EVALUATION OF REPORTING ALL TYPES OF ADVERSE DRUG REACTIONS BY PARENTS OF CHILDREN YOUNGER THAN 18 YEARS IN SOUTH AFRICA

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

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ABSTRACT

Introduction: Medicines are created with the intention of helping patients but may be harmful to the patient by causing adverse reactions. The effect of adverse drug reactions (ADRs) on patients has become more evident over the last two decades and reporting of ADRs in South Africa is low. This results in many patients, particularly children, potentially being exposed to medicinal products with an uncertain safety profile. Due to parents' typical caring and protective role, they could play a part in detecting and reporting ADRs in children, thereby contributing to making safer medicines available to children.

Aim: This research study evaluated the awareness and knowledge in South Africa of parental reporting of suspected ADRs in their children.

Method: A quantitative descriptive study was conducted based on an anonymous web-based self-administered questionnaire that was distributed through Facebook® and LinkedIn™ to parents in South Africa. The questionnaire, which was distributed between July 2018 and August 2018, was standardized for all participants and consisted of closed (n=28) and open-ended (n=4) questions. The questions were coded, data was analysed using descriptive statistics (percentage and frequency counts). Associations between categorical demographic variables were determined using the Pearson Chi-square test.

Results: The questionnaire was voluntarily completed by 206 participants. Majority of the respondents were female (n=155, 75.2%) and the most relevant age category for all respondents was 31-40 years (n=100, 48.5%). The majority of participants (n=146, 70.9%) were aware of the term ADR and significant associations between awareness of ADRs and ethnicity, marital status, education level, medical aid and access to general medical services were found. Being white (p<0.001), having a degree (p=0.001) and having private medical aid (p=0.004) were independently associated with being significantly more aware of the term ADR compared to being black (p<0.001), coloured (p=0.004), a single parent (p=0.003), not finishing school (p<0.001), having matriculated (p<0.001), having no private medical aid (p=0.004) and receiving general medical services from public clinics (p = 0.003).

More than half of the participants or their children (n=123, 59.7%) experienced an ADR. Many participants (n=137, 66.5%) reported an ADR to a healthcare professional while only 15% (n=31) reported to a product manufacturer. The most common outcome of an ADR reported was a consultation with a doctor (n=74, 35.9%). It was found that 121 participants knew how to report ADRs and 150 participants (72.8%) knew what type of ADRs to report, however a large number did not know where more information on ADR reporting can be found (n=67) or how ADRs can be reported (n=65). Motives enhancing ADR reporting included social concerns such as helping others (n=48), severity of reaction (n=34) and safety concerns (n=16). Barriers deterring ADR

reporting included process issues (n=35), minor reaction (n=11) and no feedback/ actions being taken (n=9).

Conclusion: Majority of the respondents were aware of the term ADR, they indicated a good knowledge basis on which ADRs to report and the importance of reporting ADRs. Gaps in the respondents' knowledge were identified which highlighted specific groups of individuals to be targeted to increase ADR awareness and improve knowledge on the reporting process. Greater awareness and knowledge among parents can play a considerable role in improving the safety data of medicines and may reduce the occurrence of ADRs in children and the general population.

Keywords: Adverse drug reactions, spontaneous reporting, patient reporting systems, children, parental reporting, pharmacovigilance, awareness, knowledge, views, South Africa

DECLARATION

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

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

Signed: ……

Dated: …13 December 2018……

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LIST OF ABBREVIATIONS

ADR	Adverse drug reaction
ADRU	Adverse Drug Reactions Unit
CADRMP	Canadian Adverse Drug Reaction Monitoring Program
CIOMs	Council for International Organizations of Medical Sciences
EU	European Union
FDA	Food and Drugs Authority
MCC	Medicines Control Council
MedDRA	Medical Dictionary for Regulatory Activities
MHRA	Medicines and Healthcare Products Regulatory Agency
NADEMC	National Adverse Drug Event Monitoring Centre
NDOH	National Department of Health
NPC	National Pharmacovigilance Centre
OTC	Over-the-counter
SAHPRA	South African Health Products Regulatory Authority
SOC	System Organ Classification
TGA	Therapeutic Goods Administration
UK	United Kingdom
USA	United States of America
WHO	World Health Organization
YCS	Yellow Card System

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CHAPTER 1: INTRODUCTION

1.1 Introduction

New medicines go through an intensive process, involving a wide-range of tests and trials, before being approved and released onto the market (Weigmann, 2016; Staniszewska, *et al.,* 2017). The purpose of these tests is to prove the safety and efficacy of a product; however, the studies are usually conducted under controlled conditions with a limited number of patients for a short period of time (Mehta, 2011). Therefore, little is known about the safety profile of the medicine and unanticipated side effects are observed after approval (Weigmann, 2016).

Medicines are created with the intention of helping patients, but they may be harmful to the patient by causing adverse reactions (van Grootheest and de Jong-van den Berg, 2004). The monitoring of adverse drug reactions (ADRs) to ensure patient safety is a critical component of pharmacovigilance (Avery, *et al.,* 2011). Pharmacovigilance is defined by the World Health Organization (WHO) as "the science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other drug-related problem" (WHO, 2018). Protecting patients from the harmful effects of medicines is a responsibility that should be shared between all stakeholders, including healthcare professionals and patients (Suleman, 2010).

1.2 Background

Studies conducted throughout the world found that ADRs constitute over 6% of all hospital admissions and are among the leading global causes of morbidity and mortality (Gupta, *et al.,* 2018). ADRs result in longer hospital stays and higher costs incurred for the patient and the healthcare system (Wilson and Amma, 2015). Research shows that in some countries, up to 20% of their hospital budget is spent on managing ADRs (Mehta, 2011).

A major concern is the high incidence of ADRs in children. Numerous medicines have not been adequately tested and approved for use in children (Napoleone, 2010). This results in off-label use of medicines in children which is linked to an increased risk of ADRs (Hawcutt, *et al.,* 2011; Tobaiqy, *et al.,* 2010). Pharmacovigilance is an essential component of ensuring the safe use of medicines in children (Napoleone, 2010). The foundation of pharmacovigilance programs is the reporting of ADRs spontaneously by healthcare professionals through ADR report forms (Wilson and Amma, 2015). Spontaneous reporting allows for unknown or uncommon reactions to be identified and can contribute to making safer medicines available to patients by facilitating the withdrawal of potentially unsafe medicines from the market (Mehta, 2011).

Under-reporting of ADRs has been recognized to be a common shortcoming of pharmacovigilance programs in South Africa as well as internationally (Wilson and Amma, 2015; Mehta, 2011). After reviewing the spontaneous reporting systems of 12 countries, Hazell and Shakir (2006) found that on average 94% of ADRs were not reported. Under-reporting prolongs the detection of ADRs and may result in increased death and suffering in patients (Gupta, *et al.,* 2018). While it was found that healthcare professionals are aware of the need and methods to report ADRs, factors that prevent them from reporting include time, fear of criticism, and large amounts of patient care requirements (Wilson and Amma, 2015).

1.3 Problem statement

The effect of ADRs on healthcare professionals and patients has become more evident over the last two decades, yet reporting of ADRs by healthcare professionals in South Africa remains low (Mehta, *et al.*, 2017). This results in many patients, particularly children, potentially being exposed to medicinal products with an uncertain safety profile (Mehta, 2011). Since parents have a typical caring and protective role, they could play a part in detecting and reporting ADRs in children. Parents were found to be unaware of their role in reporting ADRs in countries that have patient reporting systems (van Hunsel, *et al.,* 2012). This could mean that the awareness of parental reporting in countries without a patient reporting system may be lower. The contribution of parental reporting to pharmacovigilance in South Africa could be substantial. However, parents' awareness and knowledge of ADR reporting and the process involved had to first be considered.

1.4 Aim and objectives

The overarching aim was to evaluate the awareness and knowledge in South Africa of parental reporting of suspected ADRs in themselves and their children.

The following research questions were investigated:

- Are parents aware of adverse drug reactions?
- What is the knowledge of parents on ADRs?
- What experiences have parents had with ADRs?
- What are the processes or steps to follow when reporting ADRs?
- What are the views on ADR reporting?
- Which factors may enhance or deter ADR reporting?

To answer the above research questions the following primary and secondary objectives were set.

1.4.1 Primary objectives

- To assess parents' awareness of reporting ADRs
- To assess the knowledge of parents on the procedures to follow when reporting ADRs

1.4.2 Secondary objectives

- To explore parents' views on reporting ADRs
- To determine which factors could motivate or prevent parents from reporting ADRs experienced by their children or themselves

1.5 Significance of the study

Most of the studies in the past have evaluated ADR reporting among healthcare professionals, however, to the researchers' knowledge, this was the first investigation of parental reporting in South Africa. Little is known about what South African parents know about ADRs or whether they report ADRs. There is currently no direct patient reporting system in South Africa, therefore this evaluation of the awareness and knowledge of reporting ADRs by parents can be useful to the regulatory authorities and pharmaceutical applicants, who may consider implementing a formal patient reporting system in future.

This study highlighted challenges to reporting ADRs and possible recommendations to overcome it. It has contributed to identifying gaps and how to address it to improve parents' knowledge on ADR reporting and generate awareness among parents as to the importance of reporting. It may have also improved adult patients' understanding of what ADRs are, who they need to be reported to and why they need to be reported. The public may have been made aware of the valuable contribution that they can make to safe medicine use.

CHAPTER 2:
LITERATURE REVIEW

2.1 Introduction

This chapter reviews and discusses pertinent literature that is relevant to this study.

The WHO defines an ADR as "a response to a drug which is noxious, and unintended, and which occurs at doses normally used in man for prophylaxis, diagnosis or therapy of disease, or for the modification of physiological function" (WHO, 2002, p.5). While sometimes confused with an ADR, an adverse event refers to an untoward experience associated with the use of a drug, but which is not necessarily caused by the drug and a side effect refers to an unintended effect of a drug which is related to its pharmacological properties and occurs at normal doses (WHO, 2002).

Research has revealed that ADRs have become a universal public health matter that may need to be addressed using a different approach (Mehta, 2011). Spontaneous reporting by patients is one of the methods that is increasingly being utilized. Patient reporting systems have existed in many countries, including the United States of America (USA), Canada, Australia, the Netherlands, Italy, Sweden, the United Kingdom (UK) and more recently Norway (Wilson and Amma, 2015). Patient reporting systems were introduced in European Union (EU) legislation to improve medicine safety and has been seen as a valuable contribution to protecting public health (Rolfes, *et al.*, 2014).

As medicines are intended to benefit patients, obtaining information directly from patients plays a key role in identifying new ADRs (Weigmann, 2016). Research has shown that patients worldwide have substantial interest in the safety aspects of medicines and allowing them to report ADRs has offered a unique approach to pharmacovigilance (van Grootheest and de Jong-van den Berg, 2004).

