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KNOWLEDGE, ATTITUDES, AND PERCEPTIONS OF HEALTHCARE WORKERS ON ADVERSE DRUG REACTION REPORTING IN A GOVERNMENT HOSPITAL IN BOTSWANA

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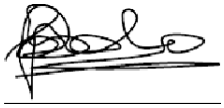
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A Dissertation submitted to the Faculty of Health Sciences, University of the Witwatersrand in fulfilment of the requirements for the degree of Master of Pharmacy.

March 2024, Johannesburg

DECLARATION

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



Lineo Lipholo

28th day of March in the year 2024

DEDICATION

I would like to dedicate this research work to my family: Kagelelo, Thabelang and Letlotlo Mphetolang, for the love and support they gave me through my study journey. Without your support this project would not have come to fruition. Thank you for your encouragement and motivation in making this dream a reality. Hopefully the joy of achieving it will compensate for the family time I spent away from you.

ABSTRACT

INTRODUCTION

Adverse Drug Reactions (ADRs) are an inherent part of using medication to treat diseases. They impact negatively on the health of an individual, potentially leading to hospitalization and increase in the cost of caring for hospitalized patients. Healthcare professionals (HCP) need to assume an active surveillance role of reporting suspected ADRs. Spontaneous reporting (SR) becomes the practice to adopt to ensure safe use of medicines. Education and training are thus necessary to equip HCPs with the necessary skills to identify and report ADRs.

OBJECTIVES

The objective of this study explored the knowledge, attitudes, and perceptions of healthcare professionals in a government hospital in Botswana when it comes to reporting ADRs.

METHOD

A questionnaire composed of both open and closed ended questions was used to collect data on the knowledge, attitudes, and perceptions of HCPs to establish their disposition towards reporting of ADRs. The research tool was checked for its face and content validity as well as internal consistency. The data collected was captured in Microsoft Excel version 16.43 and then imported to SPSS version 27.0 for data analysis.

RESULTS

Based on the findings of this study 26.3% of the participants indicated that they had attended training pertaining to ADR reporting, whilst 39.8% indicated that they had seen and reported an ADR before. There was no statistical significance in reporting of ADRs between profession and gender ($p=0.075$). When assessing for a statistical association between the participants' profession and having used an ADR reporting form before, there was no statistically significant association ($p=0.28$). The association between the average number of ADRs reported and having attended seminar/training was statistically significant ($p<0.05$). HCPs felt that reporting ADR

was of high importance with a Mean Score of 4.67 and Standard Deviation of 0.63 on Likert items measuring attitude towards reporting ADR. HCPs showed positive perception towards reporting ADRs with a Mean Score of 3.07 and Standard Deviation of 1.17 on Likert items measuring perceptions. 40% of the HCPs indicated that they would report ADRs requiring hospitalization.21.8% of HCPs felt that workload could not allow for reporting of ADRs and 5.3% said lack of feedback discouraged from authorities reporting of ADRs.

CONCLUSION

There is a lack of knowledge of ADR reporting among HCPs. The lack of ADR reporting results in unsafe practices with the use of medications. This is despite strategies suggested to curb the challenge of underreporting. Some of the discouraging reasons to report include lack of feedback and communication from the authorities, and workload. These factors affect the overall reporting behaviour among the HCPs even when there is a positive attitude and perception of the importance of reporting ADRs. Education in the form of training and seminars should be a continuous practice, to equip HCPs with the necessary knowledge and skills needed to strengthen the practice of Pharmacovigilance in ensuring medication safety.

KEYWORDS: Adverse drug reaction, Healthcare professionals, Spontaneous reporting

ACKNOWLEDGEMENTS

Firstly, my deepest acknowledgement goes to God Almighty for the mercy and compassion He provided throughout my study journey.

To my supervisors, Ass. Professor Padayachee and Dr. Vagiri, thank you for your guidance in making my research project a success.

To Tefo Mokone, thank you so much for your time and effort in assisting with this research.

To the Healthcare staff that participated in the undertaking of this study, without your participation, this study would not have happened.

Lastly to the Botswana Health Research Unit, thank you for allowing me the opportunity to conduct my research in Botswana.

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ABBREVIATIONS

ACT	Artemisinin-based Combination Therapy
ADR	Adverse Drug Reactions
AE	Adverse Events
AIDS	Acquired Immune Deficiency Syndrome
CEM	Cohort Event Monitoring
HCP	Healthcare Professionals
HIV	Human Immune Virus
PV	Pharmacovigilance
SR	Spontaneous Reporting
TSR	Targeted Spontaneous Reporting
UMC	Uppsala Monitoring Centre
WHO	World Health Organization

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CHAPTER 1: INTRODUCTION

1.1 BACKGROUND

Medicines have been in use for a long time, to treat diseases and illnesses, with the ultimate goal of use being to improve the health and well-being of an individual using them (WHO,2004).The World Health Organisation (WHO) advocates for the rational use of medications in patients and amongst communities, through the use of safe and cost- effective medications (Strengthening Pharmaceutical Systems (SPP), 2011; (WHO, 2004), more especially in resource-limited countries. However safe use of medications does not always translate into optimal health outcomes, in some cases, patients taking medication could experience Adverse Drug Reactions (ADRs) (WHO 2002; WHO, 2004).

WHO defines an ADR as a response to a drug which is noxious and unintended and occurs at doses normally used in man for the prophylaxis, diagnosis, or therapy of disease, for the modifications of physiological function (WHO, 1972). ADRs are an inevitable occurrence associated with medication use in the treatment of diseases, of which some might be known, and others not known at the time of use (WHO, 2004). When thalidomide was used to treat nausea and vomiting in pregnant women in the late 1950s to early 1960s, it was not known then that it could lead to *phocomelia* in newborn babies whose mothers took the medication during pregnancy (WHO, 2004).

In response to the thalidomide tragedy, the WHO developed a program for International Drug Monitoring (Uppsala Monitoring Centre, UMC), in 1968 (WHO, 1972).UMC compiles and analyses reports from the member states on reported Individual Case Safety Reports (ICSRs), through a database system called *Vigibase* (ICSR management system) based in Sweden, from which it identifies signals of ADRs, evaluates the hazard, undertakes research for the development of safer and more effective medications (WHO, 2002; WHO, 2004).

The consequences of the thalidomide tragedy prompted medical authorities in developed countries to ensure safe and rational medicine use by imposing standards and measures that drug manufacturing companies must adhere to during clinical drug development, and this resulted in the birth of Pharmacovigilance (PV) (WHO, 2002). According to WHO, PV can be defined as

the science and activities relating to the detection, assessment, understanding, and prevention of adverse effects or any other medicine-related problem (WHO, 1972).

The primary goal of PV is to ensure the safe use of medication, regardless of the robustness and rigour of the drug development process, since the outcome of clinical trials might not have the same results for the general public (Adhikari et al., 2017; Mehta et al., 2017; Strengthening Pharmaceutical Systems (SPP), 2011; Sultana et al., 2013). In clinical practice, as opposed to clinical trials, medications are used in patients with (co/poly) morbidities, on different medications that might have drug interactions, in age groups such as children and elderly that usually fall under the exclusion category of studies, as well as for off label use (Mehta et al., 2017; Sultana et al., 2013; WHO, 2004). There could be some safety challenges missed during clinical trials such as a lack of standard safety guidelines to determine whether a signal is true or not, a lack of guidelines to establish and classify ADRs, and limited generalizability of trials that exclude high-risk patients (Singh and Loke, 2012; Strengthening Pharmaceutical Systems (SPP), 2011).

Sub-Saharan countries like Botswana have been members of the WHO for some time, though the ICRSs sent to UMC are low, signifying a challenge of either an ineffective PV reporting system, that is unable to achieve its responsibilities or passive behaviour and indifference towards reporting of ADRs by Healthcare professionals (HCPs) (Strengthening Pharmaceutical Systems (SPS), 2011). Secondly, the use of public health programmes such as the Malaria campaign lacks follow-up on tracking ADRs associated with them, and how they merge into the mainstream of the PV reporting system (Isah et al., 2012; Olsson et al., 2015; Strengthening Pharmaceutical Systems (SPP), 2011)

In a 2011 study, to assess PV systems in Sub-Saharan Africa, Botswana was classified under group 2 countries; these countries have basic PV structures in place but lack Spontaneous Reporting (SR) to generate a signal and assess risk (Strengthening Pharmaceutical Systems (SPS), 2011). The study by Berha et al. (2015) identified key features of ADR of cardiometabolic drugs submitted via *Vigibase* by Sub-Saharan African countries; South Africa, Nigeria, Kenya, Ghana, Namibia, and Zimbabwe contributed less than 1000 reports, with no record for Botswana.

There is limited research on ADRs reporting by HCPs in Botswana, and the factors that contribute to underreporting, which continues to be a challenge in developing countries, where the PV systems are not operating to full capacity (Strengthening Pharmaceutical Systems (SPP), 2011). If the reporting trends can be identified, strategies can be developed to increase safe medication use in patients. The Botswana Medical Regulatory Authority (BOMRA) launched the Med Safe app and e-Reporting system in an effort to increase ADR reporting (Uppsala Monitoring Centre Reports, 2020). This study therefore informs on whether HCPs are knowledgeable on PV and reporting channels in Botswana.

1.2 RESEARCH PROBLEM

HCPs play a pivotal role in reducing the prevalence of ADR-related cases, through SR in their day-to-day practice (Pal et al., 2013). The reporting of ADRs reduces the financial burden that health systems may face, in the overall management of ADR-related cases and the discomfort or harm they inflict on those experiencing ADRs (Olsson et al., 2015; WHO, 2002).

The benefit of reporting may also identify new signals or ADR trends, as much as the extent of harm may not be quantified (Mehta et al., 2017), but may reduce incidence rates. In the US alone, the cost of managing ADRs is estimated to be US$ 30.1 billion annually, with the inpatient care costs varying for different hospital wards, whereby in the Intensive Care Unit (ICU) the cost to care is estimated at US$ 19 685 and non-intensive care costs US$ 13 994 (Sultana et al., 2013). Further research is needed to quantify the cost related to ADRs management in Southern Africa, as there are limited studies.

Failure to report ADRs perpetuates the use of suspected medication that poses a danger to the well-being of an individual taking them and increases the overall global challenge of underreporting (WHO, 2002). There is limited information regarding the ADR reports submitted to UMC from Botswana. When the reporting behaviour of HCPs is investigated, this could shed some light in terms of what is being practiced regarding ADR reporting and a knowledge gap can be identified. Strategies can henceforth be developed to curb identified factors that contribute to current underreporting. Motivation through providing information from reliable sources is one way to improve attitudes that can be implemented.

1.3 PURPOSE OF STUDY

The purpose of this quantitative study was to explore the knowledge, attitudes, and perceptions of healthcare professionals in a government hospital in Botswana when it comes to ADR reporting. This was carried out to understand the HCPs awareness of ADR reporting and factors that contribute to their lack of reporting behaviour. The data was collected using a questionnaire where continuous variables were described as means with standard deviations (SD), and categorical variables were presented as frequencies with percentages. Pearson Chi-square test was performed, at a confidence interval of 95% and p-value of 0.05, to determine any association between the variables.

1.4 RESEARCH QUESTIONS

What knowledge, attitudes, and perceptions do healthcare professionals in Botswana have towards Adverse Drug Reactions reporting?

1.5 RESEARCH OBJECTIVES

i. To assess the knowledge of HCPs towards ADRs reporting in a government hospital in Botswana
ii. To assess the attitudes of HCPs towards ADR reporting in their day-to-day practice
iii. To explore the perceptions of HCPS on ADRs reporting in their daily practice

CHAPTER 2: LITERATURE REVIEW

2.1 KNOWLEDGE, ATTITUDE, AND PERCEPTIONS

Knowledge can be described as information, understanding, or skill that one obtains from experience or education (Britannica dictionary 2022, definition of knowledge entry).It can influence how information is processed, interpreted, or given meaning (perception) and the tendency to behave in a particular way based on personal experience or character (attitude) (Pickens, 2005).The willingness to gain knowledge is related to motivation, independent learning, self-concept, and self-esteem (Eekelen, 2006; Carrillo, 2013). The relationship between these human characteristics i.e. knowledge (K), attitude (A), and perception (P) is shown in Figure 2.1.1.

According to the Knowledge, Attitude and Practice theory, change in human behaviour can be achieved in 3 steps; acquiring knowledge, generating attitudes/beliefs, and forming practices (Xie et. al., 2017). The use of credible sources for sharing knowledge can promote attitude change which ultimately will affect behaviour (Block-3 Attitudes, 2020).

