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Identification of Drug-Related Problems: A Prospective Study in Two General Hospitals

Maher R. Khdour[1,*], Anan S. Jarab[2], Heba O. Adas[3], Ekhlas Z. Samaro[4], Tareq L. Mukattash[5] and Hussein O. Hallak[1]

[1]*Faculty of Pharmacy, Al-Quds University, Abu-Dies, Jerusalem, P.O. Box 20002, Palestine;* [2]*Faculty of Pharmacy, Al-Zaytoonah University of Jordan, Amman, Jordan;* [3]*Department of Pharmacy, Tulkarm (Thabet-Thabet) Hospital, Tulkarm-Palestine;* [4]*Department of Pharmacy, Alwatani Hospital, Nablus-Palestine;* [5]*Department of Clinical Pharmacy, Faculty of Pharmacy, Jordan University of Science and Technology, Irbid 22110, Jordan*

Abstract: Drug-related problems (DRPs) can reduce the potential clinical benefits of treatment with medicines and waste valuable resources. No previous studies were published to examine the nature and frequency of drug related problems among hospitalized patients in Palestinian hospitals. Methodology: Prospective observational study was conducted to report and record the natural and frequency of drug related problems in two general hospitals. Results: The study included 212 patients, 54.4 % female, with a mean age 62.2 (±10.6 SD). 88% of the patients were reported with one or more DRPs, with an average of 1.9 DRPs per patient were found. The most prevalent DRP was incorrect dosing regimen which was represented by (22.2%), followed by drug-drug interaction (19.4%), drugs need laboratory tests (15.2%). Ceftriaxone, warfarin, enoxapirin and dogixin were the drugs causing most frequent DRPs. The drug groups causing most DRPs were anti-infective agents, anti-thrombotic agents and non-steroidal anti-inflammatory agents. Once discovered, the majority of DRPs (71.6%) were accepted by the physicians and solved immediately, while 11.5 % of pharmacist advice was not approved. Multiple regression analysis indicated that the number of medications (RR 1.99; 95% CI 1.31-3.76) and the number of medical conditions (RR 1.81; 95% CI 1.11-3.13) independently predicted the number of DRPs. Conclusion: DRPs in general hospitals are frequent, serious and predictable. Most of the problems identified as DRPs by the pharmacists were accepted by the physicians and solved. Pharmacists in the hospital setting are well suited to identify and resolve DRPs.

Keywords: DRPs, Pharmacist intervention, hospital setting, adverse drug reaction, Palestine.

INTRODUCTION

Drug therapy is growing more complex, thus making appropriate drug prescribing increasingly challenging. Many patients do not receive the intended beneficial effects of their treatment due to drug-related problems (DRPs) [1]. DRPs cause both unnecessary suffering and huge expenditures to society, because they necessitate extra doctor's visits and hospitalizations [2].

During the last decade, several studies have been published highlighting the significance of adverse drug reactions in hospitalized patients in terms of frequency, [3-6] consequences for the affected patients [7-9] and costs for the hospitals [10-12]. DRPs include all issues that can potentially affect the success of pharmacotherapy in a given patient, in particular medication errors, adverse drug events and adverse drug reactions [9]. A review of the literature from 1990 to 2005 found that on average 8% of hospitalized patients experience an adverse drug event (ADE), and 5-10% of all drug prescriptions or drug applications are erroneous [13]. As an example, it has been reported that 14.6% of internal medicine patients experience ADEs. Similarly, 12% to 17% of hospitalized patients experience ADE after discharge [14, 15]. Older people are particularly vulnerable because of their increased prevalence of chronic diseases and drug consumption. The associations of these factors with patient metabolic changes with age predispose older people to suffer drug-drug interactions and adverse drug events, especially as they generally have more hospital admissions and discharges [16, 17].

Literature reports indicate that the most common types of DRPs were: wrong dosage, inappropriate schedule and missing information. More detailed investigations show that DRP may stem from: non-compliance [18, 19], lack of knowledge about the medication [18] adverse drug events [20] drug interactions [21, 22] dosage problems, and practical problems [20]. Events associated with such DRPs include changes in drug therapy following hospital discharge, patient's cognition and poly-pharmacy [18, 20].

Pharmacy practitioners have a key responsibility to respond to patient DRPs. For example, Benrimoj *et al.* demonstrated the value of clinical interventions in Australian community pharmacies in terms of both the quality of care and cost savings [23]. Favorable clinical and economic outcomes of pharmaceutical care in ambulatory patients have also been shown by Strand *et al* [24].

