International Journal of Africa Nursing Sciences 12 (2020) 100191

Contents lists available at ScienceDirect

International Journal of Africa Nursing Sciences

journal homepage: www.elsevier.com/locate/ijans

Evaluating the knowledge, attitudes and practices of healthcare workers towards adverse drug reaction reporting at a public tertiary hospital in Johannesburg

Yashmay Gordhon*, Neelaveni Padayachee

Faculty of Health Sciences, School of Therapeutic Sciences, Department of Pharmacy and Pharmacology, University of Witwatersrand, 7 York Road, Parktown, Johannesburg 2193, South Africa

ARTICLE INFO

Keywords:
Pharmacovigilance
Adverse drug reaction reporting
Medicine safety
Healthcare professionals

ABSTRACT

Background: Spontaneous reporting of adverse drug reactions is a method of monitoring the safety of drugs post-marketing, providing a way to discover new, rare or unnoticed adverse drug reactions. Despite its importance, there is widespread underreporting of adverse drug reactions by health care professionals in South Africa. The study assessed the knowledge, attitudes and practices of health care professionals on adverse drug reaction reporting at a tertiary public-sector hospital in Johannesburg, South Africa.

Methods: A descriptive quantitative study using a questionnaire was conducted at a tertiary public-sector hospital in Johannesburg. A stratified sampling method was used to distribute questionnaires to doctors, nurses and pharmacists at the institution from July to November 2016.

Results: Of the 338 questionnaires sent out, 297 health care professionals responded to the questionnaire (87.87% response rate). Half of the participants knew about reporting adverse drug reactions, and pharmacists were the most likely group to know how to report (82.61%) ($p < 0.001$). Ninety-seven percent of participants who had previously received adverse drug reaction training knew how to report them. Patient management, lack of knowledge and the time-consuming requirement of reporting featured as discouraging factors. Although, 58.59% of participants had encountered adverse drug reactions, only 16.50% had reported ($p < 0.001$).

Conclusions: Despite an awareness of adverse drug reactions, participants were unlikely to report adverse drug reactions due to time constraints and a lack of knowledge. Adverse drug reaction reporting is essential to ensuring patient safety. The benefits of reporting should be emphasized by encouraging continuous professional development in pharmacovigilance and, placing more emphasis on adverse drug reactions at an undergraduate level.

1. Introduction

The safety, efficacy and quality of medicines are essential components to the overall wellbeing of patients. While medicines are intended to heal, treat and prevent ailments, there is no certainty that they won't themselves cause harm. When determining the safety of new pharmaceuticals, testing and clinical trials are conducted. These allow for a range of adverse drug reactions (ADRs) to be identified, some of which occur frequently and others that may be extremely rare. These ADRs are defined as the "response to a drug which is noxious and unintended, and which occurs at doses normally used in man for the prophylaxis, diagnosis, or therapy of disease, or for the modifications of physiological function" (WHO, 1972). Randomized controlled clinical trials have limits on the amount of time during which the drug is tested, and the patients participating; inevitably it cannot be tested on every genetic and ethnic makeup (Keller et al., 2018; Toklu & Soyalan, 2016). Post-marketing monitoring is an important feature of pharmacovigilance as it provides a means by which rare and population specific ADRs can be identified. Pharmacovigilance is defined as the "science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other drug-related problem" (WHO, 2015).

Spontaneous reporting of ADRs refers to the passive reporting of ADRs by healthcare professionals or patients as they witness them (Joubert & Naidoo, 2016). This type of reporting has been the mainstay approach to ADR reporting globally for many years. Active reporting, on the other hand, refers to activities used to "study the causal relationship between medical interventions and harmful effects" through

* Corresponding author.
E-mail addresses: yashmayg@yahoo.com (Y. Gordhon), neelaveni.padayachee@wits.ac.za (N. Padayachee).

https://doi.org/10.1016/j.ijans.2020.100191
Received 7 February 2019; Received in revised form 26 January 2020; Accepted 27 January 2020
Available online 31 January 2020

targeted surveillance (Huang, Moon, & Segal, 2014). However, more recently the analysis of electronic health records has come into prominence (Huang et al., 2014).

Historically, many life-threatening ADRs were discovered via spontaneous reporting. These include instances such as the development of liver toxicity with troglitazone; aplastic anaemia with felbamate; and fatal rhabdomyolysis with cerivastatin, which were experienced by patients taking these medicines (Ogimura et al., 2017; Thakkar et al., 2015; Chang and Green, 2002; Staffa, Chang, & Green, 2002; Kohlroser, Mathai, Reichheld, & Banner, 2000). Thalidomide became synonymous with pharmacovigilance as it brought attention to the subject of drug safety. In the 1950′s, Thalidomide was put on the market and prescribed to pregnant women after it was said to be "virtually free from side effects" (Lenz, 1988). However, thalidomide resulted in thousands of expectant mothers devastatingly giving birth to babies with a congenital defect called phocomelia, in which babies are born with underdeveloped limbs (Miller, 1991; McBride, 1961). This tragedy resulted in the establishment of the World Health Organisation (WHO) Programme for International Drug Monitoring (WHO, 2002). In 1978, all operational responsibilities were directed through the Uppsala Monitoring Centre (UMC), which holds an international database of ADRs, and plays a prominent role in signal detection and safety research (UMC, 2017).

On a clinical level, the development of pharmacovigilance advisory committees, which can report to the national centre, allows for ease of communication and the ability to deal with issues within the hospital environment. It was suggested at the First International Conference on Improving Use of Medicines (ICIUM) that hospital committees be developed (WHO, 2003). In South Africa, these hospital committees are termed Pharmaceutical and Therapeutics Committees (PTCs), and they deal with "problems of drug selection, procurement, distribution and use" (WHO, 2003). Pharmaceutical and Therapeutics Committees are pharmacist driven committees that are responsible for managing ADRs and managing medication errors, as well as "evaluating the clinical use of drugs" and "managing the formulary" (WHO, 2003). These forums provide a way in which public sector institutions can integrate gathered information, and then report this information to national centres. They also serve as a potential platform for feedback on ADR management at a clinical level. Pharmaceutical and Therapeutics Committees (PTC) have proven effective in improving rational drug use when utilized effectively, and the WHO is committed to promoting the functioning of these committees in developing countries (WHO, 2003). 'The National Policy for the Establishment and Functioning of Pharmaceutical and Therapeutics Committees in South Africa' (2015) published by the National Department of Health outlines the goals, and policies that should be adhered to in order to have an effective PTC. Members of a PTC have a "range of expertise and skills" (National Policy, 2015, pp. 8) to provide a holistic advisory committee. The emphasis on communication between healthcare professionals is important as it allows for thorough clinical problem solving and thus improved patient care.

