

Drug-Related Problems in Hospitalised Patients

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Abstract

Drug-related problems include medication errors (involving an error in the process of prescribing, dispensing, or administering a drug, whether there are adverse consequences or not) and adverse drug reactions (any response to a drug which is noxious and unintended, and which occurs at doses normally used in

humans for prophylaxis, diagnosis or therapy of disease, or for the modification of physiological function). Furthermore, adverse drug events can be defined as an injury – whether or not causally-related to the use of a drug.

Drug-related problems are relatively common in hospitalised patients and can result in patient morbidity and mortality, and increased costs. In order to get an overview of studies on drug-related problems in hospitalised patients, with specific attention to the incidence of drug-related problems and their costs, to the possibilities of prevention and to the effect of these interventions, we performed a literature search.

Incidences of medication errors reported in studies vary widely. The range of reported incidences of adverse drug reactions is even wider. These wide ranges can be largely explained by the different study methods and definitions used.

Problems related to drug therapy may be averted by preventive interventions. Several possibilities for prevention exist, especially for the prevention of medication errors. Prescribing, transcription and interpretation errors can be reduced by using computerised physician order entry. Together with the use of automated dispensing systems and bar-code technology, this will aid in the reduction of both dispensing and administration errors. Education of nursing staff involved in the process of drug distribution is another important measure for preventing medication errors. Finally, the introduction of systems for the early detection of adverse drug reactions may help to reduce problems related to drug therapy. Identifying risk factors that contribute to the development of adverse drug reactions, may aid in the prevention of these reactions.

Besides their beneficial effects, drugs may also induce morbidity in some patients. Drug-induced morbidity has become a common problem.^[1-3] Historically, adverse drug reactions have been the focus of most studies on drug-induced morbidity, but they form only a small part of drug-related problems. Medication errors, overdosage (in suicide attempts), drug dependence, noncompliance and therapeutic failure are other examples of important problems associated with drug use. Therefore, it may be more appropriate to use the term 'drug-related problems'. These are defined as 'circumstances that involve a patient's drug treatment that actually, or potentially, interfere with the achievement of an optimal outcome'.^[4]

Most of the studies on drug-related problems have been conducted in hospitals. These studies either look into the rate of hospitalisation as a result of drug-induced morbidity, or they analyse drug-related problems in hospitalised patients. There is much to gain in the prevention of drug-related problems in hospitalised patients, as they are asso-

ciated with patient morbidity, increased length of hospital stay and increased costs.^[5] Information from previous studies can assist in the development of preventive interventions in hospitals and can give information on the effect of these interventions on drug-induced morbidity. Most review articles focus either on medication errors or on adverse drug reactions, instead of looking into drug-related problems (in hospitalised patients) as a whole. Therefore, we performed a literature search of drug-related problems in order to get an overview of studies with specific attention to the incidence of drug-related problems and their costs, to the possibilities of prevention and to the effect of these interventions.

1. Literature Search

A literature search using Medline and Embase was performed. These literature databases were searched, using the keywords 'adverse drug reaction', 'adverse drug event', 'medication error' and 'hospital'. The reference sections of all retrieved

articles were manually searched for additional articles. Articles that fulfilled the following criteria were selected:

- published in 1991 or later (so that the results of the studies may be more applicable to modern hospital practice)
- concerned drug-related problems in hospitalised patients (so, articles on the subject of hospitalisation as a result of drug-induced morbidity were excluded).

This search resulted in a total of 115 articles. Of these articles, 31 were excluded because they mainly concerned adverse events (that were not specified) or because they focused on how to start a system for reporting drug-related problems in hospitals instead of describing the results of such a system. The remaining 84 articles consisted of 69 original investigations and 15 review articles or meta-analyses. Of the 84 articles, the majority (56) originated from the US.

These 84 articles were used for this review, in which, first, the different types of drug-related problems in hospitalised patients were defined. Secondly, the articles were summarised in terms of frequency of drug-related problems and influence on costs and length of hospital stay. Finally, from this summary a perspective was given on possible causes and methods for prevention.

2. Definitions of Drug-Related Problems

Drug-related problems have been defined in a very broad and different way across studies, including medication errors, adverse drug reactions, overdosages, noncompliance and therapeutic failure. The interpretation of study results depends on the definition used by the different authors for the drug-related problems. When reviewing literature, we found that the same terms are often defined in different ways. For example, the term ‘adverse drug event’ was used for an adverse drug reaction of unclear causal relationship to a drug, but also for a combination of medication errors and adverse drug reactions, which actually led to patient morbidity or mortality. We tried to define the different terms in an unequivocal way, so that they may clar-

Table I. Definitions of drug-related problems

Drug-related problem	A circumstance that involves a patient's drug treatment that actually, or potentially, interferes with the achievement of an optimal outcome ^[4]
Medication error	Any error in the process of prescribing, dispensing or administering a drug, whether there are adverse consequences or not ^[6]
Adverse drug reaction	Any response to a drug which is noxious and unintended and which occurs at doses normally used in humans for prophylaxis, diagnosis or therapy of disease, or for the modification of physiological function, given that this noxious response is not due to a medication error ^[7]
Adverse drug event	An injury related to the use of a drug, although the causality of this relationship may not be proven ^[6]

ify the different problems we describe in this review. All retrieved articles were interpreted by using these definitions.