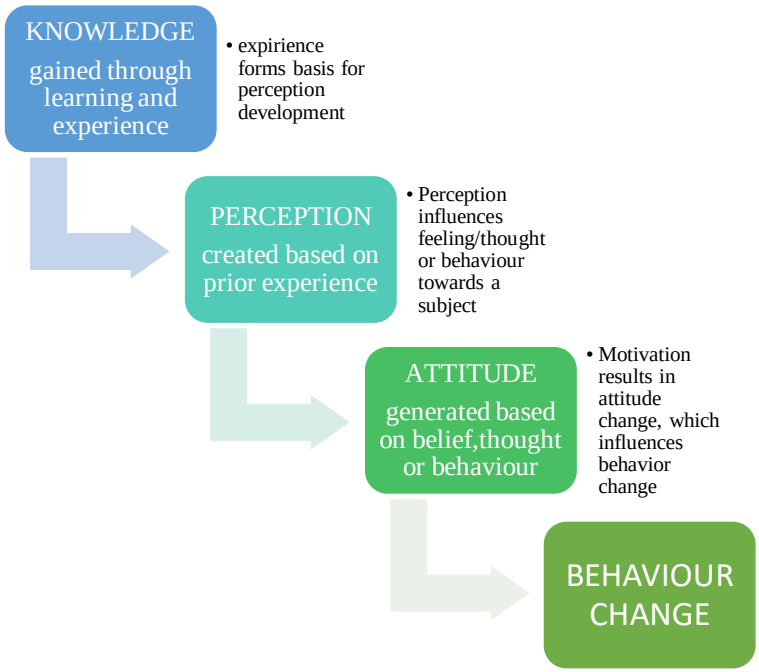


Figure 2.1.1 Conceptual framework showing relationship between knowledge, attitude and perception

2.1.1 KNOWLEDGE VERSUS PERCEPTION

Rahman and Sommer (2018) demonstrated that in-depth knowledge shapes perception, through the recollection of stored information in the memory. They argued that for an individual to perceive a stimulus there should have been prior exposure to similar stimuli, to influence behaviour. Based on their proposition, if continuous education to HCPs on ADR and reporting thereof, can be viewed as prior exposure then change in reporting behaviour can be influenced, when an ADR is met during practice. Recollection of what was taught will increase sensitivity towards ADR reporting, nevertheless, behaviour change will depend on the HCPs' attention and motivation (Pickens, 2005).

Knowledge affects perception in that it enables recognition and interpretation to occur, and it provides internal solutions which can then be accessed. Experience from knowledge acquired becomes the basis on which perception is formed (Rock, 1985). Since perception is influenced by existing beliefs, attitudes, motivation, and personality, only what is considered relevant will be perceived (Pickens, 2005). When HCPs hold positive attitudes towards ADR reporting, they are likely to perceive it as an important responsibility to carry out in practice.

2.1.2 KNOWLEDGE VERSUS ATTITUDES

There are 3 components to developing an attitude which are; effect (feeling), cognition (thought or belief), and behaviour (action) (Pickens, 2005). Since attitude is learned or influenced by experience, providing new information can challenge behaviour (Pickens, 2005). The work of Adasi and Omitogun (2019), observed positive attitudes among HCPs who had prior knowledge of ADR reporting, compared to those who had no prior knowledge. The group without prior knowledge displayed positive attitudes, influenced by their willingness to gain new knowledge. (Adasi and Omitogun, 2019)

Since attitudes influence decisions, guide behaviour, and impact what can be remembered, changing them depends on the cognitive and emotional components. (Pickens,2005) The cognitive approach of changing attitude uses new information to advocate for change (Pickens, 2005). The discussion method as opposed to lecturing has been determined to be more beneficial to attitude change (Block-3 Attitudes, 2020). There is an assumed relationship between knowledge and attitudes, whereby if one has better knowledge about a subject, there is a

likelihood that they will tend to behave positively, but this is not the case. Hussain et al., (2021) determined that positive attitudes do not translate to better reporting behaviour. Only when HCPs are motivated that they can effectively participate in ADR reporting (Hussain et al., 2021)

2.2 IMPLICATIONS OF ADVERSE DRUG REACTION INCIDENTS

ADRs come about as a result of taking medication to treat diseases (WHO, 2004). They have undesirable effects both on the welfare of the individual and the financial sustainability of a health system, through hospitalization, worsening of the disease condition, and increasing the cost of care (Adisa and Omotogun, 2019; Gunèr and Ekmeki, 2019; Mouton et al., 2016; Shanthi, 2013).ADRs contribution to hospital admissions in the USA, Canada, and Australia is estimated at 4.2-30%, 5.7-18.8%, and 2.5-10.6% respectively (Howard, 2007). The financial implications of ADR are a challenge, especially in developing countries where resources are limited (Olsson et al.,2015).

More often than not ADRs can be preventable (WHO, 2004), only if risk assessment and preventative measures are put in place at various hospital levels (Mouton et al., 2016*).*In a South African study to determine ADR contributing to hospital admissions, it was found that 8.4% of the admissions were ADR induced, with the medicines used to treat Tuberculosis (TB) and Human Immunodeficiency Virus & Acquired Immune Deficiency Syndrome (HIV&AIDS) having the highest contribution (Mouton et al., 2016). With Africa having the highest prevalence of HIV & AIDS in the world of 25.6 million people (WHO, 2023), and the contribution that HIV & AIDS has on ADR occurrences, puts financial pressure on health systems for its treatment and induced ADRs (Mouton et al., 2016). Further the lack of human capacity also places additional challenge on the health care system (WHO, 2023)

In an Australian study on some ADRs contributing to the financial burden of health systems, fever, bleeding, diarrhoea, and cardiac arrhythmia were among the most observed (Sultana et al., 2013). The medications contributing to the ADR incidences and management thereof include non- steroidal anti-inflammatory drugs (NSAIDs), antibacterial, anticoagulants, and antineoplastic agents (Sultana et al., 2013). These are commonly used medications in the healthcare system especially NSAIDS and antibacterial. Failure to observe the medications contribution to ADR occurrence poses a threat to human life and potentially increases the burden of disease (Mouton et al., 2016; Sultana et al., 2013)

2.2.1. METHODS OF ADVERSE DRUG REACTIONS REPORTING

2.2.1.1 SPONTANEOUS REPORTING

Spontaneous Reporting (SR) is a passive surveillance method that relies on HCPs to detect and report an ADR (Kasliwal, 2012). It is the most practical and cost-effective way for continual surveillance of medication safety in the daily practice of HCPs (Mehta et al., 2017; Olsson et al., 2015; Sultana et al., 2013). It helps to identify unexpected ADRs that might have been undetected during the clinical trials and point out a new aspect of a known ADR that might continue to pose a danger to the public if not identified (Kasliwal, 2012). It is also beneficial for signal generation (Khan et al., 2013; Kasliwal, 2012; Li et al, (2018); Mehta et al., 2017).

During the clinical trial phase of drug development, only a tiny sample of the population is used, and very stringent conditions are applied, and depending on the clinical trial phase, only disease-specific subjects are used (Adhikari et al., 2017). SR thus becomes helpful in giving insight into the safety profile of medication based on real-life clinical practice (Kasliwal, 2012). The outcome of clinical trials, might not have the same results for the general public, suggesting continuous surveillance from HCPs to ensure public safety (Joubert, 2016; Mehta at al., 2017; WHO 2002).

Since SR is mainly voluntary and is based on the skill and experience of HCPs, it is highly underused resulting in underreporting of ADRs (Mehta et al., 2017; Olsson et al., 2015; Sultana et al., 2013), even though it is generally less expensive and easier to implement than other methods of reporting ADRs (Kasliwal, 2012). The other disadvantages of SR include incomplete information on the reporting forms, lack of information to quantify risk, and variation in the quality of the information provided (Kasliwal, 2012).

2.2.1.2. COHORT EVENT MONITORING

Cohort Event Monitoring (CEM) is an observational cohort study of adverse events associated with using one or more medications in routine clinical practice, after the post- marketing phase (Pal et al., 2013; Rachlis et al., 2016; Suku, 2015;).An adverse event (AE) is any untoward medical occurrence that may present during treatment with a medication but does not necessarily have a causal relationship with this treatment (WHO, 2002).

CEM follows a cohort of patients taking medication of interest from the start of treatment, to identify adverse experiences. Baseline data on events happening to patients before treatment is collected against which it will be compared with the events met during treatment (Pal et al., 2013). This cohort is followed at regular intervals and all AEs are captured while the patient receives the medication, regardless of the cause or severity (Pal et al, 2013; Rachlis et al., 2016).

Some of the advantages of this method include early signal detection, the ability to calculate incidence rates and produce a near-complete profile of the AEs and/or ADRs for the medication of interest as well as the association of the incidence to risk factors (Rachlis et al., 2016). It can identify new adverse reactions or events of a new medication. Since CEM captures all clinical events for the duration of treatment, regardless of suspicion of causality, this allows for showing previously unrecognized and unsuspected ADRs (Pal et al., 2013; Suku, 2015).

The active monitoring of the cohort is based on regular clinical assessment, collection of laboratory specimens, and well-informed staff for information collection, it is considered expensive and labour-intensive, (Pal et al., 2013) especially for Low-Middle-income countries, where there are limited financial and human resources (Olsson et al., 2015).

The duration of CEM is dependent on the treatment duration of the monitored medication as well as reaching a cohort size of 10,000 patients, in addition, to have a meaningful assessment, at least there should be three events shown (Pal et al., 2013; Rachlis et al., 2016). Since the purpose of CEM is to measure the occurrence of an incidence, it is essential that duplicate entries are avoided by identifying patients correctly (Pal et al., 2013). The CEM method proved to build PV capacity in four African National Pharmacovigilance Centres when implemented to monitor artemisinin-based combination therapy (ACT), for uncomplicated malaria (Suku 2015).

2.2.1.3. TARGETED SPONTANEOUS REPORTING (TSR)

TSR is another method of reporting ADRs, and builds on the principle of SR, with the application of some aspects of CEM. A well-defined group of patients is chosen (e.g. patients on treatment of drug-resistant TB) and then monitored as part of routine clinical care for any suspected safety concerns, by HCPs. The method is concerned with addressing a specific set of questions, and therefore it becomes imperative that HCPs be trained and educated on how to assess and report the specific safety concerns suspected to be medicine-related (Pal et al., 2013; Rachlis et al., 2016) however, this method can also be adapted to capture all ADRs, those related to medication of interest, or continual general PV information (Rachlis et al., 2016).

Training and mentoring HCPs in selected facilities treating populations of interest, have demonstrated an increase in reporting rates because of shared reporting responsibility amongst the HCPs (Pal et al.,2013,Rachlis et al 2016).This reduces underreporting significantly, a challenge associated with SR (Rachlis et al., 2016). It has proven to be beneficial when implemented in public health programs, through the integration of reports generated from public health programs into the existing reporting system (Pal et al., 2013).

It is also simple to use, affordable, captures measurements over the entire length of the treatment, and is sustainable in settings with limited financial and human resources (Pal et al., 2013; Rachli, 2016). Unlike CEM, there are neither baseline measurements nor any active follow-up of members of the cohort, and, thus fewer resources are used (Pal et al., 2013).

Since it depends on the willingness of HCPs to monitor and report, the number of individuals with the suspected ADR may not be accurate, hence making completeness of reporting crucial. As a result of limited experience that HCPs have with TSR, the technique needs to be field-tested (Pal et al., 2013).

2.3. KAP AND ADVERSE DRUG REACTIONS REPORTING

ADRs impact negatively the financial sustainability of health systems as well as the welfare of the public (Güner and Ekmekci, 2019; Olsson et al., 2015). With the use of safe medication at the core of PV, it is necessary to report medications suspected to pose a safety hazard to the public, as a result of ADRs/AEs that could be experienced during/after the use of such medication (WHO, 2002). As part of continual post-marketing surveillance, HCPs become the focal point of

contact for patients to report their concerns to and through whom the health authorities can be notified (Güner and Ekmekci, 2019; WHO, 2002). When HCPs are willing to report ADRs, medication safety can be assured. The willingness to participate in reporting could be influenced by motivating the HCPs through incentives (Güner. and Ekmekci, 2019; Hussain et al., 2021) however the willingness and positive attitudes do not always translate to positive reporting behaviour.