South Africa's Medicines Control Council (MCC) (currently termed the South African Health Products Regulatory Authority (SAHPRA)) published guidelines on reporting ADRs titled: 'Post-Marketing Reporting of Adverse Drug Reactions to Human Medicines in South Africa'. The document pertains to Regulation 37 issued in terms of the Medicines and Related Substances Act, 1965 (Act 101 of 1965) and outlines clearly the relevant terminology pertaining to ADRs, as well as the process of reporting (MCC, 2017). According to the guidelines, serious and non-serious ADR reports should be submitted within 15 days of a witnessed reaction, using the prescribed national individual case safety report (ICSR) form. This form is termed the 'Adverse Drug Reaction and Quality Problem Report Form', and spontaneous reports are made via this. In the public sector, completed forms are received by the hospital or district PTC, consolidated and forwarded to the provincial PTCs, the National Adverse Drug Event Monitoring Centre (NADEMC) and finally the South African Health Products Regulatory Authority (SAHPRA) (Guidelines for Implementation of Pharmaceutical and Therapeutics Committees in Gauteng Province, 2013). The role of the PTC is to manage the formulary system to include medication-use-evaluation, adverse drug event monitoring, patient safety initiatives and development of clinical care plans and guidelines (Guidelines for Implementation of Pharmaceutical and Therapeutics Committees in Gauteng Province, 2013). The reporting healthcare professional should then be informed of progress and final outcomes to ensure continuity in terms of patient safety, and future ADR monitoring (Mittmann & Knowles, 2009). Strengthening pharmacovigilance has to include a focus on the importance of collaboration through continuous training (Maigetter et al., 2015).

Spontaneous underreporting of ADRs is a problem globally. Underreporting leads to incomplete data and can lead to signals in ADRs that go un-noticed. Healthcare professionals have an ethical responsibility to report ADRs to ensure the safety of their patients. How much information is gathered and duly reported largely depends on the awareness and assertiveness of the professional (Ampadu et al., 2016; Pimpalkhute et al., 2012). The reasons for the underreporting of ADRs by healthcare professionals have been researched globally. Isah et al. list the following reasons for underreporting in Africa: "inability to recognize ADRs, ignorance of the reporting requirements, lack of reporting forms, feeling of guilt following the occurrence of adverse effects and fear of litigation" (2012). These factors cause healthcare professionals to not adhere fully to the framework of reporting, which leads to inadequate or incomplete data.

An important consideration is the disease burden in the country, as well as the type of treatments patients use outside of western medicine such as traditionalmedicine. In South Africa, Human Immunodeficiency Virus (HIV) and Tuberculosis (TB) account for a large patient demographic, and a high incidence of ADRs as a result of the corresponding treatment, which often leads to a further need to monitor patients on their treatment (Mehta et al., 2008). A study conducted by Ampadu et al. found that in 2015 the African continent was responsible for 0.88% of the global number of reports- a fraction of the rest of the world. In 2015, 28,609 Individual Case Safety Reports (ICSRs) were submitted by South Africa, representing 0.24% of the total global reports (Ampadu et al., 2016). Fewer reports by healthcare professionals means that data is often not fed to a national system (Maigetter et al., 2015). There is a lack of collaboration between sectors, particularly the pharmaceutical industry, which leads to a "national database that does not include data from all sources" (Ouma, Africa, & Meeting, 2012). Olsson, Pal and Dodoo conducted a review of pharmacovigilance in resource limited countries and showed that due to the shortage of healthcare professionals in low to middle income countries, the perception is that it's more important to focus on clinically managing the patient than filling out the paperwork involved in spontaneous reporting (Olsson, Pal, & Dodoo, 2015).

The aim of this study was to evaluate the knowledge, attitudes and practices of healthcare professionals in the public sector towards adverse drug reporting.

2. Methods

2.1. Study design

This study was a descriptive quantitative, questionnaire-based study (Edmonds & Kennedy, 2016). A literature review was conducted between January and March 2016 to gain background knowledge on the perceptions of healthcare professionals on ADR reporting globally. A questionnaire was then compiled consisting of questions relating to knowledge, attitudes and practices of healthcare professionals. A total of 21 questions were used based on 3 similar studies (Suyagh, Farah, & Farha, 2014; Pimpalkhute et al., 2012; Desai et al., 2011). In order to achieve the aim of the study, the questions were categorised as follows: 5 questions pertaining to demographics; 7 questions on knowledge; 7

questions about the professional's previous ADR reporting involvement; 1 question pertaining to the professional's general attitude towards ADR reporting and 1 question about possible future improvements that could be made.

2.2. Site selection

A public tertiary hospital in Johannesburg, South Africa was the study site. The hospital employs > 4000 staff and is one of the largest teaching hospitals, serving a population of approximately 10.6 million (in 2016) (CMeRC, 2016). A sample size calculation was done using the number of doctors (623), nurses (2165) and pharmacists (26) employed at the hospital (total = 2814). Using a confidence interval of 0.05 and a 95% confidence level, the appropriate total sample size for this study was 338 for all the relevant healthcare professionals (i.e. nurses, doctors and pharmacists). The number sampled per profession was 238 doctors, 327 nurses and 25 pharmacists. Respondents were made up of pharmacists, nurses and medical doctors who practiced within the main hospital pharmacy and the ten highest volume inpatient wards (i.e. Pulmonology; Oncology; ICU (neonatal and adults); Surgical; Orthopaedic; Renal; Gynaecology; Diabetes; Gastroenterology; Cardiac), as permitted by the site. Subsequent to the approval by the hospital PTC, the study details were communicated to head nurses in the chosen wards. They were then responsible for announcing the study and requesting participation by doctors and nurses. All interested participants collected and subsequently returned the questionnaires to an assigned study box that was located in each of the chosen wards. The pharmacists on the other hand were easily accessible and were approached at a meeting, and all interested parties were invited to participate. A stratified sampling method was applied and only doctors, nurses and pharmacists from the chosen sites were invited to participate.

2.3. Inclusion criteria

- All qualified and registered medical doctors, nurses and pharmacists practising in the ten chosen wards in 2016/ 2017, including interns (those completing their practice training year(s) after completing their qualification) and those conducting community service (a mandatory year of work in the South African public sector after the completion of internship).
- Respondents who consented participation in the study.

