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ORIGINAL RESEARCH

Which drugs cause treatment-related problems? Analysis of 10,672 problems within the outpatient setting

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Background: Treatment-related problems (TRPs) may pose risks for patients if unaddressed. With the increased complexity of health care, it is important to target pharmacists' efforts to patients that are at high risk for TRPs.

Objectives: The present study aimed to identify medications most commonly associated with TRPs.

Setting: Outpatient departments of five public and teaching hospitals in Jordan.

Method: TRPs and drugs most commonly implicated with TRPs were assessed for patients recruited from outpatient clinics in five major hospitals in Jordan using a standardized and validated pharmaceutical care manual.

Main outcome measure: Drugs associated with different types of TRPs.

Results: Ultimately, 2,747 patients, with a total of 10,672 TRPs, were included in the study. The medication groups most commonly associated with TRPs were cardiovascular (53.0%), endocrine (18.1%), and gastrointestinal (7.7%) drugs. The most common specific drugs associated with TRPs from any category were atorvastatin (12.5%), metformin (8.5%), simvastatin (6.2%), and enalapril (5.9%). Cardiovascular medications were the most common drugs implicated with multiple subtypes of TRPs – most commonly, allergic reaction or undesirable effect (88.5%), drug product not available (87.3%), safety interaction issues (81.8%), a need for additional or more frequent monitoring (78.0%), and more effective drugs available (77.2%). Hypertension, diabetes mellitus, and dyslipidemia were the most common diseases associated with different subtypes of TRPs.

Conclusion: The present study identified high-risk drugs for TRPs, which can be used as identification of targeting approach TRPs. Such an approach would improve care provided to patients and can inform health care policies.

Keywords: drug related problems, drug therapy problems, high alert medication, Jordan, pharmaceutical care, treatment related problems

Introduction

Treatment-related problems (TRPs) are associated with the use of medications that result in decreased therapeutic outcomes, which are usually addressed by pharmacists. The impact of such problems is significant. TRPs can lead to decreased disease control and adverse effects. Such TRPs might lead to overutilization of health care resources, with associated high costs for the health care system, in particular for elderly patients.[1–9] Approximately one-tenth of hospital admissions are attributed to drugs and TRPs are common in institutionalized patients, such as those in nursing homes.[2,6,8,9] TRPs are also common in primary care, particularly after hospital discharge.[10,11] The high impact associated with TRP issues can provide a strong case for pharmacist service

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to address such important problems, particularly serious, clinically significant TRPs.

As the complexity of treatment and the number of available treatments increase, addressing TRPs might pose a challenge for the pharmacist. In direct patient care, increased emphasis should be paid to appropriate targeting or case finding for high-risk patients. A "trigger" tool that alerts the health care professional for the possibility of TRPs is an approach that can be applied in targeting. A convenient and easy trigger tools would be to formulate a list of drugs commonly associated with TRPs as a targeting mechanism. This concept has been adopted by accreditation bodies such as the Joint Commission (Oakbrook Terrace, IL, USA), which maintains a list of high-alert medications. In addition, the concept of high-alert medications is highlighted in academic curricula for pharmacy, particularly the clinical pharmacy curriculum.[12] The Institution of Safe Medication Practice (ISMP) list for high-alert medications identifies drugs associated with risk in cases of error. Examples of these medications are antiretroviral agents, chemotherapeutic agents, hypoglycemic agents and insulin, immunosuppressants, opioids, carbamazepine, midazolam (liquid), propylthiouracil, warfarin, and pregnancy category X drugs.[13]

Internationally, as clinical pharmacy is steadily developing, such targeted drug lists can be useful especially for health care systems with limited resources. In Jordan, a number of studies have been published describing typical pharmaceutical care research and the impact of clinical pharmacy interventions.[14,15] Other studies have assessed the prevalence of TRPs.[16,17] The latter studies were conducted on heterogeneous settings; one study was conducted on a single health center and found the most frequent TRPs (83.3%) are the need for education and counseling.[16] Another study that was based on home visits showed that the mean number of TRP is 7.4 per patient.[17] In a study conducted on hospitalized patients, average TRPs were 9.35 per patient.[18]