2.2 International practices on reporting by patients

Many countries allow patient reporting through existing systems for healthcare professionals or a system designed specifically for non-healthcare professionals (Matos, *et al.*, 2016). Patients in the UK submit ADR reports to the Medicines and Healthcare Products Regulatory Agency (MHRA), through the Yellow Card System (YCS) (Anderson, *et al.,* 2011). Within five years after patient reporting systems were introduced in the UK, 18% of the ADRs were reported by patients (Fortnum, *et al.,* 2012). Patients in the USA have been reporting ADRs for many years using the MedWatch program (Avery, *et al.,* 2011). In both the UK and USA, the reporting process for patients is the same as that for healthcare professionals (Avery, *et al.,* 2011). Studies, however, have shown differences between the reports submitted by patients and healthcare professionals (Avery, *et al.,* 2011). Patient reports contained more subjective information, in terms of the impact

of the ADR on their lives, whereas reports from healthcare professionals contained more objective information, such as route of administration of the drug and patient medical history (Rolfes, *et al.*, 2015).

The Adverse Drug Reactions Unit (ADRU), which forms part of the Therapeutic Goods Administration (TGA) is available for patients in Australia to report ADRs (Avery, *et al.*, 2011). A study conducted by Avery, *et al.* (2011) found that a large number of serious ADRs reported by patients in Australia were not reported by healthcare professionals. Patients in Canada can report ADRs to the Canadian Adverse Drug Reaction Monitoring Program (CADRMP) and patients in the Netherlands report to the Netherlands Pharmacovigilance Center (Lareb) (Avery, *et al.*, 2011). A downside to the Lareb system is that patients can only submit electronic reports which may have impeded patients from reporting, due to insufficient internet access (Avery, *et al.*, 2011).

In Ghana, although ADR reports were always accepted from patients, ADRs have primarily been reported by healthcare professionals (Sabblah, *et al*, 2017). A patient reporting system was launched in 2016, in which patients can report ADRs, through the Blue Form, to the National Pharmacovigilance Centre, which is part of the Ghana Food and Drugs Authority (FDA) (Darko and Sabblah, 2015). In Saudi Arabia, ADR reports can be submitted to the NPC by healthcare professionals, pharmaceutical manufacturers and patients from 2009 (Sales, *et al.*, 2017). Patients in Poland, on the other hand, were only able to report ADRs to the Department for Monitoring Adverse Reactions of Medicinal Products, with an online system being introduced in 2015 for reporting of ADRs through the patients' smartphones (Staniszewska, *et al.*, 2017).

Spontaneous reporting of ADRs has been present in Croatia since 1974, with patients being able to report ADRs to the Agency of Medicinal Products and Medical Devices, called HALMED, from 2009. Croatia was one of the first countries to introduce an online system for patients to report ADRs using their mobile devices (Glamočlija, *et al.*, 2018). Despite various countries having introduced patient reporting systems, there are still numerous countries that do not have systems in place for direct patient reporting of ADRs (Sales, *et al.*, 2017*).*

2.2.1 Potential benefits of patient reporting

Global studies have indicated that patient reports of ADRs provide supplemental information to the reports submitted by healthcare professionals because of the different point of view of the patient (Wilson and Amma, 2015; van Hunsel, *et al.*, 2012). Patient reporting systems have given the public the opportunity to be more involved in their own care and has improved reporting of ADRs on over-the-counter (OTC) products, which physicians are unlikely to report (Avery, *et al.*, 2011; Wilson and Amma, 2015). Reports from patients were found to be more detailed, in terms of the ADR description and the influence on the patient's life, and free of bias due to lack of medical expertise (Wilson and Amma, 2015; Rolfes, *et al.*, 2014). As the report comes directly

from the person who has experienced the ADR, the description was found to be more accurate (Herxheimer, *et al.*, 2010). Research also found that patients may report adverse effects sooner than healthcare professionals would (Lebanova and Getov, 2014).

Patients are sometimes hesitant to mention to healthcare professionals the array of medicines that they are taking, or the unusual effects that they experience (Mehta, 2011). By reporting to a person or authority that is not familiar with the patient, the patient may be less reluctant to provide this important information. Patients also may not report to healthcare professionals because of a belief that the healthcare professional will not do anything about it (Blenkinsopp, *et al.*, 2006). The ability to report immediately may empower the patient to speak up about his/her concern which could prevent further harm to the patient by identifying and managing the ADR timeously (Mehta, 2011).

Children are known to have a higher risk of experiencing ADRs compared to adults and because they are often not able to verbally express their experiences, the monitoring and reporting of ADRs by parents is important (Hawcutt, et al., 2011). Evidence suggests that parental reporting provides several benefits for pharmacovigilance, including increasing the rate of reporting of ADRs and identifying previously unknown ADRs in children (Oshikoya, et al., 2009). This leads to an increase in safety data available and ultimately assists in providing quality health care to children (Napoleone, 2010; Oshikoya, et al., 2009).

2.2.2 Concerns about patient reporting

Evidence has suggested that patient reports may help identify new ADRs, however, few studies have investigated the impact of patient reports on pharmacovigilance (Avery, *et al.*, 2011). There have been concerns by regulatory authorities about receiving reports from patients that are not serious or are of low quality (Blenkinsopp, *et al.*, 2006). Contrary to expectations, the quality of reports received from patients has been of good quality globally (Matos, *et al.*, 2016; Pahuja, *et al.*, 2014). There have also been concerns regarding the difference in opinions between patients and healthcare professionals about the seriousness of an ADR or determining whether the adverse reaction was likely caused by the medicine or a disease (Blenkinsopp, *et al.*, 2006). In Norway, patient reports are not assessed for causality, whereas in Australia, causality is assessed for all serious adverse reactions (van Hunsel, *et al.*, 2012). Seriousness is assessed by most countries using the Council for International Organizations of Medical Sciences (CIOMs) committee criteria and causality is often assessed using the WHO causality assessment model, which takes into account the clinical-pharmacological attributes of the case history and the quality of the report (van Hunsel, *et al.*, 2012; WHO-UMC (undated)).

Another apprehension of encouraging patients to report was that influence from the media may result in unnecessary events being reported or it may result in patients discontinuing their treatment inappropriately (Herxheimer, et al., 2010). Nevertheless, it has been noted that the patient is able

to provide a clearer description than the healthcare professional of how the ADR affected the patient's life, family and job (Sales, *et al.,* 2017). Experiences from European countries favour patient reporting but indicates that additional information from healthcare professionals may be required for a better understanding of the ADRs (Rolfes, *et al.,* 2014). A study revealed that patient reporting in Ghana has also shown positivity, while studies show low patient reporting in other developing countries (Sabblah, *et al.,* 2017; Inácio, *et al.,* 2017).

2.2.3 Patient awareness of reporting

While it is evident that patients can offer useful input to pharmacovigilance programs, there are factors which prevent patients from reporting (Lebanova and Getov, 2014). Poor economic status, resulting in the inability to post reports or access the internet to submit reports electronically, has been found to deter ADR reporting by patients in developing countries (Dweik, *et al.,* 2017). Another reason for patients not reporting ADRs is a lack of awareness (Matos, *et al.,* 2016). Raising public awareness of the need to report, what to report as well as how and to whom to report may increase the number of reports from patients (Weigmann, 2016).

Increasing publicity of patient reporting, simplifying patient reporting systems and allowing patient reports to be submitted through a variety of methods (e.g. telephone, email, post), could enhance the timeliness and value of patient reporting (van Hunsel, *et al.,* 2012). An aspect of increasing publicity is to inform healthcare professionals about the benefits of patient reporting (Avery, *et al.,* 2011).

2.3 Reporting in South Africa

Patient reporting is not actively promoted in many countries due to financial limits and a lack of resources (Matos, *et al.,* 2016). In South Africa, a spontaneous reporting system is used, in which healthcare providers are responsible for reporting suspected ADRs to the National Adverse Drug Event Monitoring Centre (NADEMC), a unit of the South African Health Products Regulatory Authority (SAHPRA), formerly known as the Medicines Control Council (MCC) (Mehta, et al., 2017; Maigetter, *et al.,* 2015). NADEMC was established by the South African National Department of Health (NDOH) and is coordinated by the National Pharmacovigilance Centre (NPC) (Mehta, 2011; Dheda, 2016). Figure 1 shows the flow of ADR information to the NPC and the safety information generated and sent back to the reporters (Dheda, 2016).

There is currently no system in place for patients to report suspected ADRs directly to the NADEMC, but they can report to pharmaceutical manufacturers, either telephonically or via the company website (Mehta, *et al.,* 2017). Pharmaceutical companies work closely with NADEMC to ensure that the regulatory authority is informed about ADRs experienced by patients in South Africa (Maigetter, *et al.,* 2015).

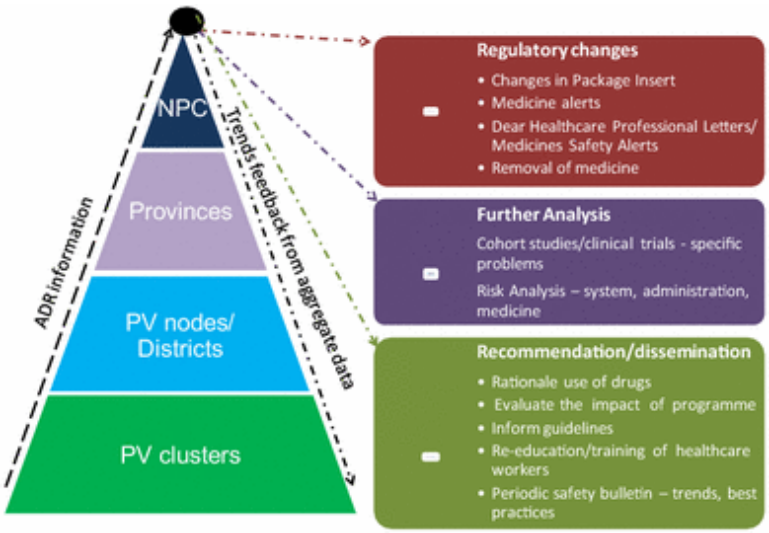

Figure 1: Pharmacovigilance system in South Africa (Taken from Dheda, 2016)

2.4 Parental reporting

In comparison to reporting by adult patients, studies evaluating the reporting of ADRs by parents are limited (Hawcutt, *et al.*, 2011). Self-medicating is a common practice in developing countries due to high costs of private healthcare and poor quality of public healthcare (Oshikoya, *et al.*, 2009). Parental self-medication, in combination with off-label use of medicines have increased the risk of ADRs in children (Hawcutt, *et al.*, 2011).

Research has found that, in countries with patient reporting systems (e.g. UK, India, Malaysia), parents were not aware of their role in reporting ADRs (Fortnum, *et al.*, 2012; Joshi, *et al.*, 2015). Findings from a study conducted by Anderson, *et al.*, (2011) indicate that the majority of patients who reported ADRs had altruistic motives while only a small number reported for personal benefit. Altruistic motives included preventing others from experiencing a similar reaction and improving medicine safety. Studies indicated that reasons for some parents not reporting is that they did not consider it their responsibility to report ADRs or they felt that their reports would be of little value due to lack of medical knowledge. Other parents were optimistic about reporting but were uncertain about who should report ADRs and what type of ADRs to report (Arnott, *et al.*, 2012).

Although reporting by parents has shown to be beneficial in helping to identify ADRs previously unknown in children and has the potential to strengthen existing pharmacovigilance programs, parental reporting globally is not frequent (Pahuja, *et al.*, 2014; Oshikoya, *et al.*, 2009; Hawcutt, et al., 2011). If the awareness that parents can report suspected ADRs in their children is low in countries where a patient reporting system exists, the awareness of parental reporting in countries without a patient reporting system may be even lower. This leads to the question of what the awareness and knowledge of parental reporting of ADRs in South Africa is.

