SJP Sarawak Journal of Pharmacy

Journal Homepage: http://jknsarawak.moh.gov.my/spj/

Knowledge of Drug-drug Interactions among Pharmacy Department Staff in Miri General Hospital: A cross-sectional study

Faizul Bin Abdul Rahman[1], Clausanta Anak Paul Joring[1], Jong Yi Wen[1], Chin Lee Yii[1], Kamarudin Ahmad[1,2]

[1]Pharmacy Department, Miri Hospital, Sarawak

[2]Clinical Research Centre Miri

Corresponding author name and email: Faizul Bin Abdul Rahman (faizul.ar.moh@1govuc.gov.my)

ABSTRACT

Introduction: Drug-drug interactions (DDIs) can be potentially harmful and although not all adverse drugs effects (ADEs) can easily predicted, exposure to a DDI is a medical error that can be prevented. Pharmacists play a key role in identifying DDIs to enhance the safety of medication management.

Objective: The objective of the study is to assess the knowledge of drug-drug interaction among pharmacy department staffs in Miri General Hospital.

Methods: A cross sectional study done involving pharmacists (Fully Registered Pharmacists and Provisionally Registered Pharmacists) and Pharmacist Assistants of Miri General Hospital (MGH). Data collection done based on questionnaire adapted from a validated Drug-drug Interaction Knowledge Assessment Instrument Questionnaire. The data analyses separated into 2 categories, which based on DDI management strategy analysis and DDI recognition analysis.

Results: Pharmacy staffs Miri General Hospital (N=55) participated in this survey study. Majority of the pharmacy staffs (85.5%) showed poor result in the DDI management strategy and only some (14.5%) were fairly good. None of the staff showed good management strategy. Analysis of the DDI recognition showed 40% of pharmacy staff was having poor DDI recognition, while the remaining 30.9% and 29.1% were fairly good and good respectively.

Conclusion: The level of knowledge of identifying DDIs among Pharmacy Department staff in Miri General Hospital is poor. Therefore, more educational sessions are necessary to train and equip pharmacists with the necessary amount of knowledge and skills to better identify DDIs and ensure safe medication regimes.

Key words: Knowledge, drug-drug interactions, pharmacy department staff

INTRODUCTION

Healthcare professionals are responsible for detecting and preventing adverse drug events (ADEs), which defined as an injury from a medication error. One of the types of medical error is knowledge-based error. In particular, a knowledge based-error typically involves the occurrence of a drug interaction due to the lack of knowledge of how that particular interaction may occur (1). Drug-drug interactions (DDIs) which are clinically significant can be life-threatening and although not all ADEs can easily predicted, exposure to a DDI is a medical mistake that can be prevented (2). Despite the advancement in information technology which assists to prevent clinically significant DDIs, hundreds of millions of potential DDIs happen every year, affecting millions of patients (3).

This scenario is especially critical in a country such as Malaysia, which has a growing older population. In Malaysia, the elderly population projected to increase from 9.2% in 2015 to nearly a quarter of the whole population (23.6%) by 2050. Consequently, age-related multi-morbidity will escalate the usage of more medications and hence, increasing the risk of polypharmacy. This is a major concern as polypharmacy highly associated with the risk of harmful drug interactions (4). Based on a cross-sectional study in Penang General Hospital, it identified that 86 DDIs caused uncontrolled glycemia in 46 patients (23%) with 1 to 4 DDIs per patient. Most of these DDIs classified as possible (77.9%) and preventable (37%) (5).

Pharmacists carry an important role in preventing prescribing errors. For instance, pharmacists can supply appropriate information and detect errors, including identifying potential DDIs by collaborating closely with physicians (6). In a study which evaluated the role of pharmacists in prevent DDIs that cause QTc prolongation, it has shown that a pharmacist consult resulted in higher attention of prescribers toward ECG recordings, which led to better monitoring and health result. This is because a pharmacist has the ability to detect potentially lethal DDIs, increasing medical awareness of prescribers and monitoring (7).

