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## REVIEW

# Systemic review on drug related hospital admissions – A pubmed based search



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#### **KEYWORDS**

Adverse drug reaction; Drug related admission; Hospital admission; PubMed; Systemic review Abstract *Background:* Drug related admissions have significantly increased over the past few decades. According to various studies on drug related hospital admissions, it was estimated that around 5-10% of hospital admissions were due to drug related problems (DRP), in which 50% of them are avoidable.

*Objective:* The objective of the study was to derive results from various studies conducted on drug related hospital admissions and have an overall view about the incidence, frequency, cost of treatment, major causative drugs, problems for drug related hospital admissions, and preventable drug related admissions and summarize the factors responsible for the occurrence of DRP.

*Method:* Relevant literatures related to 'drug related hospital admissions' were obtained from PubMed database. Articles that were published from October 2007 to September 2012 were collected. All the studies being shown in the search results were considered for the study irrespective of the specialty department.

*Results:* A total of 366 articles were found based on the keyword 'drug related hospital admission', 'drug related problem admission', and 'adverse drug event admissions' search. Out of which

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49 articles were identified to be showing relevance to the study. Non-English, abstract-only articles, and out-patient adverse drug reaction (ADR) studies were filtered from 49 articles. Finally 15 articles were taken up for the study. Systemic analysis was made on these articles and the results were summarized.

*Conclusion:* Most of DRP studies were retrospective, multicenter studies conducted in general populations in Europe. The main objective of the studies was to estimate DRP frequency, incidence, risk factors and trends of DRP hospital admissions. Anti-neoplastic agents, CVS drugs and CNS drugs were related to most of the drug related problems. These studies concluded polypharmacy and older age were the major risk factors for developing drug related problems. It was found that the cost for the management of DRP was directly proportional to severity.

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#### Contents

1.	Introduction	2
2.	Objective	2
3.	Method	2
	Results and discussion	
	Conclusion	
	Contributors	
	Funding source	
	Acknowledgements	7
	References	7

#### 1. Introduction

A drug related problem (DRP) is defined as an event or circumstance that involves a patient's drug treatment that actually, or potentially, interferes with the achievement of an optimal outcome (Bhalla et al., 2003; Roxburgh and Degenhardt, 2008).

Problems associated with the drug use have a wide set of factors that can be considered as DRP viz. adverse drug reactions, drug interactions, untreated indication, inappropriate drug selection, sub-therapeutic dosage, supra-therapeutic dosage, non-compliance and drug use without indication.

DRP admissions have been significantly increased over the past few decades. According to various studies on drug related hospital admissions, it was estimated that around 5-10% of hospital admissions were due to drug related problems, in which 50% of them are avoidable (Nelson and Talbert, 1996; Sekhar et al., 2011). DRP admissions need high attention as DRP related admissions on an average accounted for 8.36% (Conforti et al., 2012; Davies et al., 2010; Menéndez-Conde et al., 2011; Posthumus et al., 2012; Rodenburg et al., 2011; Singh et al., 2011; Stausberg and Hasford, 2011). Increased use of medicines, existence of multiple inter current disease states and polypharmacy are some of the risk factors for DRPs. Gediatric population showed a high incidence of DRP admissions. Pharmacological and pathological changes leading to alteration in pharmacodynamic and pharmacokinetic parameters of drug absorption, distribution, metabolism and excretion in elderly patients are believed to be the reasons why gediatric population is the most affected group among DRPs. Antiplatelets, anticoagulants, antineoplastics, immunosuppressive, diuretics, antidiabetics and antibiotics showed a high profile of drug related problems. Majority of DRP admitted patients presented with chief complaints of weakness due to dehydration, electrolyte imbalance; bleeding, GI

disturbances, anemia, hypoglycemia, secondary infections etc. It has been noticed that drug related problems associated with medications' use have contributed to a major portion of the health expenses in most of the countries (Carrasco-Garrido et al., 2010; Dibben et al., 2011; Stausberg and Hasford, 2010; Wu et al., 2010).