CHAPTER 3: METHODOLOGY

3.1 Introduction

This chapter presents the methodology of the study by discussing the setting, study design, population, data collection and analysis, validation of research tool and the ethical considerations. A survey refers to the process of collecting information from a sample of individuals through various methods to make an inference about the larger population (Ponto, 2015). A questionnaire is one method of obtaining information through either open or closed-ended questions or a combination of both (Boynton and Greenhalgh, 2004).

3.2 Study design

A quantitative descriptive study was used to conduct a survey, which was based on an anonymous questionnaire provided to participants to self-complete to assess their awareness and knowledge of reporting ADRs. See Appendix 2 - Questionnaire.

The questionnaire comprised of three sections that covered:

- Demographic information,
- Adverse drug reaction awareness and knowledge, and
- Views on adverse drug reaction reporting.

It consisted of 28 closed-ended questions with multiple choice (n=23) and Likert-type options, (n=5) as well as four open-ended questions where the respondents could type in their own feedback. Although the methodology was primarily quantitative, the open-ended questions (D6, D8, E3 and E4) generated qualitative data where main themes were identified by the researchers. The results of these open-ended questions, however, were reflected as frequency counts (quantitative).

Knowledge level was determined by who should report ADRs, who to report ADRs to and what type of ADRs to report.

3.3 Study population

The survey was conducted on parents living in South Africa who voluntarily responded to the posted online questionnaire.

Inclusion criteria:

- Parents over the age of 18 years living in South Africa

- Male and female parents
- Parents of adopted children
- Parents of step children
- Parents of children (< 18 years)
- Parents that can read and understand English

Exclusion criteria:

- Minors (under the age of 18 years)
- Adults who do not have any children
- South African parents living abroad

3.4 Data collection

A web-based self-administered questionnaire (research instrument) was constructed and distributed through Google Forms to parents in South Africa. The link to the questionnaire was distributed on social media platforms, such as Facebook® and LinkedIn™ for a period of 9 weeks, from July 2018 to August 2018.

The benefits of using social media include low costs, a diverse target population and the possibility of the questionnaire being shared to additional individuals (Bethlehem, 2010; Wright, 2005). Respondents were encouraged to share the questionnaire with potential participants in their social media community. A negative aspect of distributing the survey on social media was the possibility of the results being skewed due to self-selection bias. This type of bias occurs when individuals are entrusted to select themselves for the survey and usually decide to participate because of their own interest in the topic (Bethlehem, 2010).

Potential participants were required to answer the question "Do you have any children" to exclude non-parents from answering the remaining questions.

3.4.1 Reliability and validity of research tool

The research instrument (questionnaire) was validated by measuring and identifying the number of systematic or built-in errors in the questionnaire (Van Tilburg Norland, 1990). It determined whether the indicators used described the meaning of the theory that the researcher was testing. There are four different types of validity according to Neuman (2014):

- Face validity
- Content validity
- Construct validity
- Criterion validity

Face and content validity were used in this investigation. The primary researcher and the student researcher, together with colleagues and subject matter experts were involved in the questionnaire design to ensure face and content validity (Kelley, et al., 2003).

The questionnaire was designed and developed based on existing questionnaires on the same subject matter and after existing literature was reviewed and examined (Joshi, *et al.,* 2015; Pahuja, *et al.,* 2014; Sales, *et al.,* 2017; Staniszewska, *et al.,* 2017). The researchers reviewed the relevance of each main category and respective questions in relation to the set objectives.

The questionnaire was standardized for all participants to ensure reliability and was based on good writing and language principles to ensure that the questionnaire was clear and easy to understand and that the sequences of questions were easy to follow (Neuman, 2014; Kumar 2014).

3.4.2 Pilot study

The questionnaire was piloted before implementation by administering it to five volunteers who were similar to the target population and who were not included in the principal study (van Teijlingen and Hundley, 2001). Participants of the pilot study were requested to record the time it took to complete the questionnaire and provide any feedback or comments on the questionnaire.

The pilot study assisted in identifying potential problems with the structure and understandability of the questionnaire, thereby establishing questionnaire validity. The pilot study identified minor changes to be made to the informed consent and questionnaire. The informed consent was amended to include "dear potential participant" and the expected duration of the questionnaire was reduced from 20 to 15 minutes.

3.5 Data analysis

The questions were coded, and the data collected was entered and cleaned in Microsoft Office Excel (2016). To ensure that the data was of high quality, quality control activities were performed on the database. To confirm that the coding was done correctly, a proportion (20%) of the data was cross-checked.

Data was analysed using IBM® SPSS® Statistics software, version 23. Descriptive statistics were used, and the data was summarized using percentages, frequency tables, bar charts and cross tabulations. Where more than one option could have been chosen, only the frequency counts were used in the tables and figures. Associations between categorical variables were determined using the Pearson Chi-square test and differences were considered statistically significant if the p-value (α) was <0.05. Adjusted p-values (Bonferroni correction) were calculated for multiple comparisons (e.g. Ethnicity: Black; Coloured; Indian; White). For each of the multiple

comparisons, the critical *p* –value (α) in this study (0.05) was then divided by the number of comparisons being made to set a new stricter significant threshold level as a post-hoc test for probability to control possible false positives and negatives (Haynes, 2013).

Thematic analysis was performed on open-ended questions (Questions D6, E3 and E4) to identify themes within the data (Maguire and Delahunt, 2017). This process involved reviewing the data, generating initial codes, searching for themes, reviewing the themes then defining and naming the themes accordingly (Clarke and Braun, 2013). Consensus on the various themes was performed by both the primary researcher and the student researcher.

The patients' descriptions of the various ADRs experienced (Question D8) were linked to different organ systems. Each ADR was classified according to the WHO system organ classification (SOC) (WHO, 2011). The list of SOCs in alphabetical order is presented in Table 1. Fever was linked to the general disorders and administration site conditions and non-specific allergic reactions were linked to the immune system (WHO, 2011).

Table 1: The Medical Dictionary for Regulatory Activities (MedDRA) Terminology System Organ Classification List

SOC *Blood and lymphatic system disorders*
SOC *Cardiac disorders*
SOC *Congenital, familial and genetic disorders*
SOC *Ear and labyrinth disorders*
SOC *Endocrine disorders*
SOC *Eye disorders*
SOC *Gastrointestinal disorders*
SOC *General disorders and administration site conditions*
SOC *Hepatobiliary disorders*
SOC *Immune system disorders*
SOC *Infections and infestations*
SOC *Injury, poisoning and procedural complications*
SOC *Investigations*
SOC *Metabolism and nutrition disorders*
SOC *Musculoskeletal and connective tissue disorders*
SOC *Neoplasms benign, malignant and unspecified (incl. cysts and polyps)*
SOC *Nervous system disorders*
SOC *Pregnancy, puerperium and perinatal conditions*
SOC *Psychiatric disorders*
SOC *Renal and urinary disorders*
SOC *Reproductive system and breast disorders*
SOC *Respiratory, thoracic and mediastinal disorders*
SOC *Skin and subcutaneous tissue disorders*
SOC *Social circumstances*
SOC *Surgical and medical procedures*
SOC *Vascular disorders*

Taken from WHO, 2011

3.6 Ethical considerations

All participants were provided with a concise online information sheet indicating the purpose of the research and describing any risk and/or benefit to them. Potential participants were given the option to participate in the research project and contact details to ask any questions that they had. Participants were informed that they may decline to answer any of the questions, without any reason or penalty.

Participants were included in the research based on an informed consent process. A consent form was drawn up and consent was obtained from each participant before participating in the study. See Appendix 1 - Participant Informed Consent and Informational Sheet. Participants were not allowed to continue to the questionnaire unless they had selected “agree” to the statement “the study has been explained to me in a language that I understand, and I freely and voluntarily agree to participate”, which served as the participant’s consent to participate in the study. If participants selected “disagree” they were taken to the end of the questionnaire and were not able to answer any of the other questions.

Care was taken to respect participant’s privacy and ensure confidentiality. An online survey tool (Google Forms) was used to deliver the questionnaire to maintain anonymity. No traceability back to the respondents was possible via email address. The electronic filled questionnaires were saved on a password protected database and the information was not used for any other purpose apart from the purpose of this study.

The study was approved by the Biomedical Science Research Ethics Committee of the University of the Western Cape on 8 June 2018 (Reference Number: BM/18/4/5).

3.7 Timeline

The research project, inclusive of proposal writing, data collection, data analysis and writing of the final report, was conducted between February 2018 and December 2018.

3.8 Budget

No budget was required to perform this study as data was recorded electronically.

CHAPTER 4:
RESULTS

4.1 Introduction

This chapter presents the findings of this study in a descriptive format (frequencies and percentage). The results cover socio-demographic characteristics and are presented according to the research questions posed. Associations were also made between the demographics of the respondents and their awareness of the term ADR.

4.2 Socio-demographics

A total of 206 parents completed the questionnaire. The detailed socio-demographics of the respondents are summarized in Table 2.

Overall, 75.2% (n=155) of the participants were female, 24.3% (n=50) were male and 0.5% (n=1) did not respond to the question regarding gender. There was representation from each of the nine provinces, although the majority (n=141, 68.4%) of the respondents were from Gauteng.

The majority (n=100, 48.5%) of the respondents were in the age category 31-40 years and from White (n=89, 43.2%) and Indian (n=77, 37.4%) ethnicity. The marital status of respondents was reported as married by 73.8% (n=152) of respondents and 45.6% (n=94) reported having two children.

Most of the participants indicated that they have a degree (n=75, 36.4%), with the highest level of education reported as a master's degree. Primary area of employment was diverse with healthcare (n=40, 19.4%) being reported the most, followed by education and training (n=35, 17%) and financial services (n=35, 17%). The greater part of respondents had private medical aid (n=177, 85.9%) and made use of private physicians (n=177, 85.9%) for their general medical services.