*Address correspondence to this author at the Faculty of Pharmacy, Al-Quds University, Abu-Dies, Jerusalem, P.O.Box 20002, Palestine;
Tel: +97222799753; Fax: +97222471149;
E-mail: mkhdour@pharm.alquds.edu

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There is a perception in the Palestinian health care system that DRPs are common in Palestinian community, yet no studies were conducted to quantitate this problem. Furthermore, the fact that the health care system in the general does not involve an active role for the pharmacists in hospitals, suggests that the prevalence of DRP may be high. As such, a study to quantitate DRP in Palestine was deemed necessary. The objective of the study was to examine the nature and frequency of drug related problems among hospitalized patients and to evaluate the impact of the pharmacist in identifying medication related problems.

METHODS

Patients and Design

This prospective multicenter study was approved by the Committee for Clinical Research, Hospital Administration Department, Ministry of Health, Palestine. From May to November 2011, expert clinical pharmacists identified DRPs and recorded the pharmacist's advice on drug therapy. The study was performed in two medical wards at Al-Watani general hospital and two medical wards at Tulkarm general hospital (North Palestinian Territories). For participation we chose wards that had clinical pharmacists joining multidisciplinary therapeutic teams. All patients admitted to the participating wards were consecutively included, while readmissions of patients who already had been enrolled were excluded. Information on possible risk factors such as age, gender, number of drugs used at admission, total number of clinical/pharmacological risk factors and type of department were recorded and analyzed.

Classification of Drugs and DRPs

The drugs were classified according to the Anatomical Therapeutic Chemical (ATC) classification system [25]. The DRPs were defined as ''An event or circumstance involving drug therapy that actually or potentially interferes with desired health outcomes" [26]. The classification of DRPs is shown in Table **1** and was compiled according to a modified version of Strand *et al.* [27]. For the adverse drug reactions ADRs and drug interactions, only those graded as important, were included. An independent assessment team was appointed, consisting of three specialists in hospital pharmacy with long experience as clinical pharmacists. The team retrospectively assessed and assigned DRPs to their categories after each of the team members had undertaken an individual evaluation. If the individual judgment differed, the case was discussed and consensus was reached.

Data Collection and Response to Pharmacist's Advice

A special data collecting form was designed by the investigators for a structured patient information collection. The form was designed, tested and found applicable for the participating departments. Clinical pharmacists collected the data from medical charts, medical records, physicians' ward rounds and from the multidisciplinary meetings where each patient was discussed with regard to diagnosis and management.

The main section was designed to record all the data regarding the patient medication, dates and times that a prescription was written, names of medication, dosage forms, doses, dosage regimens, starting and stopping dates, if applicable, instructions and potential drug-drug interactions. Demographic and medical information about patients was obtained from flow sheets and medication administration records. Laboratory results and results of diagnostic tests were used as necessary.

Table 1. Classification of a Drug-related Problem

1. The need for an additional drug
2. Unnecessary drug
3. Non-optimal drug, including drug formulation
4. Non-optimal dosing, including optimal dosing schedule
5. No further need for the drug
6. Drug-drug interactions
7. Need for laboratory tests [e.g. therapeutic drug monitoring (TDM), laboratory values]
8. Adverse effects (being experienced) (ADRs)
9. Medical chart error (e.g. dose not stated)
10. Compliance problems
11. Patient education required (giving patient information on the physicians request, e.g. to avoid non-compliance)
12. Information/therapy discussion (regarding a specific drug regimen for a patient)
13. Others

The collected data were reviewed by the investigational pharmacists and rechecked with investigational clinical team. The investigational pharmacists participated in the process of evaluation used a standard set of definitions related to drug related problems. As primary reference sources, the Palestinian Registered Product List, Drug Information Handbook, 21st edition the Physician's Desk Reference were used.

Responses to pharmacist advice were recorded in three categories: ''Fully accepted' 'which indicates immediate acceptance by the physician and action taken. ''Rejected '' which indicates that the physician did not approve the pharmacist proposal and no action was taken. ''Partially accepted'' which indicates agreement by the physician, who took notice, but no immediate action was taken.