In a study conducted by Smith et al., the frequency of drug 'reaction' in hospitalized patients had been studied, and they had shown that more the number of drugs, higher is the incidence of DRPs. These authors attributed the increase in morbidity due to polypharmacy, mainly when the patients are on 10 or more drugs. Twenty-four percentage of DRPs were found out to be due to drug interactions (Smith et al., 1996).

#### 2. Objective

The objective of the study was to derive results from various studies conducted on drug related hospital admissions and make an overall view about the incidence, frequency, cost involved for treatment, major drugs contributing for the event, complaints on drug related hospital admissions, and percent preventable ADR admissions and summarize the factors responsible for the occurrence of DRP.

#### 3. Method

Relevant literatures related to 'drug related hospital' admissions were obtained from PubMed database. Articles that were published from October 2007 to September 2012 were collected. All the studies being shown in the search results were considered for the study irrespective of the specialty department. A total of 366 articles were found based on the keyword 'drug related hospital admission', 'drug related problem admission', and 'adverse drug event admissions' search. Out of which 49 articles

Table 1 Background information of the drug related problem studies selected for the systemic review.

Study No.	Study	Country	Study design	Setting	Study group	Mean age
1.	Posthumus et al. $(2012)^5$	Netherlands	Prospective	Single-center	Pediatrics	3 years 6 months
2.	Conforti et al. (2012) <sup>6</sup>	Italy	Prospective	Single-center	Geriatrics	81.9 years Women (83.0 years) Men (80.7 years)
3.	Wu et al. (2012) <sup>19</sup>	Canada	Retrospective cohort	Multi-center	Geriatrics	$77.0 \pm 7.1$ years
4.	Singh et al. $(2011)^7$	India	Prospective observational descriptive	Single-center	General population	$49.8 \pm 18.23$ years
5.	Stausberg and Hasford (2011) <sup>8</sup>	Germany	Retrospective longitudinal	Multi-center	General population	27.26 years
6.	Menéndez-Conde et al. (2011) <sup>9</sup>	Spain	Prospective cross-sectional	Single-center	General population	$68.2 \pm 16.1$ years
7.	Rodenburg et al. (2011) <sup>10</sup>	Netherlands	Retrospective	Multi-center	General population	-
8.	Hartholt et al. $(2010)^{18}$	Netherlands	Retrospective	Multi-center	Geriatrics	_
9.	Davies et al. $(2010)^{11}$	U.K	Retrospective cohort	Single-center	General population	62 years
10.	Carrasco-Garrido et al. (2010) <sup>12</sup>	Spain	Retrospective	Multi-center	General population	-
11.	Dibben et al. (2011) <sup>13</sup>	Scotland	Retrospective	Multi-center	General population	22.2 years
12.	Wu et al. (2010) <sup>14</sup>	England	Retrospective	Multi-center	General	70 years
13.	Stausberg and Hasford, (2010) <sup>15</sup>	Germany	Retrospective	Multi-center	General	-
14.	Shamliyan (2010) <sup>20</sup>	US	Retrospective	Multi-center	Geriatrics	-
15.	Brvar et al. (2009) <sup>16</sup>	Slovenia	Retrospective	Single-center	General population	65.6 (19–94) years

were identified to be showing relevance to the study. Non-English, abstract-only articles, and out-patient ADR studies were filtered from 49 articles. Finally 15 articles were taken up for our study. Systemic Analysis was made on these articles and the results were summarized.

#### 4. Results and discussion

Out of 15 articles, four studies were prospective analysis which was conducted at a single center, 11 studies were retrospective data base screening out of which two studies were single center based study. One study was conducted in pediatric population, four in geriatric population and 10 studies were conducted in general population (Table 1). More than two-third of the studies (12/15) were conducted in European countries, followed by one study each in US, Canada and India.