Table 2: Socio-demographic characteristics of participants

Characteristic		Number of Participants (%)
Gender	Male	50 (24.3%)
	Female	**155 (75.2%)**
Age	18-30	33 (16.0%)
	31-40	**100 (48.5%)**
	41-50	60 (29.1%)
	>50	13 (6.3%)
Ethnicity	Black	32 (15.5%)
	Coloured	8 (3.9%)
	Indian	77 (37.4%)
	White	**89 (43.2%)**
Province	Eastern Cape	12 (5.8%)
	Free State	6 (2.9%)
	Gauteng	**141 (68.4%)**
	Kwazulu-Natal	14 (6.8%)
	Limpopo	5 (2.4%)
	Mpumalanga	4 (1.9%)
	North West	4 (1.9%)
	Northern Cape	3 (1.5%)
	Western Cape	17 (8.3%)
Marital Status	Single	26 (12.6%)
	Married	**152 (73.8%)**
	Divorced	20 (9.7%)
	Separated	6 (2.9%)
	Widowed	2 (1.0%)
Number of Children	1	59 (28.6%)
	2	**94 (45.6%)**
	3	35 (17.0%)
	4 or more	18 (8.7%)
Highest Level of Education	Did not finish school	6 (2.9%)
	Matric certificate	41 (19.9%)
	Diploma	68 (33.0%)
	Degree	**75 (36.4%)**
	Other	15 (7.3%)
Primary Area of Employment	Student	3 (1.5%)
	Unemployed	11 (5.3%)
	Automotive industry	15 (7.3%)
	Education and training	35 (17.0%)
	Financial services	35 (17.0%)
	Healthcare	**40 (19.4%)**
	Information technology	10 (4.9%)
	Legal services	8 (3.9%)
	Wholesale and retail trade	9 (4.4%)
	Other	32 (15.5%)
Medical Aid	Yes	**177 (85.9%)**
	No	29 (14.1%)
General Medical Services	Private doctor	**177 (85.9%)**
	Private nurse	1 (0.5%)
	Pharmacy	15 (7.3%)
	Public clinic	12 (5.8%)

4.3 Adverse drug reaction awareness and knowledge

The research questions that were investigated in this section include:

- Are parents aware of adverse drug reactions?
- What is the knowledge of parents on ADRs?
- What experiences have parents had with ADRs?
- What are the processes or steps to follow when reporting ADRs?

One of the objectives of the study was to assess parents' awareness of reporting ADRs and another objective was to assess their knowledge on the procedures to follow when reporting ADRs. This was measured in terms of their awareness of the term ADR, their awareness of identifying an ADR and their knowledge of who should report ADRs, who to report ADRs to, what type of ADRs to report and how to report ADRs.

According to Figure 2, 70.9% (n=146) of the participants were aware of the term ADR before completing the questionnaire, while 29.1% (n=60) were not aware.

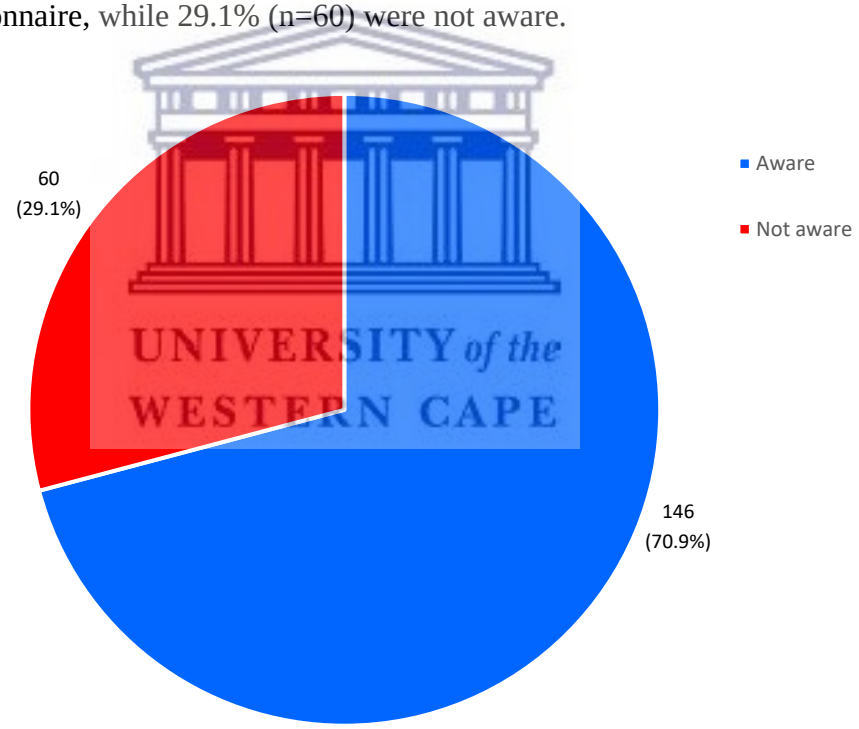

Figure 2: Participants' awareness of the term 'adverse drug reaction'

Although many of the respondents were aware of the term ADR prior to taking part in this investigation, it was important to see if certain socio-demographic factors could have played a role in this awareness more than others. The associations between certain socio-demographic variables and awareness of the term ADR are illustrated in Table 3.

Table 3: Association between different socio-demographic variables and awareness of the term 'adverse drug reaction'

Socio-demographic variables	Aware (Yes)	Not aware (No)	Pearson Chi-Square	Adjusted *p*-value (Bonferroni correction)
ETHNICITY –	**Threshold significance level when** $p < 0.006$ for multiple comparisons			
Black	13 (40.6%)	19 (59.4%)	16.8	< 0.001*
Coloured	2 (25%)	6 (75%)	8.5	0.004*
Indian	56 (72.7%)	21 (27.3%)	0.2	0.651
White	75 (84.3%)	14 (15.7%)	13.6	<0.001*
MARITAL STATUS -	**Threshold significance level when** $p < 0.005$ for multiple comparisons			
Single	12 (46.2%)	14 (53.8%)	8.8	0.003*
Married	113 (74.3%)	39 (25.7%)	3.4	0.066
Divorced	15 (75%)	5 (25%)	0.2	0.669
Separated	4 (33.3%)	2 (33.3%)	0.1	0.818
EDUCATION LEVEL -	**Threshold significance level when** $p < 0.005$ for multiple comparisons			
Did not finish school	0 (0.0%	6 (100.0%)	15.3	< 0.001*
Matric certificate	18 (43.9%)	23 (56.1%)	18.7	< 0.001*
Diploma	50 (73.5%)	18 (26.5%)	0.3	0.607
Degree	64 (85.3%)	11 (14.7%)	11.5	0.001*
Other	14 (93.3%)	1 (6.7%)	3.9	0.050
EMPLOYMENT AREA -	**Threshold significance level when** $p < 0.003$ for multiple comparisons			
Student	1 (33.3%)	2 (66.7%)	2.1	0.144
Unemployed	5 (54.5%)	5 (45.5%)	1.6	0.209
Automotive Industry	7 (46.7%)	8 (53.3%)	4.8	0.030 ns
Education and training	29 (82.9%)	6 (17.1%)	2.8	0.094
Financial services	27 (77.1%)	8 (22.9%)	0.7	0.393
Healthcare	36 (90.0%)	4 (10.0%)	8.6	0.003 ns
Information technology	7 (70.0%)	3 (30.0%)	0.01	0.931
Legal services	6 (75.0%)	2 (25.0%)	0.1	0.809
Wholesale and retail trade	3 (33.3%)	6 (66.7%)	6.6	0.01 ns
Other	19 (59.4%)	13 (40.6%)	2.6	0.106
MEDICAL AID -	**Threshold significance level when** $p < 0.013$ for multiple comparisons			
Medical aid	132 (74.6%)	45 (25.4%)	8.3	0.004*
No medical aid	14 (48.3%)	15 (51.7%)	8.3	0.004*
ACCESS TO GENERAL MEDICAL SERVICES -	**Threshold significance level when** $p < 0.006$ for multiple comparisons			
Private doctor	131 (74.0%)	46 (26.0%)	6.7	0.009 ns
Private nurse	1 (100.0%)	0 (0.0%)	0.4	0.519
Pharmacy	10 (66.7%)	5 (33.3%)	0.1	0.719
Public clinic	3 (25.0%)	9 (75.0%)	12.9	0.003*

*statistically significant

ns – not significant according to the new set threshold significance level for multiple comparisons

A large proportion of black (59.4%, *p*–value<0.001) and coloured (75%, *p*-value=0.004) participants were significantly associated with **not being aware** of the term ADR, while a large proportion of white participants (84.3%, *p*–value < 0.001) were significantly associated with being aware of the term ADR. Being Indian indicated no association with the term ADR.

Within the marital status multiple comparison, a large proportion of single participants (53.8%, *p*-value=0.003) were significantly associated with **not being aware** of the term ADR. All other marital statuses showed no association with the term ADR.

Having a degree was significantly associated with a high proportion of participants being aware of the ADR term (85.3%, *p*–value<0.001), whereas having matriculated (56.1%, *p*–value<0.001) and not finishing school (100%, *p*–value<0.001) were significantly associated with a high proportion of participants **not being aware** of the ADR term.

After adjusting for multiple comparisons, it was found that none of the various employment categories had any association with awareness of the term ADR.

Having a medical aid was significantly associated with a high proportion of participants who were aware of the term ADR (74.6%, *p*–value=0.004) and having no medical aid was significantly associated with a high proportion of participants who were not aware of the term ADR (51.7%, *p*–value=0.004). Receiving general medical services from a public clinic was significantly associated with a high proportion of participants who were **not aware** of the term ADR (75%, *p*-value=0.003)

More specific knowledge of respondents on ADRs are reflected in Table 4, many participants recognised that ADRs can harm people of all ages (n=150), all medicines can cause ADRs (n=130) and that the collection of information on ADRs contributes to improving patient safety (n=189, 91.7%).

Table 4: Participants' knowledge of adverse drug reactions

Question	Responses	Frequency
Which age group can be harmed from ADRs? #	Children	45
	Adults	21
	Elderly	23
	All ages	**150**
	I do not know	12
	No response to question	1
What type of medication can cause ADRs? #	New medicines	35
	OTC medicines	47
	Complementary medicines (traditional, herbal, etc.)	16
	All medicines	**130**
Does the collection of information on ADRs contribute to improving patient safety?	Yes	**189**
	No	14
	No response to question	3

More than one option could have been indicated

According to Figure 3, 59.7% (2.9% + 3.9% + 26.2% + 26.7%) (n=123) of the participants and/or their children experienced an ADR and 40.3% (n=83) indicated that neither they nor their children had experienced an ADR.

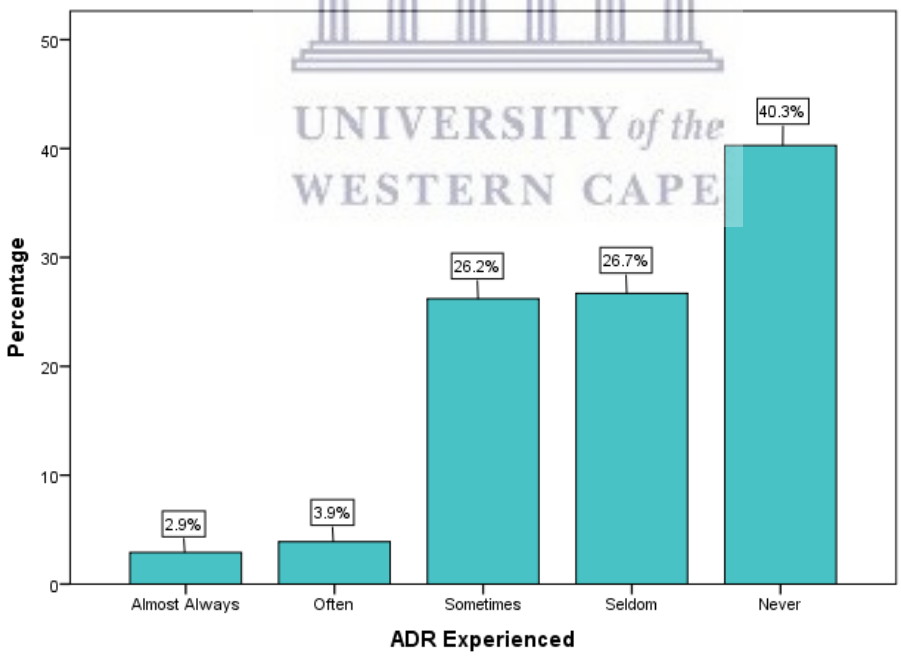

Figure 3: Adverse drug reactions experienced by participants and/or their children

Figure 4 presents how the participants became aware of the ADR experienced. Several participants (n=100, 48.5%) stated that they became aware of the ADR due to a physical reaction that was observed, while others indicated that they knew it was an ADR due to an experience from the past (n=2, 1.0%), information from others (n=2, 1.0%) or a forewarning from a healthcare professional (n=3, 1.5%).

