. The information in the national ADR database is used to identify signals of new, previously unknown or poorly understood ADRs. Ultimately, some of the signals may lead to the positive identification of ADR information about which will subsequently be included in the labelling and package insert of the product. In some situations, information derived from spontaneous reports can provide adequate evidence to facilitate the withdrawal of a potentially unsafe medicine from the market. The data from ADRI database are routinely fed into an international database of these reports housed in Sweden at the Uppsala Monitoring Centre (the WHO Collaborating Centre for International Drug Monitoring) (Metha, 2011).

In the Tshwane District, reports on ADRs should be submitted to the Tshwane Metsweding Regional Pharmacy and then discussed at the Tshwane District Pharmacy and Therapeutics Committee meeting on a quarterly basis. Over the 18 months prior to this study, very few ADRs were discussed at this committee (GDOH, 2013). It was therefore considered important to determine the knowledge, attitudes and practices of HCPs, in an attempt to understand why ADRs are not being reported. The results of this study can be used to design and initiate a programme to promote ADR reporting in the Tshwane Health District.

1.3 RESEARCH QUESTION

What are the knowledge, attitudes and practices of HCPs in provincial PHC facilities in the Tshwane Health District towards ADR reporting?
**1.4 AIM OF THE STUDY**

The aim of the study was to determine the knowledge, attitudes and practices of HCPs in provincial PHC facilities in the Tshwane Health District towards ADR reporting.

**1.5 OBJECTIVES OF THE STUDY**

The objectives of the study were as follows:

- To determine the knowledge of HCPs in PHC facilities in the Tshwane District about ADR reporting.
- To determine the attitudes of HCPs toward ADR reporting.
- To determine the practices of HCPs in ADR reporting.

**1.6 IMPORTANCE OF THE STUDY**

The objective of pharmacovigilance is to reduce the risk of drug-related harm to patients, but can only be successful if this system is managed in the correct way to achieve the objective (Arun, Bharat, Akshay, Sambit, Subrat & Debasish, 2015). The monitoring of ADRs generates an information system regarding the quality and safety of drugs, creates risk-management plans, contribute to the prevention of ADRs and improves awareness of ADRs among healthcare professionals (Sahu, Yadav, Prasad, Roy & Chandrakar, 2014). The outcomes of ADRs, namely mortality, morbidity and cost, can therefore be reduced with pharmacovigilance (Khan, 2013; Singh & Bhatt, 2012).

This study suggested that underreporting of ADRs are associated with gaps in knowledge, attitudes and practices of HCPs towards ADR reporting. Creating awareness and training of HCPs on pharmacovigilance could assist in addressing the under reporting of ADRs in Tshwane District.

**1.7 OUTLINE OF THE DISSERTATION**

Chapter 1: Gives the rationale for the study and the objectives to be achieved.

Chapter 2: The chapter discusses the literature, related to the study topic.

Chapter 3: Presents the methods used in this study and describes important factors to consider in research such as ethical considerations.
Chapter 1: Introduction

Chapter 4: In this chapter, the results collated and compiled during data collection are presented and discussed in the form of a manuscript.

Chapter 5: This chapter provides the limitations of the study, recommendations and final conclusion.
2.1 INTRODUCTION

In this chapter, the literature review related to the study is presented. The chapter begins with an overview of ADRs and factors affecting ADR reporting are discussed. A brief exploration of the framework of pharmacovigilance and patient safety is provided. This is followed by a discussion of post-marketing surveillance. Methods that complement spontaneous reporting systems and factors associated with non-reporting of ADRs conclude the chapter.

2.2 ADVERSE DRUG REACTIONS

Adverse drug reactions has been defined by the WHO as any noxious, unintended and undesired effect of a drug that occurs at doses used for prevention, diagnosis or treatment. (WHO, 1969).

2.2.1 Importance of adverse drug reactions

Adverse drug reactions are significant causes of morbidity and mortality. They may result in hospitalisation and lead to large economic burdens to patients and to society (Toklu & Uysal, 2008). The field of drug safety has been receiving a great deal of attention over recent years. Almost weekly, tabloids as well as scientific journals publish articles on drugs that cause unexpected ADRs. These articles have the unfortunate result of evoking apprehension in both patient and HCPs regarding the use of the drugs responsible. A more serious consequence may be that the patient stops taking the prescribed medication, which may lead to an even more serious situation than the ADR he/she was initially concerned about (Härmark & Grootheest, 2008).

Safety and efficacy are the major concerns about a drug. While efficacy of a drug can be quantified with relative ease, the same cannot be done for safety. The reason for this is because the adverse effect of a drug may be uncommon (but very serious) and many patients may be affected or subjected to a potential risk before the relationship with the drug is established (Gupta & Udupa, 2011).

The quality of medicines is also of great concern and the following quality problems should be reported, according to the ADR and product quality report form of the Department of Health (DOH), 2003:
• Suspected contamination
• Questionable stability
• Defective components
• Poor packaging or labelling
• Therapeutic failures

Adverse effects or reactions are not only allergic reactions such as rashes and anaphylactic shock. Adverse effects often look very similar to other diseases and can affect any organ system of the body. Hence it is important to maintain a high suspicion that a new or newly-administered medicine may be responsible for an unexplained worsening in a patient’s condition. Sometimes the ADR may not even be listed in the package insert or other references (Mkele et al., 2010).

2.2.2 Types of adverse drug reactions

Adverse drug reactions are grouped into two broad categories. Group 1 consists of reactions that are predictable, common and related to the pharmacological actions of the drug, whereas Group 2 includes reactions that are unpredictable, uncommon and usually not related to the pharmacological actions of the drug. These unpredictable immunologically mediated reactions are called drug allergies (Chen, Cheng, Lin, Hung, Chen & Lin, 2012; Rawlins & Thompson, 1991).

2.2.3 Reporting of adverse drug reactions

For all drugs, serious reactions, new and unexpected reactions, and ADRs that seems to increase in frequency and seriousness should be reported. Serious reactions are defined as suspected deaths, reactions leading to hospital admission, to prolonged hospitalisation, resulting in persistent or significant disability/incapacity or reactions that are life threatening (Bäckström, Ekman & Mjörndal, 2007).

A medicine’s side-effect is deemed as rare if its frequency of occurrence is less than 0.01% – or 1 in 10 000. Unfortunately, such side effects often cannot be captured by the Phase I, II and III clinical studies, studies that include thousands of patients but rarely get to reach 10 000. Such side effects can be captured only after the drug will enter the market and will be used by a large number of patients. The main sources for investigating the occurrence of ADRs during post marketing surveillance are as follows: (i) spontaneous reporting systems, (ii) prospective cohort or case control studies, (iii) analyses of regional or national health insurance data, (iv)
record linkage databases, and (v) registries. As the pre-registration drug trials are able to demonstrate the efficacy and safety, in ideal conditions of treatment and selected groups of patients, identification of adverse reactions to drugs used in normal conditions is based mainly on “adverse reaction reporting system.” The new ADRs detected through the surveillance systems are used to create hypotheses to be tested in subsequent studies (Paveliu M, Bengea-Luculescu, Tama & Parveliu, 2013)

The information collected during the pre-marketing of drug development is inevitably incomplete with regard to possible ADRs. This is mainly because of the following factors (WHO, 2002):

- Tests in animals are insufficient to predict human safety;
- Patients used in clinical trials are selected and limited in number, the conditions of use differ from those in clinical practice and the duration of trials are limited;
- By the time of licensing exposure of less than 5000 human subjects to a drug allows only the more common ADR to be detected;
- At least 30,000 people need to be treated with a drug to be sure that you do not miss at least one patient with an ADR which has an incidence of 1 in 10,000 exposed individuals;
- Information about rare but serious adverse reactions, chronic toxicity, use in special groups (such as children, the elderly or pregnant women) or drug interactions is often incomplete or not available.

Thus, post-marketing surveillance is important to permit detection of less common, but sometimes very serious ADRs. Hence, HCPs worldwide should report on ADRs as it can save the lives of their patients and others.

2.3 PHARMACOVIGILANCE

Pharmacovigilance (PV) is defined by the WHO as the science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other possible drug-related problems (WHO, 2002).

Pharmacovigilance is an arm of patient care. It aims at making the best use of medicines for the treatment or prevention of disease. No one wants to harm patients, but unfortunately any medicine will sometimes do just this. Good pharmacovigilance will identify the risks and the risk factors in the shortest possible time so that harm can be avoided or minimized. When communicated effectively, this information allows for the intelligent, evidence-based use of
medicines and has the potential for preventing many adverse reactions. This will ultimately help each patient to receive optimum therapy, and on a population basis, will help to ensure the acceptance and effectiveness of public health programmes (WHO, 2006).

The aims of pharmacovigilance according to the WHO (2006) are to:

- improve patient care and safety in relation to the use of medicines and all medical and paramedical interventions;
- improve public health and safety in relation to the use of medicines;
- detect problems related to the use of medicines and communicate the findings in a timely manner;
- contribute to the assessment of benefit, harm, effectiveness and risk of medicines, leading to the prevention of harm and maximization of benefit;
- encourage the safe, rational and more effective (including cost-effective) use of medicines; and
- promote understanding, education and clinical training in pharmacovigilance and its effective communication to the public.

Good PV will identify risks associated with medicines in a minimal amount of time and when communicated effectively, information will allow for intelligent, evidence-based use of medicines which will have potential to preventing many adverse reactions. National PV and ADR reporting systems in India, Uganda and South Africa are not yet functionally optimally. This is due to lack of human, technical and financial resources. According to the WHO, in many developing countries patients are not adequately safeguarded from accessing harmful and ineffective medicines due to poor PV systems. This may result in treatment failures. Particular attention needs to be paid to proper infrastructure and governance, adequate human resources, training and capacity-building and sustainable methodologies and innovation in pharmacovigilance (Maigetter et al., 2015).

The first national ADR reporting schemes were set up in the 1960’s in approximately 10 developed countries (Edwards, Lindquist, Meyboom et al., 2000). Thereafter, many other countries started pharmacovigilance. Unfortunately, only a small number of African countries have formal pharmacovigilance systems. These include Morocco, South Africa, Tanzania, Tunisia, Zimbabwe, Ghana, Egypt, Nigeria, Mozambique, Uganda and Togo, all of which are full members of the WHO Programme for International Drug Monitoring (WHO, 2016). Implementation of spontaneous reporting systems in resource-limited, developing counties is
particularly problematic where other pressing health priorities and challenges, such as remote location, poor telecommunication services and low numbers and level of education of health professionals’, are commonplace (Sevène et al., 2008).

2.3.1 The pharmacovigilance framework

The following figure illustrates the components, structures, functions and personnel of a comprehensive, on-going pharmacovigilance system.

![Pharmacovigilance Framework Diagram]


Figure 2.1: Supporting Pharmacovigilance in Developing Countries: The Systems Perspective

2.3.2 Patient safety

It was not until the disaster caused by thalidomide in 1961 that the first systematic international efforts were initiated to address drug safety issues (WHO, 2002). At that time many thousands of congenitally deformed infants born as the result of exposure in utero to an unsafe medicine promoted for use by pregnant mothers. The sixteenth World Health Assembly (1963) adopted...
Chapter 2: Literature Review

A resolution (WHA 16.36) that reaffirmed the need for early action in regard to rapid dissemination of information on ADRs and led, later, to creation of the WHO Pilot Research Project for International Drug Monitoring in 1968. The purpose of this was to develop a system, applicable internationally, for detecting previously unknown or poorly understood adverse effects of medicines. From these beginnings emerged the practice and science of pharmacovigilance. The collection of international ADR reports in a central database would serve the important function of contributing to the work of national drug regulatory authorities, improve the safety profile of medicines, and help avoid further disasters (WHO, 2002). Patient safety is a central component of the quality of healthcare. Besides the therapeutic benefits that justify their use, medicines can also induce unwanted effects. To minimize the adverse outcomes associated with the use of medicines in healthcare, pharmacovigilance appears to be an essential tool in clinical medicine and public health. The rationale for pharmacovigilance is primarily based on the necessity to mitigate the shortcomings of premarketing clinical trials, mainly designed to demonstrate efficacy. Considering the intrinsic limitations of current clinical trials, such a lack of statistical power, selection of study participants, and too-short follow-up time pharmacovigilance offers the possibility of gathering further information on the safety and effectiveness of medicines during the post marketing life, thereby permitting drug-related morbidity and mortality to be minimized; it could also help detect and prevent medication errors, another common drug-related problem. Furthermore, preventing ADRs can be cost effective as a result of reducing the financial costs associated with their medical management when they occur (Kabore, Millet, Fofane, Berdai, Adam & Haramburu, 2013).