One-third (5/15) of the articles' primary objective was to estimate frequency of DRP (Table 2) (Conforti et al., 2012; Menéndez-Conde et al., 2011; Singh et al., 2011; Stausberg and Hasford, 2011; Stausberg and Hasford, 2010). One-fifth (3/15) of the studies focused on analyzing trends in DRP hospital admissions (Dibben et al., 2011; Hartholt et al., 2010; Wu et al., 2010). Three studies were related to estimation of cost involved to treat drug related hospital admissions (Menéndez-Conde et al., 2011; Wu et al., 2012). Two articles were each on determining the incidence (Posthumus et al., 2012; Wu et al., 2012) and risk factors associated with DRPs (Menéndez-Conde et al., 2011; Rodenburg et al., 2011). There were few studies which made their objective differently viz, analyzing the potential usefulness of ICD-10 coding (Stausberg and Hasford, 2010); impact of ADRs on re-admissions (Davies et al., 2010); finding relation between gender and occurrence of ADR related admissions; impact of homelessness as the risk of death for young drug misusers (Dibben et al., 2011); ADE (Adverse Drug Event) reporting, method of detection and urgency of DRP admission (Brvar et al., 2009). DRP related admissions are on an average accounted for 8.36% (Conforti et al., 2012; Davies et al., 2010; Menéndez-Conde et al., 2011; Posthumus et al., 2012; Rodenburg et al., 2011; Singh et al., 2011; Stausberg and Hasford, 2011). Overall ADE related admission in female to male ratio was 1:0.74. ADR related hospital admission increased by 175% in males aged  $\geq 60$  years and females 112% aged  $\geq 60$  years from 1981 to 2007 (Hartholt et al., 2010).

One-third of the studies reported that antineoplastic agents (Brvar et al., 2009; Carrasco-Garrido et al., 2010; Menéndez-Conde et al., 2011; Posthumus et al., 2012; Rodenburg et al., 2011) as the major contributing drugs causing secondary infection, agranulocytosis, poisoning and constipation (Table 3). Same number of studies showed similar results by CNS drugs (Hartholt et al., 2010; Posthumus et al., 2012; Rodenburg et al., 2011; Shamliyan, 2010; Wu et al., 2012). Seven studies indicated that cardiovascular drugs (Brvar et al., 2009; Conforti et al., 2012; Davies et al., 2010; Hartholt et al., 2010; Rodenburg et al., 2011; Singh et al., 2011; Wu et al., 2010) as the major contributing class in which two studies showed diuretics (Conforti et al., 2012; Davies et al., 2010) as the major contributing drugs causing problems such as electrolyte imbalance. Antidiabetic drugs (Brvar et al., 2009; Singh et al., 2011; Shamliyan, 2010), immunosuppressive drugs (Carrasco-Garrido et al., 2010; Posthumus et al., 2012; Rodenburg et al., 2011) antibiotics (Posthumus et al., 2012; Rodenburg et al., 2011; Carrasco-Garrido et al., 2010) and anticoagulants (Carrasco-