Responses such as "I read [the] info pamphlet inside [the] pill case" and "[I] studied nursing so [I was] aware from an early age" were categorized as miscellaneous. A considerable number (n=43, 20.9%) of respondents indicated that the question "how did you become aware that you or your child may be experiencing an ADR" was not applicable, while others (n=50, 24.3%) did not answer the question.

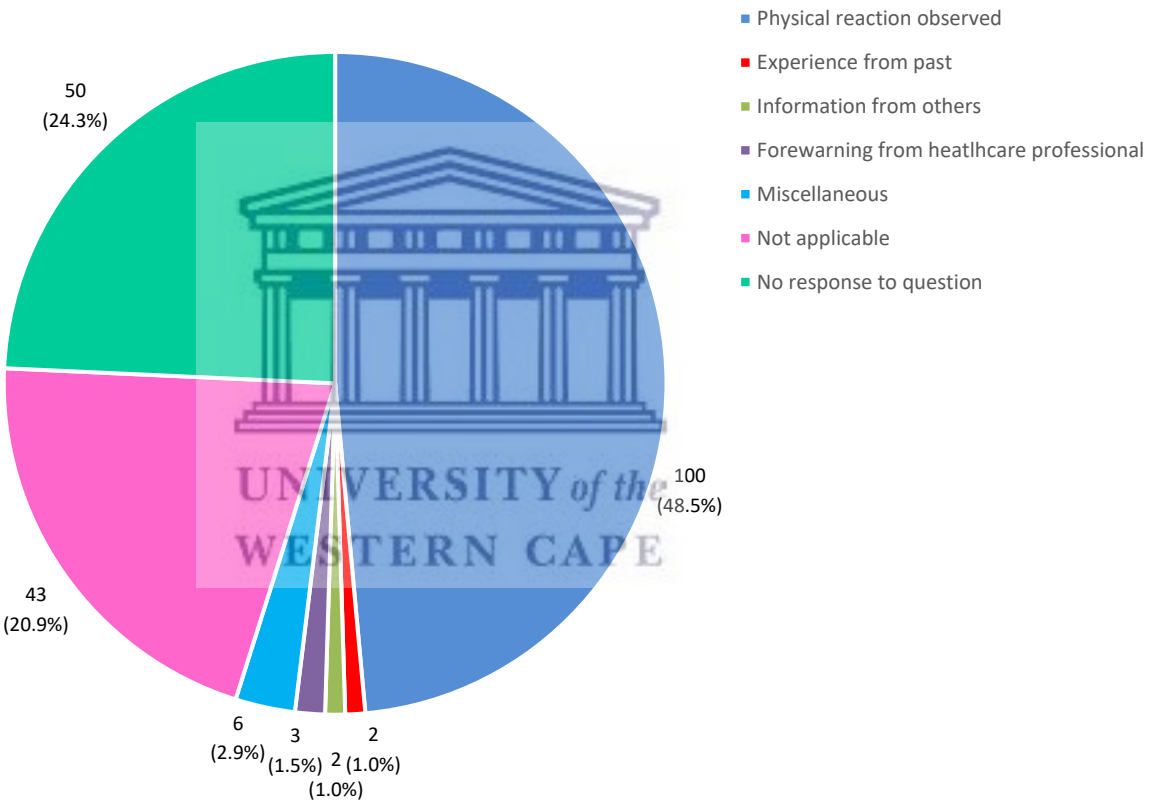

Figure 4: How participants became aware of the adverse drug reaction experienced

Table 5 represents ADRs as described by the respondents, classified according to the WHO SOC. The skin was found to be the most commonly affected organ system (n=22, 23.9%), followed by the gastrointestinal (n=20, 21.7%) and immune (n=16, 17.4%) systems.

Table 5: Adverse drug reactions classed according to system organ classification

Organ system	Frequency	Percentage
Cardiac disorders	2	2.2%
Ear and labyrinth disorders	2	2.2%
Gastrointestinal disorders	**20**	**21.7%**
General disorders and administration site conditions	5	5.4%
Immune system disorders	**16**	**17.4%**
Musculoskeletal and connective tissue disorders	1	1.1%
Nervous system disorders	13	14.1%
Psychiatric disorders	4	4.3%
Renal and urinary disorders	1	1.1%
Respiratory, thoracic and mediastinal disorders	6	6.5%
Skin and subcutaneous tissue disorders	**22**	**23.9%**
No ADR stated / no response to question	114	55.3%
Total	**206**	**100.0%**

The most common outcome of an ADR described was a consultation with a doctor (n=74, 35.9%), followed by ADR resolved on its own (n=55, 26.7%) and admission to hospital (n=17, 8.3%). A few of the respondents indicated that a visit to the clinic was necessary (n=5, 2.4% and even less indicated that the ADR resulted in a prolonged hospital stay (n=2, 1.0%) The outcomes are depicted by Figure 5.

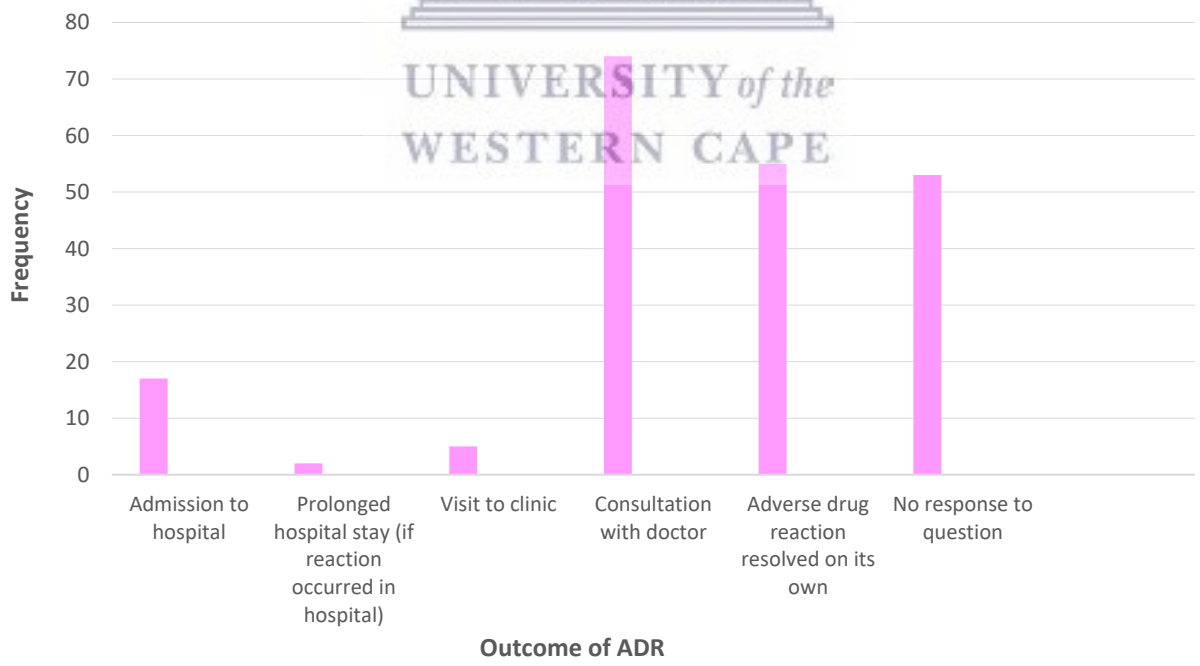

Figure 5: Outcome of one of the adverse drug reactions experienced

Figure 6 presents the reporting of ADRs by participants to healthcare professionals and product manufacturers (pharmaceutical applicants). A third of parents (n=69, 33.5%) never informed a healthcare professional about an ADR experienced by themselves or their child and most parents (n=175, 85%) never informed the product manufacturer about their ADR encounter.

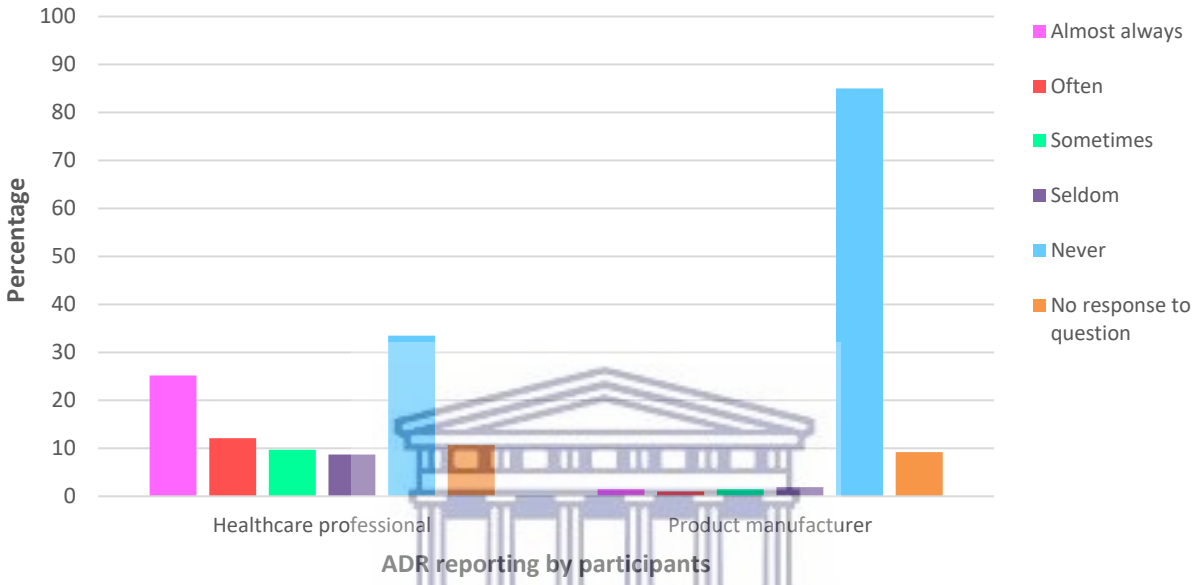

Figure 6: Reporting to healthcare professionals and product manufacturers

Table 6 presents **frequency counts** (more than one option could have been selected) to questions regarding the ADR reporting process. A pharmacy was the selection for approximately half of the respondents (n=114) with the remaining selections being a doctor's surgery (n=90), a pharmaceutical company (n=83) and a hospital (n=73). A small number of participants believed that only healthcare professionals should report ADRs (n=32), similar to those that believed that only patients should report ADRs (n=30). However, the majority (n=138) believed that reporting ADRs is both the responsibility of healthcare professionals and patients.