2.4. Exclusion criteria

- Healthcare professionals other than doctors, nurses and pharmacists were excluded from the study.
- Basic and post-basic pharmacists were not included in the study.
- Those who did not consent to participate were not included in the study.

2.5. Data collection

Participation in the questionnaire occurred over the period between July and November 2016, in which the hard copies of the questionnaires were disseminated and collected. The questionnaires were distributed to pharmacists, and to head nurses at wards, who distributed and collected the questionnaires within their departments. Reminders were sent to heads of department beforehand to ensure that staff members were made aware of the study. Those who chose to respond were required to complete the informed consent form and were given appropriate instructions for filling out the questionnaire. They were guaranteed anonymity with regards to their questionnaire responses, in that no personal or identifiable information was asked to be disclosed. Only the researchers involved had access to the questionnaires after they were completed.

2.6. Data analysis

Data was collected in the form of the hard copy questionnaire responses from pharmacists (n = 24), doctors (n = 41) and nurses (n = 230). The data was then electronically captured onto spreadsheets on Microsoft Excel™. The questionnaire responses were categorized in terms of: the demographics of the person participating; the current knowledge of the respondent; the attitude of the professional towards pharmacovigilance; any practice the respondent may have had in the form of prior pharmacovigilance involvement; and the need for further pharmacovigilance training or other suggestions. The data captured on Microsoft Excel™ spreadsheets was imported on Stata® (Version 14). Pearson chi squared and Fishers tests were run in order to discover significant associations in the data.

2.7. Ethical considerations

The questionnaire remained anonymous and confidential throughout, with only the researcher having access to the forms. Hospital approval for the conduction of the study was given in 2016 and Ethics approval was consequently granted by the University of the Witwatersrand Human Research Ethics Committee (HREC) (No. M160246).

2.8. Validity of the study

The sample for the study was all participating medical doctors; nurses and pharmacists working within the 10 chosen wards and the hospital pharmacy, representing the overall study population of the healthcare professionals at the study site. Conclusions drawn in this study are specific to the hospital site, and therefore generalisations made pertain only to the study population.

Face validity was achieved in that the objectives of the study were appropriately measured using the methodology, which was adapted from previous similar studies. The questionnaire was validated using a group of 10 randomly selected pharmacists, who were not included in the study. The questionnaire was piloted once, and again one month later in order to ensure validity and eliminate bias. All the questionnaire responses were analysed to yield an understanding of relevant and irrelevant questions. No significant changes were made to the questionnaire after the pilot, only minor grammatical changes were made. The questionnaire was adjusted appropriately to obtain a final version for distribution.

The primary consideration in this section was the effects of social interaction on the study. The study assessed three separate groups of healthcare professionals (doctors; nurses and pharmacists) in the questionnaire. Knowledge that the study was happening may have affected the respondent's responses in anticipation of what the study involved. Those that chose to respond to the questionnaire may have done so with some level of bias.

With regards to relationships among quantitative data, chi-squared tests were used to prove the statistical significance of any relationship that occurred between variables.

2.9. Reliability and dependability of the study

The study could be easily reproduced in a different study population in order to assess the knowledge, attitudes and practices of healthcare professionals in other settings. However, it is not necessarily expected that the results will be consistent in another setting, although similarities may occur, based on the literature review of similar studies and their results.

Table 1
Frequency distribution of the demographics of respondents (N = 297).

Demographic characteristics	Frequency (N)	Percentage (%)
Gender		
Male	48	16.16
Female	249	83.84
Total	**297**	
Profession		
Doctor	41	13.80
Nurse	230	77.44
Pharmacist	24	8.08
Total	**295 (* = 2)**	
Level of Practice		
Intern	27	9.09
Community Service	28	9.43
Post- community service	144	48.48
Total	**199 (*= 98)**	
Years of Practice		
<1 year	34	11.45
1–5 years	83	27.95
6–10 years	106	35.69
>10 years	68	22.90
Total	**291 (* = 6)**	

* = missing data.

3. Results

3.1. Demographics

297 questionnaires were returned out of the 338 questionnaires distributed, to yield an 87.87% response rate. The majority (84%) of respondents were female. The respondents were made up of 41 doctors (response rate of 17%); 230 nurses (response rate of 70%); 24 pharmacists (response rate of 96%) and 2 respondents did not indicate their profession. Most respondents (36%) had 6–10 years of experience (Tables 1 and 2).

3.2. Knowledge of the healthcare professionals about adverse drug reporting

Approximately half of the respondents (50%) stated they knew how to report an ADR, and most (77%) stated that they were familiar with the adverse drug reporting form. Respondents favoured all the options as the reasons for the importance of ADRs, with patient safety (94%) featuring as the most important concern.

In Table 3, more than half (54%) of the nurses were unaware of how to report an ADR, while 54% of doctors and 83% of pharmacists stated they knew how to report.

Table 4 shows the relationship between knowledge and the years the respondents had been practicing. One hundred and six respondents had been practicing as a healthcare professional for 6–10 years, which makes up 36% of the total study population. Half (54%) of the respondents in this group knew how to report, particularly the process of reporting, while respondents who were new to practicing (<1 year) (11% of the total population) had little knowledge of reporting (77%). Table 5 shows a similar result. Fifty-eight percent of post-community service respondents knew how to report ADRs, whereas only 23% of the total interns knew how to report ADRs. This shows a relationship between the level of practice and the knowledge of ADR reporting, as those that have completed training have more knowledge on ADR reporting.

3.3. Attitudes of the respondents

Table 6 shows the frequency distribution of the results pertaining to the attitudes of the respondents towards pharmacovigilance. Most respondents (90%) stated they would report an ADR based on the seriousness of the reaction. However, not knowing how to report; not knowing where to report; managing the patient being more important, and reporting being time-consuming were factors that discouraged reporting. Fig. 1 shows that 93% of respondents felt medical practitioners should be held responsible, followed by nurses and pharmacists. This was further broken down in Fig. 2, which shows the profession of participant and corresponding response of who should report. Every group of healthcare professionals believed that doctors should be held responsible for reporting before other health care professionals. Interestingly, 91% of nurses chose themselves as the responsible professional when it comes to reporting ADRs. The most common reference for ADR reporting used was the internet (80%).

Table 2
Frequency distribution of respondents knowledge of pharmacovigilance (N = 297).