Study No.	No. of subjects	No. of DRP cases	Duration	Year of study	Objective	Conclusion
l.	683	258	4.5 months	2008	Incidence and characteristics of ADR related admissions	ADR-related hospital admission occurred in 6.9% of all acutely admitted pediatric patients. All ADRs in the pediatric wards and ICU, and oncology ward were relatively mild, none of the patients suffered permanent harm
2.	1215	1023	6 months	2009	Frequency of ADRs, both in hospital admissions and occurring in hospital. To describe the types of reactions and associated drugs	11.1% of admissions were related to ADRs. ADRs in patients during hospital stay were 25%. Eighty four drugs were responsible for hospital admissions. 60 ADRs identified and concluded that ADRs are an important cause of hospital admissions
3.	Total population Data Base screening	1.65 millions	5 years	2003–2007	Incidence and costs of emergency department(ED) visits related to ADRs and to describe risk factors for experiencing severe ADRs	0.75% of total annual ED visits in adults above 66 years were found to be ADR-related, and 21.6% of these patients were hospitalized. In 2007, the cost of ADR-related visits was \$333 per visit and \$7528 per hospitalization for a total annual cost of \$13.6 million in Ontario, or an estimated \$35.7 million in Canada
ι.	3560	118	6 months	2010	Frequency, severity and classification of DRP resulting in hospitalization; and to identify any patient, prescriber, drug, and system factors associated with these events	Severity was classified as mild in 19 cases (16.1%), moderate in 91 cases (77.12%) and severe in 08 cases (6.78%). Most of the definite and possible DRP were definitely preventable
5.	Total population data base screening	48 million	5 years	2003–2007	Estimate frequency and type of drug-related admissions and hospital-acquired averse drug events (ADE)	5% of hospital admissions were found to be at least possibly drug-induced and 0.7% very likely drug-induced. About 4.5° of in-patients had experienced a hospital-acquired ADE
5.	16,566	252	l year		Identify, classify and quantify the frequency of ADR related admissions. To determine ADR preventability, risk factors, costs and identify drugs that are often involved	19.4% of admissions were the direct consequence of ADR, 65% of which were preventable. ADR associated cost was €237,377 and mean cost per admission was €4844
7.	Total population Data Base screening	9.28 million	6 years	2000–2005	Study differences in ADR-related hospitalizations between the sexes	ADR-related admissions are 0.41% of all admissions in men and 43% of all ADR-related admissions.0.47% of all admissions in women and 57% of all ADR-related admissions

 Table 2
 Summary of the drug related problem studies selected for the systemic review.

4

Study No.	No. of subjects	No. of DRP cases	Duration	Year of study	Objective	Conclusion
8.	Total population Data Base screening	0.36 million	26 years	1981–2007	Trends in ADR-related hospitalizations	Overall number of ADR related hospital admissions female: male is 1:0.74. ADR related hospital admissions increased by 175% in males age $\ge 60$ and 112% in females aged $\ge 60$
9.	1000 (selected 1st 1000 pts who are admitted to wards)	1000 followed & reason for re-admission studied	1 year	2009–2010	Impact of ADRs on re-admission to hospital after a period as an inpatient	ADR contributing to admissions in 20.8% of patients. Of the readmitted patients, 18.1% patients had at least one ADR related readmission
10.	Total population Data Base screening	0.35 million	6 years	2001–2006	Estimate the burden of hospital admissions, along with the associated total health cost	1.69% of all acute hospital admissions were associated with ADRs. Cost generated by patients due to ADR related hospital admissions increased by 19.05% from 2001 to 2006
11.	Total population Data Base screening	13,303	15 years	1986–2001	Estimate the additional impact of homelessness on the risk of death for young drug misusers	Immediately after a drug-related hospital admission there was no difference in survival between the homeless and those with a 'fixed address. Over a 3-year period the risk for those who were homeless was 3.5 times greater.
12.	Total population Data Base screening	0.55 million	10 years	1999–2009	Trends in hospital admissions associated with ADRs	Between 1999 and 2008, the total number of hospital admissions increased by 28.3%, but the total number of admissions due to ADRs increased by 76.8%
13.	11 millions	-	1 year	2006	Examine the potential usefulness of ICD-10 coded diagnoses in routine hospital data for the identification of ADE	0.7% of hospital admissions were revealed by routine data to be causally related to the administration of a drug. In 5.3% of admissions, there was at least a reason to suspect such a causal relation
14.	Total population Data Base screening	0.32 million	8 years	2000–2007	Analyze trends in hospital admissions due to ADEs	Total number of hospital admissions due to ADEs increased from 36,199 in 2000 to 42,057 in 2007. Total hospital charges increased from \$393,618,776 in 2000 to \$905,776,719 in 2007
15.	Random selection of cases (520 cases) from 17,230 in patients	30	l year	2006	Evaluate the frequency of ADR related admissions and its dependency on reporting and method of detection, urgency of admissions	ADRs cause 5.8% of admissions in medical departments. The frequency of ADR causing admissions detected by using an ICD-10 coding system was 0.2% and no patient admitted due to ADRs was reported to the national reporting system. The recognized frequency of ADR related admissions also depends on the department's specialty and acceptance of urgently admitted patients