Data Analysis

All data were coded and analyzed using the SPSS program for Windows 16.0 (SPSS Inc, Chicago, IL). Descriptive statistics are shown as means with range or standard errors. Statistical comparisons were done by the Mann-Whitney for nominal continuous data, and the Chi-squared (χ^2) test for categorical. The multivariate analysis was employed by the backward logistic regression method in order to assess the influence of number of diseases, ward type and number of medications on the number of DRPs identified. In the first stage of regression, we utilized variables for which the *p*-value in the univariate analysis was less than 0.1. For all analyses, a probability value of less than 0.05 was considered statistically significant.

RESULTS

The study included 212 patients, 54.4 % female, with a mean age 62.2 (±10.6 SD). On average, each patient used 4.8 (range 0-14) medicines. All the recruited patients were monitored during the total length of their hospital stay. The average length of hospital stay was around 5.8 days ranging from 2 to 18 days as shown in Table **2**.

Table 2. Demographic Description of Recruited Patients

Parameter	Patients with DRPs	Patients without DRPs	P-value
	N= 187	N=25	
Average age in years (S.D)	65.4 (14.2)	58.1(5.9)	0.04*
Age range	22-87	48-69	
Gender distribution (Female %)	101 (53.8%)	16 (64.0%)	0.07**
Average number of medication taken (S.D)	5.1 (1.5)	2.9 (0.4)	0.02*
Average length of hospital stay in days (S.D)	6.3 (2.1)	2.2 (0.9)	0.002*
Average number of medical conditions (S.D)	4.1(2.7)	2.8 (1.1)	0.001*

*Statistical level of significance, Mann-Whitney U-test, $p<0.05$ between the two groups, ** Statistical level of Significance at $p<0.05$, Chi-squared test. DRPs: Drugs Related Problems. SD: Standard deviation. P: Level of significance.

Table 3. Type, Example and Acceptance Rate of Interventions Made

	N=356	Acceptance Rate n (%)[a]			Examples of Drugs involved
Type of DRP	n (%)	Full	Partial [b]	Rejected	
Non optimal dose	79 (22.2)	61 (77.2)	13 (16.5)	5 (6.3)	Antibiotics NSAIDs, ACEIs, spiranolactone
Drug-Drug interaction	69 (19.4)	49 (71.0)	12 (17.4)	8 (11.6)	Carvedilol + salmeterol (β-blocker and β-agonist). Aminophylline +Ceftriaxone (incompatible) Granisetone + Ciprofloxacin (arrhythmias)
Need for laboratory tests	54 (15.2)	31 (57.4)	13 (24.1)	10 (18.5)	Warfarin, digoxtin, heparin, aminoglycosides
Unnecessary drug	42 (11.8)	35 (83.3)	5 (11.9)	2 (4.8)	Enoxapirin, Rantidin, Famotidin, Opemrazole. Antibiotics
Need additional drugs	26 (7.3)	17 (65.4)	6 (23.1)	3 (11.5)	Atorvastatin after MI, Analgesic for pain. Dopamine to achieve diuresis. Amlodipine for hypertension
Adverse effect	18 (5.0)	10 (55.6)	2 (1.1)	6 (33.3)	Furosemide (hypokalemia) Ceftriaxone (cholecystitis) NSAIDs (↑risk of bleeding)
Non optimal drug	16 (4.5)	9 (56.2)	3 (18.8)	4 (25.0)	Tetrahydrozoline-containing eye drops for treating dry eyes. Morphine replaced by pethidine. Amlodipine replaced by enalaprin
No clear indication	14 (3.9)	11 (78.6)	1 (7.1)	2 (14.3)	Ceftriaxone and Metronidazole, Enoxapirin. (many cases with no indications)
Medical Chart error	11 (3.1)	9 (81.8)	2 (18.2)	0 (0.0)	ISMN® (trade name for isosorbide mononitrate).NSAIDs, Antibiotics (missing the dose or route of administration
Therapy discussion	11 (3.1)	8 (72.7)	2 (18.2)	1 (9.1)	IgG, Tigecycline, Trastuzumab (prepared by clinical pharmacist)
Patient education	10 (2.8)	10 (100.0)	0 (0.0)	0 (0.0)	Alendronate, Methotrexate, Folic acid
Compliance problems	6 (1.7)	5 (83.3)	1 (16.7)	0 (0.0)	Carbamazepine, Phenytion, Folic acid.

[a] Acceptance rate of pharmacist advice regarding each DRP group by physicians or healthcare professionals.
[b] Advice accepted but not acted upon, or partially acted upon.