Concurrently, drug compendia, computer programmes and digital drug index commonly utilised by pharmacists to recognise drug interactions, but usage of these tools show limited usefulness. For example, DDI software detects both clinically significant and non-significant interactions, making it more difficult for pharmacists to interpret and assess DDI warnings (8, 9). Thus, it is important that pharmacists equip themselves with the necessary amount of knowledge and skills to better identify DDIs and suggest safer medication regimens to prescribers.

This study aimed to assess the knowledge of drug-drug interaction among pharmacy department staff in Miri General Hospital in hope that this study contributes to better patient care and improved medication safety.

METHODS

Pharmacy department staffs (fully registered pharmacist, provisionally registered pharmacist and pharmacist assistant) in Miri General Hospital enrolled in this DDI knowledge assessment. This population selected for involvement since they were medication professionals who are responsible for appropriate as well as rational medication use in healthcare professional era. The study design employed is a cross-sectional study. Confidentiality assured throughout the assessment as random distribution done in each pharmacy related department.

In the present study, 15 medication pairs proposed, including 11 interacting pairs and 4 noninteracting drug pairs (Appendix 1). The drug interaction pairs selected based on their clinical importance with a focus on cardiovascular drugs because of their potentials to cause serious adverse events. Non interacting drug pairs incorporated to discourage guessing. Noninteracting drug pairs involved drugs that commonly caused DDIs whereas no interaction occurred when administered concurrently with either Digoxin or Warfarin. Each of the medication involved in the DDI knowledge questionnaires listed alphabetically with both generic and brand name, according to the object (the drug affected by the interaction) and precipitant drug (the drug causing the interaction). The self-administered questionnaires also contained demographic details, length of experience, and department of practice.

There are 5 DDI management options for each interaction pairs: ‘‘avoid combination,’’ ‘‘usually avoid combination’’, ‘‘take precautions”, ‘‘no special precautions”, and ‘‘not sure’’. The last option was added to prevent guessing. “Avoid combination” is for combination with risk outweighing benefits. For “usually avoid combination”, such combination only used under special circumstances/interactions for which there are clearly preferable alternatives for one or both drugs/interactions to avoid unless the benefits of both drugs judged to outweigh the risk. “Take precautions” indicate that the combination’s risk has to be assessed and take one or more precautions if needed. Precautions include: 1) Consider available alternatives that are less likely to interact 2) Circumvent in which action is taken to minimize the interaction (e.g. adjust dosage) 3) Monitor to ensure early detection so that the risk of an adverse result minimised. “No special precautions” is to be selected when either of the following is true: 1) The risk of adverse results appears small 2) Evidence suggests the drugs do not interact.

In view of subjective nature of classifying DDIs into specific management categories, the data analysed in 2 ways: (1) DDI management strategy analysis (2) DDI recognition analysis. In DDI management strategy analysis, participants given credit for getting an interaction pair corrects only if they selected the appropriate management strategy. For instance, if the authors deemed that an interaction pair should be avoided, the credit given only for selecting the ‘‘avoid combination’’ option. In DDI recognition analysis, participants given credit for an item if they identified DDIs. For example, if the authors deemed there was sufficient evidence that a drug pair interacts, then the credit given if they selected any of the DDI management options. (ie, ‘‘avoid combination,’’ usually avoid combination,’’ or ‘‘take precautions’’). In both analyses, the ‘‘not sure’’ options scored as incorrect when selected and the non interacting pairs considered incorrect if the participant indicated that the pair interacted in any way.

SPSS Statistics Version 21 used to calculate descriptive statistics and perform Chi-square test. When the criteria of expected count (EC), which includes the number of cells with expected count less than 5, must be less than 20% of total number of cells or the smallest EC must be at least 2 are not met, Fisher’s exact test generated for all the variables under investigation. Descriptive analyses with $p < 0.05$ is defined as a significant test.

RESULTS

Table 1. Demographics details of respondents.