Notably, previous studies were focused on certain types of TRPs, particularly adverse reactions, and have been limited to hospital admissions.[19–21] Additionally, the traditional high-alert drug approach was limited to drugs that have a low safety margin in which errors associated with the use are devastating. We have previously identified the most common TRPs and their frequency in such a limited resource health care system outpatient setting.[14] However, no study has linked medications/groups to TRPs in an effort to create a sort of focused TRP medication list for this health care setting. Thus, there is a need for a large, multicenter study to identify medications that are mostly associated with TRPs in such health care settings. Such an approach will be useful for pharmacists in supporting patient medication use by addressing TRPs, as opposed to medications that would be associated with serious consequences in the case of error.

Aim of the study

The present study aimed to assess medications most commonly associated with TRPs within the outpatient setting. Thus, the current study is an advanced step of our previous study,[14] focusing on relating TRPs with specific medications/groups of medication in an effort to create a sort of focused TRP medication list.

Method

Setting

The present study was carried out in eleven outpatient departments including respiratory, endocrine, and cardiovascular in five hospitals in the northern, central, and southern areas of Jordan. These hospitals represent major hospitals in distinctive areas of Jordan and include King Abdullah University Hospital (KAUH), a teaching hospital affiliated with the Jordan University of Science and Technology in Irbid; Jordan University Hospital, a teaching hospital affiliated with the University of Jordan in Amman; Al-Basheer Hospital, a public hospital in Amman; Princess Basma Hospital, a public hospital in Irbid; and Al-Karak Hospital, a public hospital in Al-Karak.

Patients selection

During the study period (September 2102–December 2013), patients who attended cardiology, endocrine, and respiratory outpatient clinics and met the selection criteria were invited to take part in the study. The selection criteria included adult patients who have used at least two long-term medications (either new or long-standing) and who have one or more or chronic medical conditions. After explaining the study to those patients who agreed to participate, signed written informed consents were obtained from each patient. A parent or legal guardian of any participant under the age of 18 years also provided written informed consent. Furthermore, the study protocol was approved by appropriate research ethics committees and the institutional review board of Jordan University of Science and Technology.

Data collection

Pharmacist review for TRP determination

Recruited patients were assessed for TRPs by clinical pharmacists (n=11, one clinical pharmacist/department), who are involved in direct patient care and are licensed to practice pharmacy and hold Doctor of Pharmacy degree. The identification of TRPs was carried according to a

systematic pharmaceutical care manual that the clinical pharmacists were trained on using to identify and document TRPs. The manual allowed assessment for TRPs, via evidence-based approach, which incorporates best evidence in decision making. TRPs were identified via interview of patients and referral to medical records[22,23] against national and international compendiums and guidelines, where a comprehensive, full range of TRPs was identified. The TRPs classification system used was based on modified version of classification of TRPs by Aburuz et al,[20] in which it was modified to be adapted for use in outpatient setting. The validity and reliability of the classification system were established on a sample of 200 patients and were found to be valid and reliable with good inter-rater agreement. Full details of validation and reliability tests have been published elsewhere.[22] The classification system groups TRPs into indication, effectiveness, safety, patient related, and miscellaneous areas.[18] Of the most important categories of TRPs identified is adherence-related problems, which included issues related to adherence to drugs, which was assessed indirectly by interview guided by an adherence questionnaire, and adherence to self-care activities or non-pharmacological therapy (eg, smoking abstinence and dietary recommendations), which was assessed via interview of patients. Interview with each patient took ~15 minutes.