The reporting rate of ADRs to the UMC, for the African continent has been low, which according to Olsson et al. (2015) is influenced by a lack of legislative, regulatory framework, and financial support to build sustainable PV systems. Low- and Middle-income countries (LMIC) have fragmented health systems, and depend on donors for most public health programs (Hussain et al., 2021). Further collaboration and integration of safety information is weak resulting in poor regulatory oversight (Olsson et al., 2015). The work of Olsson et.al., (2015) further shows that about 50% of hospital admissions that could be prevented are ADR-related and are due to the way medication is prescribed, dispensed, administered, or even used.

WHO developed Minimum Requirements for a Functional Pharmacovigilance System as a guide on PV activities for a fully operational PV system, and indicators to determine if the expected functions of a PV centre are met, as shown in Table 2.3.1. These indicators measure the structural, process, and outcome or impact of the PV activities, on the existence of PV facilities, dynamics in the set-up, and the outcome respectively (WHO, 2015).In a 2011 study, to assess PV systems in Sub-Saharan Africa, Botswana was classified as having basic PV structures in place but lacking capacity in SR to generate a signal and assess risk (Strengthening Pharmaceutical Systems (SPS) Program, 2011); a disadvantage when it comes to meeting terms of core outcome 1 as per Table 2.3.1. Human capacity also poses a challenge to implementing PV due lack of trained professional staff and high staff turnover (Olsson et al., 2015).

Table 2.3.1: Core outcome or impact indicators (WHO, 2015)

INDICATOR ITEM	ASSESSMENT
CORE OUTCOME 1	Number of signals detected in the past 5 years by the pharmacovigilance centre
CORE OUTCOME 2	Number of regulatory actions taken in the preceding year as a consequence of national pharmacovigilance activities includes a: number of product label changes (variation); b: number of safety warnings on medicines to (i)health professionals (ii) the general public; c: number of withdrawals of medicines; d: number of other restrictions on the use of medicines
CORE OUTCOME 3	Number of medicine-related hospital admissions per 1000 admissions
CORE OUTCOME 4	Number of medicine-related deaths per 1000 persons served by the hospital per year
CORE OUTCOME 5	Number of medicine-related deaths per 100,000 persons in the population
CORE OUTCOME 6	Average cost (US$) of treatment of medicine-related illness
CORE OUTCOME 7	Average duration (days) of medicine-related extension of hospital stay
CORE OUTCOME 8	Average cost (US$) of medicine-related hospitalization

HCPs play a significant role when it comes to the success of SR in a PV reporting system (WHO, 2002). Studies have identified factors that deter HCPs from reporting; such as ignorance, complacency, insecurity, ignorance, diffidence, lethargy as well and lack of training in PV by HCPs (Abjaude et al., 2016; Güner and Ekmekci, 2019; Olsson et al., 2015).On the other hand, ways of motivating HCPs to report ADRs include; education on PV, getting feedback on reported

cases, reporting becoming a professional responsibility, and incentives (Adjaude et al., 2016; Güner and Ekmekci, 2019).

Change in reporting behaviour by HCPs is crucial to promote reporting ADRs. Tailor- made education and training of HCPs based on their clinical responsibilities have demonstrated positive results on ADR reporting and need to be continuous for on-going reporting behaviour (Abjaude et al., 2016; Güner and Ekmekci, 2019; Hussain et al., 2021). Drug safety alerts and continuous professional development impact positively on the reporting of ADRs (Abjaude et al., 2016; Hussain et al., 2021). Güner and Ekmekci (2019), observed a high reporting rate amongst HCPs with PV knowledge.

CHAPTER 3: METHODOLOGY

3.1: SELECTION OF THE INSTITUTION

The study was conducted in a government hospital in Gaborone, Botswana. The healthcare delivery system in Botswana has divided hospitals in terms of the type and level of service they provide, namely; primary, district, and referral. Hospitals are used as referral points for the lower level of service care points like clinics, health posts, and mobile stops. The hospital where the study was conducted is amongst the 3 at referral level and provides specialized care, with departments such as oncology and urology. The level of care provided at the hospital and its location, makes it ideal to use for studies in the capital city, Gaborone.

3.2 STUDY DESIGN

This study followed a cross-sectional quantitative research design with a qualitative aspect to it and used a questionnaire (research instrument) to collect data from the participants. The research instrument was adapted from similar studies by Khan et al., 2013 and Gordhon & Padayachee (2020) and changed where applicable to suit the setting of this study. A stratified random sampling method was used to choose the sample from the population whereby the number of all HCPs applicable to the study was divided into 3 subgroups namely; doctors, nurses, and pharmacy personnel (pharmacists and pharmacy technicians together).From each subgroup, the representative number of participants was calculated based on the sample size of 260 (shown below under sample size); in such a way that it was proportionally representative of the total population. Once the number of participants within the subgroups was determined, randomly in each subgroup, the participants were chosen.

3.3 POPULATION AND SAMPLE SIZE

The study population included doctors, pharmacists, pharmacy technicians, and nurses in the selected hospital from all the wards (surgical and medical wards as well as Pharmacy). Since access to staff establishment information was not allowed to third parties from the institution at the time this study was done, a reference to the population size was drawn from a study by *Ngidi* (2015), whereby there were 745

personnel applicable to this study (doctors, nurses, and pharmacy personnel) employed at the time.

Yamane's sample size formula shown below was used to determine the sample size for this study at 95% confidence interval and 5% margin of error and the calculated sample size was 260. Since the data collected in this study was categorical and the estimated population size was known, it was appropriate to use this method of sample calculation, to make inferences about the population.

$$n = \frac{N}{1 + N(e)^2}$$

Whereby:

- *N* the population size
- *e* is the acceptable margin of error.
- *n* is the sample size

3.4 INCLUSION CRITERIA

Only doctors in their different specialties, pharmacists, pharmacy technicians, and nurses who gave consent to be part of the study were included in the study

3.5 EXCLUSION CRITERIA

All the HCPs who belonged to the identified group but were unwilling to participate in the study

No interns were considered for the study.

3.6 RESEARCH QUESTIONNAIRE

The questionnaire consisted of 21 questions made up of both open-ended and close-ended questions. The breakdown of the questions was; 5 questions on the demographics of the respondents, 7 on knowledge of ADRs reporting, 1 on attitude of

HCPs on ADRs reporting, 7 on encounters with ADRs, and 1 on recommendation to improve ADRs reporting.

3.7 VALIDITY OF STUDY

3.7.1. FACE AND CONTENT VALIDITY

A pilot test on 5 HCPs was done to determine the face validity of the instrument, and it was attained by establishing the relevance, practicality, unambiguity, and clarity of the study, based on its intended audience.

Content validity, on the other hand, was established by administering the research instrument to 5 panellists (2 doctors, 2 nurses, and 1 pharmacist, who did not participate in the study) for item scoring of the expressions in each domain, based on the relevance of the item to the variables being measured. Each item on the instrument was scored on a scale of 1 to 3 corresponding to “essential”, “useful but not essential” or “not essential” respectively.

The item scores were used to determine the Content Validity Ratio (CVR) which was used to calculate Content Validity Index (CVI). A favourable number of CVI was obtained which meant the panellists agreed with the items in the domains they were supposed to measure.
In maximizing the response rate from the panellists, a face-to-face approach was used for the content validation method (Lawshe, 1975).

3.8 RELIABILITY OF THE STUDY

3.8.1 INTERNAL CONSISTENCY

The reliability of the instrument was determined by checking for internal consistency using Cronbach's alpha coefficient, whereby item scoring of items on a Likert scale measurement was done. Spreadsheet was created on Microsoft Excel and Cronbach’s alpha was determined. A score higher than 0.7 was obtained and was acceptable to render the questionnaire reliable (Sürücü & Maslakçi, 2020).

To increase the consistency of the instrument, the participants received the same questionnaire and the procedure for data collection was consistent throughout; in an effort to minimize sources of variability.

The research instrument used in this study would be able to demonstrate consistency, stability, and repeatability of results when used in similar studies, exploring the knowledge, attitudes, and perceptions of healthcare professionals in as much as the circumstances would be different.

3.9 DATA ANALYSIS

Spreadsheets of data collected from the questionnaires were created on Microsoft Excel™ version 16.43 and imported to the IBM SPSS Statistics *version 27.0* Continuous variables were described as means with standard deviations (SD), while categorical variables were presented as frequencies with percentages. Under demographics, gender was used to allow for comparison between males and females in the same professional group and across professionals.

A bivariate analysis was performed of the categorical variables and *a Pearson Chi*-square test was performed, at a confidence interval of 95% and p-value of 0.05, to determine an association between the variables.

To assess for knowledge, attitudes, and perceptions (KAPs) on ADR reporting, item scoring was performed on questions directly linking back to the KAPs whereby the actual number of an item was divided by item score and multiplied by 100. The results were then presented as a percentage. Pearson's coefficient of correlation(r) was used to determine the degree of association between the data on an interval scale.

Open-ended responses were analysed using the thematic analysis approach on Microsoft Excel™. The keywords used in the responses were first "coded" into words or phrases relevant to the research question. These words were categorized into themes and cleaned after which they were analysed using frequencies and presented as a pie chart (Braun and Clarke, 2012).

3.10 ETHICS

The data provided on the questionnaires was only accessible to the researcher, and maintenance of anonymity, and confidentiality were ensured throughout the study. No information on the questionnaires could be linked back to the participants. Ethics approval was granted by the University of the Witwatersrand Human Research Ethics Committee (HREC). (Ethics clearance certificate number M221086, approval date 11/05/2023) (See Appendix F)

CHAPTER 4: RESULTS AND DATA ANALYSIS

4.1. QUESTIONNAIRE RESULTS

Based on the calculated sample size of two hundred and sixty, 133 participants responded, resulting in a response rate of 51%. Of those who participated and responded 66.9% were females and 33.1% were males, with nurses contributing the highest proportion of the participants at 73.7 %, as indicated in Table 4.1.1

Table 4.1.1: Demographic characteristics of the participants (N=133)

		Frequency	Percentage (%)
Profession	General practitioner	20	15.0
	Medical specialist	7	5.3
	Nurse	98	73.7
	Pharmacist	2	1.5
	Pharmacy technician	6	4.5
Ward/ Department	Accident and Emergency	30	22.6
	Renal	19	14.3
	ICU	22	16.5
	Orthopaedic	26	19.5
	Dentistry	7	5.3
	Pharmacy	8	6.0
	Surgical	21	15.8
Gender	Male	44	33.1
	Female	89	66.9
Experience	Less than 5 years	43	32.3
	5 to 10 years	29	21.8
	More than 10 years	61	45.9
Age	18-24	14	10.5
	25-36	62	46.6
	37-49	44	33.1

	50-64	13	9.8

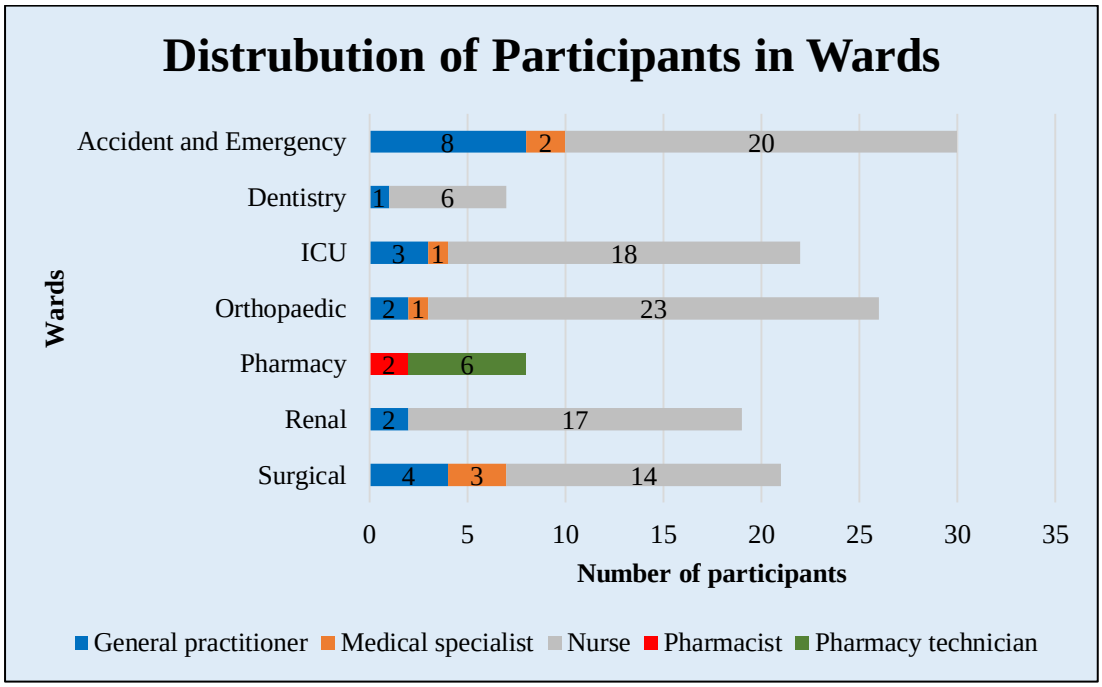


Figure 4.1.1: Distribution of participants in the hospital departments

Table 4.1.2 shows the relationship between participant's profession and gender. A Pearson Chi-square test was performed, to determine if there was any statistically significant association between gender and profession, and the results were not significant ($p=0.075$).