Demographics		Frequency
Age	21 – 30	38 (69.1%)
	31 – 40	14 (25.5%)
	41 – 50	0 (0.0%)
	51 – 60	3 (5.5%)
Gender	Male	11 (20.0%)
	Female	44 (80.0%)
Position	FRP	27 (49.1%)
	PPF	11 (20.0%)
	PRP	17 (30.9%)
Work Experience	<1 year	17 (30.9%)
	1 – 10 years	28 (50.9%)
	10 – 20 years	6 (10.9%)
	20 – 30 years	3 (5.5%)
Department of Practice	Clinical Pharmacy	7 (12.7%)
	DIS	2 (3.6%)
	OPD	19 (34.5%)
	IPD	3 (5.5%)
	Satellite	6 (10.9%)
	TDM	3 (5.5%)

	CDR	4 (7.3%)
	Production	2 (3.6%)
	Logistics	5 (9.1%)
	MTAC	4 (7.3%)

Table 2. Different variables and the DDI knowledge of Hospital Miri Pharmacy Staffs based on Management Strategy Analysis and DDI Recognition Analysis.

		DDI Management Strategy Analysis					DDI Recognition Analysis				
		Good (%)	Fairly Good (%)	Poor (%)	Total	P-value	Good (%)	Fairly Good (%)	Poor (%)	Total	P-value
Age	24-30	0 (0)	5 (13.2)	33 (86.8)	38	0.794	12 (31.6)	14 (36.8)	12 (31.6)	38	0.242
	31-40	0 (0)	3 (21.4)	11 (78.6)	14		4 (28.6)	3 (21.4)	7 (50.0)	14	
	41-50	0 (0)	0 (0)	0(0)	0		0 (0)	0 (0)	0(0)	0	
	51-60	0 (0)	0 (0)	3 (100)	3		0 (0)	0 (0)	3 (100)	3	
Gender	Male	0 (0)	1 (9.1)	10 (90.9)	11	0.492	2 (18.2)	2 (18.2)	7 (63.6)	11	0.299
	Female	0 (0)	7 (15.9)	37 (84.1)	44		14 (31.8)	15 (34.1)	15 (34.1)	44	
Position	FRP	0 (0)	4 (14.8)	23 (85.2)	27	1.000	12 (44.4)	10 (37.0)	5 (18.5)	27	0.001*
	PRP	0 (0)	2 (11.8)	15 (88.2)	17		2 (11.8)	7 (41.2)	8 (47.1)	17	
	PPF	0 (0)	2 (18.2)	9 (81.8)	11		2 (18.2)	0 (0)	9 (81.8)	11	
Work Experience	<1	0 (0)	2 (11.8)	15 (88.2)	17	1.000	2 (11.8)	7 (41.2)	8 (47.1)	17	0.062
	1-10	0 (0)	4 (14.3)	24 (85.7)	28		12 (42.9)	9 (32.1)	7 (25.0)	38	
	11-20	0 (0)	1 (16.7)	5 (83.3)	6		1 (16.7)	1 (16.7)	4 (66.7)	6	

	21-30	0 (0)	0 (0)	3 (100)	3		0 (0)	0 (0)	3 (100)	3	
Department of Practice	Clinical	0 (0)	0 (0)	7 (100)	7	0.007*	1 (14.3)	2 (28.6)	4 (57.1)	7	0.023*
	DIS	0 (0)	0 (0)	2 (100)	2		0 (0)	1 (50)	1 (50)	2	
	OPD	0 (0)	2 (10.5)	17 (89.5)	19		6 (31.6)	3 (15.8)	10 (52.6)	19	
	IPD	0 (0)	0 (0)	3 (100)	3		0 (0)	1 (33.3)	2 (66.7)	3	
	Satellite	0 (0)	0 (0)	6 (100)	6		1 (16.7)	2 (33.3)	3 (50.0)	6	
	TDM	0 (0)	0 (0)	3 (100)	3		0 (0)	2 (66.7)	1 (33.3)	3	
	CDR	0 (0)	3 (75.0)	1 (25.0)	4		4 (100)	0 (0)	0 (0)	4	
	Production	0 (0)	2 (100)	0 (0)	2		2 (100)	0 (0)	0 (0)	2	
	Logistics	0 (0)	1 (20)	4 (80)	5		2 (40)	2 (40)	1 (20)	5	
	MTAC	0 (0)	0 (0)	4 (100)	4		0 (0)	4 (100)	0 (0)	4	