Table 4. Variables Associated with Occurrence of Drug-related Problems (DRPs)

	Univariate Analysis			Multivariate Analysis		
Variables	**RR**	**CI 95%**	***P*-Value**	**RR**	**CI 95%**	***P*-Value**
Gender (female=1)	1.06	0.71-1.21	(0.3)	---	----	---
Age per 10 years	1.03	0.66-1.33	(0.3)	---	----	---
No. of medical conditions	2.1	1.21-3.45	(0.001)	1.81	1.11-3.13	(0.001)
No. of medication used	2.4	1.70-3.99	(0.001)	1.99	1.31-3.76	(0.001)
Department						
Rheumatology	1	0.78-1.11	(0.11)	0.87	0.70-0.99	(0.13)
Surgical	0.95	0.72-1.09	(0.12)	0.83	0.66-1.01	(0.06)
Internal medicine	0.90	0.84-1.22	(0.08)	0.98	0.79-1.21	(0.09)
ICU	1.04					

ICU: Intensive care unit.

The 212 recruited patients were using a total of 1018 medicines classified according to ATC classification system. Cardiovascular agents accounted for the majority of the medications consumed by the participants (25%) followed by anti-infective (16%), alimentary tract and metabolism (12%), anticoagulants and antiplatelets (10%), anti-inflammatory (10%) and gastrointestinal drugs.

The pharmacists identified 356 DRPs in 187 of the 212 patients (mean per patient 1.9; SD 0.8).

Ceftriaxone, enoxaparin, warfarin, and digoxitin were the drugs causing most frequent DRPs. The drug groups causing most DRPs were J01A-antiifective agents, B01A-anti-thrombotic agents, M01A-non-steroidal anti-inflammatory agents and A02B-drugs for peptic ulcer disease.

Table **3** represents the most commonly reported DRPs. Among the detected problems, incorrect dosing regimen represented the highest percentage (22.2%) followed by drug-drug interaction (19.4 %), drugs that required therapeutic monitoring (15.2%), unnecessary drug therapy (11.8%) and the need for additional drug therapy (7.3%).

The majority (~90%) of the pharmacists' interventions related to DRPs involved direct contact with the physician. For example, contraindications and adverse reactions were generally solved by immediate contact with the physician. Pharmacists were able to resolve some of the DRPs by themselves. This primarily included those related to adherence problems, and medications prescribed without indication.

Of 356 DRPs, 255 (71.6%) DRPs were solved immediately (i.e. "Full acceptance"). An additional 60 (16.8%) were accepted as DRPs, but immediate action was not taken (i.e. ''Partial acceptance''). Pharmacist advice was rejected for 41 (11.5%) DRPs (Table **3**).

Age, gender, type of department, number of medication and number of medical conditions were analyzed to determine whether they could predict the occurrence of DRPs. Multiple regression analysis found that number of medications (RR 1.99; 95% CI 1.31-3.76) and number of medical conditions (RR 1.81; 95% CI 1.11-3.13) independently predicted the number of DRPs. There was no relationship between age or gender and the number of DRPs identified (Table **4**).

DISCUSSION

The majority of patients have one or more DRPs in clinical departments in general hospitals. On average the pharmacists identified 1.9 DRPs per study patient. Our findings are well comparable with studies previously conducted in the European countries [1, 2, 28] revealed an average of 2.5 DRPs per patient. The little differences may be explained by different study populations. In consistence with our study, other researchers have also found high frequencies of inappropriate dosing [1, 29, 30-32], inappropriate drugs [33-35], need for laboratory tests [36] and need for additional drugs [37].

Drug dosing was considered too high in several cases including: Paracetamol 4 grams/day, Ceftriaxone intravenous 2g/day, Lactulose 30 ml/day and Spiranolactone 100mg in the presence of ACEI and heart failure. Ranitidine or Famotidine and Omeprazole combination represented the most unnecessary combination specially when used as prophylaxis against stress ulcer.

In this study, cardiovascular drugs are highly involved. However cardiovascular drugs were especially associated with probably unavoidable side effects. These problems could lead to early discontinuation of treatment which has been reported frequently as an important problem with cardiovascular preventive therapy such as antihypertensive and lipid lowering drugs. Gastrointestinal drugs such as laxatives and antacids were also highly involved, and have been reported as possible predictors of prescribing errors by Fijn *et al.* [38].