Responses	Frequency (%)	Percentage (%)
Knowing how to report an ADR		
Yes	149	50.17
No	145	48.82
Total	294 (* = 3)	
Familiar with the reporting form		
Yes	229	77.10
No	65	21.89
Total	294 (* = 3)	
Where to Report ADRs		
The National Adverse Event Monitoring Centre (NADEMC)	176	59.26
Pharmaceutical and Therapeutics Committee (PTC)	145	48.82
The Medicines Control Council (MCC)/ SAHPRA	143	48.15
Medical Supply Depot (MSD)	38	12.79
The Safety and Quality Subcommittee	70	23.57
Other	12	4.04
“Doctor and Pharmacy in Hospital”	3	
“Pharmaceutical Company”	1	
“The Drug Controller”	2	
“Supplier”		
Total	584	
Why it's Important to Report ADRs		
To identify new ADRs	1375	92.59
To improve patient safety	1401	94.34
To measure the incidence of ADRs	1376	92.66
To share information about ADRs with colleagues	1347	90.71
To identify relatively safe drugs	1357	91.38
It is a requirement	1315	88.55

* = missing data.

Table 3
Knowledge of how to report ADRs by profession (N = 292).

Profession of respondent				
Response	Doctor	Nurse	Pharmacist	All
Yes	23 (53.49%)	105 (46.46%)	19 (82.61%)	147 (50.34%)
No	18 (41.86%)	121 (53.54%)	4 (17.39%)	143 (48.97%)
Invalid response	2 (4.65%)	0 (0.00%)	0 (0.00%)	2 (0.68%)
Total	43 (100%)	226 (100%)	23 (100%)	292 (100%)

*Pearson Chi-square = 23.1900, p-value = 0.000, *Fisher's exactfor scores < 5 = 0.000. The results are significant at p < 0.001.

3.4. Practices of the respondents

Table 7 shows that a mere 11% of respondents had received previous pharmacovigilance training. Of the 174 respondents (59%) who encountered an ADR in practice, a meagre 49 respondents (17%) reported the encountered ADR. The vast majority of respondents (74%) submitted <1 ADR per year.

Table 4
Knowledge of how to report ADRs by years of practice (N = 288).

Years of experience of respondents					
Response	<1 year	1–5 years	6–10 years	>10 years	All
Yes	6 (17.65%)	34 (41.46%)	57 (53.77%)	50 (75.76%)	146 (51.04%)
No	26 (76.47%)	48 (58.54%)	49 (46.23%)	16 (24.24%)	139 (48.26%)
Invalid Response	2 (5.88%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (0.69%)
Total	34 (100%)	82 (100%)	106 (100%)	66 (100%)	288 (100%)

*Pearson Chi-square- = 47.2773, p-value = 0.000, * Fisher's exact for scores < 5 = 0.000 The results are significant at p < 0.001.

Table 5
Knowledge of How to Report ADRs by Level of Practice of Respondent (N = 195).

Level of practice of respondents				
Response	Intern	Community service	Post-community service	All
Yes	6 (23.08%)	12 (42.86%)	82 (58.16%)	100 (51.28%)
No	18 (69.23%)	16 (57.14%)	59 (41.84%)	93 (47.69%)
Invalid Response	2 (7.69%)	0 (0.00%)	0 (0.00%)	2 (1.03%)
Total	26 (100%)	28 (100%)	141 (100%)	195 (100%)

*Pearson Chi-square = 22.7846, p-value = 0.000, *Fisher's exact for scores < 5 = 0.001 *The results are significant at p < 0.001.

4. Discussion

4.1. Knowledge of healthcare professionals on ADR reporting

Respondents in this study had some knowledge of pharmacovigilance, side effects and ADRs. Healthcare professionals have demonstrated a relative awareness for the presence of ADRs as seen in studies similar to this one, conducted in other developing countries (Agrawal et al., 2018; Gurmesa & Dedefo, 2016; Suyagh et al., 2014). However, these studies also found a lack of knowledge of the process of reporting. Gurmesa and Dedefo found that although 77.4% of respondents felt that ADR reporting is essential to patient safety, only 37.4% were aware of the actual reporting form (2016).

The knowledge of the pharmacovigilance reporting system, although positive, unfortunately does not translate to practice, with very few ADR reporting occurring (<1 on average annually in this study). The awareness of the PTC role in ADR reporting and pharmacovigilance provides a positive outlook on the National Department of Health's initiative to bring pharmacovigilance and ADR reporting into the forefront (Mehta, 2008). Although the NADEMC is the national monitoring centre in South Africa, the PTC should also be recognised as an important channel for communication within the institution. Provincial PTCs play a pivotal role in the collection, signal detection and feedback of ADR reports to SAHPRA and healthcare professionals. However, a recent South African study by Matlala et al. revealed that reporting of ADRs and medication errors to PTCs were poor at all hospital levels (2017). Communication and collaboration among the different health disciplines may help to give holistic care, and in many ways, this can make the involved persons more motivated.

The study found different levels of knowledge among the different professions, with nurses showing the least knowledge on how to report. The study revealed that an alarming 92% of respondents believed that doctors should be responsible for reporting. Questions need to be raised about who is responsible for adverse drug reporting. De Angelis et al. concluded that "Nurses are not fully aware of their role in adverse drug reaction reporting" (2015), and Hanafi et al. had a similar finding with 89% of nurses preferring to refer the report to the doctor for completion (2013). Other studies have stated a variety of possible reasons for low reporting rates by nurses, including workload; inattention; confidence about reporting; and fear of litigation (Agrawal et al., 2018; Salk & Ehrenpreis, 2016).

Table 6
Frequency distribution of respondent's attitudes (N = 297).