Outcomes of the study

The following outcomes were recorded for each TRP:

1. Drugs associated with TRPs.
2. The disease associated with TRPs.

The implicated medications with TRPs were recorded together with the linked disease. The British National Formulary drug classification system was adopted. Assessment of most common drugs associated with TRPs of any category was carried out. For each category of TRPs, the most common drugs associated with each category of TRPs were documented. In addition, the disease linked to each type of TRPs was investigated. The present study was an advance of a previous study that assessed medication-related problems; full details are shown elsewhere.[14] Data were coded using the SPSS, version 21.0 (SPSS Inc., Chicago, IL, USA) entry program. The data were summarized using frequency tables including mean values and/or percentage.

Results

General characteristics of the patients recruited

During the study period (September 2012–December 2013), the total number of patients recruited was 2,747 patients. Approximately two-thirds (68.3%) of the patients were between 18 and 64 years old, and about 60% of the patients were females. Regarding the level of education of the study sample, 16.3% of patients recruited were illiterate, with approximately one-quarter of the patients having completed primary (29.3%), secondary (29.0%), or tertiary (ie, university; 25.3%) education.

In addition, 96.5% of patients were insured. After assessing the patients, it was noted that 9.1% of the patients had a problem in medication adherence, 48.7% of the patients had a problem in illness knowledge, and 86.8% of the patients were nonadherent to self-care and nonpharmacological recommendations relevant to their disease. Table 1 summarizes the demographic, social, and clinical characteristics of the patients recruited.

Table 1 Demographic, social, and clinical characteristics of the patient recruited

Variables	%
Age	
<18 years old	1.1
18–64 years	68.3
>65 years old	30.6
Missing	0.2
Sex	
Male	41.2
Female	58.5
Missing	0.4
Educational level	
Illiterate	16.3
Primary	29.3
Secondary	29.0
Tertiary	25.3
Missing	0.1
Health insurance	
Insured	96.5
Uninsured	3.3
Missing	0.2
Problem in adherence to medications	
Yes	9.1
No	90.9
Missing	0.0
Problem in illness knowledge	
Yes	48.7
No	51.3
Nonadherence to self-care and nonpharmacological recommendations	
Yes	86.8
No	13.2
Missing	0.9

Table 2 Frequency of drug groups (BNF drug class) causing any TRPs

Drugs	%	n (total 10,672)
Cardiovascular drugs	53	5,656
Endocrine drugs	18.1	1,932
Respiratory drugs	11.4	1,217
Gastrointestinal drugs	7.7	822
Blood and nutrition	4.7	502
Musculoskeletal drugs	1.9	203
Nervous drugs	1.6	171
All medications	1	107
Infection	0.2	21
Genitourinary drugs	0.2	21
Malignancy and immunosuppressant drugs	0.2	21

Abbreviations: BNF, British National Formulary; TRPs, treatment-related problems.

Most patients had cardiovascular disease and diabetes while some patients had respiratory diseases.

Drug groups associated with TRPs

After assessing the 2,747 patients recruited, it was determined that they were prescribed an average of 5.6 medications and had a total of 10,672 TRPs. This yields an average of 11.1 TRPs per patient. The medication groups most commonly associated with TRPs of any category were cardiovascular (53.0%), endocrine (18.1%), and gastrointestinal (7.7%) systems. Full details are illustrated in Table 2. Table 3 shows the specific medications associated with TRPs of any category, which were atorvastatin (12.5%), metformin (8.5%), simvastatin (6.2%), enalapril (5.9%), isosorbide dinitrate (4.6%), albuterol (4.6%), aspirin (4.5%), lansoprazole (4.2%), and insulin (any type; 4.0%).