With increased access to newly introduced essential medicines, there is a greater need to monitor and promote their safety and effectiveness. Although many drugs have been used and studied in developed countries, their safety profiles may not necessarily be applicable to other settings, where the incidence, pattern, and severity of ADRs may differ because of local environmental and genetic influences. Further, scant data on the global burden of ADRs associated with new artemisinin-based combination therapy (ACT) and antiretrovirals (ARVs) are available. Thus, the importance of surveillance of medicines-related problems, particularly in Africa with the vulnerable populations receiving treatment for HIV/AIDS, TB and malaria, is becoming increasingly evident (SPS, 2011).

Many other issues are also of relevance to the science:

- Substandard medicines
- Medication errors
- Lack of efficacy reports
Chapter 2: Literature Review

- Use of medicines for indications that are not approved and for which there is inadequate scientific basis
- Case reports of acute and chronic poisoning
- Assessment of drug-related mortality
- Abuse and misuse of medicines
- Adverse interactions of medicines with chemicals, other medicines, and food (WHO, 2002)

The importance of pharmacovigilance for safe medicines use has increasingly been recognised during the last few years, pharmacovigilance has been subject of intense research and regulation (Huang, Moon & Segal, 2014) and in particular, it has earned more and more importance and attention in low-resource countries. This is largely due to the globalisation of trade and availability of new, highly effective but potentially harmful chemical medicinal products in those parts of the world where traditional treatments, in particular herbal or other complementary remedies, used to prevail. A plethora of publications, guidelines and information about newly observed or further investigated ADRs from all over the world creates a growing burden for people working with medicines or patients to keep abreast of this development. Largely due to global availability of information through the internet, patients are nowadays, more and more critical and often concerned about, or even frightened of, potential ADRs of their medicines. This poses an additional demand on the up-to-date competencies of their doctors and other HCPs. A particular challenge is the multidisciplinary character of PV which requires know-how in topics as different as molecular mechanisms of ADRs, clinical medicine, pharmacoepidemiology, legal aspects, public health situations on various levels, and tradition in different regions of the world (Beckmann, Hageman, Bahri, Bate, Boyed, Pan et al., 2014).

Appropriate pharmacovigilance systems to monitor the potential occurrence of both expected and unexpected ADRs to pharmacotherapy are needed to optimise the health of the local population. Where such pharmacovigilance systems are not available, simple techniques to promote and facilitate reporting of unusual clinical events that could be considered as ADRs are recommended (Edwards, 1998). Currently, WHO is promoting the introduction of pharmacovigilance into public health programmes since public health programmes are well established, operate according to standard guidelines and are well supported and funded. An opportunity exists to form a mutually beneficial relationship with pharmacovigilance activities (Sevene et al., 2008).
South Africa is one of the few developing countries in Africa with an existing pharmacovigilance system. The Medunsa National Pharmacovigilance Centre (MNPC), functional since the year 2007, is the only pharmacovigilance centre in South Africa using a structured surveillance system to assess and monitor the safety profile and impact of ARV medicine in adults and adolescents (Dube, Summers, Tint & Mayayise, 2012).

The specific aims of pharmacovigilance are to (WHO, 2002)

- improve patient care and safety in relation to the use of medicines and all medical and paramedical interventions,
- improve public health and safety in relation to the use of medicines,
- contribute to the assessment of benefit, harm, effectiveness and risk of medicines, encouraging their safe, rational and more effective (including cost-effective) use, and
- promote understanding, education and clinical training in pharmacovigilance and its effective communication to the public.

Despite its 40-year history, pharmacovigilance remains a dynamic clinical and scientific discipline. It continues to play a crucial role in meeting the challenges posed by the ever increasing range and potency of medicines, all of which carry an inevitable and sometimes unpredictable potential for harm. When adverse effects and toxicity do appear – especially when previously unknown – it is essential that these are reported, analysed and their significance communicated effectively to an audience that has the knowledge to interpret the information (WHO, 2004).

### 2.4 POST-MARKETING SURVEILLANCE

Post-marketing surveillance includes identifying, reporting, and responding to risk-benefit issues arising with marketing medicines. Post-marketing surveillance programmes use information generated from spontaneous reports and from active surveillance to re-evaluate marketing approval. In South Africa among measures that have been taken to implement post-marketing surveillance, are the establishment of Pharmacovigilance Centres, which includes NADEMC, the Pharmacovigilance office of the MRA and the MNPC (Mkele et al., 2010).

The effectiveness of a national post-marketing surveillance programme is directly dependant on the active participation of health professionals’. Health professionals’ are in the best position to report on suspected ADRs observed in their everyday patient care. All healthcare providers (physicians, pharmacists, nurses, dentists and others) should report ADRs as part
of their professional responsibility, even if they are doubtful about the precise relationship with the given medication (WHO, 2002).

Currently it is medical practitioners who mainly report adverse events (AEs) or other unintended results from medicines, regardless of cause, severity or unexpectedness. Their reports may go to pharmaceutical or medical device manufacturers and the medicines regulatory authorities (the MCC in SA’s case). However, medical practitioners are most commonly involved in the initiation of treatment. Often they do not participate in the follow-up process, particularly where life-time medication is involved, e.g. in the case of antiretroviral medicines for the treatment of human immunodeficiency virus (HIV). Here it is pharmacists and clinical nurses who sees patients regularly, when they come to refill prescriptions for their medicines (Mkele et al., 2010).

Voluntary ADR reporting is a fundamental tool of drug safety surveillance. It is therefore, important to identify the knowledge and attitudes relating to under-reporting, because this would enable targeted educational strategies that is expected to stimulate ADR reporting (Bello & Umar 2011)

According to the WHO (2002), the following ADRs should be reported:

- For “new” drugs – report all suspected reactions, including minor ones. (In many countries drugs are still considered “new” up to five years after marketing authorization);
- For established or well-known drugs – report all serious unexpected (unusual) suspected ADRs;
- Report if an increased frequency of a given reaction is observed;
- Report all suspected ADRs associated with drug-drug, drug-food or drug-food supplements (including herbal and complementary products) interactions;
- Report ADRs in special fields of interest such as drug abuse and drug use in pregnancy and during lactation;
- Report when suspected ADRs are associated with drug withdrawals;
- Report ADRs occurring from overdose or medication error;
- Report when there is a lack of efficacy or when suspected pharmaceutical defects are observed.
Chapter 2: Literature Review

2.4.1 Spontaneous reporting of adverse drug reactions

In 1961, a letter from the Australian physician WG McBride was published in The Lancet. In this letter, he shared his observation that babies whose mothers had used thalidomide during pregnancy were born with congenital abnormalities more often than babies who had not been exposed to thalidomide in utero (Härmark & van Grootheest, 2008; McBride, 1961). In the years to come it became evident that thousands of babies had been born with limb malformations due to the maternal use of thalidomide. In order to prevent a similar disaster from occurring, systems were set up all over the world with the aim of regulating and monitoring the safety of drugs. Spontaneous reporting systems (SRS) were created, and these have become the primary method of collecting post-marketing information on the safety of drugs. The main function of SRS is the early detection of signals of new, rare and serious ADRs. A spontaneous reporting system enables physicians and, increasingly more often, pharmacists and patients to report suspected ADRs to a pharmacovigilance centre (Härmark & van Grootheest, 2008; van Grootheest, Olsson, Couper et al., 2004; van Grootheest & de Jong-van der Berg, 2004; van Grootheest, Passier & van Puijenbroek, 2005).

Spontaneous reporting of suspected ADRs has long been the cornerstone of pharmacovigilance worldwide for the identification of early signals of problems of safety related to the use of medicines. Spontaneous reporting systems operate at the level of individual pharmaceutical companies and regional and national pharmacovigilance centres. In addition, there are overarching multinational pharmacovigilance databases: Eudravigilance, operated by the European Medicines Agency (EMA) and EU Member States, and WHO’s global individual case safety report (ICSR) database, VigiBase®, managed by the Uppsala Monitoring Centre (UMC) (Pal, Olsson & Brown. 2015).

Many developed countries have strong and efficient pharmacovigilance systems. Good pharmacovigilance system will identify the risks and the risk factors in the shortest possible time so that harm can be avoided or minimized (WHO, 2006). These systems among others use spontaneous reporting to collect and analyse adverse events associated with the use of drugs. Though this process is not perfect, it can provide evidence that can be used to establish regulatory action to protect public health. (Amrain & Bečić, 2014).

2.4.2 Advantages of spontaneous reporting of adverse drug reactions

Spontaneous reporting of ADRs has contributed significantly to successful pharmacovigilance. The contribution of health professionals’ to ADR databases has encouraged on-going investigation of the benefit-risk ratio of some drugs. It also contributed to signal detection of
unsuspected and unusual ADRs, previously undetected during the initial evaluation of a drug (Kamtane & Jayawardhani, 2012).

Safety data obtained in premarket trials are often inadequate owing to limitations of such trials, and consequently it is only after drugs have been on the market for some time that the rarer and more serious ADRs tend to be detected. Spontaneous ADR reporting systems are thus the basic component for comprehensive post-marketing surveillance of drug-induced risks (WHO, 2002).

Spontaneous ADR reporting is important to monitor known and unknown adverse effects of medicines. Furthermore, spontaneous reporting of ADRs has played an important role in the detection of serious and unusual ADRs during marketing of the drug in actual practicing in the market. This has led to the withdrawal of many drugs in the past such as rofecoxib, cisapride and terfenadine (Upadhyaya, Vora, Nagar & Patel, 2015).

2.4.3 Limitations of spontaneous reporting of adverse drug reactions

Low voluntary reporting rates greatly limit the advantages offered by this surveillance method (Erill, 1973). It is estimated that only 10% of all adverse reactions are reported (Smith et al., 1996; Pirmohamed et al., 1998). For example, in Portugal, an ADR system was introduced in 1992, yet the country’s ADR reporting figure of 175 per million population in 2008 falls far short of the WHO target of 250 per million. Under reporting is the principal limitation of ADR reporting systems in all countries (Pernas, 2012).

Spontaneous reporting of ADRs by healthcare workers remains an important method of ADRs detection. Such monitoring and reporting system contributes to signal detection of unsuspected and unusual ADRs previously undetected during the initial evaluation of a drug. It encourages documentation of ADRs as well as provides a mechanism for monitoring the safety of drug use in high-risk patient populations. This system also stimulates the education of health workers regarding potential ADRs. In spite of these benefits, under-reporting remains a major drawback of spontaneous reporting (Ezeuko, Ebenebe, Nnebue & Ugoji, 2015).

2.5 METHODS THAT COMPLEMENT SPONTANEOUS REPORTING SYSTEMS

2.5.1 Cohort Event Monitoring (CEM)

Cohort Event Monitoring (CEM) (WHO, 2009a, WHO, 2009b) is a prospective, observational, cohort study of adverse events associated with one or more medicines. A CEM programme is essentially an observation of a new medicine in routine clinical practice in the early post-
marketing phase, but it can be used for older medicines. It is based on the principles of the New Zealand Intensive Medicines Monitoring Programme (Coulter, 2002) and the UK Prescription Event Monitoring (Shakir, 2005) except that in most resource-limited countries, treatment within public health programmes (such as TB and HIV) is not provided on a prescription basis. CEM is thus an early warning system that interviews patients on a certain treatment (the cohort), for capturing problems (the events) with new medicines in public health programmes (Pal, Duncombe, Falzan & Olsson, 2013).

Post-marketing drug surveillance for adverse drug events (ADEs) has typically relied on spontaneous reporting. Recently, regulatory agencies have turned their attention to more preemptive approaches that use existing data for surveillance, called active surveillance (Huang, Moon & Segal, 2014). The Medunsa National Pharmacovigilance Centre (MNPC), functional since the year 2007, is the only pharmacovigilance centre in South Africa using a structured surveillance system to assess and monitor the safety profile and impact of ARV medicines in adults and adolescents (Dube et al., 2012).

2.5.2 Targeted Spontaneous Reporting (TSR)

The WHO proposes targeted spontaneous reporting (TSR) as a methodology that builds on the principles of spontaneous reporting but applied in a defined setting (WHO, 2012). In this method, health professionals managing a well-defined group of patients [e.g. patients on treatment for drug-resistant TB or those switching from first-line to second-line antiretroviral therapy (ART)] are sensitized to report specific safety concerns suspected to be medicine related. TSR addresses a distinct set of questions and provides a comprehensive monitoring method that is affordable, feasible and sustainable in settings with limited financial and human resources. It also promotes the role of pharmacovigilance as a best practice that improves quality of care (Pal et al., 2013).

2.6 FACTORS ASSOCIATED WITH NON-REPORTING OF ADVERSE REACTIONS

Physicians, pharmacists, dentists and nurses are in a position to play a major key role in pharmacovigilance programs but underreporting is very common, with an estimated median underreporting rate (defined as percentage of ADRs detected from intensive data collection that were not reported to relevant spontaneous reporting systems) of 94% (Amrain M et al., 2014).
Factors associated with non-reporting or under-reporting of ADRs include lack of knowledge of the forms for reporting, ignorance of the rules and procedures for reporting and not being sure of the type of reactions that must be reported (O Fadare et al., 2011).