Study No.	Major contributing drug	Problems on admission	Risk factors	
1.	Anti-neoplastic and immunomodulation drugs (6.7%), vaccines, anti-infective for systemic use and medicines for nervous system	Neutropenic fever (increased infection)	Neutropenia due to cancer chemotherapy	
2.	Diuretics, anti-thrombotic agents and ACE inhibitors	Electrolyte imbalance, GI Disturbance, Anemia and altered INR	Age, elderly people are at greater risk	
3.	Psychoactive agents, Opioids, sedatives and hypnotics	Agranulocytosis (9.44%), heart failure (3.64%) and coagulation defects (3.17%)	Polypharmacy (60.0%) Polyphysicians (85%) Prescription re-filled in different pharmacies (50%)	
4.	Oral hypoglycemic agents and insulin, antihypertensive agents and chemotherapy (antiretroviral)	-	Noncompliance (46.6%)	
5.	-	Enterocolitis due to Clostridium difficile infection was the most frequent cause of a drug-related admission	-	
6.	Hormone therapy, anti-neoplastics and immunosuppressive therapy accounted for 38%; digestive & metabolic treatment 90.5% and respiratory medicine 13.89%	Respiratory failure (36.7%) and cardiovascular problems	Medical error, including both prescription errors and medication follow-up errors	
7.	Anti-neoplastic & immunosuppressive, anti-rheumatics, anti- coagulants & Salicylates, CNS drugs, CVS drugs, steroids and antibiotics	Agranulocytosis, GI Bleeding, poisoning and constipation, osteoporosis, hypoglycemia	Poly pharmacy, female gender	
8.	Cardiovascular agents, analgesics, hormones, water and mineral acids, psychotropic drugs and systemic agents	Bleeding, GI symptoms, anemia, cardiac system, pulmonary system, hypoglycemic coma, electrolyte disturbances, UTI, Cartilage disease, Agranulocytosis, constipation and pulmonary embolism	Age (elderly patients at a higher risk)	
9. 10.	Antiplatelet drugs, loop diuretics Anti-neoplastics & immunosuppressive, adrenal corticosteroids, anticoagulants and antibiotics	Bleeding and renal impairment Neutropenia (5%), obstructive chronic bronchitis (4.9%) and CHF (3.1%)	Age (elderly patients at a higher risk) Age (elderly patients at a higher risk)	
11.	-	-	-	
12.	Systemic agents (19.2%), analgesic (13.3%) and CVS drugs (12.9%)	Nephropathy, cardiovascular and mental and behavior disorders	Multiple long term disease, polypharmacy and age	
13.		-		
14.	Opioids, benzodiazepines, insulin, anti-diabetic drugs, anti- coagulants	Gastroenteritis with or without hemorrhage	Multi centered treatment, polypharmacy	
15.	NSAIDs, acetyl salicylic acid, warfarin, CVS medication, anti-neoplastic agents & immunosuppressive agents, corticosteroids and anti-diabetic drugs	GI bleeding, hemorrhage, hypoglycemia, electrolyte imbalance and secondary infections	Age (elderly patients at a higher risk)	

Garrido et al., 2010; Rodenburg et al., 2011; Shamliyan, 2010) were found as the major causal drug in 20% of the studies causing problems like hypoglycemia, osteoporosis, GI bleed, gastroenteritis and hemorrhage. Two studies each suggested that systemic agents and analgesics as the major drugs causing GI bleed and nephropathy. (Hartholt et al., 2010; Wu et al., 2010) One study implied warfarin (Brvar et al., 2009) and aniplatelets (Davies et al., 2010) as major contributing drugs causing complications such as bleeding.