*P-value generated from Fisher's Exact Test

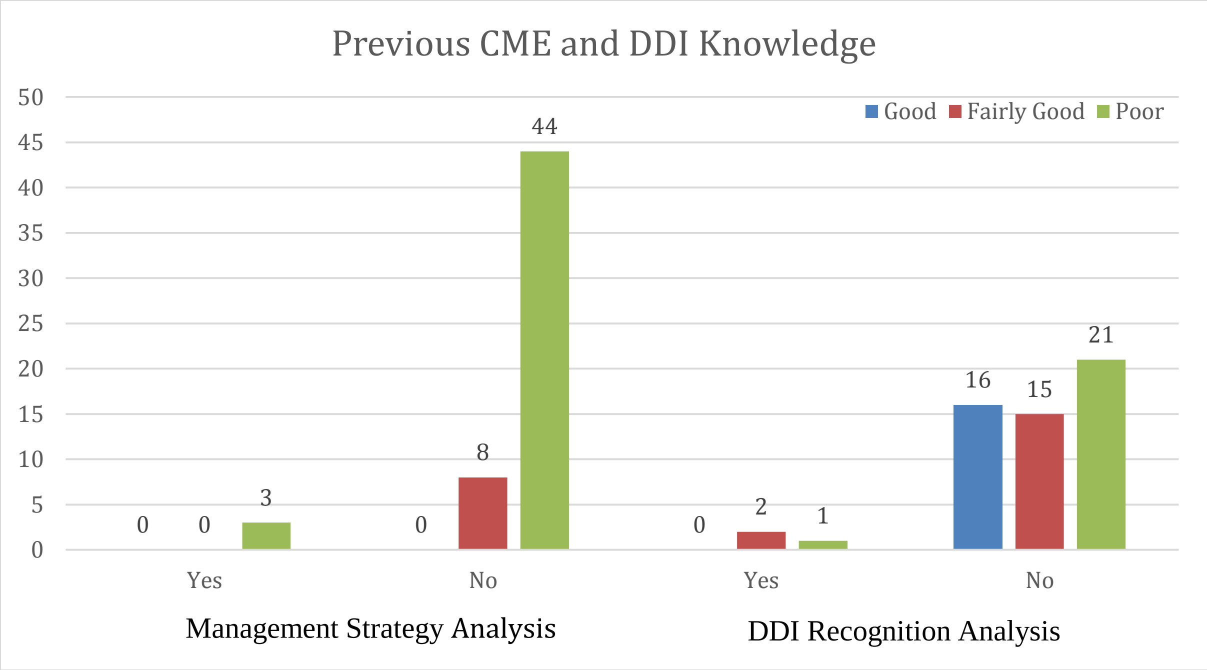

Figure 1. Previous CME and DDI Knowledge based on Management Strategy Analysis and DDI Recognition Analysis.