Healthcare workers were encouraged to report ADRs if the reaction was serious, if the reaction was to a new product and was unusual in nature. Concern that the report may be inaccurate, difficulty in deciding whether an ADR has occurred or not, lack of time to complete an ADR form and lack of time to look actively for ADRs while at work were the most discouraging factors (Khan et al., 2013).

The ‘seven deadly sins’ of under-reporting were described by Inman (1996) as the following attitudes relating to professional activities (Gupta & Udupa, 2011):

- Financial incentives: rewards for reporting.
- Legal aspects: fear of litigation or enquiry into prescribing costs: and ambition to compile or publish a personal case series and problems associated with ADR-related knowledge and attitudes.
- Complacency: the belief that very serious ADRs are well documented by the time a drug is marketed.
- Diffidence: the belief that reporting an ADR would only be done if there was certainty that it was related to the use of a particular drug.
- Indifference: the belief that the single case an individual doctor might observe could not contribute to medical knowledge.
- Ignorance: the belief that it is only necessary to report serious or unexpected ADRs.
- Lethargy: the procrastination and disinterest in reporting or lack of time to find a report card and other excuses.

In a study that was conducted by Hazel and Skakir in 2006, the reasons for non-reporting were given as a lack of time, different care priorities, uncertainty about the drug causing the ADR, difficulty in accessing reporting forms, lack of awareness of the requirements for reporting and the lack of understanding of the purpose of spontaneous reporting systems. Well-known and trivial ADRs are less likely to be reported. In addition, physicians attitude towards reporting ADRs contribute to under-reporting (Hazell & Shakir, 2006).
2.7 SUMMARY

Adverse drug reaction reporting through post marketing surveillance is the main source for investigating the occurrence of ADRs. It could detect less common, but very serious ADRs and could reduce the morbidity and mortality of patients. Pharmacovigilance systems need further development and although PV systems exist in South Africa, it is still not fully functional. Access to new medicines increase the need to promote the safe and effective use of medicine and with information available for patients on the internet, HCPs should stay up to date with new medicines and developments. The effectiveness of post marketing surveillance is directly dependant on the active participation of HCPs. However HCPs knowledge, attitude and practices towards ADR reporting are serious constraints on effective reporting.
CHAPTER 3
METHODOLOGY

3.1 INTRODUCTION

The methodology used in this study is discussed in this chapter. In the first part of the chapter, the study design, which followed a descriptive, cross-sectional design, the study site (PHC facilities and CHCs in Tshwane Health District) and the study population are described. Details on the study sample, and inclusion and exclusion criteria, are discussed. The data collection process is described, along with the data capture and analysis process. This is followed by an outline of how the reliability, validity and trustworthiness of the data were ensured, including bias that might have affected the study. A discussion of the ethical considerations concludes the chapter.

3.2 STUDY DESIGN

This study followed a descriptive, cross-sectional design where mainly quantitative data were collected with a self-administered questionnaire.

3.3 STUDY SITE

The study was conducted in eight public sector CHCs and 40 PHC facilities in the Tshwane District (see Table 3.1). These facilities fall under the Gauteng Department of Health, Region C and are under the management of Tshwane Health District, where a Chief Director takes responsibility. These facilities render PHC services to the people in the community. The CHCs and PHC clinics in the Tshwane Health District are managed by facility managers who report to an area manager. The area manager reports to a PHC manager, who reports directly to the Chief Director of the District. The HCPs working in the CHC’s and PHC clinics include medical practitioners, professional nurses, enrolled nurses, pharmacists and pharmacist assistants.

Figure 3.1 shows a map of Tshwane and indicated on the map are all the PHC facilities in the Tshwane District that have been used in this study.
3.4 STUDY POPULATION AND SAMPLE

3.4.1 Study population

The target population of this study consisted of the HCPs working at all 48 Provincial PHC facilities in the Tshwane District (see Table 3.1). One of these facilities served as a pilot site and was excluded from the final sample. The HCPs for the purpose of this study included pharmacists, pharmacist assistants, nurses and medical practitioners.

3.4.2 Sample selection

A breakdown of the total number of 363 HCPs including pharmacists, nurses and medical practitioners employed at the study facilities at the time of data collection, is shown in Table 3.1. A reasonable expectation was that at least 60% of these HCPs would agree to participate in the study.

Sample size estimation was performed on nQuery Advisor, Release 7.0. It was estimated that with a sample size of 218 respondents, a two-sided 95% confidence interval for the percentage HCPs with satisfactory knowledge, attitude and practices, will be within ±5% of the percentage that will be calculated from the sample, assuming that 80% of the respondents will have satisfactory knowledge, attitudes and practices.
Participants for the study were recruited from all 48 facilities listed in Table 3.1. Convenience sampling was employed where individuals who were available at a particular study facility on the day of data collection were asked to participate in the study. That included all pharmacists, pharmacist assistants, professional nurses and medical practitioners.

The following **inclusion criteria** applied for the study:

- Employed by the Gauteng Department of Health (DOH) on a permanent basis.
- Registered HCPs pharmacists, professional nurses, medical practitioners, HCPs and qualified post basic pharmacist assistants
- Willing to participate in the study and provided written consent.

The following **exclusion criteria** applied:

The following exclusion criteria applied for the study:

- Staff members who are not employed by the DOH on a permanent basis.
- Potential participants not present at the facility on the day that data was collected.
### Table 3.1: Health care professionals employed at PHC facilities in the Tshwane District

<table>
<thead>
<tr>
<th>Type of PHC facility</th>
<th>Facility</th>
<th>Pharmacists</th>
<th>Professional Nurses</th>
<th>Medical practitioners</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Community Health Care Centres (CHC's)</strong></td>
<td>Dark City CHC</td>
<td>0</td>
<td>13</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Eersterust CHC</td>
<td>0</td>
<td>25</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Kgabo CHC</td>
<td>0</td>
<td>20</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Laudium CHC</td>
<td>2</td>
<td>16</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Phedisong 4 CHC</td>
<td>0</td>
<td>10</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Soshanguve 3 CHC</td>
<td>2</td>
<td>16</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Stansa Bopape CHC</td>
<td>2</td>
<td>18</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>Temba CHC</td>
<td>0</td>
<td>13</td>
<td>3</td>
</tr>
<tr>
<td><strong>Sub-total</strong></td>
<td>6</td>
<td>131</td>
<td>13</td>
<td></td>
</tr>
<tr>
<td><strong>Clinics</strong></td>
<td>Dewagensdrift</td>
<td>0</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Ubuntu</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Bronkhorstspruit</td>
<td>0</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Kanana</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Kekana Gardens</td>
<td>0</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Rayton</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Refilwe</td>
<td>0</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>Rethabiseng</td>
<td>0</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Sokhulumi</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Zithobeni</td>
<td>0</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Adelaide Tambo</td>
<td>0</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Block JJ</td>
<td>0</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Block TT</td>
<td>0</td>
<td>11</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Boekenhout</td>
<td>0</td>
<td>11</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Boikutsong</td>
<td>0</td>
<td>6</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Bophelong</td>
<td>0</td>
<td>4</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Dilopye</td>
<td>0</td>
<td>4</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Ekangala</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Garankuwa View</td>
<td>0</td>
<td>9</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Holani</td>
<td>0</td>
<td>4</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Jack Hindon</td>
<td>0</td>
<td>6</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Jubilee Gateway</td>
<td>0</td>
<td>10</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>KT Motubatse</td>
<td>1</td>
<td>9</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Kekanastad</td>
<td>0</td>
<td>5</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Mandisa Schiceka</td>
<td>0</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Maria Ranto</td>
<td>0</td>
<td>5</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Phedisong 1</td>
<td>0</td>
<td>9</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Phedisong 6</td>
<td>0</td>
<td>5</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Ramotse</td>
<td>0</td>
<td>5</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Refentse</td>
<td>0</td>
<td>7</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Block X</td>
<td>0</td>
<td>5</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Sedilega</td>
<td>0</td>
<td>6</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Skinner</td>
<td>1</td>
<td>10</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Sosh 2</td>
<td>0</td>
<td>8</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Suurman</td>
<td>0</td>
<td>7</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Tlamelong</td>
<td>0</td>
<td>4</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Winterveldt</td>
<td>0</td>
<td>7</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>New Eersterust</td>
<td>0</td>
<td>4</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Kekanastad</td>
<td>0</td>
<td>1</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td>Mercy</td>
<td>0</td>
<td>5</td>
<td>0</td>
</tr>
<tr>
<td><strong>Sub-total</strong></td>
<td>2</td>
<td>186</td>
<td>25</td>
<td></td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>8</td>
<td>317</td>
<td>38</td>
<td></td>
</tr>
</tbody>
</table>

Source: Tshwane District Office Human Resource Department: Personnel Records for Tshwane District as at end of May 2013

Total number of health care professionals: 363
3.5 DATA COLLECTION INSTRUMENT

A self-administered, structured questionnaire was used as the data collection instrument. The questionnaire was administered as a once-off exercise to assess the knowledge, attitudes and practices of HCPs toward the reporting of ADRs. The questionnaire was only available in English, as it is the language of communication in the workplace (Appendix 1).

The questionnaire was developed by the researcher based on practice experience, discussion with experts and consideration of the literature (Gupta & Udupta, 2011). To ensure the content validity of the questionnaire, it was then given to two experts in the field of pharmacovigilance, for review and input. Based on the experts’ review, the questionnaire was amended and was further tested in a pilot study.

3.6 PILOT STUDY

The aim of the pilot study was to determine the relevance of the data collection tool and to identify any problems that the participants might have had with the questions, so that modifications could be made to the questionnaire accordingly (Struwig & Stead, 2001).

The pilot study was conducted at Skinner Clinic immediately after the Medunsa Research and Ethics Committee (MREC) had granted ethical clearance for the study. The sample for the pilot study included a pharmacist, two professional nurses and a medical practitioner. Skinner Clinic was therefore excluded from the final sample.

The pilot study showed that the questionnaire was appropriate and that participants did not experience any problems with the questions. It was furthermore determined that the time to complete the questionnaire was approximately 15 minutes. The results of the pilot study showed that the questionnaire was adequate for the purpose of this study and no changes were necessary.

3.7 DATA COLLECTION

3.7.1 Data collection period

Data were collected over a period of 12 months in 2014 and 2015.
3.7.2 Data collectors and training

Data were collected by the researcher herself and six Community Service Pharmacists (CSPs) who were supervising the 48 public service PHC facilities in the Tshwane District. They were part of the Monitoring and Evaluation Team at the Tshwane Metsweding Regional Pharmacy and had to conduct visits to all the facilities on a monthly basis. The CSPs who collected the data, underwent data collection training before the commencement of the study to ensure standardisation of the data collection procedures. The data collection training was conducted by the researcher and took place prior to the pilot study. Data collection training included the following aspects:

- Clear written instructions on how the instrument is to be administered.
- Each item on the instrument was discussed, to ensure consistency in case of any questions of respondents.
- Communication and ethical principles in research.
- A clear schedule of dates when the collection of data will occur.

3.7.3 Data collection process

All pharmacists, pharmacist assistants, professional nurses and doctors present at the facility and who complied with the inclusion criteria for the study were invited to participate. The data collectors approached the potential participants, explained the aim and objectives of the study and provided them with information about the study (see Appendix 2). They were informed that participation in the study is voluntary and that the questionnaire will be completed anonymously.

After reading the study information leaflet, potential participants were allowed the opportunity to ask questions about the study. After agreeing to participate, participants were requested to complete the written informed consent form (see Appendix 3). The questionnaire was handed to them for immediate completion in a private area in the facility, e.g. office or consultation room, after which they placed the questionnaire in a sealed box provided in the facility, to ensure anonymity.

3.8 DATA ENTRY AND ANALYSIS

The data were captured electronically using a Microsoft Excel™ spread sheet. All entered data were proof-read for accuracy and completeness and the necessary corrections were made
prior to the commencement of the data analysis. The data analysis was mainly descriptive and took place in consultation with a statistician.

Data were captured using Microsoft Excel™, checked for accuracy and cleaned before analysis with SAS, release 9.2, running under Microsoft Windows.

Responses were categorised according to knowledge, attitudes and practices based on the questions included on the questionnaire. For knowledge, attitudes and practices, correct or preferred responses were summarised by frequency counts and percentages for each item as well as for medical practitioners, professional nurses, pharmacists and pharmacist assistants separately. An overall score (%) with 95% confidence interval based on responses from all participants was calculated for knowledge, attitudes and practices.

An individual overall score (%) was calculated for each participant, for knowledge, attitudes and practices, based on positive or preferred responses. A mean (%) for knowledge, attitudes and practices was calculated for each profession (medical practitioners, professional nurses, pharmacists and pharmacist assistants). Mean knowledge, attitude and practice levels (%) of the different professions were compared by an analysis of variance (ANOVA), followed by pair wise comparisons by t-test.

3.9 RELIABILITY AND VALIDITY

To ensure the content validity of the questionnaire and that the objectives of the study were achieved, the questionnaire was given to two experts in the field of pharmacovigilance for their comments and input (see Section 3.5).