Regarding to whom ADRs can be reported, a large number (n=183) of participants selected product manufacturers, 165 selected NADEMC, 154 selected doctors, 136 selected pharmacists and 104 indicated that ADRs should be reported to nurses. It was surprising to note that more than half (n=121) of the respondents had knowledge of how to report ADRs (by post, telephone, email/website), while 19 respondents were incorrect (only be post/ only by telephone/ only by email/website) and 65 respondents indicated that they did not know how to report ADRs. The responses to the questions regarding the ADR reporting process can be seen in Table 6.

Table 6: Participants' responses regarding the reporting process or steps to be taken

Question	Responses	Frequency
Where can you find more information on ADR reporting?[#]	From a hospital	73
	From a pharmacy	**114**
	From a doctor's surgery	90
	From a pharmaceutical company	83
	I do not know	67
Whose responsibility is it to report ADRs?[#]	Healthcare professionals (doctors, nurses, pharmacists)	32
	Patients	30
	Healthcare professional(s) and patients	**138**
	Reporting is not necessary	2
	No response to question	4
To whom can ADRs be reported?[#]	Doctors	154
	Nurses	104
	Pharmacists	136
	Product manufacturers	**183**
	NADEMC	165
	No response to question	3
How can ADRs be reported?[#]	Only by post	1
	Only by telephone	6
	Only by email/website	12
	By post, telephone, email/website	**121**
	I do not know	65
	No response to question	1

More than one option could have been indicated

Figure 7 shows participants' responses regarding what type of ADRs are to be reported. Majority of the respondents (n=150, 72.8%) indicated that all suspected ADRs are to be reported, while 14.6% (n=30) selected serious or life-threatening ADRs, 8.3% (n=17) selected ADRs not indicated on package insert, and 2.4% (n=5) selected uncommon ADRs. It is important to note that four respondents (1.9%) indicated that reporting of ADRs is not necessary.

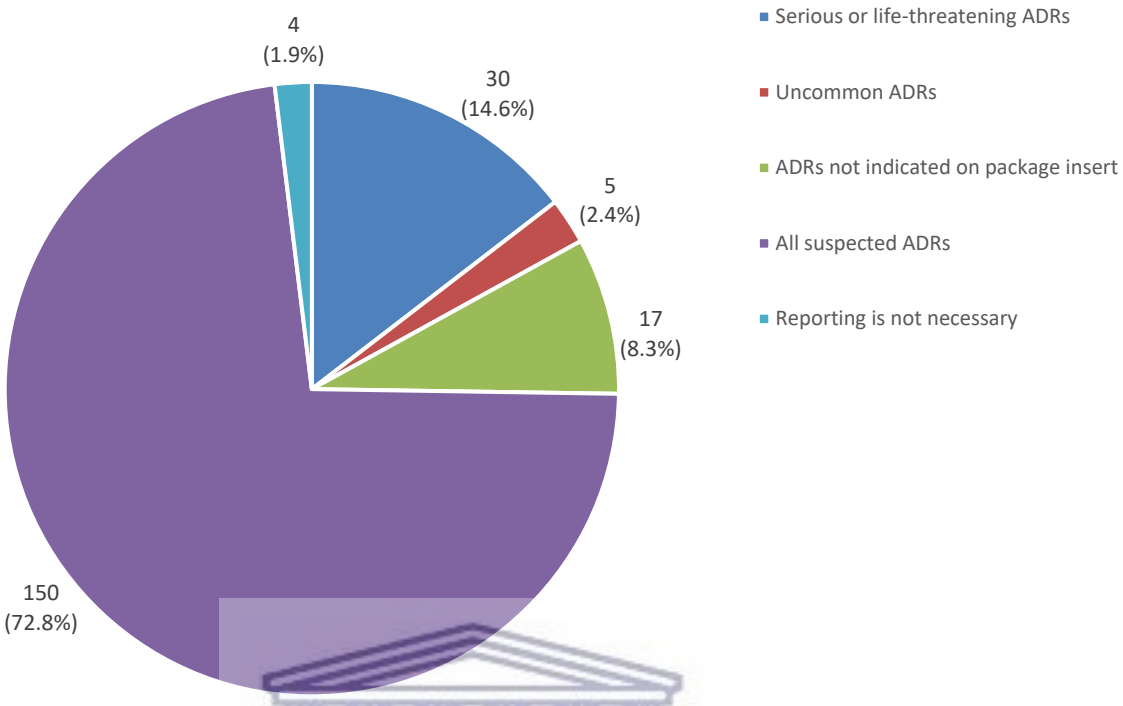

Figure 7: Participants' responses regarding what type of adverse drug reactions are to be reported

4.4 Views on adverse drug reaction reporting

The research questions that were investigated in this section include:

- What are the views on ADR reporting?
- Which factors may enhance or deter ADR reporting?

One of the objectives of the study was to explore parents' views on reporting ADRs. Participants' views on public reporting is shown in Table 7. Majority of the participants (n=152+49+3, 99%) believed that reporting of ADRs by the public is important, while only one participant (0.5%) believed that it is not important at all. Participants were generally positive about reporting ADRs. All but four (2%) said that they would consider reporting ADRs in future.

Table 7: Participants' views on public reporting

Question	Responses	Frequency	Percentage
How important do you think it is for the public to report ADRs?	Absolutely Essential	**152**	**73.8%**
	Very Important	49	23.8%
	Moderately Important	3	1.5%
	Not Important At All	1	0.5%
	No response to question	1	0.5%
Would you consider reporting suspected ADRs in future?	Definitely	**169**	**82.0%**
	Probably	23	11.2%
	Possibly	10	4.9%
	Probably Not	2	1.0%
	Definitely Not	1	0.5%
	No response to question	1	0.5%

Another objective was to determine which factors could motivate or prevent parents from reporting ADRs experienced by their children or themselves. Figure 8 reflects the most frequent responses reported to possibly motivate participants to reporting ADRs.

The most prominent positive theme that emerged from the open-ended questions was a social concern (n= 48). Participants were particularly concerned with helping others: "I will not want someone else to have a bad experience," "I would report it so that no other child or person goes through it," "So my feedback can help other parents or people." Other factors motivating the reporting of ADRs included severity of the reaction (n=34), safety concerns (n=16) and ADRs experienced by self / family (n=14). Less frequent responses include: product improvement, receiving feedback, receiving more information about the reporting process, fear/anxiety, increasing healthcare professional awareness, if the reaction is unexpected and if a causal relationship has been established. It should be noted that 35 participants (17%) did not respond to this question.

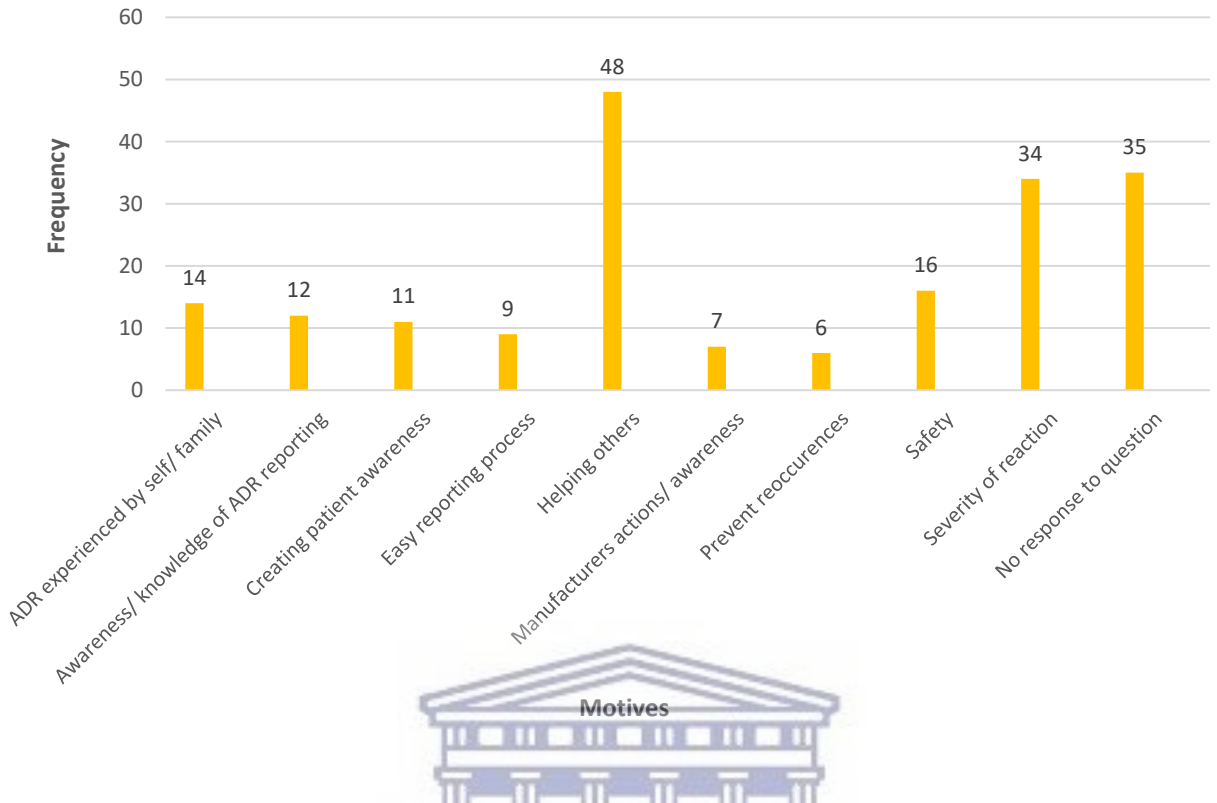

Figure 8: Motives for reporting adverse drug reactions

Figure 9 presents the most frequent barriers that were identified from the responses. Almost one third of participants (n=67, 32.5%) indicated that nothing would prevent them from reporting ADRs experienced by themselves or their children. Some barriers reported by participants were process issues (n=35, 17%): "long hauled process of reporting", time constraints (n=4, 1.9%): "just being busy and not having time to report it" and no feedback or actions taken (n=9, 4.4%): "should no action be taken, I would feel less motivated to report it." Some patients indicated that they would be reluctant to report ADRs because the ADR was minor (n=11, 4.3%), or they were uncertain about whether the medicine caused the reaction (n=5, 2.4%). Less frequent barriers reported include forgetting, procrastination, fear of intimidation and condemnation, lack of awareness, lack of resources, lack of guidance from healthcare professionals, unapproachable medical staff, making an appointment to see a healthcare professional, a common reaction, a non-prescription drug, recommended dose not given and informing people about complementary medicine use. Approximately one quarter of participants (n=53, 25.7%) did not respond to this question.