Among the 212 patients reviewed, 51 (24.0%) received one or more of those drugs described as having narrow therapeutic index and required careful monitoring. Out of those 51 patients, only 6 patients (11.8%) were monitored for those medications. This lack of monitoring can be

attributed to several factors; the major will be cost related [36]. Not all the physicians were familiar with which drugs should be closely monitored and even those who were familiar did not know the availability of the monitoring tests in their hospital. When the physicians were verbally asked about the importance of therapeutic drug monitoring some of them believed that clinical manifestation would be the best indicator to count on rather than the drug plasma sample.

Regarding drug-drug interaction, there was no special pattern for the identified drug-drug interactions in the screened patients. Only major interactions as classified using the Lexi-comp software were reported. This included prescribing Granisetone together with the Ciprofloxacin.

The most commonly prescribed medications with no clear indication were metronidazole and ceftriaxone which were prescribed for a sole reason which is prophylaxis, regardless of the patient case and kidney or liver function.

The effectiveness of pharmacists' interventions can be evaluated by means of physicians acceptance rates of the pharmacists' recommendations. Our study revealed 71.8% acceptance and full implementation of pharmacists' interventions. Previous studies report acceptance rates between 39% and 92% [39, 40]. This is probably due to different communication models when addressing DRPs. Direct communication between healthcare providers in general reveals higher acceptance rates than indirect contact, e.g. written reports [2]. This proactive approach may also have contributed to the high rate of problem-solving achieved in this study, as interventions were planned and executed during round discussion.

In general, 33.3% of the identified adverse drug effects and 25.0% of non-optimal prescribed drugs were not approved by the clinical teams, while proposed DRPs regarding "Unnecessary drug" and "no clear indication" were highly accepted by the physicians. This is possibly explained by the fact that most adverse effects were considered of minor clinical importance. Another explanation is that risk-benefit analyses have already been performed by physicians when prescribing the actual drugs and combinations. A previous study has reported that in 32.1% of cases when an adverse drug event occurred and reported to a healthcare provider, the drug was continued as before, with no further intervention from the healthcare provider [41]. This may be explained by that the pharmacist considered the side effect to be tolerable and not avoidable.

The major findings included an indication of several factors associated with DRPs. The number of medical conditions and the number of medications prescribed were independently associated with the number of DRPs. This implies that poly-pharmacy and co-morbidities are major risk factors for experiencing DRPs, which is consistent with other studies [42, 43]. Furthermore, the number of medications and co-morbidities appear to be strong predictors for the development of certain DRPs such as drug-drug interactions, need for laboratory tests, dosage problems and the need for additional drugs.

Future studies need to evaluate possible solutions that may prevent these drug related mistakes from happening. Some of the measures that may be considered include frequent chart reviews that may help identify DRP followed by communication of those DRP to respective physicians. Another measure may include bar codes for proper drug identification. Education and publicizing of the findings of this study may also help increase awareness in Palestinian hospitals. Finally, the study clearly indicates that the pharmacist may play an important role in identifying DRP. As such, effort needs to be made to increase opportunities for pharmacist support in drug treatment.

LIMITATION

The main limitation is that the study is small and that a control group was not included. The process of identification of the DRPs depended mainly on an observational experience which is more subjective and may be a source of bias. Another limitation is that the study was restricted to two hospitals and therefore cannot be assumed that the results are representative of other hospitals. The intervention revealed a significant reduction in number of DRPs. However, effects on clinical endpoints and drugs costs were not examined, as this was beyond the scope of this study. Future research should focus on studying the optimal strategy to improve prescribing practices and monitoring, particularly among high-risk patients or patients taking high-risk medications.

CONCLUSION

DRPs in general hospitals are frequent, serious and predictable. Most of the problems identified as DRPs by the pharmacists were accepted by the physicians and solved. Pharmacists in the hospital setting are well suited to identify and resolve DRPs. Policy-makers should consider implementing systematic medication reviews on a regular basis to achieve and maintain high-quality drug treatment in general hospitals. Future research should include clinical end-points to substantiate beneficial patient-related outcomes, e.g. reductions in side effects, and possible cost-savings.

CONFLICTS OF INTEREST

Declared none.

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REFERENCES

[1] Blix HS, Viktil KK, Reikvam A, *et al.* The majority of hospitalised patients have drug-related problems: results from a prospective study in general hospitals. Eur J Clin Pharmacol 2004; 60: 651-8.