A pilot study was conducted prior to the study to test the feasibility of the data collection process and the appropriateness of the questions included in the questionnaire (see Section 3.6).

The data were collected by the researcher herself with the assistance of six CSPs, who were trained in the data collection procedures prior to the study. They practiced the sequence of events so that all questionnaires were administered in the same way, to ensure a standardised data collection process (see Section 3.7.2).

All captured data were cross-checked and proof-read by the researcher to ensure the reliability of the data entry (see Section 3.8).
3.10 BIAS

Participants in this study were not influenced by the data collectors, nor were they led to answer in a particular way, as the questionnaire was self-administered. All questionnaires were completed anonymously as the names of the participants were not requested and were not provided for in the questionnaire. Each participant placed his/her completed questionnaire in a sealed box in the facility so that confidentiality and anonymity were maintained.

Selection bias was avoided by including all PHC facilities in Tshwane Health District in the study. Participants were not selected specifically, as all pharmacists, professional nurses, medical practitioners and pharmacist assistants who were available at the PHC facility on the day of the data collection were invited to participate. The pilot site was selected randomly to prevent selection bias. Participants in the pilot study were excluded from the main study, to prevent any information bias that could have been introduced.

3.11 ETHICAL CONSIDERATIONS

Ethical clearance for the study was obtained from the Medunsa Research Ethics Committee (MREC) of the University of Limpopo, now Sefako Makgatho Health Sciences University, prior to the commencement of the study (MREC/H/270/2013). Ethical approval was also obtained from the Gauteng Health Ethics Committee (see Appendix 5).

Permission to conduct the study in the PHC facilities in Tshwane District was obtained from the Chief Director of the Tshwane District (see Appendix 5). As the study is related to pharmaceutical services in the district, a copy of the final report will be made available to the Tshwane District Offices and the District Pharmacy and Therapeutics Committee. All HCPs were informed of the study.

All participants gave written informed consent before participating in the study and were allowed to withdraw from the study at any time, without any negative consequences (see Appendices 1 and 2). Access to the data collection forms was controlled by the researcher and data collection forms were kept under lock and key. Raw data collection materials were locked away and kept for backup and record purposes. The identity of the participants was not known, as the questionnaire was completed anonymously. All data were handled in confidence.
Chapter 3: Methodology

3.12 SUMMARY

This chapter described the methodology used for data collection in this study, which was descriptive and cross-sectional in which mainly quantitative data were collected with a self-administered questionnaire.

The study was conducted in 48 PHC facilities in Tshwane Health District. The data were captured electronically using a Microsoft Excel™ spread sheet and checked for accuracy and correctness and imported into SAS® release 9.2 for statistical analysis.

Ethical clearance and permission for the study was obtained from all necessary authorities.

The results of the data collected in this study, are presented and discussed in Chapter 4, in the form of a manuscript for publication in an accredited journal.
CHAPTER 4
RESULTS AND DISCUSSION

4.1 INTRODUCTION

The results of the study and discussion thereof are presented in the format of a manuscript according to the requirements and guidelines of the journal. The manuscript is followed by the letter to the editor of the particular journal.

The manuscript will be submitted to Primary Health Care Research and Development under the title “Knowledge, Attitudes and Practices of Health Care Professionals towards Adverse Drug Reaction Reporting in Public Sector Primary Health Care Facilities in Tshwane District”. The author guidelines for this journal are attached in Appendix 8 and can be accessed electronically at: https://www.cambridge.org/core/journals/primary-health-care-research-and-development.
4.2 MANUSCRIPT

This section contains the manuscript formatted according to the journal’s requirements. For the purpose of the dissertation, single line spacing was used for tables, which are included in the text.

Title:
Knowledge, Attitudes and Practices of Health Care Professionals towards Adverse Drug Reaction Reporting in Public Sector Primary Health Care Facilities

Running title:
Knowledge, Attitudes and Practices towards Adverse Drug Reaction Reporting
Authors:

Mrs Hester Michelle Haines, Pharmacy Manager Tshwane Regional Pharmacy, District Pharmacist, BPharm.

Johanna C Meyer, Associate Professor Faculty of Health Sciences Sefako Makgatho Health Sciences University, BPharm, MSc (Med), PhD (Pharmacy);

Robert Summers, Professor Faculty of Health Sciences Sefako Makgatho Health Sciences University, BSc (Pharm), MSc (Pharm), PhD.

Corresponding author: Prof JC Meyer

Address: Sefako Makgatho Health Sciences University, Department of Pharmacy, Molotlegi Street, Ga-Rankuwa, South Africa, 0208

Tel: +27 12 521 4567

Fax: +27 12 521 3992

Email: hannelie.meyer@smu.ac.za; hannelie.meyer@gmail.com
Abstract

Aim

The aim was to determine the knowledge, attitudes and practices of health care professionals (HCPs) towards adverse drug reaction (ADR) reporting in primary health care (PHC) facilities in the Tshwane District in the Gauteng province of South Africa.

Background

In Tshwane District reports on ADRs should be submitted to the Tshwane District Pharmacy and Therapeutics Committee meeting on a quarterly basis. At the time of the study, very few ADRs were submitted to the committee, hence it was important to determine the knowledge, attitude and practices of HCPs to understand the under-reporting of ADRs. The findings could be used to direct future practice towards initiating programmes to promote ADR reporting in Tshwane District.

Methods

This study followed a descriptive, cross-sectional design using quantitative methodology. Study sites included eight public sector Community Health Care Centres (CHCs) and 40 PHC facilities in the Tshwane District. A self-administered questionnaire was distributed to 218 HCPs, including medical practitioners, professional nurses, pharmacists and pharmacist assistants (PBPA). Ethical clearance was obtained and HCPs provided written informed consent.

Findings

The final sample size was 200, with a response rate of 91.7%. Although an appropriate attitude for ADR reporting existed, the actual frequency of ADR reporting was low. The lack of awareness (57.5%) of respondents about the existence of an ADR reporting system, ultimately will affect the reporting process. The majority of HCPs (89.0%) felt that ADR reporting is a professional obligation, and will be encouraged to report it if the reaction was serious (89.5%), linked to a new product (89.5%) and if it was unusual (78.0%). Unfortunately 11.0% of HCP’s were unaware of the professional obligation to report ADRs. Only 12.0% of HCPs knew where the ADR forms were kept in the facilities. When responses of all HCPs were combined, overall 79.6% (95% CI: 76.9% - 82.3%) of responses were positive or preferred in terms of knowledge of ADRs, overall positive attitude was 63.3% (95% CI 60.7%-65.8%) and 24.6% (95% CI 21.7%-27.4%) of responses were positive in terms of practice.
Conclusion

The findings suggest that underreporting of ADRs is associated with gaps in knowledge, attitudes and practices regarding pharmacovigilance amongst HCPs. There is a serious and urgent need for education and training of HCPs on ADRs, and to create awareness and promote the reporting of ADRs amongst HCPs.

**Keywords:** adverse drug reaction, health care professionals, pharmacovigilance, pharmacist, pharmacist assistant, professional nurse, medical practitioner
Introduction

Adverse drug reactions (ADRs) are a major public health problem because they directly cause an increase in mortality, morbidity and costs (Pernas et al., 2012). Physicians, pharmacists, dentists and nurses are in a position to play a major key role in pharmacovigilance programmes, however under-reporting of adverse drug reactions (ADRs) is very common (Amrain M et al., 2014).

If health care professionals (HCPs) took responsibility for detecting, identifying, managing and reporting medication-associated adverse events as they happen, a situation could occur in which pharmaceutical manufacturers and regulators, health care providers, funders and patients would not have to be concerned about the safety of approved medicines, vaccines or devices. Should HCPs work together to establish effective pharmacovigilance systems, it will produce confidence in the services to which patients entrust their lives. Safety signals would be detected early on, and better and quicker safety decisions would be made (Mkele et al., 2010).

Adverse drug reaction (ADR) spontaneous reporting systems are currently the basic methods for the comprehensive post-marketing surveillance of drug-induced risks. Spontaneous reporting systems are inexpensive and simple to operate. However, their strength is tightly connected to the actual reporting rate by HCPs, under-reporting being the main disadvantage (Vessel et al., 2009).

Many factors are associated with ADR under-reporting among HCPs. These factors have been broadly classified as personal and professional characteristics of health carers, and their knowledge and attitude to reporting, referred to as ‘the seven deadly sins’ of pharmacovigilance (Inman, 1996). Factors associated with non-reporting or under-reporting of ADRs include lack of knowledge about the forms used for reporting, ignorance of the rules and procedures for reporting and not being sure of the type of reactions that must be reported (O Fadare et al., 2011).

The first national ADR reporting schemes were set-up in the 1960’s in approximately 10 developed countries (Edwards et al., 2000). Thereafter, many other countries started pharmacovigilance systems and activities, but unfortunately only a small number of African countries have formal systems. They include Morocco, South Africa, Tanzania, Tunisia, Zimbabwe, Ghana, Egypt, Nigeria, Mozambique, Uganda and Togo, all of which are full members of the WHO Programme for International Drug Monitoring (WHO, 2016).

Implementation of spontaneous reporting systems in resource-limited, developing counties is particularly problematic where other pressing health priorities and challenges, such as remote
location, poor telecommunication services and low numbers of and low level of education of
health professionals, are commonplace (Sevence et al., 2008).

South Africa is one of the few developing countries in Africa with an existing
pharmacovigilance system. The Medunsa National Pharmacovigilance Centre (MNPC),
functional since 2007, is the only pharmacovigilance centre in South Africa using a structured
surveillance system to assess and monitor the safety profile and impact of ARV medicines in
adults and adolescents (Dube et al., 2012).

In Tshwane District, reports on adverse drug reactions (ADRs) are discussed at the Tshwane
District Pharmacy and Therapeutics Committee meeting on a quarterly basis. Over the 18
months period prior to the study very few ADRs were discussed by the committee. It would
therefore be important to determine the knowledge, attitudes and practices of HCPs, hence
the aim of this study, in an attempt to understand why ADRs are not being reported. The
results of this study can be used to design and initiate programmes to promote ADR reporting
in Tshwane District.

Methods

Study design and setting

This study followed a descriptive, cross-sectional design, using quantitative methodology and
a self-administered questionnaire. The study was conducted in 48 Primary Health Care (PHC)
facilities in the Tshwane Health District, which consists of eight Community Health Care
Centres and 40 PHC clinics. Tshwane Health District is situated in the Gauteng Province in
South Africa. Services are rendered to the people in the community by the PHC facilities.

Target population and participants

The target population of this study consisted of HCP (medical practitioners, professional
nurses, pharmacists and pharmacist assistants) working at 48 PHC facilities in the Tshwane
District. At the time of the study, a total number of 363 HCPs were employed at the PHC
facilities. A reasonable expectation was that at least 60% of these HCPs would agree to
participate in the study, and will therefore be included in the sample.

Sample size estimation was performed on nQuery Advisor, Release 7.0. It was estimated that
with a sample size of 218 respondents, a two-sided 95% confidence interval for the percentage
HCPs with satisfactory knowledge, attitude and practices, will be within ± 5% of the percentage
that will be calculated from the sample, assuming that 80% of the respondents will have
satisfactory knowledge, attitudes and practices.
Convenience sampling was employed in which HCPs who were available at a particular study facility on the day of data collection, were approached to participate in the study. Inclusion criteria were HCPs permanently employed by the Gauteng Department of Health (DOH), registered pharmacists, professional nurses, medical practitioners and qualified post-basic pharmacist assistants, willingness to participate in the study and provide written informed consent.

**Data collection instrument and process**

A self-administered, structured questionnaire was used to assess the knowledge, attitudes and practices of HCPs towards the reporting of ADRs. The questionnaire was developed based on practice experience, discussion with experts and consideration of the literature (Gupta & Udupta, 2011). Two experts in the field of pharmacovigilance reviewed the questionnaire for content validity, after which it was tested in a pilot study for feasibility.

Data were collected by six Community Service Pharmacists (CSPs) who received data collection training, before the commencement of the study, to ensure standardisation of the data collection procedures. They were supervising the 48 PHC facilities in the Tshwane District and had to conduct visits to all facilities on a monthly basis, as part of the Monitoring and Evaluation Team at the Tshwane Metsweding Regional Pharmacy.

Potential participants were approached by the data collectors, the aim and objectives of the study were explained and written consent obtained on agreement to participate. The structured questionnaire was handed to them for completion in a private room at the facility. The completed questionnaire was placed by the participants in a sealed box provided at the facility, to ensure confidentiality.

**Data entry and analysis**

Data were captured using Microsoft Excel™, checked for accuracy and cleaned before analysis with SAS, release 9.2, running under Microsoft Windows.