Six studies indicated age (Brvar et al., 2009; Carrasco-Garrido et al., 2010; Conforti et al., 2012; Davies et al., 2010; Hartholt et al., 2010; Wu et al., 2010) as the major risk factor. The other risk factors included polypharmacy (Rodenburg et al., 2011; Shamliyan, 2010; Wu et al., 2010, 2012), polyphysician (Shamliyan, 2010; Wu et al., 2012), noncompliance (Singh et al., 2011) and prescription errors (Menéndez-Conde et al., 2011)(Table 3). Out of 15 articles, four articles also investigated the severity of ADRs. In a prospective study on ADR based on Le algorithm and Schumock algorithm for preventability, the severity of ADRs in patients exposed to cancer chemotherapy was comparable with the severity of nonexposed patients. All ADRs were classified as severe, due to hospitalization, but they were clinically mild cases, not resulting in permanent impairment to the patient or significant hemodynamic instability or directly or indirectly leading to patient death. Only 10% of ADRs was avoidable in this study. In a study by Singh et al., severity was classified as mild in 16.1% cases, moderate in 77.12% cases and severe in 6.78% cases. Most of the definite and possible DRPs were definitely preventable (Singh et al., 2011). In a study by Brvar et al., 90% of ADRs were potentially preventable (Brvar et al., 2009).

In a study by Menéndez-Conde et al., with regard to ADR severity, 77.6% were level 4, 20.4% were level 5 and 2% were level 6. They estimated ADR costs according to severity and found a mean cost per admission were \$342 for level 4 episodes, \$438 for level 5 episodes and \$726 for level 6 episodes. They reported significant differences in consumption of thyroid drugs (23.5% vs 4.9%, P = .003) and systemic corticosteroids (41.2% vs 11.3%, P = .001) for the unpreventable ADR and non-ADR groups, respectively. There were also significant differences in the use of cytostatic drugs among patients with both preventable and unpreventable ADRs (18.4% vs 6.4%, P = .019) and in use of antiplatelets among patients with preventable ADRs (Brvar et al., 2009).

In another study by Wu et al. on the incidence and economic burden of ADRs among 7222 elderly patients in Ontario emergency departments (EDs), found that severe ADRs were associated with age, sex, multiple drugs, comorbidity, polypharmacy, newly prescribed drugs, recent ED visits, recent hospitalizations and long term care (LTC) residents (Wu et al., 2012).

Shamliyan study reported that the average cost incurred for the treatment of DRP admission was \$10,873 in 2000, which increased to \$ 21,536 per individual in the year 2007. Total cost for treating DRPs in the year 2000 in US population was \$ 393,618,776 that is increased to 2.3 times in 2007 (Shamliyan, 2010).

#### 5. Conclusion

Majority of DRP studies were conducted in developed countries in Europe. Most of these were retrospective, multicenter studies conducted in general populations. The primary objective of the studies was to estimate DRP frequency, incidence, risk factors and trends of DRP hospital admissions. Anti-neoplastic agents, CVS drugs and CNS drugs were identified to precipitate most of the Drug Related Problems. Polypharmacy, polyphysician, non-compliance and prescription errors were underlying reasons for developing DRPs. Few studies classified DRPs based on severity and preventability. It was found that the cost for the management of DRP was directly proportional to Severity. It was quoted in an article that there was 100% under reporting of ADRs. Many articles stated that ADR related admissions were preventable up to 50% on an average. Hospital could bring down therapy cost incurred to treat DRP admissions to a greater extent. This gives an idea on how much extent a clinical pharmacist could play a vital role in preventing the drug related problems.

#### 6. Contributors

Mr. Sonal Sekhar M wrote the manuscript and shall act as the guarantor for the paper; Ms. Nivya Kolli, Ms. Sri Sai Kiran Vempati and Ms. Nandita Ragoo collected the data and involved in manuscript preparation; and Dr. Jayaprakash B critically reviewed the manuscript.