Table 4.1.2: Gender versus Profession of participants (N=133)

What is your profession?	What is your gender?		Total
	Male	Female	
General practitioner	12 (27.3%)	8 (9%)	20 (15%)
Medical specialist	2 (4.5%)	5 (5.6%)	7 (5.3%)
Nurse	28 (63.6%)	70 (78.7%)	98 (73.7%)
Pharmacist	1 (2.3%)	1 (1.1%)	2 (1.5%)
Pharmacy technician	1 (2.3%)	5 (5.6%)	6 (4.5%)
Total	44 (100%)	89 (100%)	133 (100%)

Pearson Chi-square = 8.5, p-value = 0.075, The results not significant at *p< 0.05*

4.2 KNOWLEDGE OF PARTICIPANTS ON ADR REPORTING

Only 26.3% of the participants attended a seminar or training before on ADR reporting. 39.8% indicated having used an ADR reporting form before, although 62.4% said they did not know where ADR reporting forms were in their department as indicated in Figure 4.2.1.

27.9% said that ADRs were submitted to the Botswana Medical Regulatory Authority and 35.1% said the reports were submitted to the Princess Marina Pharmacovigilance Centre in Figure 4.2.2. There were more female (56.6%) than male (43.4%) participants who gave positive responses across the knowledge items, as demonstrated in Figure 4.2.3.

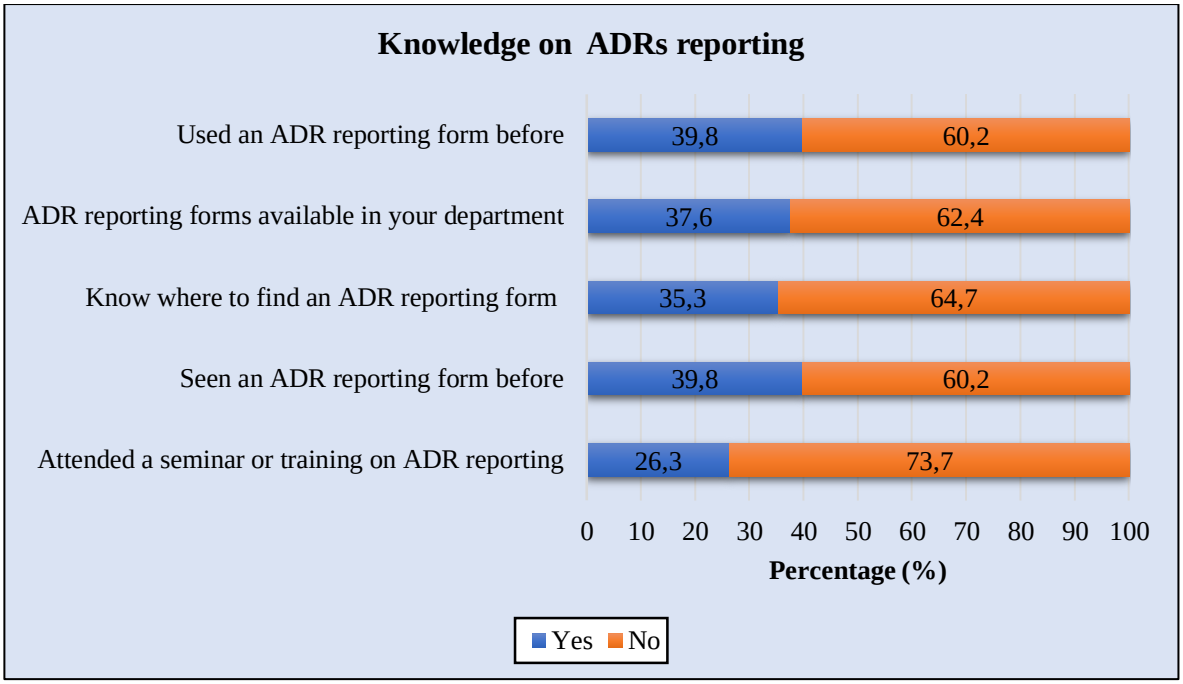


Figure 4.2.1: Knowledge on ADR reporting among participants

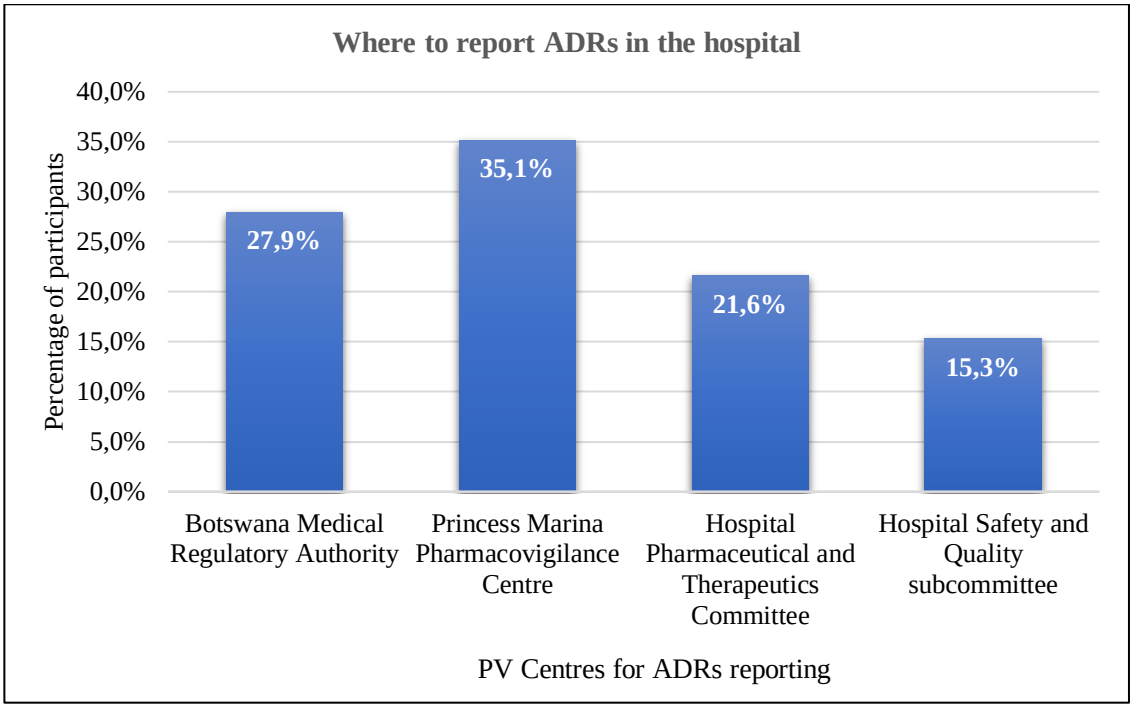


Figure 4.2.2: Adverse drug reactions reporting centres

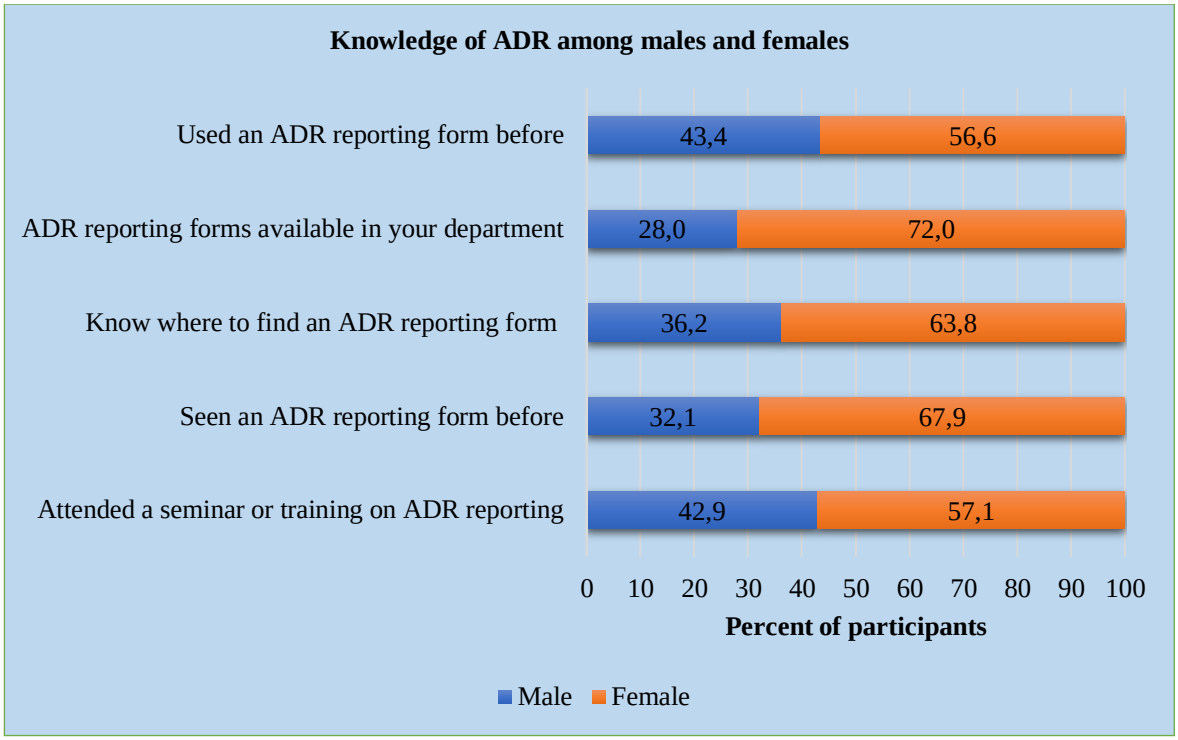


Figure 4.2.3: Knowledge of ADR reporting against gender

74.5% of the participants with less than 10 years of work experience knew where to find ADR reporting forms in their department.9.4% of those with more than 5 years of work experience had seen an ADR reporting form before. Of those who had between 5 -10 years of work experience only 32.1% had used an ADR reporting form before, as shown in Table 4.2.1.

Table 4.2.1: Knowledge of ADR reporting according to years of work experience (N=133)

Knowledge of ADRs	Years of Experience (%)		
	<5	5-10	>10
Attended a seminar or training on ADR reporting	14.3	17.1	68.6
Seen an ADR reporting form before	9.4	18.9	71.7
Know where to find an ADR reporting form	10.6	14.9	74.5
ADR reporting forms available in your department	20.0	30.0	50.0
Used an ADR reporting form before	37.7	32.1	30.2

Table 4.2.2 shows the relationship between knowledge on the use of an ADR reporting form and the healthcare profession. To determine if there was a significant association between the two categorical variables, a Pearson Chi-square test was performed. The results showed that there was no statistically significant association between participants' profession and knowledge on the use of ADR reporting forms (*p=0.28*).

Table 4.2.2: Knowledge of use of ADR reporting form versus profession (N=133)

What is your profession?	Have you ever used an ADR reporting form before?		Total
	Yes	No	
General practitioner	11 (20.8%)	9 (11.3%)	20 (15%)
Medical specialist	4 (7.5%)	3 (3.8%)	7 (5.3%)
Nurse	35 (66%)	63 (78.8%)	98 (73.7%)
Pharmacist	0 (0%)	2 (2.5%)	2 (1.5%)
Pharmacy technician	3 (5.7%)	3 (3.8%)	6 (4.5%)
Total	53 (100%)	80 (100%)	133 (100%)

Pearson Chi-square = 5.071, p value = 0.28, The results not significant at *p<0.05*

The results presented in Table 4.2.3 show a relationship between gender and having used an ADRs reporting form before. More female participants (56.6%) had utilized an ADR reporting form compared to male participants (43.4%). To determine if there was any significant association between gender and the use of ADR reporting forms, a Pearson Chi-square test was conducted. The results indicated statistical significance at a 5% level of significance (*p<0.05*).