Responses were categorised according to knowledge, attitudes and practices based on the questions included in the questionnaire. For knowledge, attitudes and practices, correct or preferred responses were summarised by frequency counts and percentages for each item as well as for medical practitioners, professional nurses, pharmacists and pharmacist assistants separately. An overall score (%) with 95% confidence interval based on responses from all participants was calculated for knowledge, attitudes and practices.

An individual overall score (%) was calculated for each participant, for knowledge, attitudes and practices, based on positive or preferred responses. A mean (%) for knowledge, attitudes
and practices was calculated for each profession (medical practitioners, professional nurses, pharmacists and pharmacist assistants). Mean knowledge, attitude and practice levels (%) of the different professions were compared by an analysis of variance (ANOVA), followed by pair wise comparisons using the t-test.

Ethical considerations

Ethical clearance for the study was obtained from the Medunsa Research Ethics Committee of the University of Limpopo, now Sefako Makgatho Health Sciences University, prior to the commencement of the study (MREC/H270/2013). Permission to conduct the study at the PHC facilities was obtained from the Chief Director of the Tshwane Health District. All participants provided written informed consent.

Results

Two hundred of the 218 questionnaires distributed were completed, giving a response rate of 91.7%.

Demographic characteristics

The demographic characteristics of the respondents are summarised in Table 1. The majority (83.0%) of the respondents were female and a third (35.5%) between 31 and 40 years of age. Professional nurses constituted the largest proportion of the respondents (44.5%). The majority (73%) of the respondents were from PHC facilities.

Table 1 Demographic characteristics of participants

<table>
<thead>
<tr>
<th></th>
<th>Number (%) of health care professionals</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Medical practitioner (n=23)</td>
</tr>
<tr>
<td><strong>Gender</strong></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>7 (3.5%)</td>
</tr>
<tr>
<td>Female</td>
<td>16 (8.0%)</td>
</tr>
<tr>
<td><strong>Age group (years)</strong></td>
<td></td>
</tr>
<tr>
<td>21-30</td>
<td>4 (2.0%)</td>
</tr>
<tr>
<td>31-40</td>
<td>10 (5.0%)</td>
</tr>
<tr>
<td>41-50</td>
<td>5 (2.5%)</td>
</tr>
<tr>
<td>51-60</td>
<td>2 (1.0%)</td>
</tr>
<tr>
<td>&gt;61</td>
<td>2 (1.0%)</td>
</tr>
<tr>
<td><strong>Working environment</strong></td>
<td></td>
</tr>
<tr>
<td>Community Health Care centre</td>
<td>9 (4.5%)</td>
</tr>
<tr>
<td>Primary Health Care clinic</td>
<td>14 (7.0%)</td>
</tr>
</tbody>
</table>
Health care professionals’ knowledge on what should be reported as ADRs

Table 2 shows that 75.6% of respondents understood the term ‘adverse drug reaction’ and 92.5% were aware that ADRs must be reported. However, only 57.5% were aware of an ADR reporting and monitoring system in the district. Only a third (33.0%) was aware of the actual form that must be used for ADR reporting with six of the 10 pharmacists being aware of the form. Only eighteen (9.0%) of all HCPs knew where to submit the form when reporting an ADR.

The majority (94.0%) of respondents were aware that one of the objectives of pharmacovigilance was to ‘improve patient care and safety’. Other objectives namely to ‘contribute to the assessment of risk/benefit of medicine’ (92.5%), ‘promote understanding, education and clinical training’ (91.5%) and ‘ensure effective communication of adverse drug reaction reporting to the public’ (90.5%) were perceived as almost equally important (Table 2).
<table>
<thead>
<tr>
<th>Item</th>
<th>Correct response from number (%) of health care professionals</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Pharmacist (n=10)</td>
</tr>
<tr>
<td>Understanding the term ‘adverse drug reaction’</td>
<td>10 (100%)</td>
</tr>
<tr>
<td>Know that ADRs must be reported</td>
<td>10 (100%)</td>
</tr>
<tr>
<td>Know of the existence of an ADR reporting and monitoring system in the district</td>
<td>7 (70.0%)</td>
</tr>
<tr>
<td>Know where to find the form to complete for reporting ADRs</td>
<td>6 (60.0%)</td>
</tr>
<tr>
<td>Know where the ADR reporting form must be submitted to</td>
<td>3 (30.0%)</td>
</tr>
<tr>
<td>An event related to these items must be reported</td>
<td></td>
</tr>
<tr>
<td>Allopathic drugs</td>
<td>9 (90.0%)</td>
</tr>
<tr>
<td>Herbal drugs</td>
<td>9 (90.0%)</td>
</tr>
<tr>
<td>Traditional and complementary medicine</td>
<td>8 (80.0%)</td>
</tr>
<tr>
<td>Blood products</td>
<td>8 (80.0%)</td>
</tr>
<tr>
<td>Biological</td>
<td>9 (90.0%)</td>
</tr>
<tr>
<td>Medical devices</td>
<td>10 (100%)</td>
</tr>
<tr>
<td>Vaccines</td>
<td>8 (80.0%)</td>
</tr>
<tr>
<td>Main objectives of PV in the public sector</td>
<td></td>
</tr>
<tr>
<td>Improve patient care and safety</td>
<td>10 (100%)</td>
</tr>
<tr>
<td>Improve public health and safety</td>
<td>10 (100%)</td>
</tr>
<tr>
<td>Contribute to the assessment of risk/benefit of medicines</td>
<td>10 (100%)</td>
</tr>
<tr>
<td>Promote understanding, education and clinical training in this field</td>
<td>9 (90.0%)</td>
</tr>
<tr>
<td>Ensure effective communication of adverse drug reaction reporting to the public</td>
<td>10 (100%)</td>
</tr>
</tbody>
</table>
The respondents showed reasonably good knowledge of the type of adverse events that should be reported, ranging from 65.5% for congenital anomaly to 89.5% for reaction to a new drug and a serious event (see Figure 1).

When all knowledge questions and statements were combined for all HCPs, overall 79.6% (95% CI: 76.9-82.3%) of responses were positive or preferred in terms of knowledge of ADRs.

An individual overall knowledge score (%) was calculated for each participant, based on positive or preferred responses. Mean and median (%) for knowledge were calculated for each profession (see Table 3). Mean knowledge levels (%) of the different professions were compared by an analysis of variance (ANOVA), followed by pair wise comparison by t-test. The mean knowledge scores of medical practitioners (82.8%; p=0.017), pharmacists (91.4%; p=0.003) and professional nurses (84.0%; p<0.0001) were significantly greater compared to that of PBPAs (72.2%).

**Table 3** Mean and median (%) knowledge levels on ADRs by profession

<table>
<thead>
<tr>
<th>Profession</th>
<th>Medical Practitioner (n=23)</th>
<th>Pharmacist (n=10)</th>
<th>Professional Nurse (n=89)</th>
<th>Post-basic pharmacist assistant (n=78)</th>
<th>Overall (n=200)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mean (SD)</strong></td>
<td>82.8 (14.7)</td>
<td>91.4 (12.3)</td>
<td>84.0 (17.0)</td>
<td>72.2 (22.0)</td>
<td>79.6 (19.6)</td>
</tr>
<tr>
<td><strong>Median</strong></td>
<td>85.7</td>
<td>95.2</td>
<td>90.0</td>
<td>76.2</td>
<td>85.7</td>
</tr>
<tr>
<td><strong>IQR</strong></td>
<td>71.4-95.2</td>
<td>85.7-100</td>
<td>76.2-95.2</td>
<td>61.9-90.5</td>
<td>71.4-95.2</td>
</tr>
<tr>
<td><strong>Min/Max</strong></td>
<td>42.9-100</td>
<td>61.9-100</td>
<td>9.5-100</td>
<td>9.5-100</td>
<td>9.5-100</td>
</tr>
</tbody>
</table>

SD= standard deviation; IQR= inter quartile range.
Attitudes towards adverse drug reaction reporting

Table 4 shows that the majority (91.0%) of respondents acknowledged that ADR reporting is necessary, with 89.0% agreeing that reporting ADRs is a professional obligation, and 89.0% agreeing on the need for training. More than 70% of HCPs felt that ADR reporting should be compulsory. Nearly two thirds (63%) of HCPs regarded pharmacovigilance in everyday work as very important.
### Table 4: Health care professionals’ attitudes towards the reporting of adverse drug reactions

<table>
<thead>
<tr>
<th>Item</th>
<th>Correct response</th>
<th>Correct response from different health care professionals</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Pharmacist (n=10)</td>
</tr>
<tr>
<td>ADR reporting is necessary</td>
<td>Yes</td>
<td>10 (100%)</td>
</tr>
<tr>
<td>ADR reporting is a professional obligation</td>
<td>Yes</td>
<td>10 (100%)</td>
</tr>
<tr>
<td>Training on ADR reporting</td>
<td>Yes</td>
<td>7 (70.0%)</td>
</tr>
<tr>
<td>Adverse drug reaction reporting should be</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Voluntary</td>
<td>Yes</td>
<td>4 (40.0%)</td>
</tr>
<tr>
<td>Compulsory</td>
<td>Yes</td>
<td>6 (60.0%)</td>
</tr>
<tr>
<td>Remunerated</td>
<td>Yes</td>
<td>0</td>
</tr>
<tr>
<td>Health care workers role</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Preventing adverse drug reactions</td>
<td>Yes</td>
<td>9 (90.0%)</td>
</tr>
<tr>
<td>Detecting adverse drug reactions</td>
<td>Yes</td>
<td>10 (100%)</td>
</tr>
<tr>
<td>Managing adverse drug reactions</td>
<td>Yes</td>
<td>10 (100%)</td>
</tr>
<tr>
<td>Reporting adverse drug reactions</td>
<td>Yes</td>
<td>10 (100%)</td>
</tr>
<tr>
<td>The importance of pharmacovigilance in everyday work</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Very important</td>
<td>Yes</td>
<td>5 (50.0%)</td>
</tr>
<tr>
<td>Important</td>
<td>Yes</td>
<td>5 (50.0%)</td>
</tr>
<tr>
<td>Slightly important</td>
<td>Yes</td>
<td>0</td>
</tr>
<tr>
<td>Not important at all</td>
<td>Yes</td>
<td>0</td>
</tr>
</tbody>
</table>
Major factors which discourage reporting are listed in Table 5. Nearly two thirds of participants (60.5%) did not know how to report, where to report or when to report an ADR and half of them (51.5%) said that the level of their clinical knowledge makes it difficult to decide whether or not an ADR has occurred.

**Table 5** Major factors which discourage reporting of ADRs

<table>
<thead>
<tr>
<th>Factors discouraging ADR reporting</th>
<th>Number (%) of HCPs (n=200)</th>
</tr>
</thead>
<tbody>
<tr>
<td>A single unreported case may not affect the ADR data base</td>
<td>38 (19.0%)</td>
</tr>
<tr>
<td>Non-remuneration for reporting</td>
<td>47 (23.5%)</td>
</tr>
<tr>
<td>Lack of confidence to discuss the ADRs with other colleagues</td>
<td>56 (28.0%)</td>
</tr>
<tr>
<td>Concern that reporting may generate extra work</td>
<td>67 (33.5%)</td>
</tr>
<tr>
<td>Lack of time to actively look for ADRs while at work</td>
<td>79 (39.5%)</td>
</tr>
<tr>
<td>Lack of time to complete a report</td>
<td>88 (44.0%)</td>
</tr>
<tr>
<td>Concern that the report may be incorrect</td>
<td>93 (46.5%)</td>
</tr>
<tr>
<td>Level of clinical knowledge makes it difficult to decide whether or not an ADR has occurred</td>
<td>103 (51.5%)</td>
</tr>
<tr>
<td>Do not know how to report, where to report and when to report</td>
<td>121 (60.5%)</td>
</tr>
</tbody>
</table>

Health care workers perception about their role in adverse drug reaction reporting is presented in Figure 2 with the majority (more than 90%) of HCPs who said that they had an important role to play in preventing, detecting, managing and reporting of ADRs.

**Figure 2** Health care professionals’ role in ADR reporting

When all attitude questions and statements for all HCPs were combined, overall 63.3% (95% CI: 60.7-65.8%) of responses were positive or preferred in terms of attitude towards ADRs.
An individual overall attitude score (%) was calculated for each participant, based on positive or preferred responses. Mean and median (%) for attitude were calculated for each profession (see Table 6). Mean attitude levels (%) of the different professions were compared by an analysis of variance (ANOVA), followed by pair wise comparison by t-test. The mean attitude scores of medical practitioners (66.7%; \( p = 0.006 \)), pharmacists (73.9%; \( p = 0.001 \)) and professional nurses (68.3%; \( p < 0.001 \)) was significantly greater compared to PBPAs (55.2%).