Response	Frequency (N)	Percentage (%)
Cases most likely to report ADR		
Seriousness of the ADR	268	90.24
Unusualness of the reaction	160	53.87
Involvement of a new drug	139	46.80
Level of certainty that it is an ADR	85	28.62
None of the above	2	0.67
Total	**654**	
Factors discouraging participants from reporting ADRs		
Do not know how to report	97	32.66
Not knowing where to report	96	32.32
Did not think it was important to report	65	21.89
Managing the patient was more important than reporting ADRs	115	38.72
Lack of access to ADR reporting form	49	16.50
Patient confidentiality	46	15.49
It is time-consuming	95	31.99
There is a lack of feedback after forms have been submitted	65	21.89
Other	7	2.36
"Inexperience"	1	
"No discouraging factors"	2	
Total	**635**	
ADRs that should be reported		
None	1	0.34
All ADRs	182	61.28
All serious ADRs	132	44.44
ADRs to new drugs	59	19.87
Unknown ADRs to old drugs	47	15.82
ADRs to herbal and non-allopathic drugs	23	7.74
ADRs to vaccinations	28	9.43
Other	3	1.01
Total	**475**	
Professionals who should report ADRs		
Medical practitioners	275	92.59
Nurses	264	88.89
Pharmacists	228	76.77
Other	7	2.36
"Patient"	2	
Total	**774**	
Reference materials participants would use		
Textbook	177	59.60
Colleague	211	71.04
Internet	236	79.46
Package Insert	224	75.42
Other	3	1.01
Total	**851**	

* = missing data.

The statistical association between knowledge of ADR reporting and the years of experience of respondents was interesting. Only 23% of the total interns (pharmacists and doctors) knew how to report ADRs, yet 62% were aware of the reporting form, having seen it before ($p < 0.001$). A possible reason for this finding was demonstrated by Van Eekeren et al. who found that "no standard exists for teaching

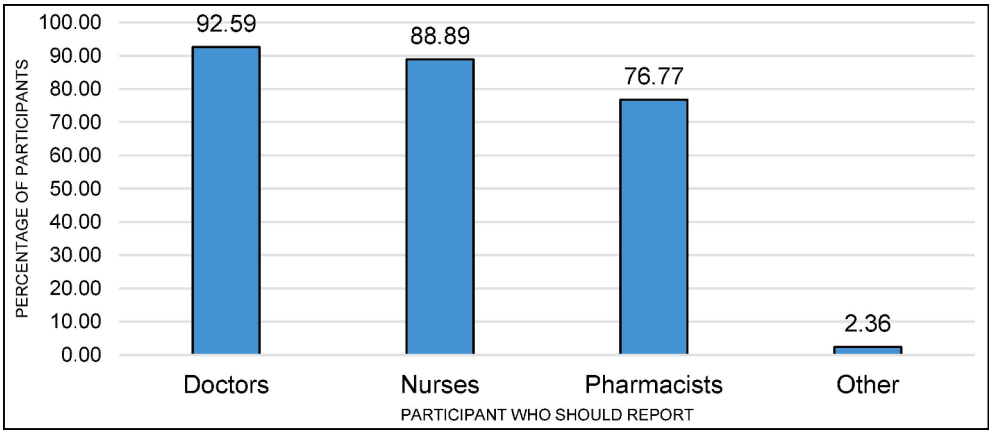

Fig. 1. Perceived responsibility for reporting ADRs.

(pharmacovigilance) at universities" (2018).

4.2. Attitudes of healthcare professionals on ADR reporting

Attitudes in this study were measured by the factors that encouraged and discouraged healthcare professionals, as well as the cases in which they were most likely to report ADRs. These factors accounted for some of the gaps between knowledge and practice. Believing that ADR reporting is important is an inevitable start to reporting ADRs, and this study found that only 22% of all respondents chose "did not think it was important to report" as a reason for underreporting. Similarly, Gurmesa and Dedefo found that 77.4% of healthcare professionals thought reporting ADRs was essential (2016), and Joubert and Naidoo found that 79.4% of respondents "regarded (pharmacovigilance) as a valuable tool" (2016).

A range of factors discouraged respondents from reporting ADRs, including feelings that it is more important to prioritise managing the patient. Other reasons included a lack of knowledge about the reporting system, which is consistent with other studies (Abdel-Latif & Abdel-Wahab, 2015). Most healthcare professionals cited the seriousness of the ADR (90%) as the main encouraging factor in deciding whether to report an ADR. This is comparable to the 89% of respondents who believed that all serious ADRs should be reported regardless of uncertainty (O'Callaghan, Griffin, Morris, & Bermingham, 2018).

4.3. Practices of healthcare professionals on ADR reporting

The practices of healthcare professionals were assessed through responses based on encountered ADRs versus reported ADRs. There was a concerning disconnect between the number of respondents encountering an ADR in practice (59%) and the proportion that reported an ADR (17%). Agrawal et al. similarly found a low level of practice by healthcare professionals despite "good knowledge and awareness on ADRs" (2018, p.24). Fadare et al. (2011) showed that while 80% of respondents witnessed an ADR, less than half of them (42.7%) chose not to report it (2011). This could be attributed to the low percentage of respondents who had previously attended pharmacovigilance training (32%), echoed by similar studies (Roy, Agarwal and Ahmed, 2017; Toklu and Soyalan, 2016).

Vallano et al. found the availability of reporting forms to be a major barrier of reporting (2005). Similarly, Toklu and Soyalan found that healthcare professionals had little knowledge of where to obtain the forms (2016). In this study, respondents (59%) stated the forms were easily available to them in practice which is encouraging however does not reflect in the ADR reporting patterns.

4.4. Suggestions and future recommendations

Education should remain a priority in the field of pharmacovigilance, shown by increases in reports after training, and higher rates

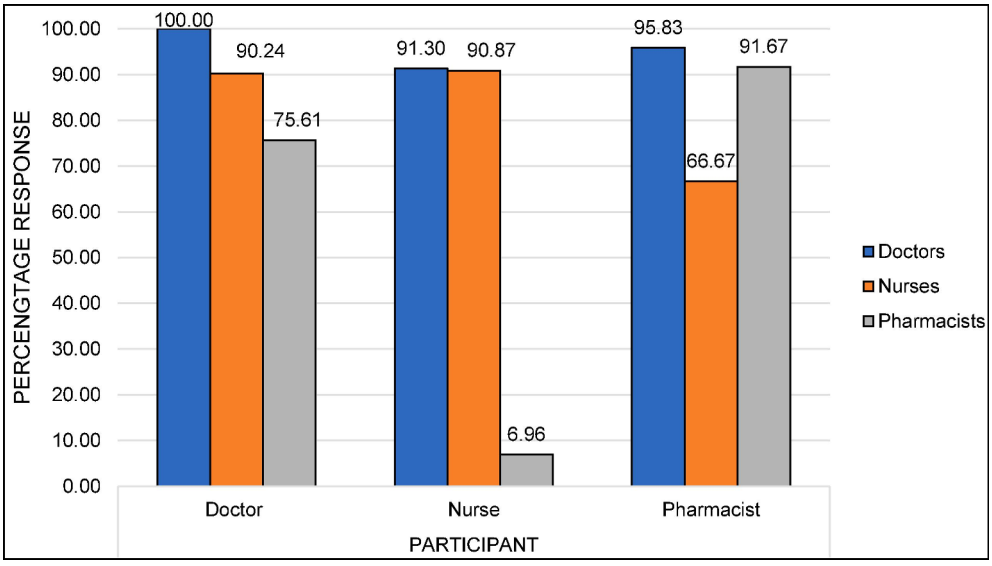

Fig. 2. Percentage of who should report according to each profession.