Table 4.2.3: Knowledge of use of ADR reporting form by Gender (N=133)

Gender	Have you ever used an ADR reporting form before?		Total
	Yes	No	
Male	23 (43.4%)	21 (26.3%)	44 (33.1%)
Female	30 (56.6%)	59 (73.8%)	89 (66.9%)
Total	53 (100%)	80 (100%)	133 (100%)

Pearson Chi-square = 4.234, p value = 0.04, The results significant at *p<0.05*

Table 4.2.4. presents the relationship between years of work experience and having used an ADR reporting from before.Participants with less than 5 years of experience were the group that had used the ADR reporting forms before at 37.7% unlike 56.3% of participants with more than 10 years' experience who showed that they had not used an ADR reporting form before.To assess the relationship between years of experience and having used an ADR reporting from before, a Pearson Chi-square test was performed, and the results showed an association between the two categorical variables (*p<0.05)*

Table 4.2.4: Knowledge of use of ADR reporting form by years of work experience (N=133)

Years of Experience	Have you ever used an ADR reporting form before?		Total
	Yes	No	
Less than 5 years	20 (37.7%)	23 (28.8%)	43 (32.3%)
5 to 10 years	17 (32.1%)	12 (15%)	29 (21.8)
More than 10 years	16 (30.2%)	45 (56.3%)	61 (45.9%)
Total	53 (100%)	80 (100%)	133 (100%)

Pearson Chi-square = 9.78, p value = 0.008, The results are significant at p<0.05)

4.3 ATTITUDES OF PARTICIPANTS ON ADR REPORTING

Table 4.3.1 presents the percentage of participants who encountered and reported ADRs they encountered.76.7% of participants said that they never reported ADRs that the encountered and 58.6% said they never encountered an ADR before

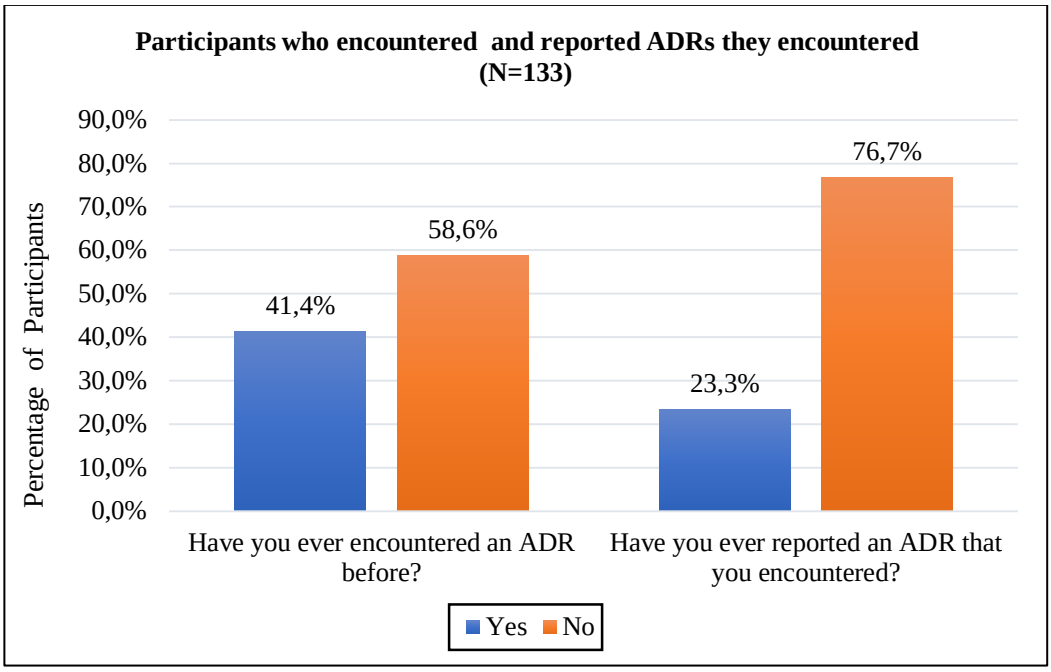


Figure 4.3.1: Adverse drug reactions encountered and reported by participants

Table 4.3.1 shows the relationship between ADRs that were encountered and those that were reported. A test for association using the Pearson Chi-square test was performed, and there was a statistically significant association between encountering and reporting an ADR. *($p<0.05$)*

Table 4.3.1: Encountered versus reported ADRs (N=133)

Have you ever encountered an ADR before?	Have you ever reported an ADR that you encountered?		Total
	Yes	No	
Yes	29(93.5%)	26(25.5%)	55(41.4%)
No	2(6.5%)	76(74.5%)	78(58.6%)
Total	31(100%)	102(100%)	133(100%)

Pearson Chi-square = 45.406, p value = 0.000, The results significant at p<0.05

Table 4.3.2. Shows the frequency distribution of the participants on the number of ADRs reports submitted over a given time period.Of the 133 participants 98 said they never submitted an ADR report before at any given time.

Table 4.3.2: Average number of ADR reports submitted over a given time (N=133)

How many ADR reports have you submitted on average?	Frequency	Percentage (%)
Less than 1 in a month	7	5.3
Less than 1 in a year	20	15.0
Between 1-10 in a month	2	1.5
Between 1-10 in a year	6	4.5
None	98	73.7
Total	133	100

Table 4.3.3 shows the results of an association between attending a seminar or training and the average number of reports submitted.To test for the association, a Pearson Chi-square test was performed, and the results showed a statistically significant relationship *(p<0.05)*

Table 4.3.3: Number of ADR reports submitted based on attending a seminar or training (N=133)

How many ADR reports have you submitted on average?	Have you ever attended a seminar or training on ADR reporting?		Total
	Yes	No	
Less than 1 in a month	5 (14.3%)	2 (2%)	7 (5.3%)
Less than 1 in a year	10 (28.6%)	10 (10.2%)	20 (15%)
Between 1-10 in a month	0	2 (2%)	2 (1.5%)
Between 1-10 in a year	2 (5.7%)	4 (4.1%)	6 (4.5%)
None	18 (51.4%)	80 (81.6%)	98 (73.7%)
Total	35 (100%)	98 (100%)	133 (100%)

Pearson Chi-square = 17.192, p value = 0.002, The results significant at p<0.05

Table 4.3.4 shows the results of mean scores observed on Likert items measuring the importance of reporting ADRs. The observed overall mean score was 4.67 with a Standard deviation of 0.63.

Table 4.3.4: Importance of reporting ADRs

Statement	1	2	3	4	5	M	SD
To identify new ADRs	1	3	8	21	100	4.62	0.765
To improve patient safety	1	0	0	12	120	4.88	0.444
To measure the incidence of ADRs	0	0	6	27	100	4.71	0.547
To share information about ADRs with colleagues	0	0	7	38	88	4.61	0.588
To identify safe drugs	0	1	2	21	109	4.79	0.493
It is a requirement	5	2	8	35	83	4.42	0.955
	Average					4.67	0.63

1=Not important, 2=Slightly important, 3=Important, 4=Fairly important, 5=Very important, M=Mean, SD=Standard deviation

Figure 4.3.2 shows the participants' responses on the question, "when are you most likely to report an ADR?'', and 72% indicated that they would report it as soon as they encounter it, with 24% not sure if they would at all report.

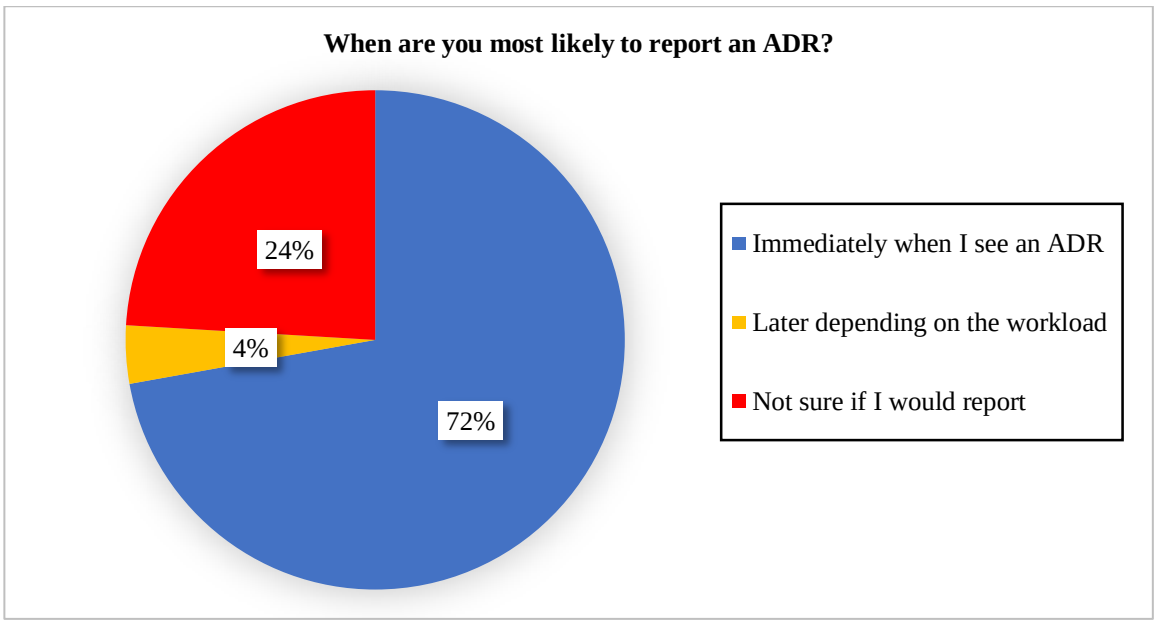


Figure 4.3.2: The timing of reporting adverse drug reactions

Figure 4.3.3 shows some of the factors that discourage participants from reporting ADRs, and 54.9% indicated that nothing discouraged them from reporting and 21.8% said workload and administrative issues.

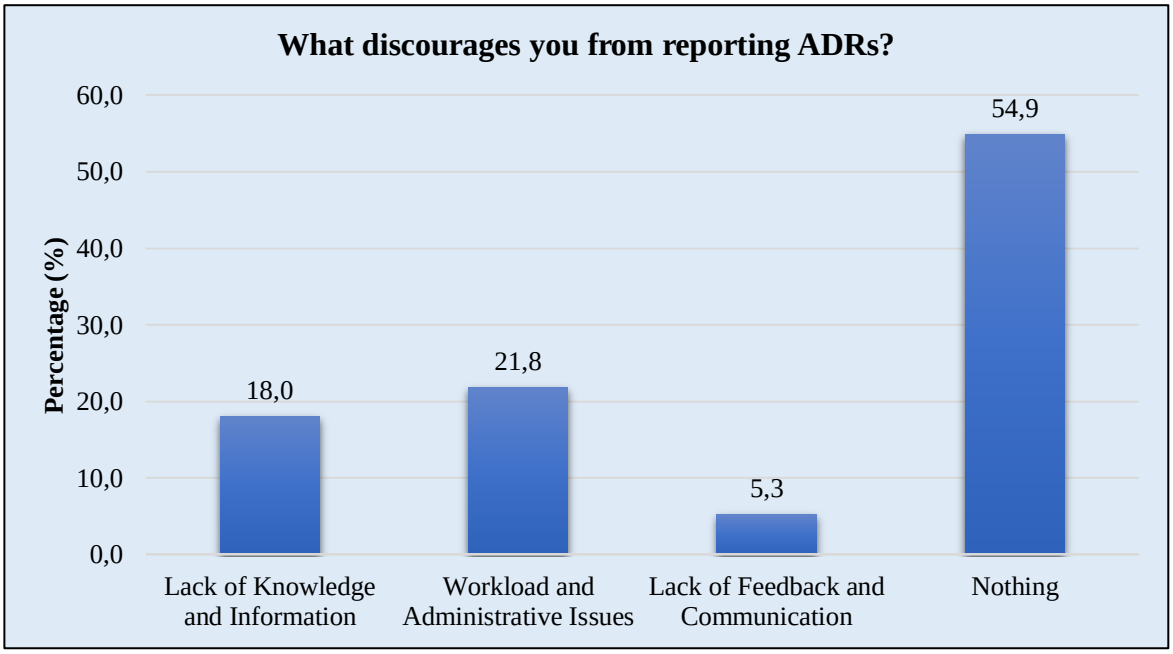


Figure 4.3.3: Factors that discourage healthcare professionals from reporting ADRs