**Table 6** Mean and median (%) attitude levels on ADRs by profession

<table>
<thead>
<tr>
<th>Profession</th>
<th>Mean (SD)</th>
<th>Median</th>
<th>IQR</th>
<th>Min/Max</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medical Practitioner (n=23)</td>
<td>66.7 (15.5)</td>
<td>66.7</td>
<td>61.1-83.3</td>
<td>38.9-88.9</td>
</tr>
<tr>
<td>Pharmacist (n=10)</td>
<td>73.9 (18.5)</td>
<td>77.8</td>
<td>66.7-83.3</td>
<td>33.3-100</td>
</tr>
<tr>
<td>Professional Nurse (n=89)</td>
<td>68.3 (17.8)</td>
<td>72.2</td>
<td>55.6-83.3</td>
<td>27.8-100</td>
</tr>
<tr>
<td>Post-basic Pharmacist assistant (n=78)</td>
<td>55.2 (16.9)</td>
<td>50.0</td>
<td>44.4-66.7</td>
<td>16.7-94.4</td>
</tr>
<tr>
<td>Overall (n=200)</td>
<td>63.3 (18.3)</td>
<td>63.9</td>
<td>44.4-66.7</td>
<td>16.7-100</td>
</tr>
</tbody>
</table>

Health care professionals practice of adverse drug reaction reporting

According to Table 7 only 16% of HCPs have ever reported any suspected ADR with 65% who said that the ADR form is available in their facilities. However, only 12% knew where it was kept and only 12 (6%) could attach a copy of the form to their questionnaire.

Just more than a third (36.5%) of respondents said that they kept copies of the forms they submitted but only three could attach a copy of the completed form. Only 17% of respondents had received training on ADR reporting (Table 7).

When all practice questions and statements for all HCPs were combined, overall 24.6% (95% CI: 21.7-27.4%) of responses were positive or preferred in terms of the practice of ADR reporting.
### Table 7: Practice of HCPs in adverse drug reaction reporting

<table>
<thead>
<tr>
<th>Item</th>
<th>Correct response</th>
<th>Correct response from different health care professionals</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Pharmacist (n=10)</td>
<td>Medical practitioner (n=23)</td>
</tr>
<tr>
<td>Have you ever reported any suspected adverse drug reaction</td>
<td>Yes</td>
<td>4 (40.0%)</td>
</tr>
<tr>
<td>Have you reported any suspected adverse drug reaction to the ADR reporting and monitoring system in your District</td>
<td>Yes</td>
<td>1 (10.0%)</td>
</tr>
<tr>
<td>Do you have the adverse reporting form available in your facility</td>
<td>Yes</td>
<td>7 (70.0%)</td>
</tr>
<tr>
<td>Where are the ADR forms kept in your facility</td>
<td>Pharmacy/ managers office</td>
<td>3 (30.0%)</td>
</tr>
<tr>
<td>Copies of the submitted ADR forms are kept</td>
<td>Yes</td>
<td>2 (20.0%)</td>
</tr>
<tr>
<td>Copy of form attached to questionnaire</td>
<td>Yes</td>
<td>0</td>
</tr>
<tr>
<td>Training received on ADR reporting</td>
<td>Yes</td>
<td>4 (40.0%)</td>
</tr>
</tbody>
</table>
Chapter 4: Results and Discussion

An individual overall practice score (%) was calculated for each participant, based on positive or preferred responses. Mean and median (%) for practice were calculated for each profession (see Table 8). Mean practice levels (%) of the different professions were compared by an analysis of variance (ANOVA), followed by pair wise comparison by t-test. The mean practice score for PBPA’s (20.9%) was significantly lower than the mean for pharmacists (33.3%; \( p=0.050 \)).

**Table 8 Mean and median (%) practice levels on ADRs by profession**

<table>
<thead>
<tr>
<th>Profession</th>
<th>Medical Practitioner (n=23)</th>
<th>Pharmacist (n=10)</th>
<th>Professional Nurse (n=89)</th>
<th>Post-basic pharmacist assistant (n=78)</th>
<th>Overall (n=200)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean (SD)</td>
<td>21.7 (24.3)</td>
<td>33.3 (31.4)</td>
<td>27.5 (18.0)</td>
<td>20.9 (20.4)</td>
<td>24.6 (20.7)</td>
</tr>
<tr>
<td>Median</td>
<td>16.7</td>
<td>25.0</td>
<td>33.3</td>
<td>16.7</td>
<td>16.7</td>
</tr>
<tr>
<td>IQR</td>
<td>0.0-33.3</td>
<td>0.0-66.7</td>
<td>16.7-33.3</td>
<td>0.0-33.0</td>
<td>8.3-33.3</td>
</tr>
<tr>
<td>Min/Max</td>
<td>0.0-66.7</td>
<td>0.0-83.3</td>
<td>0.0-83.3</td>
<td>0.0-83.3</td>
<td>0.0-83.3</td>
</tr>
</tbody>
</table>

**Discussion**

Underreporting of ADRs is a major threat to the success of the pharmacovigilance system in the Tshwane District. From the literature, various factors have been found to be responsible for under-reporting of ADRs. These factors were mainly related to the knowledge and attitudes of health workers (Inman, 1996). Very few studies have been conducted to determine which factors are related to under-reporting of ADRs amongst HCPs in PHC settings specifically. Hence, the importance of the present study.

This study showed that while a positive attitude to ADR reporting existed among HCPs, the actual practice of ADR reporting was lacking. Studies done in India in Mumbai (Gupta, et al., 2011), Mysore (Ramesh et al., 2009) and Muzzafarnagar (Ghosh et al., 2010) have shown high knowledge but poor practice of ADR reporting.

The results reflected a lack of awareness (57.5%) of HCPs about the existence of an ADR reporting system (Table 2), which will ultimately affect the reporting. More alarming is the fact that very few HCPs had ever reported an adverse event (16.0%) or contributed to the ADR monitoring system in the district (7.0%), which is similar to the results obtained by Gupta et al. (2011) and Li Qing et al. (2004) (Table 7).

Although the majority of HCPs surveyed (89.0%) felt that ADR reporting is a professional obligation (Table 4), they would be encouraged to report if the reaction were serious (89.5%), it is to a new product (89.5%), and is unusual (78.0%) (Figure 1), which are similar to the
results obtained in other studies (Belton, 1997; Li et al., 2004). However, 22 (11.0%) of HCPs were unaware of the professional obligation to report ADRs (Table 4). Personal discussions and awareness programmes will help to remove misconceptions and modify the attitude of HCPs, so that ADR reporting is perceived as an integral part of clinical practice (Khan et al., 2013). The attitude of HCPs that a single unreported case may not affect the ADR database (19.0%) also needs to be changed (Table 5). This may lead to enhanced spontaneous reporting in the long term.

Adverse drug reactions of herbal and traditional medicines are well known and reported in the literature (Edzard, 2002), but 39.5% of HCPs in this study considered it not necessary to report events related to herbal drugs (Table 2).

A number of factors impacted negatively on willingness to report ADRs of which, ‘Do not know how to report, where to report and when to report’ (60.5%) was the most prominent (Table 5). These findings suggest that underreporting of ADRs is associated with gaps in the knowledge, attitudes and practices, which have been identified in previous studies (Belton, 1995; McGettigan, 1995; Hosford et al., 2002).

The present study found a spontaneous reporting rate by HCPs of only 16.0% (Table 7). Similarly, previous studies also reported low spontaneous reporting rates (Li, 2004; McGettigan et al., 1995). Another concern was that only 12.0% of HCPs knew where the ADR forms were kept in the facilities (Table 7). These findings are of great concern and suggest that there is a serious and urgent need of education and training of HCPs on ADRs, from identification to reporting, which should improve the rate of spontaneous reporting.

Considering the results of this study, a number of measures may assist in improving the spontaneous reporting of ADRs (Khan et al., 2013). Awareness of ADR reporting must be increased through communication and training. All HCPs must be encouraged to report all suspected ADRs irrespective of the level of association with the possible cause. Reporting of all suspected ADRs, whether known, unknown, common, uncommon and serious or mild, even with established drugs must be encouraged. Training in pharmacovigilance must include special emphasis on the risk perceptions of drugs, including newly marketed drugs, over the counter medicines and herbal medicines.

This study had some limitations. Unequal distribution of responses from the different professions, limits the generalisability to all HCPs. The study was conducted in only one district, thus not representative of the entire Gauteng Province and the rest of South Africa. Qualitative research methodologies would have provided a more in-depth understanding of the knowledge, attitudes and practices of HCPs towards ADR reporting.
Conclusion

The results of the study strongly suggest that underreporting of ADRs is associated with gaps in knowledge, attitudes and practices of HCPs. There is a great need to create awareness about and to promote the reporting of ADRs amongst HCPs in the Tshwane District. Training sessions will clarify the role of the different cadres in pharmacovigilance, the types of events to report and to address the various perceived obstacles to spontaneous reporting. Adverse drug reaction reporting must be seen as an integral part of the clinical activities of all HCPs at PHC level.

Acknowledgements

The authors would like to thank all HCPs in the Tshwane District who participated in this study. The authors would also like to thank all the data collectors and the Department of Health in Tshwane who supported the study. A special thanks to Prof Herman Schoeman who assisted with the statistical analysis of the data.

References


Chapter 4: Results and Discussion


Chapter 4: Results and Discussion


4.3 LETTER TO THE EDITOR

A cover letter to the editor of Primary Health Care Research and Development Journal, which will accompany the manuscript, is included in this section.
Prof Sally Kendall and Prof Rosamund Bryar
The Editors
Primary Health Care Research and Development

Dear Prof Kendall and Prof Bryar

RE: SUBMISSION OF A MANUSCRIPT FOR PUBLICATION

I am pleased to submit an original research article entitled “Knowledge, Attitudes and Practices of Health Care Professionals towards Adverse Drug Reaction Reporting in Public Sector Primary Health Care Facilities” for consideration of publication in Primary Health Care Research and Development.

It is known that knowledge, attitudes and practices of health care professionals are paramount to the reporting of adverse drug reactions. The results of this study showed that at primary health care facilities, the knowledge, attitudes and practices of healthcare professionals towards adverse drug reaction reporting and pharmacovigilance are not optimum. Furthermore, very few studies on pharmacovigilance have been done in the primary health care environment, despite the fact that it is the patient’s first point of access to health care services.

With the submission of this manuscript I would like to declare that the above-mentioned manuscript has not been published elsewhere, accepted for publication elsewhere or under editorial review for publication elsewhere, and that my Institution (Department of Health) has granted permission for publication of this article.

I further declare that all the authors have critiqued and approved the content of the manuscript and have contributed significantly to the work. The authors have no conflict of interest to disclose and no sponsorship was received for the study.

Thank you for your consideration of our manuscript.

_______________________
Michelle Haines (first author)
Date: ________________
Tel: 012 356 9201; Cell: 071 679 0059
LIMITATIONS, RECOMMENDATIONS AND CONCLUSIONS

5.1 INTRODUCTION

In this chapter the limitations of the study are outlined, followed by recommendations offered based on the results. This chapter ends with the final conclusions to this study.

5.2 LIMITATIONS OF THE STUDY

The response rate was good, however responses from the different types of HCPs were not equally distributed with medical practitioners and pharmacists in the minority. The results can therefore not be generalised to all the professions.

Furthermore, the study was conducted in only one district, making the results not representative of the entire Gauteng Province.

Better insight into and understanding of the knowledge, attitude and perceptions of the HCPs would have been possible with qualitative research methodologies, such as in-depth interviews and/or focus group discussions.

5.3 RECOMMENDATIONS

The following measures are recommended to improve the spontaneous reporting of ADRs (Khan et al, 2013):

- Awareness of ADR reporting must be increased through effective communication and training of HCPs at all levels of service.
- Encourage HCPs to report all suspected ADRs whether known, unknown, common, uncommon and serious or non-serious, even with established drugs.
- Training in pharmacovigilance with special emphasis on the risk perceptions of drugs including newly marketed drugs, OTC medicines, and herbal medicines.

A further recommendation is that pharmacists in clinical and policy practice must be mentored to improve the reporting of ADRs and that all facilities have an standard operating procedure available for reporting of ADRs.
The study could be extended to other districts in the country to identify their trends and levels of ADR reporting, which would also allow for comparisons of trends across different districts and provinces.

5.4 CONCLUSIONS

The results of the study strongly suggest that underreporting of ADRs is associated with gaps in knowledge, attitudes and practices of HCPs. The results of the study showed that when all questions and statements were combined for all HCPs, overall 79.6% (95% CI 76.9%-82.3%) of responses were positive or preferred in terms of knowledge, attitude was 63.3% (95% CI 60.7%-65.8%) and practice was 24.6% (95% CI 21.7%-27.4%). The study suggests that there is a great need to create awareness and to promote the reporting of ADRs amongst HCPs in the Tshwane District. Training sessions will clarify the role of the different health care professionals in pharmacovigilance, the events to consider and report, and to address the various perceived obstacles to spontaneous reporting. Adverse drug reaction reporting must be seen as an integral part of the activities of all HCPs at PHC level.
REFERENCES


References


References


References


Appendices

APPENDICES

Appendix 1: Study information leaflet

Knowledge, Attitudes and Practices of Health Care Professionals towards Adverse Drug Reaction Reporting in Public Sector Primary Health Care Facilities in the Tshwane District

Please read this information about the study and feel free to ask any questions should you need any clarity before deciding to take part in this study.