Cardiovascular medications were the most common drugs implicated with many subtypes of TRPs, including allergic reactions or undesirable effects (88.5%), unavailable drug products (87.3%), safety interaction issues (81.8%), and more effective drugs available (77.2%). Gastrointestinal medications were the most common drugs implicated with "drugs with no indication" (70.5%) and "efficacy interaction issues" (60.0%). Central nervous system medications were most commonly implicated with "addiction or recreational drug use" (40.0%). Endocrine medications were most commonly implicated with "the DRP of being contraindicated or unsafe for the patient's condition" (55.4%). Blood and nutrition medications were the most common drugs implicated with "a need for an additional diagnostic test" (50.0%). Regarding adherence to medications, 211 patients had a problem; of these, 48.8% were nonadherent to all medications, 20.4% to cardiovascular medications, 16.1% to respiratory medications, and 11.8% to endocrine medications (Table 4).

Table 3 Most common drugs causing any TRPs

Drugs	%	n (total 10,672)
Atorvastatin	12.5	1,334
Metformin	8.5	907
Simvastatin	6.2	662
Enalapril	5.9	630
Isosorbide dinitrate	4.6	491
Albuterol (salbutamol)	4.6	491
Aspirin	4.5	480
Lansoprazole	4.2	448
Insulin (any)	4.0	427
Furosemide	2.4	256

Abbreviation: TRPs, treatment-related problems.

Diseases linked with TRPs

The present study assessed the most common diseases linked with different types of TRPs. As summarized in Table 5, hypertension, diabetes mellitus, and dyslipidemia were the most common diseases associated with different subtypes of TRPs.

Discussion

The present study identified medication groups associated with TRPs, which researchers consistently agree are common, undesirable, and costly.[1–9] The identification of medications associated with TRPs can prove useful in targeting pharmacists' efforts to patients most at risk for such problems. In addition to clinical value, such an enhanced targeting approach helps to improve the logistics of the delivery of pharmacists' service and would be useful for documenting the value of pharmacist interventions. An interesting finding of the present study is that cardiovascular and gastrointestinal drugs were implicated with most categories of TRPs, thereby qualifying as high-risk drugs for TRPs. The present study assessed TRPs in a comprehensive manner, using a standardized and validated methodology, and included medical TRPs in addition to drug-specific problems. The present study increases the understanding of the medications associated with care issues according to different categories, suggesting that the pharmacist could play a key role in TRPs identification and care.

In the present study, ~80% of TRPs were related to endocrine, cardiovascular, nervous, or respiratory drugs. The results indicated that a limited number of drug groups are considered high-risk medications for TRPs and can