Figure 4.3.4 shows the ADRs that participants felt need to be reported to authorities.40% of participants indicated that life threatening ADRs should be reported

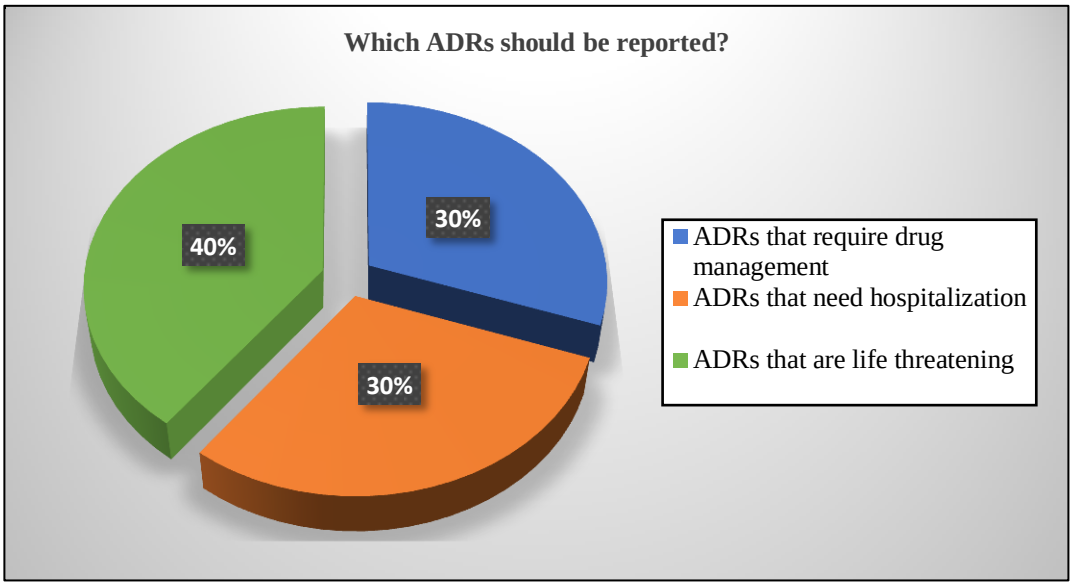


Figure 4.3.4: ADRs that need to be reported

Figure 4.3.5.presents the opinion of participants in terms of which healthcare professionals should report ADRs.76% of participants said all healthcare personnel should report ADRs and only 2% felt pharmacists were the better healthcare professionals suited to report ADRs.

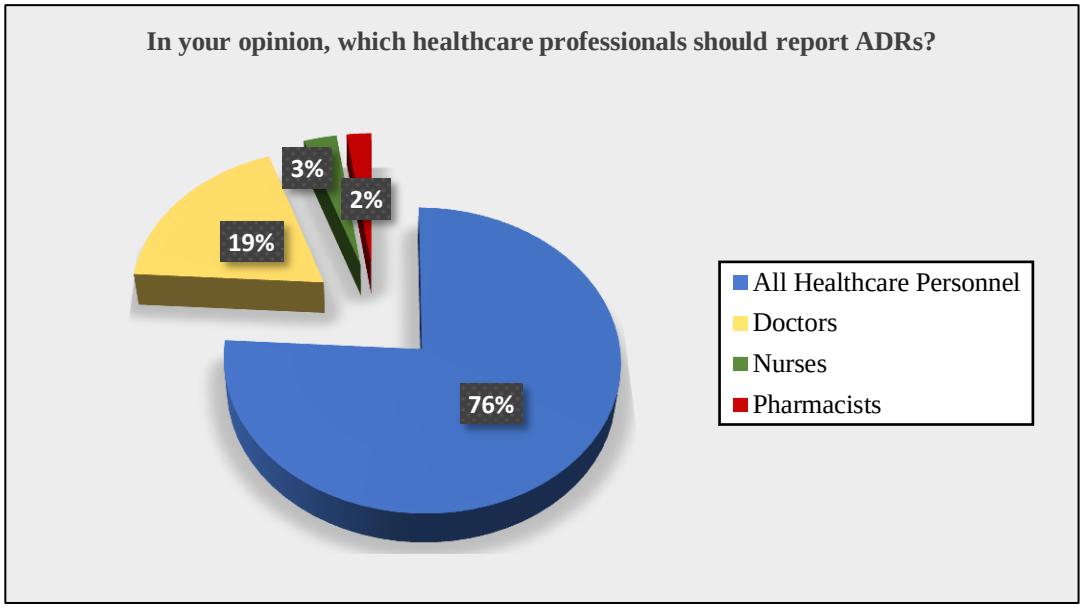


Figure 4.3.5: Healthcare professionals to report ADRs

4.4 PERCEPTIONS OF PARTICIPANTS ON ADR REPORTING

Table 4.4.1 shows the mean scores on Likert scale data on perceptions of HCPs on ADRs reporting and the overall mean score for the perception was 3.07, with a Standard Deviation of 1.17

Table 4.4.1: Perceptions of HCPs on ADRs reporting (N=133)

Statement	1	2	3	4	5	M	SD
ADR reporting is a professional obligation	1	1	22	23	86	4.44	0.848
I know how to report an ADR	39	23	23	32	16	2.72	1.416
I have received sufficient ADR reporting training	84	19	16	6	8	1.76	1.194
I know how to fill in an ADR reporting form	60	21	19	19	14	2.29	1.429
ADRs reporting adds up to unnecessary workload	70	25	22	6	10	1.95	1.248
An allergic reaction to a medicine is an ADR	7	4	24	33	65	4.09	1.125
I always check the patent's allergies before I give them any medicines	4	6	18	36	69	4.20	1.035
I would like to receive more training on ADR reporting	4	0	3	32	94	4.59	0.808
I have seen a patient experience an ADR	34	16	15	29	39	3.17	1.588
Nobody really benefits if I report an ADR	103	16	4	4	6	1.45	1.019
	Average					3.07	1.17

1=Strongly Disagree, 2=Disagree, 3=Neutral, 4=Agree, 5=Strongly Agree, M=Mean, SD=Standard deviation

The results in Table 4.4.2 show the association between interval variables measuring perceptions.Pearson's correlation coefficient was used to determine the strength and direction of the relationship between the variables. There was a positive correlation observed between having received training on ADR reporting and knowing how to fill an ADR reporting form ($r=0.70$, $p<0.05$) which was also found to be statistically significant.

Table 4.4.2: Pearson Correlation of Perceptions of HCPs on ADRs reporting

		A	B	C	D	E	F	G	H	I	J
A	R	1.00	0.20	0.20	0.06	-0.22	0.24	0.02	0.07	0.20	-0.16
	p-value		0.02	0.02	0.49	0.01	0.01	0.84	0.45	0.02	0.06
B	R	0.20	1.00	0.57	0.68	-0.02	0.16	-0.01	-0.15	0.24	-0.02
	p-value	0.02		0.00	0.00	0.78	0.07	0.88	0.08	0.00	0.84
C	R	0.20	0.57	1.00	0.70	0.00	-0.01	-0.06	-0.24	0.25	0.11
	p-value	0.02	0.00		0.00	0.98	0.89	0.51	0.00	0.00	0.21
D	R	0.06	0.68	0.70	1.00	0.10	0.12	0.05	-0.19	0.32	0.04
	p-value	0.49	0.00	0.00		0.25	0.19	0.60	0.03	0.00	0.66
E	R	-0.22	-0.02	0.00	0.10	1.00	-0.14	-0.07	-0.36	-0.20	0.37
	p-value	0.01	0.78	0.98	0.25		0.11	0.39	0.00	0.02	0.00
F	R	0.24	0.16	-0.01	0.12	-0.14	1.00	0.17	-0.12	0.17	-0.02
	p-value	0.01	0.07	0.89	0.19	0.11		0.06	0.18	0.05	0.86
G	R	0.02	-0.01	-0.06	0.05	-0.07	0.17	1.00	0.01	0.08	-0.07
	p-value	0.84	0.88	0.51	0.60	0.39	0.06		0.92	0.33	0.45
H	R	0.07	-0.15	-0.24	-0.19	-0.36	-0.12	0.01	1.00	0.16	-0.63
	p-value	0.45	0.08	0.00	0.03	0.00	0.18	0.92		0.07	0.00
I	R	0.20	0.24	0.25	0.32	-0.20	0.17	0.08	0.16	1.00	-0.13
	p-value	0.02	0.00	0.00	0.00	0.02	0.05	0.33	0.07		0.13
J	R	-0.16	-0.02	0.11	0.04	0.37	-0.02	-0.07	-0.63	-0.13	1.00
	p-value	0.06	0.84	0.21	0.66	0.00	0.86	0.45	0.00	0.13	

r = Pearson Correlation Coefficient, A=ADR reporting is a professional obligation, B=I know how to report an ADR, C=I have received sufficient ADR reporting training, D=I know how to fill in an ADR reporting form, E=ADRs reporting adds up to unnecessary workload, F=An allergic reaction to a medicine is an ADR, G=I always check the patent's allergies before I give them any medicines, H=I would like to receive more training on ADR reporting, I=I have seen a patient experience an ADR, J=Nobody really benefits if I report an ADR

Figure 4.4.1 shows some of the ways suggested when it comes to improving ADRs reporting and 22.8% of participants said training and seminars would improve ADR reporting while 16.6% recommended having monthly meeting of rare ADRs.

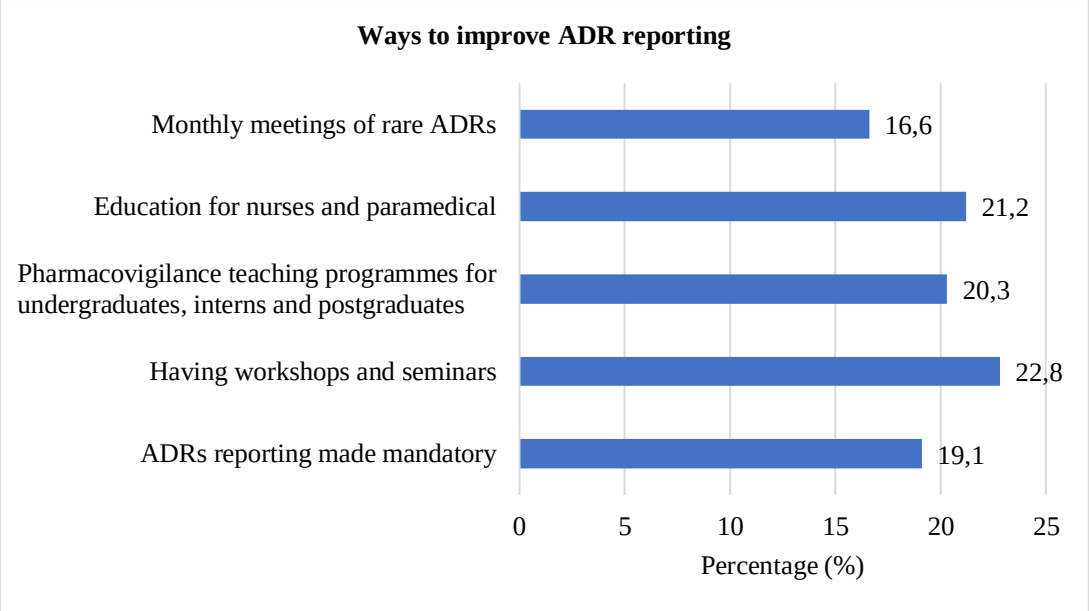


Figure 4.4.1: Ways to improve ADR reporting

CHAPTER 5: DISCUSSION

5.1 DEMOGRAPHICS

The response rate for this study was 51%, which is similar to that observed in studies from Nigeria by Fadare et al. (2011) (59%), Portugal by Herdeiro et al. (2005) (54.3%), and the Netherlands by Passier et al. (2009) (47%).This response rate however presents a challenge on the representativeness of the sample on the population it was drawn from, as it presents a 49% nonresponse bias (Fincham, 2008). In this study, the highest proportion of participants was nurses at 73.7% and a high number of nurse participants was observed in other studies from Pakistan by Hussain et al. (2021) (56.9%) and Uganda by Katusiime et al. (2015) (52.9%).

Nurses form the supporting structure of health systems at all levels of care, as a result, they are employed in high numbers compared to other categories of HCPs. According to the Ministry of Health Botswana Human Resources Strategic Plan for Health (2012), there were 1820 doctors, 9297 nurses, and 764 pharmacists and pharmacy technicians registered with both the Botswana Health Professions Council and Nursing and Midwifery Council of Botswana in 2012. This presented a proportion of nurses across the country of 68%, highlighting the high number of nurses compared to other categories of HCPs.