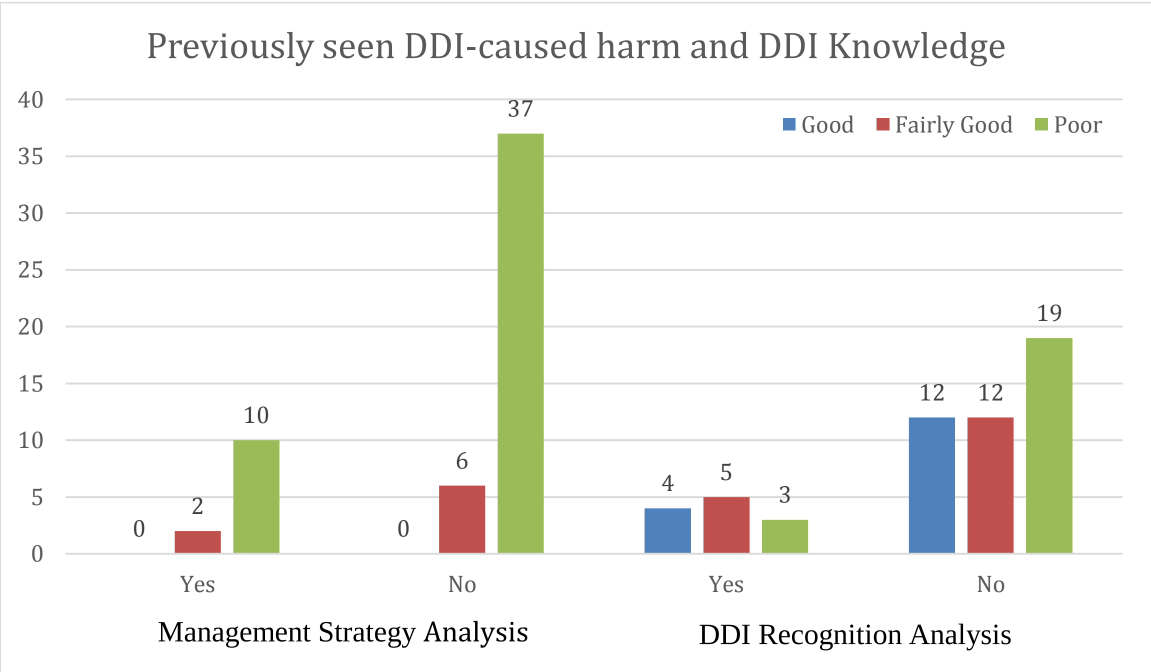

Figure 2. Previously seen DDI-caused harm and DDI Knowledge based on Management Strategy Analysis and DDI Recognition Analysis.

Among 55 participants, none of them were having good management strategy while 8 of the 55 participants (14.5%) were fairly good while the remaining of them, 47 out of 55 participants (85.5%) found to have poor result in the management strategy.

When analysed with the DDI recognition analysis, 16 of the 55 participants (29.1%) were having good DDI recognition. 17 out of 55 of them (30.9%) found to perform fairly good in the analysis with the descriptive statistic. The remaining of them (40%) indicated as poor after the evaluation.

As shown in Table 2, none of the pharmacy staffs show good DDI knowledge based on Management strategy analysis. According to both types of analysis, female pharmacy staffs generally present with better DDI knowledge than male staffs, however the difference is of no statistical significance. Also, increased work experience does not result in better DDI knowledge, regardless of the analysis used.

There is no significant difference in DDI knowledge between different age groups, gender and work experience, regardless which analysis used. However, when DDI recognition analysis applied, there is a significant difference in DDI knowledge among FRP, PRP and PPF, with higher percentage of FRP showing good DDI knowledge. In addition, both types of analysis show that department of practice does have statistically significant effect on the staff's DDI knowledge.

According to Figure 1 and Figure 2, when analysed with Management Strategy Analysis, previous CME course on DDI and previously seen DDI-induced harm does not guarantee good DDI knowledge. However, when analysed with DDI Recognition Analysis, previous exposure to these two variables results in a better DDI knowledge.

DISCUSSION

The objective of the study is to assess the knowledge of drug-drug interaction among pharmacy department staff in Miri General Hospital. Generally, the knowledge of DDIs is insufficient as 85.5% of participants showed poor result in DDI management strategy and 40% of participants showed poor result in DDI recognition analysis. This result is alarming as pharmacists are the medication experts that should be able to identify common DDIs. This finding is similar to a study in King Salman Hospital, Saudi Arabia, whereby the healthcare professionals demonstrated inadequate ability to identify clinically significant warfarin-drug and herb-warfarin interactions (10). Additionally, a study conducted in hospitals across six Massachusetts regions also showed the knowledge of health care professionals in assessing drug-nutrient interactions involving vitamin K was inadequate (11). Due to different selections of drug pairing, findings of these studies may not be directly comparable to our study. However, these studies reported that the knowledge of drug-drug interactions indeed generally poor.

Findings of this study showed that longer working experience in the pharmacy does not directly correlate to a higher result in knowledge of recognising drug-drug interactions. Despite that, our study able to portray the FRP contributed to a higher result of recognising DDI compared to the PRP. This could be due to the extent of work exposure in pharmacy between FRP and PRP. FRP were more familiar with the medication interactions from the longer years of learning and education compared to PRP who only have roughly one year of work exposure. This is concordant with the results of a study at a Veteran Affairs medical centre, in which the higher number of years of pharmacy training increased the ability of pharmacists to identify drug-drug interactions (12).