Table 4 Drug categories implicated with individual TRPs

TRPs	n	BNF drug class (%)										
		GI	CVS	Respiratory	CNS	Infection	Endocrine	GUS	Malignant	Blood and nutrition	Musculoskeletal	All drugs
Drug without an indication	789	70.5	7.0	2.3	3.4	1.3	0.6	0.0	0.0	12.5	2.4	0.0
Addiction or recreational drug use	20	5.0	35.0	0.0	40.0	0.0	5.0	0.0	0.0	15.0	0.0	0.0
The patient treatment should be stepped down	289	22.5	37.0	11.8	0.3	0.0	17.0	0.0	0.0	10.4	1.0	0.0
Duplication	96	1.0	57.3	27.1	1.0	0.0	6.3	3.1	0.0	4.2	0.0	0.0
Avoidable adverse reaction	3	0.0	66.7	0.0	0.0	0.0	33.3	0.0	0.0	0.0	0.0	0.0
Untreated condition	526	0.6	58.0	0.8	4.7	0.2	16.0	0.0	0.2	17.7	3.2	0.0
More effective drug is available	426	0.5	77.2	3.1	5.4	0.2	12.7	0.0	0.0	0.9	0.7	0.0
The patient requires additional/combinational therapy	2,374	0.4	55.7	4.3	11.9	0.0	33.3	0.0	0.2	3.0	0.8	0.0
Dosage regimen issue	513	0.6	56.7	13.8	0.2	0.2	25.3	0.0	0.0	2.5	0.4	0.0
Efficacy interaction issue	40	60.0	30.0	0.0	0.0	0.0	5.0	0.0	0.0	2.5	2.5	0.0
A current drug is contraindicated unsafe for patient condition	74	1.4	24.3	0.0	2.7	0.0	55.4	0.0	0.0	1.4	14.9	0.0
A safer drug is recommended	51	2.0	56.9	0.0	7.8	0.0	15.7	2.0	0.0	0.0	15.7	0.0
The patient is at high risk of developing ADRs	42	0.0	64.3	2.4	4.8	0.0	14.3	0.0	9.5	4.8	0	0.0
Allergic reaction or an undesirable effects	26	0.0	88.5	0.0	0.0	0.0	11.5	0.0	0.0	0.0	0.0	0.0
Safety dosage regimen issues	54	7.4	55.6	9.3	1.9	0.0	14.8	0.0	0.0	7.4	3.7	0.0
Safety interaction issues	77	0.0	81.8	0.0	14.3	0.0	1.3	1.3	0.0	0.0	1.3	0.0
The patient is not instructed or does not understand important information regarding his medications	3,148	3.2	47.3	25.7	1.6	0.2	16.8	0.4	0.3	3.3	1.2	0.0
A problem in patient's adherence to medications	211	0.0	20.4	16.1	0.0	0.0	11.8	0.0	0.5	1.4	0.9	48.8
Drug product not available	142	0.0	87.3	0.7	0.0	0.0	8.5	0.0	1.4	1.4	0.0	0.0
A need for additional or more frequent monitoring	1,726	0.1	78.0	1.0	0.2	0.0	13.8	0.0	0.2	2.5	4.3	0.0
A need for additional diagnostic test	16	0.0	37.5	0.0	0.0	0.0	12.5	0.0	0.0	50.0	0.0	0.0
A need for consultation	26	26.9	34.6	0.0	19.2	0.0	3.9	0.0	0.0	15.4	0.0	0.0
The chosen medications are not cost-effective	3	33.3	66.7	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0

Abbreviations: ADR, adverse drug reaction; BNF, British National Formulary; CNS, central nervous system; CVS, cardiovascular system; GI, gastrointestinal; GUS, genitourinary system; TRPs, treatment-related problems.