Table 7
Frequency distribution of previous pharmacovigilance practice activity (N = 294).

Response	Frequency (N)	Percentage (%)
Any previous training seminars/workshops on ADR reporting?		
Yes	32	10.77
No	262	88.22
Total	**294 (* =3)**	
Are ADR reporting forms easily available to you in practice?		
Yes	176	59.26
No	93	31.31
Total	**269 (* =28)**	
Have you ever encountered an ADR in practice?		
Yes	174	58.59
No	115	38.72
Total	**289 (* =8)**	
Have you ever reported an ADR that you encountered?		
Yes	49	16.50
No	238	80.13
Total	**287 (* =10)**	
How many ADR reports have you submitted on average?		
<1/year	219	73.74
1–10/year	23	7.74
<1/month	5	1.68
1–10/month	2	0.67
Total	**249 (* =48)**	

* = missing data

of reports from healthcare professionals with a higher level of education (De Angelis et al., 2016; Steurbaut & Hanssens, 2014; Lopez-Gonzalez, Herdeiro, & Figueiras, 2009; Backstrom, Mjorndal, & Dahlqvist, 2002). One study, focused on pharmacovigilance in resource-limited countries, mentioned continuous training, public awareness and the importance of feedback in reporting ADRs (Adepu & Shariff, 2010). Training should be consistent from the undergraduate level to routine internal training sessions in the workplace, in order to encourage awareness of ADR reporting (Agrawal et al., 2018).

Pimpalkhute et al. noticed gaps in "undergraduate training" (2012), while Olsson, Pal and Dodoo noted the importance of introducing pharmacovigilance training into undergraduate studies (2015). An approach targeted at students saw a "student- run pharmacovigilance programme" being piloted in the Netherlands (Netherlands Pharmacovigilance Centre Lareb & Student-Run Pharmacovigilance, 2017). This idea allowed for students to learn in a more practical way the importance of pharmacovigilance, which they can then carry into their professions. Their awareness of reporting was said to significantly increase following the program and the reports drawn up were given a 92% accuracy rating by permanent staff (Netherlands Pharmacovigilance Centre Lareb & Student-Run Pharmacovigilance, 2017).

Postgraduate training should also emphasize pharmacovigilance practices (Bigi & Bocci, 2017). A possible idea for this, while also utilising the idea of incentives, is the allotment of Continuous Development Points (CPDs) to reporting healthcare professionals. A study conducted in India found positive results following the implementation of this idea. Sixty-seven percent of healthcare professionals had no awareness of ADR reporting prior to the study, but results showed an increased rate of reporting after the program was introduced (Adepu & Shariff, 2010). Similarly, an idea implemented in the United Kingdom in the form of "e-learning modules" allows healthcare professionals to familiarise themselves with ADR reporting (Medicines and Healthcare Products Regulatory Agency, 2017). This allows for a continuous platform for training on ADRs, as well as the added incentive of receiving CPD credits. Another study utilised ADR reporting assignments to emphasize the importance of pharmacovigilance to specialist oncology nurses, and yielded encouraging results. Respondents produced quality reports, and showing elevated levels of interest in reporting ADRs for the sake of patient safety (Schutte et al., 2018).

5. Conclusion

Pharmacovigilance is the back bone to the safety and success of a drug. South Africa is diverse in its population with a myriad of diseases like HIV, TB and diabetes which provides the perfect landscape for possible ADRs. Further investigations into the gaps in the undergraduate pharmacovigilance curriculum should be conducted. Education, resources and support to healthcare professionals are key to the success of improving pharmacovigilance.

6. Limitations of the study

The study was conducted in 10 wards, and the pharmacy at one institution. The data obtained and conclusions drawn were specific to this environment, however similar studies could be done in other hospitals in order to get a more complete picture of pharmacovigilance in South Africa.

References

Abdel-Latif, M. M. M., & Abdel-Wahab, B. A. (2015). Knowledge and awareness of adverse drug reactions and pharmacovigilance practices among healthcare professionals in Al-Madinah Al-Munawwarah, Kingdom of Saudi Arabia. *Saudi Pharmaceutical Journal, 23*(2), 154–161. https://doi.org/10.1016/j.jsps.2014.07.005.

Adepu, R., & Shariff, A. (2010). Development, validation and implementation of continuous professional development programmes for community pharmacists. *Indian Journal of Pharmaceutical Sciences, 72557*(5), https://doi.org/10.4103/0250-474x.78520.

Agrawal, M., Singh, P., Hishikar, R., Joshi, U., Maheshwari, B., & Halwai, A. (2018). Adverse drug reactions at adverse drug reaction monitoring center in Raipur: Analysis of spontaneous reports during 1 year. *Indian Journal of Pharmacology, 49*(6), 432. https://doi.org/10.4103/ijp.ijp_781_16.

Ampadu, H. H., Hoekman, J., De Bruin, M. L., Pal, S. N., Olsson, S., Sartori, D., Leufkens, H. G., & Dodoo, A. N. (2016). Adverse drug reaction reporting in Africa and a comparison of individual case safety report characteristics between Africa and the rest of the world: analyses of spontaneous reports in VigiBase® *Drug Safety, 39*(4), 335–345. https://doi.org/10.1007/s40264-015-0387-4.

Backstrom, M., Mjorndal, T., & Dahlqvist, R. (2002). Spontaneous reporting of adverse drug reactions by nurses. *Pharmacoepidemiology and Drug Safety, 11*(8), 647–650. https://doi.org/10.1002/pds.753.

Bigi, Caterina, & Bocci, Guido (2017). The key role of clinical and community health nurses in pharmacovigilance. *European Journal of Clinical Pharmacology, 73*(11), 1379–1387. https://doi.org/10.1007/s00228-017-2309-0.

CMeRC – Charlotte Maxeke Research Cluster . 2016. Available at: http://www.inahta.org/members/cmerc/.