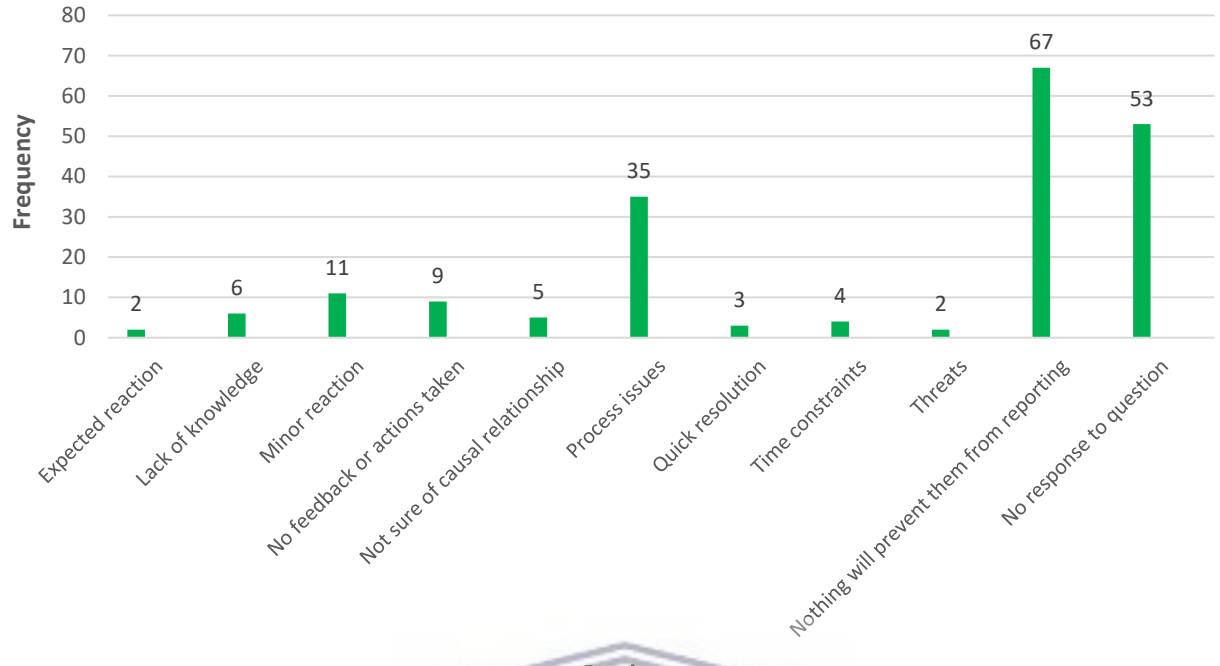

Figure 9: Barriers to reporting adverse drug reactions

The opinion of the respondents regarding methods to better educate and inform the public about ADR reporting are reflected in Table 8. The respondents could have indicated more than one option. Awareness campaigns through tv, radio, etc. was chosen by the majority (n=174) as most appropriate, followed by patient education by healthcare professionals (n=171), information on product packaging/ leaflet (n=140) and published articles on ADR reporting (n=110). Other specific suggestions that were specified by the respondents include: internet campaigns through social media; verified information via online parenting forums; and awareness campaigns at schools for parents to attend.

Table 8: Methods to educate and inform the public about reporting

Methods	Frequency*
Patient education by healthcare professionals	171
Awareness campaign through tv, radio, etc.	174
Information on product packaging/leaflet	140
Published articles on ADR reporting	110
Other	18

* More than one option could have been indicated

CHAPTER 5: DISCUSSION

5.1 Introduction

In this chapter, the principle findings of this study will be discussed in comparison to other literature on the same or similar topic where applicable.

5.2 Principle findings

The context of reporting ADRs in children is important to consider given the high incidence of ADRs experienced by children in South Africa. Most of the South African studies (Joubert and Naidoo, 2016; Terblanche, *et al.,* 2017; Williams, 2015) investigated the knowledge and perceptions of healthcare professionals toward ADR reporting, however studies evaluating ADR reporting among parents are lacking.

Studies conducted through interviews in the UK, US Australia, Canada, Netherlands, Malaysia and a few other countries, found that parents' awareness of ADR reporting was low (Arnott, *et al.*, 2012; van Hunsel, *et al.*, 2012). This study on the other hand, revealed that the participants were aware of ADRs and the importance of reporting them. Being white, having a degree and having private medical aid were associated with being significantly more aware of the term ADR compared to the other demographical variables. The findings suggest that South African parents are aware of what ADRs are and they recognised that it can harm people of all ages, that all types of medicines can cause ADRs and that reporting of ADRs can contribute to improving patient safety. Despite the infrequent reporting of ADRs by participants in this study, participants had knowledge of where to find more information on ADR reporting and surprisingly, how ADRs can be reported. The infrequent reporting by the public was consistent with other studies conducted in Saudi Arabia and the UK (Sales, *et al.,* 2017).

It is important to note that most of the participants in this study were well educated (i.e. completed matric or higher), employed and the clear majority had medical aid and received general medical services from the private sector. After conducting a study in India, Joshi, *et al.*, (2015) found that participants who lived in urban areas were more aware of ADR reporting than those that lived in rural areas and that awareness of ADR reporting increased as education level increased. A similar study relating to patient knowledge in Poland, revealed that participants who lived in urban areas had more knowledge on ADR reporting compared to those that lived outside of the city (Staniszewska, *et al.,* 2017). In a study conducted in Saudi Arabia, where a large percentage of participants (62.2%) were students or unemployed, it was found that patients were unaware of ADRs and ADR reporting (Sales, *et al.,* 2017).

Several participants in this study indicated that they or their child experienced an ADR in the past, with the most common outcome of the ADR being a consultation with a doctor. Although ADRs are a concern for healthcare professionals, manufacturers and patients, the primary contributors of ADR reports have been healthcare professionals (Suleman, 2010). Research has shown that this responsibility should be shared between all parties and this was supported by most participants in this study, who stated that ADR reporting should neither be the healthcare professional's nor the patient's sole responsibility. This may be related to a finding from Kai's study (1996) that suggested that parents were inevitably concerned about their child when they were unwell. Parents may feel that they have a responsibility to report ADRs to help their child or prevent similar occurrences in other children.

As reported by Tobaiqy, *et al.* (2010) and Pahuja *et al.* (2014) in previous studies, participants displayed a positive attitude towards reporting ADRs. However, the results of this study provide evidence of under-reporting of ADRs, with more than a third (33.5%) of respondents not reporting it to healthcare professionals and an unsurprisingly larger number (85%) not reporting it to the product manufacturers. A lack of awareness has been identified as a contributing factor to under-reporting and a study conducted by Joshi, *et al.,* (2015) found that improving patients' awareness can increase spontaneous reporting of ADRs. Although awareness was high in this study, the findings indicate a low participation rate in reporting ADRs, particularly to product manufacturers. Early research revealed that there were noteworthy differences between countries in the number of reports submitted from patients to product manufacturers, with the largest number of reports found in the USA (Talbot and Nilsson, 1998). Patient reporting to pharmaceutical manufacturers has increased over recent years, possibly due to the reduced time spent with physicians during consultations and the increased involvement of patients in their own healthcare (Fleuranceau-Morel, 2002).

A recurrent negative theme from the open-ended question was that participants were unsure of the reporting process. This is possibly due to a lack of knowledge, although the results indicated that many participants had knowledge of the reporting process or the steps to be taken. More than a third (35.5%) of participants answered, "I do not know" to the questions "Where you can find more information on ADR reporting?" and "How can ADRs be reported?" (31.6%). Perhaps, if the option of "I do not know" was available for other questions, more participants would have selected it. When asked what type of ADRs should be reported, almost one third of participants did not indicate "all suspected ADRs" suggesting that there is a lack of knowledge regarding ADR reporting.

Two crucial problems affecting ADR reporting were identified in this study. These include patients anticipating a complex process and having insufficient knowledge about the process. Previous studies conducted by Arnott, *et al.,* (2012) in the UK showed that after the aim and procedure were explained, parents were supportive of ADR reporting and found that the process was not

complicated. The findings from Arnott's studies suggest that in order to overcome under-reporting, patients' knowledge regarding ADR reporting needs to be improved. If appropriate information is communicated to patients, they may report ADRs more frequently, thus contributing towards better management of medicine safety.

This study revealed multiple motives and barriers to reporting ADRs. Identifying the factors influencing reporting was a central step in determining measures to enhance reporting. Parents had altruistic motives for reporting ADRs and many were motivated by the severity of the ADR, and experiences by themselves or their families. The altruistic motives such as preventing similar experiences in others, increasing awareness and improving product safety, was consistent with previous research (Anderson, *et al.,* 2011; Arnott, *et al.,* 2012; Dweik, *et al.,* 2017).

Major barriers included time constraints, problems with the reporting process and concern that no actions would be taken. These results are similar to a systematic review that described barriers to ADR reporting conducted by Dweik *et al.,* (2017) in several countries, including the UK, Netherlands, Australia, Uganda and Saudi Arabia, to determine the factors affecting patient reporting of ADRs.

Educating the public and highlighting the valuable contribution that patients can make in improving medicine safety may assist in overcoming these barriers. A notable finding from this study was that a large number of participants indicated that nothing would prevent them from reporting ADRs experienced by themselves or their children. This was not consistent with the low participation rate in reporting as described earlier in this chapter, however, this study may have contributed to this positive response by increasing participants' awareness of ADRs and ADR reporting.

All patients should be encouraged to report suspected ADRs and it is evident that interventions are needed to improve the public's knowledge regarding pharmacovigilance and ADR reporting procedures. The results reveal opportunities for public education through various methods such as awareness campaigns, published articles, and through healthcare professionals and product packaging. During their investigation, van Hunsel, *et al.* (2012) found that information about ADR reporting needs to be distributed using several methods in order to reach a larger audience. In Saudi Arabia, ADR reporting was promoted through educational campaigns and dissemination of flyers. Patients recommended that information can be provided through product labels and packaging as well as notices on regulatory authority websites (Sales, *et al.,* 2017). Compared to previous years, there are now more information sources available to the public, which can be used to promote ADR reporting. These include health magazines, face-to-face wellness programs, radio and tv programs as well as the internet (Fleuranceau-Morel, 2002).

To summarise, the results suggest that parents were aware and willing to report ADRs, however uncertainty as to who reports ADRs and to whom, difficulties with ADR reporting procedures, and time constraints were found to affect parents' likelihood to report, as observed in previous studies (Dweik, *et al.,* 2017; Tobaiqy, *et al.,* 2010). This study indicates that reporting of ADRs in South Africa may be increased if sufficient knowledge is imparted to parents.

CHAPTER 6:
CONCLUSION AND RECOMMENDATIONS

6.1 Introduction

A global public health matter is the occurrence of ADRs in patients, particularly children. Reporting of ADRs by patients contributes to making safer medicines available and has been seen as a valuable contribution to protecting public health (Rolfes, *et al.,* 2014).

The aim of this investigation was to evaluate the awareness and knowledge in South Africa of parental reporting of suspected ADRs in themselves and their children.

The following objectives were met:

- To assess parents' awareness of reporting ADRs
- To assess the knowledge of parents on the procedures to follow when reporting ADRs
- To explore parents' views on reporting ADRs
- To determine which factors could motivate or prevent parents from reporting ADRs experienced by their children or themselves

The section to follow focuses on the highlights and conclusion of the study, as well as the study limitations, strengths and recommendations.

6.2 Conclusion

This study provides some insight into the awareness, knowledge and views of ADR reporting among parents in South Africa. It has provided an understanding of what parents knows about ADRs and ADR reporting and where there are gaps that need to be addressed. Despite the willingness of parents to report ADRs, their knowledge of ADR reporting was insufficient and could be improved.