I am a pharmacist an MPharm student from the University of Limpopo, Medunsa Campus. For the purposes of my master’s degree, I am going to conduct a study at all Public Sector Primary Health Care facilities in the Tshwane District to find out what the knowledge, attitudes and practices are of the health care workers in these facilities about pharmacovigilance.

A questionnaire will be used to collect the data. The questionnaire will be completed anonymously, in a private area and will take approximately 30 minutes to complete. You should ask the data collector if any of the questions included in the questionnaire are not clear.

At any time you are free to let us know if you no longer wish to participate. Your name will not be recorded and all personal information about you will be kept confidential during and after the study.

The study has been approved by the University of Limpopo, Medunsa Campus Research and Ethics Committee, by the Chief Director of the Tshwane District and by the facility manager of each facility where the research will be conducted.

If you agree to participate in the study, you will be required to sign a consent form to indicate your willingness to participate. We will be very thankful if you will be prepared to take part in this study.

Please feel free to contact myself on 071 679 0059 or my supervisor, Dr JC Meyer on 012-521 4741/5, if you have any further questions regarding this study.

Kind regards

Michelle Haines
Researcher / MPharm student
Appendices

 Appendix 2: Written Consent Form

UNIVERSITY OF LIMPOPO (Medunsa Campus) ENGLISH CONSENT FORM

Statement concerning participation in a Research Project

Knowledge, Attitudes and Practices of Health Care Professionals towards Adverse Drug Reaction Reporting in Public Sector Primary Health Care Facilities in the Tshwane District

The researcher explained the aims and objectives to me and I was provided the opportunity to ask questions and given adequate time to rethink the issue. The aim and objectives of the study are sufficiently clear to me. I have not been pressurized to participate in any way.

I understand that participation in this study is completely voluntary and that I may withdraw from it at any time without supplying reasons.

I know that this study has been approved by the Medunsa Research Ethics Committee (MREC), University of Limpopo (Medunsa Campus) / Department of Health / Tshwane District. I am fully aware that the results of this Study will be used for scientific purposes and may be published. I agree to this, provided my privacy is guaranteed.

I hereby give consent to participate in this Study.

____________________________                                   ___________________
Name of participant                                          Signature of participant
Appendices

Appendix 3: Questionnaire

Knowledge, Attitudes and Practices of Health Care Professionals towards Adverse Drug Reaction Reporting in Public Sector Primary Health Care Facilities in the Tshwane District

Date:_____________ Data Collector: _____________________ Study ID: ____________

Please tick the appropriate box and/or give the necessary information in the space provided.

<table>
<thead>
<tr>
<th>Facility:</th>
<th>CHC</th>
<th>PHC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Qualification:</td>
<td>Pharmacist</td>
<td>Medical Practitioner</td>
</tr>
<tr>
<td>Gender:</td>
<td>Male</td>
<td>Female</td>
</tr>
<tr>
<td>Age range:</td>
<td>≤ 20</td>
<td>21-30</td>
</tr>
<tr>
<td></td>
<td>41-50</td>
<td>51-60</td>
</tr>
<tr>
<td>Race:</td>
<td>Black</td>
<td>Coloured</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Questions</th>
<th>Office use*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Please explain what you understand under the term adverse drug reaction.</td>
<td>K1</td>
</tr>
</tbody>
</table>

| Are you aware that adverse drug reactions must be reported? | Yes (1) | No (2) | K1 |
| Have you ever reported any suspected adverse drug reactions? | Yes (1) | No (2) | P1 |
| If yes, when did you report and how often? | D |

| Are you aware of the existence of an adverse drug reaction (ADR) reporting and monitoring system in your District? | Yes (1) | No (2) | K1 |
| Have you reported any suspected adverse drug reactions to the ADR reporting and monitoring system in your District? | Yes (1) | No (2) | P1 |
| What form must you use when reporting an adverse drug reaction? | K1 |

| Do you have the adverse reporting form available in your facility? | Yes (1) | No (2) | P1 |
| Where are the ADR forms kept in your facility? | P1 |

Attach a copy of the form
Where must the adverse drug reaction form be submitted to when an adverse drug reaction is reported?

<table>
<thead>
<tr>
<th>Yes (1)</th>
<th>No (2)</th>
<th>K1</th>
</tr>
</thead>
</table>

Do you keep copies of the ADR forms you submit?
If yes, please attach a copy of a form which you have submitted.

<table>
<thead>
<tr>
<th>Yes (1)</th>
<th>No (2)</th>
<th>P1</th>
</tr>
</thead>
</table>

Do you think that ADR reporting is necessary?

<table>
<thead>
<tr>
<th>Yes (1)</th>
<th>No (2)</th>
<th>A1</th>
</tr>
</thead>
</table>

Do you think that reporting ADRs is a professional obligation?

<table>
<thead>
<tr>
<th>Yes (1)</th>
<th>No (2)</th>
<th>A1</th>
</tr>
</thead>
</table>

How many ADRs have been reported altogether at your facility over the past year? State number.

<table>
<thead>
<tr>
<th>D</th>
</tr>
</thead>
</table>

Have you ever received training on adverse drug reaction reporting?
If YES, when and where did you receive training on adverse drug reaction reporting?

<table>
<thead>
<tr>
<th>Yes (1)</th>
<th>No (2)</th>
<th>P1</th>
</tr>
</thead>
</table>

If not, would you like to receive training on adverse drug reaction reporting?

<table>
<thead>
<tr>
<th>Yes (1)</th>
<th>No (2)</th>
<th>A1</th>
</tr>
</thead>
</table>

Did you study pharmacovigilance in your undergraduate study?
If yes please stipulate at which institution you studied.

<table>
<thead>
<tr>
<th>Yes (1)</th>
<th>No (2)</th>
<th>D</th>
</tr>
</thead>
</table>

Adverse drug reaction reporting should be? Please tick the relevant box

<table>
<thead>
<tr>
<th>Voluntary (1)</th>
<th>Compulsory (2)</th>
<th>Remunerated (3)</th>
<th>A1 &amp; A2</th>
</tr>
</thead>
</table>

What kind of event will you be inclined to report?

<table>
<thead>
<tr>
<th>Yes (1)</th>
<th>No (2)</th>
<th>I don’t know (3)</th>
<th>K1</th>
</tr>
</thead>
</table>

1. Reaction to a new drug
2. Serious event
3. Unusual event
4. Well recognised adverse reaction of a drug
5. Any suspected drug interaction
6. Death of patient due to a suspected interaction
7. Congenital anomaly
8. Other events. Please specify.

Must an event related to the following be reported?

<table>
<thead>
<tr>
<th>Yes (1)</th>
<th>No (2)</th>
<th>I don’t know (3)</th>
<th>K1</th>
</tr>
</thead>
</table>

1. Allopathic drugs
2. Herbal drugs
3. Traditional and complementary medicine
4. Blood products
5. Biological
6. Medical devices
7. Vaccines
8. Other events. Please specify.
### What will be the factors that will discourage you to report?

<table>
<thead>
<tr>
<th></th>
<th>Yes (1)</th>
<th>No (2)</th>
<th>I don’t know (3)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Concern that the report may be wrong.</td>
<td>A2</td>
<td></td>
</tr>
<tr>
<td>2.</td>
<td>Do not know how to report, where to report and when to report.</td>
<td>A2</td>
<td></td>
</tr>
<tr>
<td>3.</td>
<td>Lack of time to complete a report.</td>
<td>A2</td>
<td></td>
</tr>
<tr>
<td>4.</td>
<td>A single unreported case may not affect the ADR database</td>
<td>A2</td>
<td></td>
</tr>
<tr>
<td>5.</td>
<td>Non-remuneration for reporting.</td>
<td>A2</td>
<td></td>
</tr>
<tr>
<td>6.</td>
<td>Concern that reporting may generate extra work.</td>
<td>A2</td>
<td></td>
</tr>
<tr>
<td>7.</td>
<td>Lack of time to actively look for ADRs while at work.</td>
<td>A2</td>
<td></td>
</tr>
<tr>
<td>8.</td>
<td>Level of clinical knowledge makes it difficult to decide whether or not an ADR has occurred.</td>
<td>A2</td>
<td></td>
</tr>
<tr>
<td>9.</td>
<td>Lack of confidence to discuss the ADR with other colleagues.</td>
<td>A2</td>
<td></td>
</tr>
<tr>
<td>10.</td>
<td>Other factors. Please specify.</td>
<td>A</td>
<td></td>
</tr>
</tbody>
</table>

### Do you think as a health care worker you have a role to play in the following?

<table>
<thead>
<tr>
<th></th>
<th>Yes (1)</th>
<th>No (2)</th>
<th>I don’t know (3)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Preventing adverse drug reactions.</td>
<td>A1</td>
<td></td>
</tr>
<tr>
<td>2.</td>
<td>Detecting adverse drug reactions.</td>
<td>A1</td>
<td></td>
</tr>
<tr>
<td>3.</td>
<td>Managing adverse drug reactions.</td>
<td>A1</td>
<td></td>
</tr>
<tr>
<td>4.</td>
<td>Reporting adverse drug reactions.</td>
<td>A1</td>
<td></td>
</tr>
</tbody>
</table>

### Within the public sector, the main objectives of pharmacovigilance are as follows:

<table>
<thead>
<tr>
<th></th>
<th>Yes (1)</th>
<th>No (2)</th>
<th>I don’t know (3)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Improve patient care and safety</td>
<td>K1</td>
<td></td>
</tr>
<tr>
<td>2.</td>
<td>Improve public health and safety</td>
<td>K1</td>
<td></td>
</tr>
<tr>
<td>3.</td>
<td>Contribute to the assessment of risk / benefit of the medicine</td>
<td>K1</td>
<td></td>
</tr>
<tr>
<td>4.</td>
<td>Promote understanding, education and clinical training in this field</td>
<td>K1</td>
<td></td>
</tr>
<tr>
<td>5.</td>
<td>Ensure effective communication of adverse drug reaction reporting to the public</td>
<td>K1</td>
<td></td>
</tr>
<tr>
<td>6.</td>
<td>Other objectives. Please specify.</td>
<td>K1</td>
<td></td>
</tr>
</tbody>
</table>

### How do you rate the importance of pharmacovigilance in your everyday work?

<table>
<thead>
<tr>
<th></th>
<th>Very important (1)</th>
<th>Important (2)</th>
<th>Slightly important (3)</th>
<th>Not important at all (4)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>A1 &amp; A2</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Office use and not for printing: K = Knowledge; A = Attitudes; P = Practices; D = Descriptive

Thank you for your participation!
Appendix 4: Permission to conduct pilot study

University of Limpopo
Department of Pharmacy
P.O. Box 218, Medunsa, 0204, South Africa
Tel: (012) 521 3699/4567, Fax: (012) 521 3992, Email:haines.michelle19@gmail.com

The Facility Manager

Dear Sister

Re: Permission requested to conduct a pilot study at your facility.

I am a post-graduate student at the Department of Pharmacy, University of Limpopo, Medunsa Campus. As part of the requirements for my MPharm post-graduate qualification, I have to conduct a research project. The title of my study is “The knowledge, attitudes and practices of health care professionals towards adverse drug reaction reporting in public sector primary health care facilities in the Tshwane District”. The study has received ethical clearance from the Medunsa Campus Research and Ethics Committee (MREC............).

I therefore kindly request your permission to conduct the pilot study to test the feasibility of the questionnaires, at your facility. Attached please find a copy of the protocol as well as the MREC clearance certificate.

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

Kind regards

________________________
Ms Michelle Haines
Date:

Cc: Dr JC Meyer (Supervisor)
Appendix 5: Permission to conduct study in the Tshwane District

University of Limpopo
Department of Pharmacy
P.O. Box 218, Medunsa, 0204, South Africa
Tel: (012) 521 3699/4567, Fax: (012) 521 3992, Email:haines.michelle19@gmail.com

The Chief Director
Tshwane District

Dear Mr Pitsi

Re: Permission requested to conduct a study in the Community Health Centres and Primary Health Care Clinics in the Tshwane District.

I am a post-graduate student at the Department of Pharmacy, University of Limpopo, Medunsa Campus. As part of the requirements for my MPharm post-graduate qualification, I have to conduct a research project. The title of my study is “The knowledge, attitudes and practices of health care professionals towards adverse drug reaction reporting in public sector primary health care facilities in the Tshwane District”. The study has received ethical clearance from the Medunsa Campus Research and Ethics Committee (MREC...........).

I therefore kindly request your permission to conduct the study in the Community Health Centres and Primary Health Care Clinics in the Tshwane District. Attached please find a copy of the protocol as well as the MREC clearance certificate.