There were more female participants than males at 66.9% in this study, which is similar to results found by Katusiime et al. (2015) (62.3%) from Uganda, unlike Khan et al. (2013) from India, where there were more male than female participants (48:20). There was no statistically significant association between gender and the professional group the participants belonged to ($p < 0.075$)

5.2 KNOWLEDGE OF ADR REPORTING

There is a lack of knowledge on ADR reporting amongst healthcare professionals which perpetuates the challenge of underreporting as presented in this study Figure 4.2.1. This is supported by the response rate of 26.3% when participants were asked if they had attended a seminar or training before Figure 4.2.1. This provides evidence for

a need to educate HCPs regarding ADR reporting. The findings of the current study were consistent with similar studies by Khan et al. (2013) (25%) and Sabblah et al. (2014) (27.4%).

HCPs' knowledge and awareness of the reporting procedure, impact the overall participation in the reporting of ADR and this directly translates into the observed numbers of reports submitted. In this study, only 39.8% indicated that they had used an ADR reporting form before Figure 4.2.1, which suggests a need to determine if HCPs know how to fill in an ADR reporting form and are aware of the procedure that needs to be followed for reporting. This unfamiliarity with the reporting procedure supports diffidence and fails on HCPs' responsibility of ensuring the safety of the public at all times. This also compromises the spontaneous reporting of ADRs and results in failure to report medications suspected of causing ADRs.

Low reporting rate was observed in other studies by Katusiime et al. (2015) (16.6%), Khan et al. (2013) (19.1%), and Sabblah et al. (2014) (20%). Abjaude et al. (2016) established that one method of reporting (yellow card method) was not as effective in increasing the number of reports and hence suggested the use of other ways to promote the reporting of ADRs.

In this study, 39.8% of the participants indicated that they had seen an ADR reporting form before. On the contrary 64.7% did not know where to find them in their working location. Not knowing where the forms were kept, shows a lack of taking full responsibility for ensuring safe medication use, and there is a likelihood that encountered ADRs would therefore not be reported. Communication and training as part of Standard Operating Procedures implementation could alleviate the challenge of negligence and improve on overall participation by HCPs in the safe use of medication.

Lack of time due to work responsibilities was cited as the reason for not participating in ADR reporting Figure 4.3.4. However, HCPs need to ensure the safety of patients, especially from a Pharmacovigilance perspective at all times. Similar to the findings of this study, Katusiime et al. (2015) reported a 37.7% response on knowledge of ADR reporting forms by HCPs.

The inability to assess and identify an ADR underestimates the importance of medication safety, which renders HCPs unlikely to realize an ADR even when it presents itself and report it. Studies have identified some of the factors that hinder HCPs from reporting ADR to include ignorance, diffidence, lack of interest or time to report, lethargy, indifference, or complacency (Abjaude et al., (2016), Khan et al.,(2013) Sabblah et al.,(2014). However, the number of years of work experience should sensitize HCPs to ADR and instil a sense of commitment to act appropriately but this was inconsistent with the findings of the current study. The HCPs with less than 5 years of work experience (n=20) used an ADR reporting form more than those with longer years of experience and the association between knowledge of using an ADR form and years of experience was found to be statistically significant ($p= 0.008$) Table 4.2.4. This was also reported by Hussain et al. (2021) where 51.4% of the participants had less than 5 years of work experience.

The proportion of pharmacists who participated in this study was 1.5% and that of pharmacy technicians was 4.5%. A low participation rate of pharmacists was also observed by Katusiime et al. (2015) (3.6) % and Nisa et al. (2018) (3.6%). This shows how the pharmacy personnel fail to recognize their role in ensuring medication safety. It was reported in Ghana that there were 619 pharmacists to 2.9 million people, this was just to highlight the skewness in the distribution of pharmacists to patients and how this remains a challenge in developing countries (Owusu-Daaku et al., 2008). Pharmacists are the custodians of medications and therefore their knowledge of ADR reporting is crucial in upholding and enforcing the principles of PV when it comes to medication safety. Khan et al. (2013), Olsson et al. (2015) suggested the inclusion of PV in undergraduate curriculum to increase the awareness amongst HCPs.

The Botswana Medical Regulatory Authority (BOMRA) is the main reporting centre in the country, however, some hospitals have been identified as collection points for ADR reports, which collect and organize reports for submission to BOMRA. HCPs' awareness of the procedures within the reporting system should be increased in order to encourage ADR reporting. This needs to be explored further to determine HCPs' awareness of the reporting system and recommendations made to improve the reporting behavior amongst HCPs.

Lack of knowledge in terms of how, where, when, and whom to report discourages HCPs from participating in ADR reporting. This is demonstrated by the responses given by the participants when asked to identify where the ADR reports should be reported, whereby 35.1% indicated the Princess Marina Pharmacovigilance Centre as the place to report and 27.9% indicated BOMRA. The results were consistent with other studies by Chopra et.al. (2011) (30%) and Shailesh et al. (2013) (25%).

5.3 ATTITUDES ON ADRs REPORTING

The participants showed a positive attitude when asked when they would report an ADR, with 72% of them saying immediately when they see an ADR, as much as it was encouraging, only 23.3% reported those ADRs they encountered. This shows a gap between willingness to report and knowledge of how to report, which needs to be addressed to promote ADR reporting behaviour. The association between an ADR encounter and reporting it was found to be statistically significant ($p< 0.05$).

The findings of this study show that HCPs have a positive attitude toward ADR reporting, as indicated by the overall importance of reporting (Mean(M)=4.67, Standard Deviation(SD)= 0.63). HCPs rated professional obligation high (M=4.4.2, SD=0.63) which then suggests the awareness of professional responsibility when it comes to medication safety. Some of the reasons for reporting ADRs by HCPs were to improve patient safety (M=4.88, SD=0.444) and identify new drugs (M=4.62, SD=0765). These reasons were also mentioned in similar studies such as Abjaude et al. (2016), Desai et al. (2011) and Hussain et al. (2021).

It is worth noting that 54.9% of the participants had no interest to report which is worrisome as HCPs play a vital role in ensuring the safety of medication in patients. Some of the reasons provided for not reporting are lack of knowledge (18%) and workload (21.8%). It becomes imperative to determine ways of motivating and giving incentives to HCPs in an effort to improve ADR reporting (Fadare et al., (2011). When asked which ADRs should be reported, 40% said ADRs that are life-threatening, and 30% said those that require drug management and hospitalization.

The challenge in this regard is failure to report any suspected ADRs exposes patients to further harm and promotes diffidence and a lack of responsibility amongst HCPs. HCPs need to be made aware that every suspected ADR matters even when certainty of causality cannot be proven. The responsibility of reporting should be shared amongst HCPs and 76 % of participants said all HCPs should report and only 2% said pharmacists should be the ones reporting, which indicates a lack of awareness amongst HCPs on the roles of the different professions within the healthcare system. Sabblah et al., (2014) observed 96.4% of HCPs agreeing that it is their responsibility to report ADRs.

5.4 PERCEPTIONS ON ADR REPORTING

Since perception is created based on prior exposure and influenced by attitudes, it becomes necessary to increase the motivation of HCPs in order to promote reporting behaviour, through providing information and communication using reliable sources. HCPs had positive perceptions of ADR reporting (M=3.07, SD=1.17).

Recommendations were made in terms of ways of improving reporting, and continuous education for HCPs were cited across similar studies: Abjaude et al., 2016; Bisht et al. (2014) and Desai et al., (2011).In the current study, 21.2% of participants said educating the nurses and the paramedical professionals, and 22.8% mentioned having workshops and training as some of the ways of improving ADR reporting. Lack of knowledge and need for training for HCPs to equip them with the necessary skills is important for increasing efforts of Spontaneous reporting of ADRs. Katusiime et al., (2015), found that 56.5% of the HCPs stated that a lack of training to equip HCPs with PV results in a low reporting rate. Bisht et al. (2014) found out that continuous educational intervention has a positive effect on the reporting of ADRs, as much as it does not always translate to improved practice. Since perceptions are motivated by the experience of what is taught, it is important to educate HCPs to motivate them to improve reporting behaviour.

Having been provided with the necessary education on ADR reporting will likely increase familiarity with the ADR reporting form and this can impact positively on the overall reporting. There was a high association observed between knowing how to fill an ADR reporting form and having received sufficient training on ADR reporting($r=0.70$, $p<0.05$).

CHAPTER 6: RESEARCH LIMITATIONS

Staff establishment at the hospital where the research took place could not be made available to third parties. The sample size calculation for this study was based on previous research at the same hospital, which could have changed over time, resulting in misleading inferences made about the population.

CHAPTER 7: RECOMMENDATIONS

The results of the current study show that there is a lack amongst HCPs on knowledge and practice of PV and further research could be done to explore the benefits of educating HCPs on PV in order to bridge knowledge gaps and suggest ways of correcting current practices not in line with PV.

CHAPTER 8: CONCLUSION

Safe medication use in patients for optimal health outcomes can be achieved through the active participation of HCPs in the delivery of care. When treatment outcomes are compromised as a result of ADRs, it becomes imperative to reduce or avoid their occurrence by reporting suspected medications that could be giving rise to these ADRs.The responsibility of reducing ADRs lies with HCPs' skill to identify and report suspected medications to authorities. Globally there is a challenge of underreporting of ADRs by HCPs especially in developing countries, due to a lack of expertise and human capital within PV systems to perform duties adequately. Spontaneous reporting becomes the ideal way to use for curbing underreporting and upholding the principles of PV. However, lack of knowledge of ADR reporting amongst HCPs contributes to the use of unsafe medications by the public, as a result, morbidity and mortality due to the suspected medication.

When there is a lack of knowledge on reporting ADRs, even if HCPs perceive ADR reporting to be important it becomes nearly impossible to participate in such, as causality cannot be ascertained, and this instils a sense of hesitancy in HCPs to report. Positive attitudes as well are not enough to motivate improved patient safety through reporting ADRs. It is, therefore, necessary for on-going educational programmes to be implemented in the workplace to encourage reporting behaviours amongst HCPs and increase awareness of PV. Studies are needed to determine the effects of education and training intervention on reporting behaviour amongst HCPs and also the discrepancies in the practice of PV, based on the HCPs' current practice.

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APPENDICES

APPENDIX A: QUESTIONNAIRE

Knowledge, attitudes, and perceptions of Healthcare Professionals on Adverse DrugReactions Reporting in a government hospital in Botswana

Please take a few minutes to answer the following questions on Adverse Drug Reactions(ADRs) reporting and feel free to elaborate where applicable.

1. What is your profession? (please tick the one applicable to you)

General practitioner	
Medical specialist	
Nurse	
Pharmacist	
Pharmacy technician	

2. Which ward/department do you work in?

Pulmonary	
Renal	
ICU	
Gastroenterology	
Ophthalmology	
Oncology	
Orthopaedic	
Dentistry	
Pharmacy	

Surgical	

3. What is your gender?

Male	
Female	

4. For how many years have you been practicing?

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5. How old are you?

---

6. Have you ever attended a seminar or training on Adverse Drug Reactions reporting?

Yes	
No	

7. Have you ever seen an ADR reporting form before? **Please refer to the form attached on the last page. (Appendix B)**

Yes	
No	

8. Do you know where to find an ADR reporting form in your department?

Yes	
No	

9. Are ADR reporting forms available in your department?

Yes	
No	

10. Have you ever used an ADR reporting form before?

Yes	
No	

11. To whom should you report ADRs? You may cross/tick more than one box.

Botswana Medical Regulatory Authority	
Princess Marina Pharmacovigilance Centre	
Hospital Pharmaceutical and Therapeutics Committee	
Hospital Safety and Quality Subcommittee	
Other	

If you selected "other", please specify:

_____

12. Have you ever encountered an ADR before?

Yes	
No	

13. Have you ever reported an ADR that you encountered? If you answered "no", skipquestion 14)

Yes	
No	

14. How many ADRs reports have you submitted that you encountered?

At least 1 in a month	
At least 1 in a year	
Between 1-10 in a month	
Between 1-10 in a year	

15. Why is it important to report ADRs? Please rate on a scale of 1 to 5, 1 being notimportant and 5 being very important.