De Angelis, Alessia, Colaceci, Sofia, Giusti, Angela, Vellone, Ercole, & Alvaro, Rosaria (2016). Factors that condition the spontaneous reporting of adverse drug reactions among nurses: An integrative review. *Journal of Nursing Management, 24*(2), 151–163. https://doi.org/10.1111/jonm.2016.24.issue-210.1111/jonm.12310.

Desai, C. K., Iyer, G., Panchal, J., Shah, S., & Dikshit, R. K. (2011). An evaluation of knowledge, attitude, and practice of adverse drug reaction reporting among prescribers at a tertiary care hospital. *Perspectives in Clinical Research, 2*(4), 129. https://doi.org/10.4103/2229-3485.86883.

Edmonds, W., & Kennedy, T. (2016). *An applied guide to research designs* (2nd ed.). SAGE Publications, Inc.

Fadare, J. O., Enwere, O. O., Afolabi, A. O., Chedi, B. A. Z., & Musa, A. (2011). Knowledge, attitude and practice of adverse drug reaction reporting among healthcare workers in a tertiary centre in Northern Nigeria. *Tropical Journal of Pharmaceutical Research, 10*(3), 235–242. https://doi.org/10.4314/tjpr.v10i3.4.

Guidelines for Implementation of Pharmaceutical and Therapeutics Committees in Gauteng Province. 2013. Johannesburg: Gauteng Provincial Pharmaceutical and Therapeutics Committee, 1st ed.

Gurmesa, Lense Temesgen, & Dedefo, Mohammed Gebre (2016). Factors affecting adverse drug reaction reporting of healthcare professionals and their knowledge, attitude, and practice towards ADR Reporting in Nekemte Town, West Ethiopia. *BioMed Research International, 2016*, 1–6. https://doi.org/10.1155/2016/5728462.

Hanafi, S., Torkamandi, H., Kheirollah, A., & Mohammad, R. (2013). An educational intervention to improve nurses knowledge, attitude, and practice toward reporting of adverse drug reactions. *Iranian Journal of Nursing and Midwifery Research, 19*(1), 101–106.

Huang, Yu-Lin, Moon, Jinhee, & Segal, Jodi B. (2014). A comparison of active adverse event surveillance systems worldwide. *Drug Safety, 37*(8), 581–596. https://doi.org/10.1007/s40264-014-0194-3.

Isah, A. O., Pal, S. N., Olsson, S., Dodoo, A., & Bencheikh, R. S. (2012). Specific features of medicines safety and PV in Africa. *Therapeutic Advances in Drug Safety, 3*(1), 25–34. https://doi.org/10.1177/2042098611425695.

Joubert, M. C., & Naidoo, Panjasaram (2016). Knowledge, perceptions and practices of

pharmacovigilance amongst community and hospital pharmacists in a selected district of North West Province, South Africa. *Health SA Gesondheid, 21*, 238–244. https://doi.org/10.1016/j.hsag.2016.04.005.

Keller, S., Na, Lu. F., Blumenthal, K. G., Rai, S. K., Yokose, C., Choi, J. W. J., et al. (2018). Racial/ethnic variation and risk factors for allopurinol-associated severe cutaneous adverse reactions: a cohort study. *Annals of the Rheumatic Diseases*. https://doi.org/10.1136/annrheumdis-2017-212905.

Kohlroser, J., Mathai, J., Reichheld, J., & Banner, B. F. (2000). Hepatotoxicity due to troglitazone: report of two cases and review of adverse events reported to the United States Food and Drug Administration. *American Journal of Gastroenterology, 95*(1), 272–276. https://doi.org/10.1016/s0002-9270(99)00766-2.

Lenz, W. (1988). A short history of thalidomide embryopathy. *Teratology, 38*(3), 203–215. https://doi.org/10.1002/tera.1420380303.

Lopez-Gonzalez, Elena, Herdeiro, Maria T., & Figueiras, Adolfo (2009). Determinants of under-reporting of adverse drug reactions: A systematic review. *Drug Safety, 32*(1), 19–31. https://doi.org/10.2165/00002018-200932010-00002.

Maigetter, K., Pollock, A. M., Kadam, A., Ward, K., & Weiss, M. G. (2015). Pharmacovigilance in India, Uganda and South Africa with reference to WHO's minimum requirements. *International Journal of Health Policy and Management, 4*(5), 295. https://doi.org/10.15171/ijhpm.2015.55.

Matlala, Moliehi, Gous, Andries GS, Godman, Brian, & Meyer, Johanna C (2017). Structure and activities of pharmacy and therapeutics committees among public hospitals in South Africa; findings and implications. *Expert Review of Clinical Pharmacology, 10*(11), 1273–1280. https://doi.org/10.1080/17512433.2017.1364625.

MCC (Medicines Control Council). (2017). Reporting of Post-marketing Adverse Drug Reactions to Human Medicinal Products in South Africa. Guideline 2.33, version 5. [Accessed 1 May 2019] Available at: https://www.sahpra.org.za/Publications/DownloadDoc/5534.

Mcbride, W. G. (1961). Thalidomide and congenital abnormalities. *The Lancet, 278*(7216), 1358. https://doi.org/10.1016/s0140-6736(61)90927-8.

Medicines and Healthcare Products Regulatory Agency (2017). New CPD e-learning module on reporting suspected adverse drug reactions. gov.uk, [online]. [Accessed 24 October 2017]. Available at: https://www.gov.uk/drug-safety-update/new-cpd-e-learning-module-on-reporting-suspected-adverse-drug-reactions.

Mehta, Ushma, Durrheim, David N., Blockman, Marc, Kredo, Tamara, Gounden, Ronald, & Barnes, Karen I. (2008). Adverse drug reactions in adult medical inpatients in a South African hospital serving a community with a high HIV/AIDS prevalence: Prospective observational study. *British Journal of Clinical Pharmacology, 65*(3), 396–406. https://doi.org/10.1111/bcp.2008.65.issue-3.

Miller MT. Thalidomide embryopathy: a model for the study of congenital incomitant horizontal strabismus. Trans Am OphthalmolSoc. 1991; 89: 623. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1298636/.

Mittmann, N., & Knowles, S. (2009). A survey of pharmacy and therapeutic committees across Canada: scope and responsibilities. *The Canadian Journal of Clinical Pharmacology, 16*(1), 171–177.