Table 5 Linked disease with individual TRPs

TRPs	Linked disease (%)														
	HTN	DM	IHD	Dyslipidemia	HF	Hyperthyroidism	Hypothyroidism	Renal disease	Hepatic disease	Asthma	COPD	RA	Gout	Dep	Others
Drug without an indication	0.5	1.3	1.3	1.3	0.0	0.0	0.0	0.8	0.0	1.6	0.8	0.3	0.0	0.0	92.1
Addiction or recreational drug use	0.0	0.0	50.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	50.0
The patient treatment should be stepped down	8.2	10.0	13.8	2.2	9.3	0.4	3.7	1.1	0.0	12.6	0.4	1.5	0.7	0.0	36.1
Duplication	39.2	4.1	5.2	10.3	2.1	0.0	0.0	0.0	0.0	24.7	3.1	0.0	0.0	0.0	11.3
Avoidable adverse reaction	66.7	33.3	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Untreated condition	4.7	13.4	11.7	33.4	0.9	0.3	3.0	5.2	0.0	0.5	0.0	0.3	2.6	0.2	23.7
More effective drug is available	41.9	16.5	16.3	8.2	6.8	0.0	0.0	0.6	0.0	2.3	1.5	0.0	0.0	0.0	5.9
The patient requires additional combination therapy or stepping up	14.3	31.6	20.3	14.7	4.3	0.0	0.5	0.5	0.1	7.4	1.4	0.2	0.5	0.0	4.1
Dosage regimen issue	16.9	24.7	4.5	32.2	0.8	0.0	1.4	0.4	0.0	8.5	5.8	0.2	0.4	0.0	4.3
A current drug is contraindicated unsafe for patient condition	23.4	31.2	2.6	2.6	14.3	0.0	0.0	13.0	0.0	1.3	0.0	0.0	0.0	0.0	11.7
A safer drug is recommended	37.7	22.6	3.8	5.7	1.9	0.0	0.0	1.9	0.0	1.9	0.0	0.0	0.0	0.0	24.5
The patient is at high risk of developing ADRs	29.5	9.1	9.1	9.1	6.8	0.0	0.0	2.3	0.0	2.3	0.0	13.6	2.3	2.3	13.6
Allergic reaction or an undesirable effects	60.0	12.0	0.0	12.0	0.0	0.0	4.0	0.0	0.0	0.0	0.0	4.0	0.0	0.0	8.0
Safety dosage regimen issues	22.9	14.5	3.1	40.5	0.8	0.0	0.0	2.3	0.0	4.6	0.0	0.8	0.0	0.0	10.7
The patient is not instructed or does not understand	31.3	34.4	6.1	7.3	2.0	0.0	0.7	0.4	0.0	10.0	3.6	0.3	0.3	0.0	3.8
A problem in patient's adherence to medications	25.1	20.2	8.3	12.0	2.3	0.0	1.1	0.0	0.0	15.2	7.1	0.9	1.4	0.0	6.4
Drug product not available	44.9	34.3	6.1	7.7	1.6	0.0	0.1	0.1	0.0	0.9	0.3	0.1	0.0	0.0	3.8
A need for additional or more frequent monitoring	21.0	61.3	0.7	10.9	1.0	0.1	0.7	1.1	0.0	0.9	0.3	0.1	0.6	0.0	1.3
A need for additional diagnostic test	9.9	34.4	0.3	38.0	0.5	0.3	0.8	4.3	0.0	0.0	0.0	0.3	0.0	0.0	11.2
A need for consultation	0.0	79.8	0.7	0.2	0.0	0.0	0.5	9.5	0.0	0.0	0.0	0.8	0.0	0.2	8.3
The chosen medications are not cost-effective	18.2	81.8	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0

Abbreviations: ADR, adverse drug reaction; Dep, depression; DM, diabetes mellitus; HF, heart failure; HTN, hypertension; IHD, ischemic heart disease; RA, rheumatoid arthritis; TRPs, treatment-related problems.

qualify as a priority for pharmacists in primary care. It is well-known that cardiovascular drugs are among the drugs that have a high risk of adverse drug reactions. Diabetes mellitus is among the ambulatory care sensitive conditions were inappropriate case management in primary care, can lead to hospital admissions.[9,24]

When comparing the ISMP high-alert drugs list[13] with the drugs suggested from the current study, some differences are noted, which could be attributed to the definition of the "risk." In addition, the high-risk medications identified in the present study are more directed toward patient care.

The TRPs identified in this study occurred in real outpatients with routine medication use and clinical care. Insulin and metformin have contributed to the biggest share of the endocrine medication associated with TRPs. Thus, the present study highlighted that these medications are a high risk for TRPs.

Different age groups and linked outcomes can result in different high-risk medication lists. For example, in elderly patients, antipsychotics as well as some nonprescription drugs, such as nonsteroidal anti-inflammatory drugs (NSAIDs), are commonly implicated in TRPs.[6,25] Initial thoughts might suggest that the use of certain medications (eg, idiosyncrasy) increases the odds for TRPs; however, care quality also appears to be an important factor. For example, if patient treatment is not stepped up by the health care professional, the patient treatment goals will remain unmet.