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#### References

- Bhalla, N., Duggan, C., Dhillon, S., 2003. The incidence and nature of drug-related admissions to the hospital. Pharm. J. 270, 583–586.
- Brvar, M., Fokter, N., Bunc, M., Mozina, M., 2009. The frequency of adverse drug reaction related admissions according to method of detection, admission urgency and medical department specialty. BMC Clin. Pharmacol. 9, 8.
- Carrasco-Garrido, P., de Andrés, L.A., Barrera, V.H., de Miguel, G.A., Jiménez-Garcíal, R., 2010. Trends of adverse drug reactions related-hospitalizations in Spain (2001–2006). BMC Health Serv. Res. 10, 287.
- Conforti, A., Costantini, D., Zanetti, F., Moretti, U., Grezzana, M., Leone, R., 2012. Adverse drug reactions in older patients: an Italian observational prospective hospital study. Drug Healthc. Patient Saf. 4, 75–80.
- Davies, E.C., Green, C.F., Mottram, D.R., Rowe, P.H., Pirmohamed, M., 2010. Emergency re-admissions to hospital due to adverse drug reactions within 1 year of the index admission. Br. J. Clin. Pharmacol. 70 (5), 749–755.
- Dibben, C., Atherton, I., Doherty, J., Baldacchino, A., 2011. Differences in 5-year survival after a 'homeless' or 'housed' drugs-related hospital admission: a study of 15–30-year olds in Scotland. J. Epidemiol. Community Health. 65, 780–785.
- Hartholt, K.A., van der Velde, N., Looman, C.W., et al, 2010. Adverse drug reactions related hospital admissions in persons aged 60 years and over, The Netherlands, 1981–2007: less rapid increase, different drugs. PLoS One 5, e13977.

- Menéndez-Conde, P.C., Vicedo, B.T., Silveira, D.E., Accame, C.E., 2011. Adverse drug reactions which provoke hospital admission. Farm. Hosp. 35, 236–243.
- Nelson, K.M., Talbert, R.M., 1996. Drug-related hospital admissions. Pharmacotherapy 16, 701–707.
- Posthumus, A.A., Alingh, C.C., Zwaan, C.C., et al, 2012. Adverse drug reaction-related admissions in paediatrics, a prospective single-centre study. BMJ Open. 2, e000934.
- Rodenburg, E.M., Stricker, B.H., Visser, L.E., 2011. Sex-related differences in hospital admissions attributed to adverse drug reactions in the Netherlands. Br. J. Clin. Pharmacol. 71, 95– 104.
- Roxburgh, A., Degenhardt, L., 2008. Characteristics of drug-related hospital separations in Australia. Drug Alcohol Depend. 92, 149– 155.
- Sekhar, S.M., Mary, A.C., Anju, P.G., Hamsa, A.N., 2011. Study on drug related admissions in a tertiary care hospital in South India. Saudi Pharm. J. 19, 273–278.
- Shamliyan, T., 2010. Adverse drug effects in hospitalized elderly: data from the healthcare cost and utilization project. Clin. Pharmacol. 2, 41–63.

- Singh, H., Kumar, B.N., Sinha, T., Dulhani, N., 2011. The incidence and nature of drug-related hospital admission: a 6-month observational study in a tertiary health care hospital. J. Pharmacol. Pharmacother. 2, 17–20.
- Smith, J.W., Seidl, L.G., Cluff, L.E., 1996. Studies on the epidemiology of adverse drug reactions. V. Clinical factors influencing susceptibility. Ann. Intern. Med. 65, 629–640.
- Stausberg, J., Hasford, J., 2011. Drug-related admissions and hospitalacquired adverse drug events in Germany: a longitudinal analysis from 2003 to 2007 of ICD-10-coded routine data. BMC Health Serv. Res. 11, 134.
- Stausberg, J., Hasford, J., 2010. Identification of adverse drug events: the use of ICD-10 coded diagnosis in routine hospital data. Dtsch. Arztebl. Int. 107, 23–29.
- Wu, C., Bell, C.M., Wodchis, W.P., 2012. Incidence and economic burden of adverse drug reactions among elderly patients in Ontario emergency departments: a retrospective study. Drug Saf. 35, 769–781.
- Wu, T.Y., Jen, M.H., Bottle, A., Molokhia, M., Aylin, P., Bell, D., Majeed, A., 2010. Ten-year trends in hospital admissions for adverse drug reactions in England 1999–2009. J. R. Soc. Med. 103, 239–250.