[2] Viktil KK, Blix HS, Reikvam A, *et al.* Comparison of drug-related problems in different patient groups. Ann Pharmacother 2004; 38: 942-8.

[3] Bates DW, Cullen DJ, Laird N, *et al.* Incidence of adverse drug events and potential adverse drug events: implications for prevention. ADE Prevention Study Group. JAMA 1995; 274 (1): 29-34.

[4] Fattinger K, Roos M, Vergeres P, *et al.* Epidemiology of drug exposure and adverse drug reactions in two Swiss departments of internal medicine. Br J Clin Pharmacol 2000; 49 (2): 158-67.

[5] Moore N, Lecointre D, Noblet C, *et al.* Frequency and cost ofserious adverse drug reactions in a department of generalmedicine. Br J Clin Pharmacol 1998; 45 (3): 301-8.

[6] Lazarou J, Pomeranz BH, Corey PN. Incidence of adverse drug reactions in hospitalized patients: a meta-analysis of prospective studies. JAMA 1998; 279 (15): 1200-5.

[7] Bond CA, Raehl CL, Franke T. Medication errors in United States hospitals. Pharmacotherapy 2001; 21 (9): 1023-36.

[8] Classen DC, Pestotnik SL, Evans RS, *et al.* Adverse drug events in hospitalized patients: excess length of stay, extra costs, and attributable mortality. JAMA 1997; 277 (4): 301-6.

[9] van den Bemt PM, Egberts TC, de Jong-van den Berg LT, *et al.* Drug-related problems in hospitalised patients. Drug Saf 2000; 22 (4): 321-33.

[10] Bates DW, Spell N, Cullen DJ, *et al.* The costs of adverse drug events in hospitalized patients. Adverse Drug Events Prevention Study Group. JAMA 1997; 277 (4): 307-11

[11] Bordet R, Gautier S, Le Louet H, *et al.* Analysis of the direct cost of adverse drug reactions in hospitalised patients. Eur J Clin Pharmacol 2001; 56 (12): 935-41.

[12] Gautier S, Bachelet H, Bordet R, *et al.* The cost of adverse drug reactions. Expert Opin Pharmacother 2003; 4 (3): 319-26.

[13] Kra¨henbu¨hl-Melcher A, Schlienger R, Lampert M, Haschke M, Drewe J, Kra¨henbu¨hl S. Drug related problems in hospitals a review of the recent literature. Drug Saf 2007; 30: 379-407.

[14] Schlienger RG, Luescher TF, Schoenenberger RA, Haefeli WE. Academic detailing improves identification and reporting of adverse drug events. Pharm World Sci 1999; 3: 110-5.

[15] Forster AJ, Murff HJ, Peterson JF, Gandhi TK, Bates DW. The incidence and severity of adverse events affecting patients after discharge from the hospital. Ann Intern Med 2003; 138: 161-7.

[16] Hilmer S, Gnjidic D. The effects of polypharmacy in older adults. Clin Pharmacol Ther 2009; 85: 86-8.

[17] Parsons PL, Gifford C. Characteristics and outcomes of elderly patients receiving transitional care. Outcomes Manag 2002; 6: 182-5.

[18] Nikolaus T, Kruse W, Bach M, Specht-Leible N, Oster P, Schlierf G. Elderly patients' problems with medication. An in-hospital and follow-up study. Eur J Clin Pharmacol 1996; 49: 255-9.

[19] Gray SL, Mahoney JE, Blough DK. Medication adherence in elderly patients receiving home health services following hospital discharge. Ann Pharmacother 2001; 35: 539-45.

[20] Forster AJ, Murff HJ, Peterson JF, Gandhi TK, Bates DW. The incidence and severity of adverse events affecting patients after discharge from the hospital. Ann Intern Med 2003; 138: 161-7.

[21] Kohler GI, Bode-Boger SM, Busse R, Hoopmann M, Welte T, Boger RH. Drug-drug interactions in medical patients: effects of in-hospital tratment and relation to multiple drug use. Int J Clin Pharmacol Ther 2000; 38: 504-13.

[22] Egger SS, Drewe J, Schlienger RG. Potential drug-drug interactions in the medication of medical patients at hospital discharge. Eur J Clin Pharmacol 2003; 58: 773-8.