It is not surprising most of the pharmacy staff have poor knowledge of DDI due to the availability of medicine-related applications which allow them to have ready access to drug-drug interaction checkers. Given this fact, it reduces the need to memorise interactions between medications as they could easily check for drug interactions from their mobile phone apps. Medical applications have been a very useful tool in clinical decision making, allowing convenient access to drug information and improving work efficiency as well as minimizing potential errors (13). As our study excluded the usage of drug references from mobile apps or those available online, pharmacy staffs solely depended on their memory, therefore restraining their ability to detect drug interactions. Nevertheless, it is still essential for pharmacists to have the reasonable amount of knowledge identify DDIs without the usage of references.

The ability to identify DDIs is crucial and the poor knowledge of DDIs among pharmacy department staff is of utmost concern especially in a hospital setting such as MGH. A study showed the overall prevalence of DDIs were higher in hospital pharmacies as patients have more serious comorbidities and conditions which require many medications. This increases the likelihood of drug interactions occurring. The drugs involved also have lower therapeutic index and more severe interactions and side effects (14). Pharmacists have a critical role in identifying potentially harmful DDIs as DDIs are associated with a higher incidence of hospitalisations, adverse events and death (15).

In view of the importance of identifying DDIs, initiatives must be taken to improve the poor knowledge of DDIs among pharmacy staff in Miri General Hospital. Incorporating DDI-specific educational sessions is one of the ways to ensure that staffs are regularly trained in identifying DDIs. One of the talks that are already available in Miri General Hospital is Medication Safety. However, there is a lack of emphasis given on educating staff with common DDIs. An appropriate education session is effective as one study showed significant improvement in healthcare professional students' DDI knowledge after participating in an educational session. The session included DDI terminology and definitions, interaction mechanism explanation, various DDI management strategies and an overview of selected, clinically important DDIs (2).

One of the limitations of the study is the small sample size. Associations made might not be representative of the general populations in terms of their DDI knowledge. The study also done in one practice setting and the level of knowledge may vary between healthcare institutions. In addition, a pharmacist assistant is also included in the study and as their main role in Miri General Hospital is to fill prescriptions, their level of knowledge might not reflect the level of knowledge among pharmacists.

CONCLUSION

In conclusion, the poor level of knowledge of identifying DDIs among Pharmacy Department staff in Miri General Hospital is concerning. Pharmacists are the entrusted medication experts that play a key role in identifying potentially harmful DDIs which may cause adverse health outcomes in patients. Therefore, it is imperative that educational initiatives are taken in order to continuously equip pharmacists with necessary amount of knowledge and skills to guarantee safer medication regimes to patients.

ACKNOWLEDGEMENTS

We would like to show our appreciation to Clinical Research Centre and Mr. Kamarudin Ahmad who generously provided expertise and insight on statistical analysis during the writing of this manuscript.

REFERENCES

1. Aronson JK. Medication errors: what they are, how they happen, and how to avoid them. QJM: An International Journal of Medicine. 2009;102(8):513-21.
2. Harrington AR, Warholak TL, Hines LE, Taylor AM, Sherrill D, Malone DC. Healthcare Professional Students' Knowledge of Drug-Drug Interactions. American Journal of Pharmaceutical Education. 2011;75(10):199.
3. Warholak TL, Menke JM, Hines LE, Murphy JE, Reel S, Malone DC. A drug-drug interaction knowledge assessment instrument for health professional students: a Rasch analysis of validity evidence. Research in social & administrative pharmacy : RSAP. 2011;7(1):16-26.
4. Lim LM, McStea M, Chung WW, Nor Azmi N, Abdul Aziz SA, Alwi S, et al. Prevalence, risk factors and health outcomes associated with polypharmacy among urban community-dwelling older adults in multi-ethnic Malaysia. PLoS ONE. 2017;12(3):e0173466.
5. Hammad MA, Tangiisuran B, Kharshid AM, Abdul-Aziz N, Hassan Y, Aziz NA, et al. Drug-drug Interaction-related Uncontrolled Glycemia. Journal of Pharmacy &Bioallied Sciences. 2017;9(4):221-8.
6. Vonbach P, Dubied A, Beer JH, Krahenbuhl S. Recognition and management of potential drug-drug interactions in patients on internal medicine wards. European journal of clinical pharmacology. 2007;63(11):1075-83.
7. Calvarysky B, Yelin D, Superstine SY. PS-088 The impact of a clinical pharmacist's consults on doctor's management of drug–drug interactions with potential qt prolongation in an internal medicine ward. European Journal of Hospital Pharmacy. 2017;24(Suppl 1):A266-A.
8. Chui M. Evaluation of Online Prospective DUR Programs in Community Pharmacy Practice. Journal of Managed Care Pharmacy. 2000;6(1):27-32.
9. Peng CC, Glassman PA, Marks IR, Fowler C, Castiglione B, Good CB. Retrospective drug utilization review: incidence of clinically relevant potential drug-drug interactions in a large ambulatory population. Journal of managed care pharmacy : JMCP. 2003;9(6):513-22.
10. Al-Arifi MN, Wajid S, Al-Manie NK, Al-Saker FM, Babelgaith SD, Asiri YA, et al. Evaluation of knowledge of Health care professionals on warfarin interactions with