National Department of Health, South Africa. National Policy for the Establishment and Functioning of Pharmaceutical and Therapeutics Committees in South Africa. 2015. Available from: www.health.gov.za/index.php/pharmaceutical-and-therapeutics-committees.

Netherlands Pharmacovigilance Centre Lareb. A Student-Run Pharmacovigilance Programme. 2017. Available at: https://www.lareb.nl/en/news/a-student-run-pharmacovigilance-programme/.

O'Callaghan, J., Griffin, B. T., Morris, J. M., & Bermingham, Margaret (2018). Knowledge of adverse drug reaction reporting and the pharmacovigilance of biological medicines: A survey of healthcare professionals in Ireland. *BioDrugs, 32*(3), 267–280. https://doi.org/10.1007/s40259-018-0281-6.

Ogimura, E., Nakagawa, T., Deguchi, J., Sekine, S., Ito, K., & Bando, K. (2017). Troglitazone inhibits bile acid amidation: A possible risk factor for liver injury. *Toxicological Sciences, 158*(2), 347–355. https://doi.org/10.1093/toxsci/kfx091.

Olsson, Sten, Pal, Shanthi N, & Dodoo, Alex (2015). Pharmacovigilance in resource-limited countries. *Expert Review of Clinical Pharmacology, 8*(4), 449–460. https://doi.org/10.1586/17512433.2015.1053391.

Ouma C, Abwao E. Africa Pharmacovigilance Meeting 2012: Technical Report. Submitted to the US Agency for International Development by the Systems for Improved Access to Pharmaceuticals and Services Program. 2012. Arlington, VA: Management Sciences for Health. Available from: http://apps.who.int/medicinedocs/en/d/Js21029en/.

Pimpalkhute, S. A., Jaiswal, K. M., Sontakke, S. D., Bajait, C. S., & Gaikwad, A. (2012). Evaluation of awareness about pharmacovigilance and adverse drug reaction monitoring in resident doctors of a tertiary care teaching hospital. *Indian Journal of Medical Sciences, 66*(3), 55. https://doi.org/10.4103/0019-5359.110902.

Roy, V., Agarwal, M., & Ahmed, J. (2017). Knowledge, attitude, and practice about pharmacovigilance among healthcare providers of a tertiary care teaching hospital in New Delhi (India). *MAMC J. Med. Sci. 3*(3), 146. https://doi.org/10.4103/mamcjms.mamcjms_31_17.

Salk, Allison, & Ehrenpreis, Eli D. (2016). Attitudes and usage of the food and drug administration adverse event reporting system among gastroenterology nurse practitioners and physician assistants. *Gastroenterology Nursing, 39*(1), 25–31. https://doi.org/10.1097/SGA.0000000000000193.

Schutte, Tim, van Eekeren, Rike, Richir, Milan, van Staveren, Jojanneke, van Puijenbroek, Eugène, Tichelaar, Jelle, & van Agtmael, Michiel (2018). The adverse drug reaction reporting assignment for specialist oncology nurses: A preliminary evaluation of quality, relevance and educational value in a prospective cohort study. *Naunyn-Schmiedeberg's Archives of Pharmacology, 391*(1), 17–26. https://doi.org/10.1007/s00210-017-1430-z.

Staffa, Judy A., Chang, Jennie, & Green, Lanh (2002). Cerivastatin and reports of fatal rhabdomyolysis. *New England Journal of Medicine, 346*(7), 539–540. https://doi.org/10.1056/NEJM200202143460721.

Steurbaut, Stephane, & Hanssens, Yolande (2014). Pharmacovigilance: Empowering healthcare professionals and patients. *International Journal of Clinical Pharmacy, 36*(5), 859–862. https://doi.org/10.1007/s11096-014-0004-0.

Suyagh, Maysa, Farah, Doaa, & Abu Farha, Rana (2015). Pharmacist's knowledge, practice and attitudes toward pharmacovigilance and adverse drug reactions reporting process. *Saudi Pharmaceutical Journal, 23*(2), 147–153. https://doi.org/10.1016/j.jsps.2014.07.001.

Thakkar, Karan, Billa, Gauri, Rane, Jay, Chudasama, Hiren, Goswami, Sailendra, & Shah, Rajen (2015). The rise and fall of felbamate as a treatment for partial epilepsy – aplastic anemia and hepatic failure to blame? *Expert Review of Neurotherapeutics, 15*(12), 1373–1375. https://doi.org/10.1586/14737175.2015.1113874.

Toklu, H. Z., & Soyalan, M. (2016). The knowledge and attitude of the healthcare professionals towards pharmacovigilance and adverse drug reaction reporting in northern cyprus. *Journal of Pharmacovigilance*. https://doi.org/10.4172/2329-6887.1000193.

Uppsala Monitoring Centre (UMC). Members of the WHO Programme for International Drug Monitoring. 2017. Available from: https://www.who-umc.org/global-pharmacovigilance/members/who-programme-members.

Vallano, A., Cereza, G., Pedròs, C., Agustí, A., Danés, I., Aguilera, C., & Arnau, J. M. (2005). Obstacles and solutions for spontaneous reporting of adverse drug reactions in the hospital. *British Journal of Clinical Pharmacology, 60*(6), 653–658. https://doi.org/10.1111/j.1365-2125.2005.02504.x.

van Eekeren, Rike, Rolfes, Leàn, Koster, Andries S., Magro, Lara, Parthasarathi, Gurumurthy, Al Ramimmy, Hussain, Schutte, Tim, Tanaka, Daisuke, van Puijenbroek, Eugène, & Härmark, Linda (2018). What future healthcare professionals need to know about pharmacovigilance: introduction of the WHO PV core curriculum for university teaching with focus on clinical aspects. *Drug Safety, 41*(11), 1003–1011. https://doi.org/10.1007/s40264-018-0681-z.

World Health Organization (WHO). Essential Drugs Monitor No. 032: Drug And Therapeutics Committees: Vehicles For Improving Rational Drug Use. 2003. Available from: http://apps.who.int/medicinedocs/en/d/Js4940e/6.html.

World Health Organization (WHO) Pharmacovigilance Available from 2015. http://www.who.int/medicines/areas/quality_safety/safety_efficacy/pharmvigi/en/.

World Health Organization (WHO). Technical Reports No 498. International drug monitoring: the role of national centres. 1972. Available from: http://apps.who.int/iris/handle/10665/40968.

World Health Organization (WHO). The Importance of Pharmacovigilance. 2002. Available at: http://apps.who.int/medicinedocs/en/d/Js4893e/.