Statistically significant differences in awareness based on ethnicity, marital status, education level, medical aid and access to general medical services were observed. Inadequate representation was seen from the individuals living outside of Gauteng. This study, although limited with regard to participant distributions, highlighted which groups of individuals could possibly be targeted to increase ADR awareness and improve knowledge on the reporting process in future studies. Being black, coloured, a single parent, not finishing school, having no private medical aid and receiving general medical services from public clinics were significantly associated with being less aware of the term ADR compared to the other demographic variables. Future public health educational programs could be targeted more towards the above populations in order to raise their awareness on ADRs and the reporting process.

Reporting of ADRs by parents can assist in addressing the problem of under-reporting. As stated by Joshi, *et al.* (2015), parental reporting can be considerably increased if parents are knowledgeable about the reporting procedure. Greater awareness and knowledge among parents can play a considerable role in improving the safety data of medicines and may reduce the occurrence of ADRs in children and the general population. Some challenges in reporting of ADRs have been identified, which could be used to determine the methods of promoting patient reporting to adult patients and parents. Utilizing multiple methods for distributing information about ADR reporting, such as dissemination of flyers, education campaigns at schools or on social media, and inclusion of information on product packaging, in health magazines and on various websites, would be essential to reach a wide audience.

Patients worldwide are becoming more involved in decisions regarding their healthcare and parents are naturally involved in the healthcare of their children. The number of ADR reports submitted globally by healthcare professionals and patients have continuously been increasing over the last few years, however in South Africa ADR reporting remains low. Therefore, it is essential to increase public reporting in order to address under-reporting of ADRs and to make safer medicines available to all.

6.3 Study limitations

This study had several limitations, particularly related to the study population. The questionnaire was only made available in English and therefore excluded participants who cannot read or understand English. The study methodology excluded the voice of the less literate and individuals in poorer communities who did not have access to internet and social media. Self-selection bias may have been introduced due to distribution of the survey on social media, which could have skewed the results of this study. The majority of participants lived in Gauteng, therefore the results could not be generalized to the larger population of parents in South Africa.

6.4 Strengths of the study

Voluntary responses were received from 206 individuals with different socio-demographic characteristics. By using a web-based survey, a large number of individuals could be reached if willing to respond and respondents could respond to the questionnaire at their chosen time and own pace. It was a convenient method to gather data with minimal costs. Anonymity was maintained through the online survey tool, which provided an opportunity for honest and unambiguous responses.

6.5 Recommendations

Parental reporting of suspected ADRs in children can help identify unfamiliar ADRs and may contribute to better signal detection of ADRs. Various pharmacovigilance awareness programs should be conducted to encourage the reporting of ADRs by parents. Strategies to increase patient reporting should focus on frequent and feasible barriers to address. In addition to raising awareness, greater attention should be given to improving the public's understanding of the reporting procedure, where and how to report and to also emphasize the importance of reporting ADRs. Letters of acknowledgement, which are provided to patients in the Netherlands, can be sent to patients who report ADRs in South Africa to assure patients that their voice is heard and to encourage further reporting (Dweik, *et al.*, 2017).

Incorporating healthcare professionals in the education campaigns may be of great benefit as they are usually the primary source of information for patients when they have questions or concerns regarding medicines. Healthcare professionals need to be informed of the benefits of patient reporting and reminded that patients can report ADRs on their own. Healthcare professionals can also play a vital role in improving patient reporting by encouraging patients to report suspected ADRs.

More extensive research is required to evaluate the awareness, knowledge and views of ADR reporting by parents in other provinces, including rural areas. Special efforts should be made to specifically reach and educate populations identified as being less aware and to raise awareness of ADRs, i.e. blacks, coloureds, single parents, individuals who have not finished school, individuals who have no private medical aid and individuals who visit public clinics for general medical services.

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Appendix 1
Participant Informed Consent and Informational Sheet

Title of research project: Evaluation of reporting all types of adverse drug reactions by parents of children younger than 18 years in South Africa

Dear potential participant

You are invited to participate in a research project, which is being conducted by Shavani Pillay for a Master's degree in Pharmacy Administration and Policy Regulation at the University of the Western Cape as part of a mini-thesis.

This study was approved by the Biomedical Science Research Ethics Committee of the University of the Western Cape on 8 June 2018 (Reference Number: BM/18/4/5).

Purpose of the Study
The aim of the study is to evaluate the awareness and knowledge in South Africa of parental reporting of suspected adverse drug reactions in their children.

An adverse drug reaction can be described as a response to a drug which is harmful, and unintended, and which occurs at doses normally used in humans for prevention of diseases, for diagnostic purposes, to treat diseases or to change certain physiological function in the body.

Who can take part in this study?
Any parent (male or female) living in South Africa over the age of 18 years, parents of adopted children (younger than 18 years) and step children (younger than 18 years).

Participation & Confidentiality
Participation in this study is voluntary and you may decline to answer any questions without any reason or penalty.

Your response is anonymous and will be kept confidential. The electronic filled questionnaires will be saved on a password protected database and the information will not be used for any other purpose apart from the purpose of this study.

Risks
There are no anticipated risks to taking part in this study apart from the time it will take to complete the questionnaire

Benefits and Rewards
Your participation in the study will enable us to collect information on what the South African parent knows about how, when and who to report suspected adverse drug reactions in themselves and their children to.

There will be no incentives for participating.

If you have any questions about the research study itself, please contact Shavani Pillay 3763728@myuwc.ac.za.

Should you have any questions regarding this study and your rights as a research participant or if you wish to report any problems you have experienced related to the study, please contact:

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If you agree to participate, click on the link below which will take you to the study questionnaire. The questionnaire should take no longer than 15 minutes to complete. Please respond **by 31 August 2018** and only submit your response once.

https://docs.google.com/forms/d/e/1FAIpQLSeoKIHb17klgKByfkhNkB60SB-FzAwkDD6P2bNIJRC0dfUZqw/viewform?usp=sf_link

Appendix 2
Questionnaire

A. Informed Consent

1. The study has been explained to me in a language that I understand, and I freely and voluntarily agree to participate.	
Agree ☐	Disagree ☐

B. Inclusion/ exclusion

1. Do you have children younger than 18 years old (including adopted and step children)?	
Yes ☐	No ☐

C. Demographics

1. What is your gender?			
Male ☐		Female ☐	
2. What is your age?			
18-30 ☐	31-40 ☐	41-50 ☐	>50 ☐
3. What is your ethnicity?			
Black ☐	Coloured ☐	Indian ☐	White ☐	Other ☐ please specify: _____

4. Which province do you live in?

Eastern Cape	Free State	Gauteng	KwaZulu-Natal	Limpopo	Mpumalanga	North West	Northern Cape	Western Cape
☐	☐	☐	☐	☐	☐	☐	☐	☐

5. What is your current marital status?

Single	Married	Divorced	Separated	Widowed
☐	☐	☐	☐	☐

6. How many children do you have (including adopted and step children)?

0	1	2	3	4 or more
☐	☐	☐	☐	☐

7. What is the highest level of education you have completed?

Did not finish school	Matric certificate	Diploma	Degree	Other
☐	☐	☐	☐	☐ please specify: _____

8. Which of the following categories best describes your primary area of employment?

Student	Unemployed	Automotive industry	Education and training	Financial services
☐	☐	☐	☐	☐

Healthcare	Information technology	Legal services	Wholesale and retail trade	Other
☐	☐	☐	☐	☐ please specify: _____

9. Do you belong to a medical aid?

Yes	No
☐	☐

10. Where do you go to access general medical services (doctor care, emergency health care, preventive health care services)?

Private doctor	Private nurse	Pharmacy	Public clinic
☐	☐	☐	☐

D. Adverse Drug Reaction Awareness and Knowledge

1. Were you aware of the term 'adverse drug reaction' before today?				
Yes ☐			No ☐	
2. Which age group can be harmed from adverse drug reactions? More than one option may be applicable.				
Children ☐	Adults ☐	Elderly ☐	All ages ☐	I do not know ☐
3. What type of medication can cause adverse drug reactions? More than one option may be applicable.				
New medicines ☐	Over-the-counter (OTC) medicines ☐	Complementary medicines (traditional, herbal, etc.) ☐	All medicines ☐	I do not know ☐
4. Does the collection of information on adverse drug reactions contribute to improving patient safety?				
Yes ☐			No ☐	
5. Have you or your child experienced an adverse drug reaction(s) after taking/being given medication?				
Almost Always ☐	Often ☐	Sometimes ☐	Seldom ☐	Never ☐
6. How did you become aware that you or your child may be experiencing an adverse drug reaction?				
7. What was the outcome of one of the adverse drug reactions?				
Admission to hospital ☐	Prolonged hospital stay (if reaction occurred in hospital) ☐	Visit to clinic ☐	Consultation with doctor ☐	Adverse drug reaction resolved on its own ☐
8. Describe briefly what **one** of the adverse drug reactions was about?				

9. Did you ever tell your doctor/nurse/pharmacist about an adverse drug reaction you / your child experienced?				
Almost Always ☐	Often ☐	Sometimes ☐	Seldom ☐	Never ☐
10. Have you ever informed the product manufacturer (pharmaceutical company) of an adverse drug reaction?				
Almost Always ☐	Often ☐	Sometimes ☐	Seldom ☐	Never ☐
11. Where can you find more information on adverse drug reaction reporting? More than one option may be applicable.				
From a hospital ☐	From a pharmacy ☐	From a doctor's surgery ☐	From a pharmaceutical company ☐	I do not know ☐
12. Whose responsibility is it to report adverse drug reactions? More than one option may be applicable.				
Doctors ☐	Nurses ☐	Pharmacists ☐	Patients/Parents ☐	Reporting is not necessary ☐
13. What type of adverse drug reactions (ADRs) should be reported?				
Serious or life-threatening ADRs ☐	Uncommon ADRs ☐	ADRs not indicated on package insert ☐	All suspected ADRs ☐	Reporting is not necessary ☐
14. To whom can adverse drug reactions be reported? More than one option may be applicable.				
Doctors ☐	Nurses ☐	Pharmacists ☐	Product manufacturers ☐	National Adverse Drug Event Monitoring Centre (a unit of the South African Health Products Regulatory Authority) ☐
15. How can adverse drug reactions be reported? More than one option may be applicable.				
Only by post ☐	Only by telephone ☐	Only by email/website ☐	By post, telephone, email/website ☐	I do not know ☐

E. Views on Adverse Drug Reaction Reporting

1. How important do you think it is for the public to report adverse drug reactions?				
Absolutely Essential ☐	Very Important ☐	Moderately Important ☐	Of Little Importance ☐	Not Important At All ☐
2. Would you consider reporting suspected adverse drug reactions in future?				
Definitely ☐	Probably ☐	Possibly ☐	Probably Not ☐	Definitely Not ☐
3. What would motivate you to report adverse drug reactions experienced by you and/or your child?				
4. What would prevent you from reporting adverse drug reactions experienced by you and/or your child?				
5. In your opinion, how can the public be better educated and informed about adverse drug reaction reporting? More than one option may be applicable.				
Patient education by healthcare professionals (doctor/nurse/ pharmacist) ☐	Awareness campaign through tv, radio, etc. ☐	Information on product packaging/leaflet ☐	Published articles on ADR reporting ☐	Other ☐ please specify: _____