[23] Benrimoj SI, Langford JH, Berry G *et al.* Economic impact of increased clinical intervention rates in community pharmacy. A randomised trial of the effect of education and a professional allowance. Pharmacoeconomics 2000; 18: 459-468.

[24] Strand LM, Cipolle RJ, Morley PC, Frakes MJ. The impact of pharmaceutical care practice on the practitioner and the patient in the ambulatory practice setting: twenty-five years of experience. Curr Pharma Des 2004; 10, 3987-4001.

[25] World Health Organisation. The anatomical therapeutic chemical classification system with defined daily doses (ATC/DDD). http: //www.who.int/classifications/atcdd/en (2009). Accessed 1 Jul 2011.

[26] Pharmaceutical care network Europe. DRP-classification. http:// www.pcne.org (2011). Accessed 1 Jul 2011.

[27] Strand LM, Morley PC, Cipolle RJ, Ramsey R, Lamsam GD. Drug-related problems: their structure and function. DICP 1990; 24: 1093-1097.

[28] Blix HS, Viktil KK, Moger TA, Reikvam A. Characteristics of drug-related problems discussed by hospital pharmacists in multidisciplinary teams. Pharm World Sci 2006; 28: 152-158.

[29] McDonnell PJ, Jacobs MR. Hospital admissions resulting from preventable adverse drug reactions. Ann Pharmacother 2002; 36: 1331-1336.

[30] Alderman CP, Farmer C. A brief analysis of clinical pharmacy interventions undertaken in an Australian teaching hospital. J Qual Clin Pract 2001; 21: 99-103

[31] Gattis WA, Larsen RL, Hasselblad V, Bart BA, O'Connor CM. Is optimal angiotensin-converting enzyme inhibitor dosing neglected in elderly patients with heart failure? Am Heart J 1998; 136: 43-48.

[32] Gambassi G, Forman DE, Lapane KL, *et al.* Management of heart failure among very old persons living in long-term care: has the voice of trials spread? The SAGE study group. Am Heart J 2000; 139: 85-93.

[33] Hanlon JT, Fillenbaum GG, Schmader KE, Kuchibhatla M, Horner RD. Inappropriate drug use among communitydwelling elderly. Pharmacotherapy 2000; 20: 575-582.

[34] Oborne CA, Hooper R, Li KC, Swift CG, Jackson SH. An indicator of appropriate neuroleptic prescribing nursing homes. Age Ageing 2002; 31(6): 435-439.

[35] Flaherty JH, Perry HM, Lynchard GS and Morley JE. Polypharmacy and hospitalization among older home care patients. J Gerontol A Biol Sci Med Sci 2000; 55(10): 554-559.

[36] Gilbert AL, Roughead EE, Beilby J, Mott K, Barratt JD. Collaborative medication management services: improving patient care. Med J Aust 2002; 177: 189-192.

[37] Gurwitz JH, Rochon P. Improving the quality of medication use in elderly patients: a not-so-simple prescription. Arch Intern Med 2002; 162: 1670-1672.

[38] Fijn R, Van den Bemt PM, Chow M, De Blaey CJ, De jong-Van den Berg LT, Brouwers JR. Hospital prescribing errors: epidemiological assessment of predictors. Br J Clin Pharmacol 2002; 53: 326-31.

[39] Roberts MS, Stokes JA, King MA, *et al.* Outcomes of a randomized controlled trial of a clinical pharmacy intervention in 52 nursing homes. Br J Clin Pharmacol 2001; 51: 257-65.

[40] Zermansky AG, Petty DR, Raynor DK, Freemantle N, Vail A, Lowe CJ. Randomised controlled trial of clinical medication review by a pharmacist of elderly patients receiving repeat prescriptions in general practice. BMJ 2001; 323: 1340-3.

[41] Gray SL, Mahoney JE, Blough DK. Adverse drug events in elderly patients receiving home health services following hospital discharge. Ann Pharmacother 1999; 33: 1147-53.

[42] Ruths S, Straand J, Nygaard HA. Multidisciplinary medication review in nursing home residents: what are the most significant drug-related problems? The Bergen District Nursing Home (BEDNURS) study. Qual Saf Health Care 2003; 12(3): 176-80.

[43] Krska J, Cromarty JA, Arris F, *et al.* Pharmacist-led medication review in patients over 65: a randomised, controlled trial in primary care. Age Ageing 2001; 30(3): 205-10.

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