Cardiovascular drugs were implicated with many categories of TRPs, including indication, efficacy, safety, adherence, and miscellaneous TRPs (eg, monitoring problem), suggesting that these cardiovascular medications are a high risk, subject to many TRPs, and are commonly implicated with hospital admissions.[9,26,27] As expected, gastrointestinal drugs were commonly associated with the DRP "drugs without indication," as these drugs are commonly prescribed without a prescription by community pharmacists without formal assessment by a medical practitioner. They were also highlighted as being implicated with "drug use without an indication" within the hospital setting in Jordan.[18] Blood and nutrition medications were commonly associated with "the need for additional diagnostic tests." In Jordan, within the hospital setting, important drugs associated with DRPs were gastrointestinal drugs (indication-related problems), cardiovascular drugs (efficacy-related problems), and NSAIDs (adverse effects).[16]

The present study showed a major problem related to illness knowledge (48.7% of patients) and adherence to self-care and nonpharmacological recommendation (86.8% of patients) among patients. This highlights a major issue in relation to the quality of professional patient counseling delivered primarily by pharmacists and, sometimes, other health care professionals. This was the case despite the fact that most (>85%) of the study samples received primary, secondary, or tertiary education and most of the study samples were somewhat young. In the present study, 211 problems related to adherence to medication were noted; and in about half of these problems, nonadherence was related to all medications. Nonadherence figures for medications are considerably lower than those for self-care and nonpharmacological recommendations. Within the hospital setting in Jordan, 4.4% of patients had a problem with adherence to drugs and 2.9% had a problem with adherence to self-care activities, which is many folds lower than those in the outpatient setting identified in the present study (9.1% and 86.8% of patients, respectively).[16] Two studies carried out in Jordan (outpatient clinics and community pharmacies) highlighted that 46.1% and 73.4% of patients, respectively, were nonadherent to medications.[28,29] The differences in the percentages of nonadherence/adherence among studies might be attributed to differences in the methodology and study settings.

Limitations

Although the present study identified a multitude of TRPs, the rate of acceptance and implementation of recommendations by medical practitioners and the clinical relevance of these TRPs were unknown. Such data provide an indication about the importance of the problems identified and reflect on medical practitioners' views of the TRPs and value they perceive for pharmacist input. Yet, the present study still provided insights regarding patients' medication management situation in the outpatient setting, and the results can guide further research in this area and improve clinical practice. The TRPs in the present study were assessed only by one practitioner. It is unknown whether there would be any discrepancies in terms of identified TRPs if there was an input from another rater. Most of the TRPs identified were associated with drugs or diseases affecting cardiovascular, endocrine, and respiratory system, which can be related to the study that was conducted in cardiovascular, endocrine, and respiratory clinics. Results of the present study are most likely generalizable for patients from Jordan. Additionally, a wider range of patients' selection criteria is recommended for future studies where patients with acute medical condition are to be included in the analysis of TRPs.

The present study highlights a major need for enhanced medication management for patients; such need is relevant to medical practitioners and clinical pharmacists and can be extrapolated to the community pharmacies and hospitals given the large magnitude of the TRPs and their risk

potential. Thus, more is needed from pharmacists to address such an important matter. Another recommendation of the present study relevant to the major finding is that targeting high-risk medications is a key at the present limited resource health care environment. Efforts should be made to disseminate knowledge about the magnitude and risk of TRPs and important high-risk drugs to the practicing pharmacists, via professional workshops, for example. Application of the targeting approach in routine care or in robust clinical trials to assess the impact of pharmacist intervention for TRPs to facilitate routine implementation. Other targeting approach can be suggested for future research making use of "more clinical" factors associated with TRPs or use a composite targeting approach taking input from different targeting strategies.

Conclusion

The present study identified medication groups implicated and linked diseases with TRPs from an outpatient sample from a number of hospitals in Jordan. TRPs were commonly associated with cardiovascular, endocrine, or gastrointestinal drugs. Cardiovascular medications were the most common drugs implicated with multiple subtypes of TRPs. Hypertension, diabetes mellitus, and dyslipidemia were the most common diseases associated with different subtypes of TRPs. Targeting patients utilizing high-risk drugs by pharmacists can improve patient health outcomes and can be useful to prioritize pharmacists' efforts to those most at need.

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Disclosure

The authors report no conflicts of interest in this work.

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