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

Kind regards

Ms Michelle Haines
Date:

Cc: Dr JC Meyer (Supervisor)
Appendix 6: MREC Clearance Certificate

MEETING: 09/2013
PROJECT NUMBER: MREC/27/2013: PG

PROJECT:
Title: Knowledge, Attitudes and Practices of Health Care Professionals Towards Adverse Drug Reaction Reporting in Public Sector Primary Health Care Facilities in the Tshwane District

Researcher: Mrs M Haines
Supervisor: Dr JC Meyer
Co-supervisor: Prof RS Summers
Health Care Manager: Mr Pitsi Chief Director – Tshwane District
Department: Pharmacy
School: Health Care Sciences
Degree: M Pharm

DECISION OF THE COMMITTEE:
MREC approved the project.

DATE: 03 October 2013

PROF N EBRAMH
DEPUTY CHAIRPERSON MREC

The Medunsa Research Ethics Committee (MREC) is registered with the US Department of Health and Human Services as an Institutional Review Board (IRB) (IRB000031B), as an Institutional Review Board (IRB) (IRB000031B), and functions under a Federal Wide Assurance (FWA00003419)
Expiry date: 11 October 2016

Note:
i) Should any departure be contemplated from the research procedure as approved, the researcher(s) must re-submit the protocol to the committee.

ii) The budget for the research will be considered separately from the protocol. PLEASE QUOTE THE PROTOCOL NUMBER IN ALL ENQUIRIES.

Finding Solutions for Africa
Appendices

Appendix 7: Approval from Tshwane Research Committee

Gauteng Province

Health
Republic of South Africa

Kuyaphepha! Gauteng Working Better

427 Hico Street, The Hords Building, Pretoria 0001, South Africa. Tel: +27 12 451 9000 Fax: +27 12 451 9126
Enquiries: Dr K E Letebole-Hartell
e-mail: Marcel.Letebole@gauteng.gov.za

Tshwane Research Committee

Clearance Certificate

Meeting Date: N/A

Project Number: 51/2013

Title: Knowledge, Attitudes and practices of health care professionals towards a diverse drug reaction reporting in Public sector primary health care facilities in Tshwane district.

Researcher: Michelle Haines
Supervisor: Dr JC Meyer
Department: Pharmacy (Medunsa Campus)

Decision of the Committee:

Approved

NB: This office requests a full report on the outcome of the research done

Date: 22 November 2013

[Signatures]

Dr K E Letebole-Hartell
Chairperson Tshwane Research Committee
Tshwane District

Ms J Morowana
Director, District Health Services Support
Tshwane District

NOTE: Resubmission of the protocol by researcher(s) is required if there is departure from the protocol procedures as approved by the committee.
Appendices

Appendix 8: Author Guidelines

Primary Health Care Research & Development

Editors:
Sally Kendall, University of Kent, UK
Rosamund Bryar, City University, London, UK

Primary Health Care Research & Development is available at Cambridge Journals Online:
www.journals.cambridge.org/jid_phc
Submission is exclusively via Editorial Manager: www.editorialmanager.com/phc/default.asp
Print ISSN: 1463-4326 --- Online ISSN: 1477-1128

Instructions for Contributors

The Editors invite papers in one of four categories: Research Papers, Development Papers, Networking Papers, and Short Reports.

Research Papers
PHCR&D welcomes papers that present primary research or disseminate evidence, including systematic reviews and meta analysis. All papers should make clear the relevance of their research to an international PHC audience and implications for policy and practice. All papers are independently peer reviewed by a minimum of two referees. All material prepared for publication is assumed to be written exclusively for Primary Health Care Research & Development, and not to have been submitted for publication elsewhere. All authors are required to sign a copyright assignment form before publication and return this to journalscopyright@cambridge.org. The Editors, who retain the right to edit, if necessary, any material accepted for publication, decide priority and time of publication. UK spelling will be used.

NB: All submissions to the Journal should be exclusively be made via the electronic submission and tracking system, Editorial Manager: www.editorialmanager.com/phc/default.asp Authors whose first language is not English are requested to have their manuscript checked carefully for linguistic corrections before submission. Please supply a structured abstract (maximum 300 words) for your article; to include the following 4 headings: aim, background, methods, and findings. Articles should normally be up to 5000 words long. We will consider linked papers. Submissions from the Society for Academic Primary Care (SAPC) will be highlighted as ‘SAPC Hot Topics’ in the article title.

Development Papers
Authors less familiar with Development Papers are requested to read the following guidelines:
The Editors are keen to encourage papers from all areas of PHC which address the developmental aspects of work which is informing both practice and the research agenda. This is seen as an area which is often overlooked in peer-reviewed journals, partly because development is not recognised as 'real research', and partly because we have been limited by the criteria which are usually used to judge research but are not appropriate for development. To ensure that we can publish high-quality Development Papers, we have drawn upon notions of validity which have been adopted widely for qualitative research. For example, the concept of trustworthiness of information and the need to provide an 'audit trail' may be used rather than the concept of validity. Additionally, the concept of 'transferability' needs to be considered rather than 'generalisability'. Development Papers need to be defined as such by the authors, but the Editors will also make a decision about the status of a paper including criteria such as whether it:
• discusses a local issue;
• discusses the introduction of an innovation;
• discusses matters relating to reflective practice or developing practice;
• relates to issues of learning and dissemination in PHC;
• informs a new area for research;
• addresses issues of evaluation.
Appendices

Authors should note that when reviewing such a paper we ask reviewers to consider the following questions:

1. How has the author drawn on existing evidence to inform the discussion of the development? It is expected that Development Papers should make sufficient use of the literature and background theory to inform their thinking, as well as evidence from other sources such as expert advice.

2. What was the rationale for the development? Is this clearly argued?

3. How sufficient is the description of the development? The context should be discussed in some detail, including any policy context in which it might be embedded.

4. Where case study examples or scenarios are used, how are these documented? Is there enough information to make a trustworthy judgement of the development work? Are examples appended? In other words, the reader should be convinced that this is not just evangelism.

5. Is the discussion of the development conducted in light of the existing evidence?

6. How are conclusions drawn from the development? What message is the author trying to convey? Is this achieved? Are there key points for further research or practice development to be undertaken?

7. Does the author offer a critical analysis of the development which recognises limitations as well as strengths?

8. Has the development been evaluated? If so, are the methods appropriately discussed? If not, is a rationale provided or plans for future evaluation?

9. Referencing is as important in a Development Paper as in research (see below).

Networking Papers

We welcome contributions to the Networking section, either on the working of networks, or other initiatives to promote collaboration or build capacity in PHC research. Articles can report local or national initiatives, raise issues, inform or invite others to collaborate on future work. Short contributions of up to 1500 words, subject to editorial review, will be published as quickly as space allows. Longer contributions are also welcome and will be subject to peer review in the same way as other items submitted to the Journal.

Short Reports

PHCR&D now welcomes Short Reports. These are invited from all areas of primary healthcare research and development. Short Reports will typically report primary research that the authors feel in insufficient in scope for a full paper. For example Short Reports may describe pilot studies, exploratory studies, scoping studies, brief narrative reviews or smaller research projects conducted with fewer resources and in less time than those normally reported in full papers. PHCR&D wish to receive Short Reports from all members of the primary health care community but are particularly keen to attract Short Reports from relatively inexperienced members of the research community, including medical students conducting intercalated degrees, masters students, and professionals conducting research placements. Brief reports should be between 1500 and 2000 words in length. They need not include a structured abstract, but a summary of the paper in approximately 150 words will facilitate the editorial and review process. Normally, brief reports will comprise an introduction and/or background to the work, a brief explanation of any methods employed, results (tables or figures are preferred) and a discussion of the implications of the work. Prospective contributors are directed to the “Guidance Applicable to All Papers” for details on how to prepare their manuscript. Brief reports will be peer reviewed by at least two reviewers.

Book Reviews

We welcome Publication Reviews. These are not limited to books, but may also be websites, CDs, or other media. For further information on submitting a Publications Review, please follow this link: Cambridge Journals Online - Book Review Information

Guidance Applicable to All Papers

All pages must be numbered.

Microsoft Word is the preferred software. No artwork should be included in text files. Any artwork should be in either TIFF or EPS format, and saved as individual files per Figure. When preparing your paper:

• Use the minimum formatting;
• Roman, bold and italic type can be used, but only one typeface and font;
• Capitals should be used only where they are to appear in the finished text;
• The text should be ranged left and unjustified, with hyphenation cancellation;
• Indents, underlining and tabs should be avoided unless absolutely necessary;
• Heading and paragraphs should be separated by two carriage returns;
• There should only be one space between words and only one space after punctuation.

Give the title of the paper and a running title if the main title is longer than 12 words or 50 characters.

On a separate page authors should include: their first and family name; their post at the time they did the work; their current appointments and qualifications; the name and address of the author to whom correspondence, proofs and offprints should be sent, together with email, telephone and fax numbers.

Avoid using more than three levels of heading.

Abbreviations should be kept to a minimum and must be clearly defined when used first time. Abbreviations should be typed with no full point.
Avoid excessive capitalization.
Use italics for emphasis sparingly.
Scientific measurements should be given in SI units, but blood pressure should be expressed as mmHg and haemoglobin as g/dl.
For numbers, adopt a rule that all numbers under 10 should be written as words except when attached to a unit of quantity (e.g. 1 mm or 3 kg), and that numbers of over 10 should be written as digits except at the beginning of a sentence.
Generic names should be used for drugs. Authors should be aware of different names and availability in the UK, North America and Australia, and give alternative names of drugs in the text.

Tables and Figures should be submitted separately from the text and legendary illustrations should also be separate. Colour figures are subject to a special charge and the author should meet the cost of colour reproduction.

Care should be taken that all statistical methods are relevant and that it is clear which methods were used. Any statistical tests should be reported as well as the p value.

Papers should be prepared in accordance to the Harvard system arranged in alphabetical order by the first letter of the surname of the author. Journal articles and titles should be referred to in full. For example:


In the text when referring to more than one source please list these in the order of oldest source first e.g. (Silverman, 1993; Slater, 1996; Kendall and Bloomfield, 2005)
When using quotations please include the page number of the quotation e.g. (Silverman, 1993:15)

Authors must obtain permission from the publishers to reproduce all Tables and Figures that have been previously published. As a rule it is also necessary to obtain permission for single passages of prose exceeding 250 words, or scattered passages totalling 400 words from any one work. Please supply the Editor with full information for any cited work, including author name, date published, publisher, and page references. EU copyright extends to 70 years after the death of an author, or 70 years after publication of scholarly edition, whichever is longer. Special considerations apply for clinical photographs of patients. Please contact the Editor if you wish to include them in your paper. Please include the following sections at the end of your paper, before the References:

Acknowledgements You may acknowledge individuals or organisations that provided advice, support (non-financial). Formal financial support and funding should be listed in the following section.

Financial Support Please provide details of the sources of financial support for all authors, including grant numbers. For example, “This work was supported by the Medical research Council (grant number XXXXXXXX)”. Multiple grant numbers should be separated by a comma and space, and where research was funded by more than one agency the different agencies should be separated by a semi-colon, with
“and” before the final funder. Grants held by different authors should be identified as belonging to individual authors by the authors’ initials. For example, “This work was supported by the Wellcome Trust (A.B., grant numbers XXXX, YYYY), (C.D., grant number ZZZZ); the Natural Environment Research Council (E.F., grant number FFFF); and the National Institutes of Health (A.B., grant number GGGG), (E.F., grant number HHHH).” Where no specific funding has been provided for research, please provide the following statement: “This research received no specific grant from any funding agency, commercial or not-for-profit sectors.”

Conflict(s) of Interest Please provide details of all known financial, professional and personal relationships with the potential to bias the work. Where no known conflicts of interest exist, please include the following statement: “None.”

Ethical Standards Where research involves human and/or animal experimentation, the following statements should be included (as applicable): “The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national and institutional guidelines on human experimentation (please name) and with the Helsinki Declaration of 1975, as revised in 2008.” and “The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national and institutional guidelines on the care and use of laboratory animals (please name).” For more information on the ethical standards and procedures of Cambridge Journals, please visit CambridgeJournals Online. Proofs will be supplied in the form of a PDF file. Please remember that:

i. Proof corrections are disproportionately expensive. For example the insertion of three commas on a page will frequently costs as much as, or more than, the original setting cost of the entire page.

ii. If you return proofs even a few days after the date stipulated, it may be not be possible to include your corrections in the final version of the journal.

An offprint order form is supplied with the proofs. Offprints and copies of the Issue can be purchased if ordered at the proof stage.
There are no page charges.

**Cambridge Journals Language Editing Service**

Cambridge recommends that authors have their manuscripts checked by an English language native speaker before submission; this will ensure that submissions are judged at peer review exclusively on academic merit. We list a number of third-party services specialising in language editing and/or translation, and suggest that authors contact as appropriate. Use of any of these services is voluntary, and at the author's own expense.

http://journals.cambridge.org/action/stream?pagid=8728&level=2&menu=Authors&pagid=3608

(Last updated 21/03/2014)