drug and herb medicinal in Central Saudi Arabia. Pakistan Journal of Medical Sciences. 2016;32(1):229-33.

11. Couris RR, Tataronis GR, Dallal GE, Blumberg JB, Dwyer JT. Assessment of healthcare professionals' knowledge about warfarin-vitamin K drug-nutrient interactions. Journal of the American College of Nutrition. 2000;19(4):439-45.
12. Weideman RA, Bernstein IH, McKinney WP. Pharmacist recognition of potential drug interactions. American journal of health-system pharmacy : AJHP : official journal of the American Society of Health-System Pharmacists. 1999;56(15):1524-9.
13. Ventola CL. Mobile Devices and Apps for Health Care Professionals: Uses and Benefits. Pharmacy and Therapeutics. 2014;39(5):356-64.
14. Dirin MM, Mousavi S, Afshari AR, Tabrizian K, Ashrafi MH. Potential drug-drug interactions in prescriptions dispensed in community and hospital pharmacies in East of Iran. Journal of Research in Pharmacy Practice. 2014;3(3):104-7.
15. Saverno KR, Malone DC, Kurowsky J. Pharmacy Students' Ability to Identify Potential Drug-Drug Interactions. American Journal of Pharmaceutical Education. 2009;73(2):27.

APPENDIX 1

	Avoid Combination	Usually Avoid Combination	Take Precautions	No Special Precautions	Not Sure
1. **Acetaminophen/codeine** (Tylenol w/ Codeine) + **Amoxicillin** (Amoxil)	☐	☐	☐	☐	☐
2. **Carbamazepine** (Tegretol) + **Clarithromycin** (Biaxin)	☐	☐	☐	☐	☐
3. **Digoxin** (Lanoxin) + **Amiodarone** (eg.Cordarone)	☐	☐	☐	☐	☐
4. **Digoxin** (Lanoxin) + **Clarithromycin** (Biaxin)	☐	☐	☐	☐	☐
5. **Digoxin** (Lanoxin) + **Itraconazole** (Sporanox)	☐	☐	☐	☐	☐
6. **Digoxin** (Lanoxin) + **Sildenafil** (Viagra)	☐	☐	☐	☐	☐
7. **Metformin** (Glucophage) + **Erythromycin** (E-mycin)	☐	☐	☐	☐	☐
8. **Nitroglycerine** (Nitro-Dur) + **Sildenafil** (Viagra)	☐	☐	☐	☐	☐
9. **Simvastatin** (Zocor) + **Itraconazole** (Sporanox)	☐	☐	☐	☐	☐
10. **Warfarin** (Coumadin) + **Amiodarone** (Cordarone)	☐	☐	☐	☐	☐
11. **Warfarin** (Coumadin) + **Digoxin** (Lanoxin)	☐	☐	☐	☐	☐
12. **Warfarin** (Coumadin) + **Fluconazole** (Diflucan)	☐	☐	☐	☐	☐
13. **Warfarin** (Coumadin) + **Gemfibrozil** (Lopid)	☐	☐	☐	☐	☐
14. **Warfarin** (Coumadin) + **Naproxen** (Naprosyn)	☐	☐	☐	☐	☐
15. **Warfarin** (Coumadin) + **Sulfamethoxazole / Trimethoprim** (Bactrim)	☐	☐	☐	☐	☐