Reason	1	2	3	4	5
To identify new ADRs					
To improve patient safety					
To measure the incidence of ADRs					
To share information about ADRs with colleagues					
To identify safe drugs					
It is a requirement					

16. When are you most likely to report an ADR?

_____

17. What discourages you from reporting ADRs?

18. In your view, which ADRs should be reported?

ADRs that require drug management	
ADRs that need hospitalization	
Life-threatening ADRs	
Other (Specify)	

If you selected other, please specify

19. In your opinion, which healthcare professionals should report ADRs?

20. Do you agree or disagree with the following statements? Please rate on a scale of 1 to5, whereby 1 strongly disagrees, 2 disagree, 3 neutral, 4 agree and 5 strongly agree.

STATEMENT	1	2	3	4	5
ADR reporting is a professional obligation					
I know how to report an ADR					
I have received sufficient ADR reporting training					
I know how to fill in an ADR reporting form					
ADRs reporting adds up to the unnecessary workload					
An allergic reaction to a medicine is an ADR					
I always check the patient's allergies before I give them any medicines					
I would like to receive more training on ADR reporting					

I have seen a patient experience an ADR					
Nobody really benefits if I report an ADR					

21. How can reporting of ADRs be improved? You may cross/tick more than one box.

ADRs reporting made mandatory	
Having workshops and seminars	
Pharmacovigilance teaching programmes for undergraduates, interns, and postgraduates	
Education for nurses and paramedical	
Monthly meetings of rare ADRs	
Other	

If you selected “other”, please specify:

Thank you for your cooperation

APPENDIX B: ADVERSE DRUG REPORTING FORM



NATIONAL PHARMACOVIGILANCE CENTRE, BOTSWANA

<table>
<tr><td colspan="7">ADVERSE REACTIONS REPORTING FORM</td></tr>
<tr><td colspan="7">I. PATIENT INFORMATION:</td></tr>
<tr><td colspan="7">Patient identity/Omang number: Age(yrs.): Sex(M/F):
Weight(kgs): Ethnicity:</td></tr>
<tr><td colspan="7">II. SUSPECT MEDICATION(S)/VACCINE/HERBAL:</td></tr>
<tr><td rowspan="2">List of drugs being used by the patient (please tick the suspect drug)</td><td rowspan="2">Route</td><td rowspan="2">Dail y Dose</td><td rowspan="2">Manufacturer</td><td colspan="2">Date Drug</td><td rowspan="2">Reason sfor Use</td></tr>
<tr><td>Started</td><td>Stopped</td></tr>
<tr><td></td><td></td><td></td><td></td><td></td><td></td><td></td></tr>
<tr><td></td><td></td><td></td><td></td><td></td><td></td><td></td></tr>
<tr><td></td><td></td><td></td><td></td><td></td><td></td><td></td></tr>
<tr><td></td><td></td><td></td><td></td><td></td><td></td><td></td></tr>
<tr><td colspan="7">III. ADVERSE REACTION EXPERIENCED/OBSERVED:</td></tr>
<tr><td colspan="2">Date of onset of Reaction:</td><td colspan="4">Reaction Subsided after Suspect Drug Discontinuation:</td><td>Rechallenged?</td></tr>
</table>

Description of Adverse Event: **(including laboratory test** **results)**			
Outcome:	Recovered Death(D/M/Y)	Hospitalized Unknown	Disability
Treatment for Reaction:			
Results:			
Other Pre-existing medical conditions: (E.g. Allergies, Pregnancy, Smoking, Alcohol, Hepatic/Renal Dysfunction, others)			
Additional Information: (if any)			
IV. REPORTER:			
Name & Professional Address :			
Telephone No. Yes No	**Occupation & Specialty:**		**Health professional:**
Signature:	**Date:**		
For office use only:			
Received on:	Registration No.		Received by:

APPENDIX C: PARTICIPANT INFORMATION SHEET





Dear potential participant

My name is Lineo Lipholo. I am a Master of Pharmacy student at University of the Witwatersrand, Johannesburg. As part of the requirements for my degree, I am expected to do research on a particular topic and I have decided to conduct a research study on knowledge, attitudes and perceptions of healthcare professionals on adverse drug reactions reporting.

I am inviting you to take part in this study by completing a questionnaire and should you decide to take part, your participation in this research study will only take about 10 minutes of your time. The completion of the questionnaires will take place here at Princess Marina hospital during working hours and it is expected to last for a period of 2 weeks, in order to reach every participant in the study.

Once the questionnaires have been completed and collected, they will be stored securely in a locked box that is only accessible to the researcher, for a period of 2 years after which they will be destroyed or deleted. On the questionnaires, I will need to ask for some personal information about you, including your age, profession, years of employment as well as gender. This data will be kept confidential and anonymity will be maintained.

When I share the results of the research study, I will not include your name or anything else that could identify you. With your permission, other researchers may use the data collected from this study, they will however be expected to apply for ethics clearance from their applicable research committees and authorities to access such, and your personal information will be passed on.

If you decide to take part in the research study, it should be because you want to volunteer and should you decide to withdraw from this study, you are free to do so at any stage of the study, up to the submission of the questionnaires, in which case the questionnaire you filled will be eliminated from the findings of the study, unless your consent to retain them is granted. Participation or non-participation in this study, carries no implications on your employment status, and will not cost you anything nor will it make you lose any services, benefits or rights you would normally have.

This research study will be written up as a research report and the findings will be made available on the university library website, and also to the management of Princess Marina hospital. If you would like to receive a summary of this report, I will be happy to send it to you.

This study has been approved by the Human Research Ethics Committee (Medical) of the University of the Witwatersrand Johannesburg and Princess Marina Hospital IRB Committee. The principal function of this Committee is to safeguard the rights and dignity of all human subjects who agree to participate in a research project and the integrity of the research.

If you have any concerns over the way the study is being conducted, please contact the chairperson of the Committee who is Dr Clement Penny, who may be contacted on telephone number +27 11 717 2301, or by email Clement.Penny@wits.ac.za. The telephone numbers for the Committee secretariat are +27 11 717 2700/1234 and email addresses are Zanele.Ndlovu@wits.ac.za and Rhulani.Mukansi@wits.ac.za.

If you have any questions during or afterwards about this research study, feel free to contact me or my supervisor on the details listed below.

Contact details of researcher:
Lineo Lipholo
Email: 763720@students.wits.ac.za
Tel: + 267 72911143

Supervisor contact details:

Associate Professor Neelaveni Padayachee

Email: neelaveni.padayachee@wits.ac.za

Tel: +27 11 717 2269

Thank you very much for your time.



Yours sincerely,

APPENDIX D: TURNITIN RECEIPT

turnitin

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This receipt acknowledges that Turnitin received your paper. Below you will find the receipt Information regarding your submission.

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File size:	10
Page count:	2,421
Word count:	13,970



TITLE To determine the knowledge, attitudes and perceptions of Healthcare Professionals on Adverse Drug Reactions reporting in a provincial hospital in Botswana.

INVESTIGATORS CONTACT DETAILS

Lineo Lipholo-Mphetolang

Email 783720@students.wits.ac.za

Cell: 076 972 4687

INTRODUCTION/BACKGROUND

According to the World Health Organization (WHO), pharmacovigilance (PV) is defined as "the science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other drug-related problems"[1]. The objectives of PV are to improve patient care through proper use of medicines and promote understanding in healthcare professionals and the public in medicine safety.[1,2]

Pharmacovigilance came to being, after the 1961 worldwide thalidomide tragedy, which saw babies born, with limb deformities (phocomelia), due to the use of the drug by pregnant women to treat nausea and vomiting, at the early stages of pregnancy.[2,3]Prior to this there was no formal system in place for monitoring medicine safety after release into the public, except for letters and concerns raised to pharmaceutical companies by clinicians. After the thalidomide tragedy, in many developed countries, pharmacovigilance systems were put in pace to monitor and evaluate medicine safety.[2,3]

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APPENDIX E: SIMILARITY REPORT

To determine knowledge, attitude and perceptions of healthcare professionals on Adverse Drugs Reactions reporting in a provincial hospital in Botswana

ORIGINALITY REPORT

11%	8%	8%	4%
SIMILARITY INDEX.	INTERNET SOURCES	PUBLICATIONS	STUDENT PAPERS

PRIMARY SOURCES

1 Yashmay Gordhon, Neelaveni Padayachee. "Evaluating the knowledge, attitudes and practices of healthcare workers towardsadverse drug reaction reporting at a public tertiary hospital in Johannesburg", International Journal of Africa Nursing Sciences, 2020 Publication	1%
2 www.hindawi.com Internet Source	1%
3 hdl.handle.net Internet Source	1%
4 clinicalsafetygeek.com Internet Source	1%
5 "Mann's Pharmacovigilance", Wiley, 2014 Publication	1%
	1%

6 Sophia Bogolubova, Neelaveni Pa. dayachee, Natalie Schellack. "Knowledge, attitudes and practices of nurses and pharmacists towards adverse drug reaction reporting in the South African private hospital sector", Health SA Gesondheid, 2018 Publication	
7 jurnal.ugm.ac.id Internet Source	1%
8 Submitted to iGroupStudent Paper	1%
9 www.moh.gov.bw Internet Source	1%
10 repository.nwu.ac.za Internet Source	<1%
11 www.jddt.in Internet Source	<1%
12 www.omicsonline.org Internet Source	<1%
13 www.researchsquare.com Internet Source	<1%

Exclude quotes. On Exclude matches Off Exclude bibliography On

APPENDIX F: ETHICS CLEARANCE

UNIVERSITY OF THE WITWATERSRAND JOHANNESBURG

R49 Ms L Lipholo

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)
CLEARANCE CERTIFICATE NO. M221086

NAME: (Principal Investigator)	Ms L Lipholo
DEPARTMENT:	School of Therapeutic Sciences Department of Pharmacy and Pharmacology Medical School University
PROJECT TITLE:	*Knowledge, attitudes and perceptions of healthcare workers of adverse drug reaction reporting in a government hospital in Botswana*
DATE CONSIDERED:	2022/10/28
DECISION:	Approved unconditionally
CONDITIONS:	
NOTE:	If contact information regarding student study participants is required, please contact the Registrar's office - <Nicoleen.Potgieter@wits.ac.za>
SUPERVISOR:	Dr N Padayachee
APPROVED BY:	Dr CB Penny, Chairperson, HREC (Medical)
DATE OF APPROVAL:	2023/05/11

This Clearance Certificate is valid for 5 years from the date of approval. An extension may be applied for.

DECLARATION OF INVESTIGATORS

To be completed in duplicate and **ONE COPY** returned to the Research Office secretariat on the 3rd floor, Phillip Tobias Building, Parktown, University of the Witwatersrand, Johannesburg.

I/we fully understand the conditions under which I am/we are authorized to carry out the above-mentioned research and I/we undertake to ensure compliance with these conditions. Should any departure be contemplated from the research protocol as approved, I/we undertake to submit details to the Committee. **I agree to submit a yearly progress report**. When a funder requires annual re-certification, the application date will be one year after the date when the study was initially reviewed. In this case, the study was initially reviewed in **October** and therefore reports and re-certification will be due in the month of **October** each year. Unreported changes to the study may invalidate the clearance given by the HREC (Medical).

Signature of Principal Investigator

22/05/2023
Date

APPENDIX G: HOSPITAL APPROVAL LETTER

PLOT 1836 HOSPITAL WAY
TELEPHONE: 3621400
FAX: 3973776

REPUBLIC OF BOTSWANA

PRINCESS MARINA HOSPITAL
P.O. Box 258
GABORONE

BOTSWANA

28 June 2022

Protocol Reference: PMH 2/2A(7)/210

Principal Investigators: Dr Lineo Lipholo-Mphetolang

Study Title: Knowledge, Attitudes and Perceptions of healthcare professionals on adverse drug reactions reporting in a government hospital in Botswana

Application Type: Initial application
Date of Approval: 28 June 2022
Expiration date: 28 June 2023

Permission is granted by the PMH IRB for you to conduct the above study for a duration of one year, beyond which you will need to submit an application for extension of study period. You need to note the following:

1. You will not change any aspect of your research without permission from the Princess Marina Hospital IRB.
2. You need to report any unforeseen circumstances including the termination of the study.
3. You must allow Princess Marina Hospital IRB access to the study at any time for purposes of auditing.
4. At the end of the study you should give Princess Marina Hospital IRB a hard copy and soft copy of your report.

Wishing you success in your study

Yours Sincerely



Mpapho Motsumi
Chairperson Princess Marina Hospital IRB Committee
Cell: 00267 72858907
Work: 00267 3621400
Email: josephmotsumi@yahoo.com