We divided drug-related problems in hospitalised patients into 2 categories: problems that involve an error (extrinsic drug-related problems) and problems that involve no errors (intrinsic drug-related problems). In the first category a mistake is made somewhere in the drug distribution and/or production process (from the prescribing of the drug to the administration of the drug). These drug-problems can be called medication errors. Medication errors may or may not result in patient morbidity.

The second category consists of problems that occur even when no errors have been made in the entire process of drug distribution. These problems are called adverse drug reactions. Adverse drug reactions always result in discomfort or harm to the patient.

We defined adverse drug events as a combination of medication errors and adverse drug reactions, with the condition that this combination leads to patient morbidity. Finally, in our definitions, overdosage (in suicide attempts) and thera-

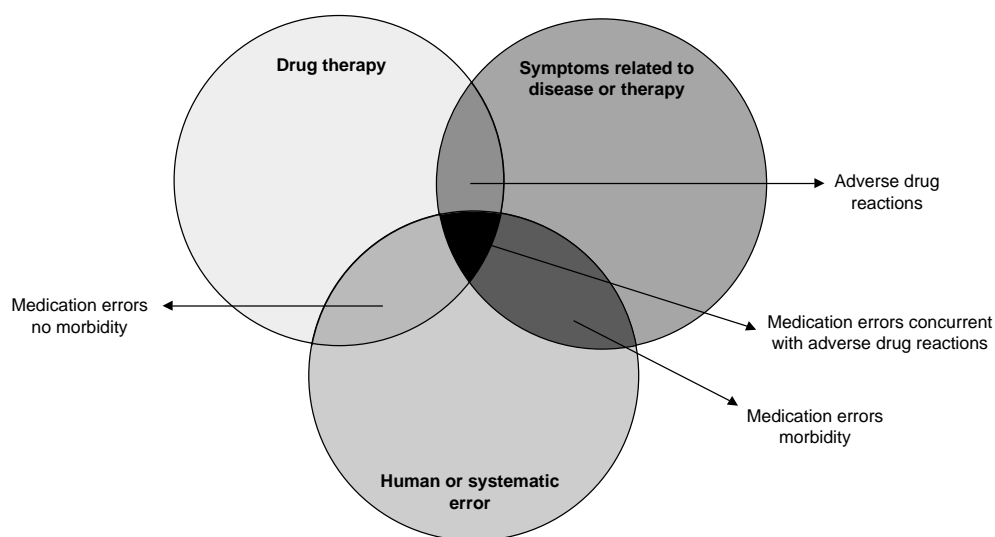


Fig. 1. Relationships between the definitions of drug-related problems.

peutic failures are excluded, which is in accordance to the definitions used in the literature.

These definitions can be found in table I, and figure 1 shows the relationship between the definitions.^[6,7]

3. Frequency of Drug-Related Problems in Hospitalised Patients

3.1 Medication Errors

Medication error rates found in observational studies are reported to vary between 1.7 and 59%, but generally accepted rates are 15% for floor stock distribution systems and 2 to 5% for unit-dose distribution systems.^[8] These rates do not include prescribing errors. The rates for prescribing errors are reported to be between 0.3 to 2.6%.^[9]

Although medication errors are an important part of drug-related problems, relatively few studies have been published since 1991. Table II gives an overview of published studies on the frequency of medication errors, including the type of medica-

tion errors studied, the number of patients, the setting and the method(s) used.^[10-20] For the type of medication error, a distinction was made between distribution errors (i.e. deviations from the prescription) and prescribing errors. Bates et al.^[18] found that almost 1% of medication errors resulted in an adverse drug event.

3.2 Adverse Drug Reactions

Adverse drug reactions are regularly encountered in hospitalised patients. Incidences reported in studies published since 1991 vary between 1.9 and 37.3% (table III).^[21-46] The wide range of incidences depends largely on the methods used to gather information on adverse drug reactions (e.g. intensive monitoring, spontaneous reporting).^[47,48] A recent meta-analysis reports an incidence of 10.9% for both serious and nonserious adverse drug reactions; fatal reactions occurred in 0.32% of hospitalised patients.^[49]

Table II. Frequencies of medication errors (MEs) in hospitalised patients

Study	Type of ME studied	No. of opportunities ^a	Settings	Distribution system ^b	Method ^c	Frequency (%)
Dean et al. ^[10] (American vs British hospital)	Distribution	US 919 UK 2756	US med surg UK gen med UK gen surg UK ger	US 1 UK 2	1	US 6.9 UK 3.0
Taxis et al. ^[11] (British vs German hospital)	Distribution	UK 842 Germany 973 Germany 1318	UK gen med German gen surg German rehab German resp German urol	UK 2 Germany 3 Germany 1	1	UK 8.0 Germany 5.1 Germany 2.4
McNally & Sunderland ^[12] (before and after improvements)	Distribution	Before 5451 After 7347	Gen surg	3	2	Before 3.3 After 2.3
Schneider et al. ^[13]	Distribution	275	Paediatric ICU	3	1	26.9 (18.2 when excluding wrong time errors)
Tissot et al. ^[14]	Distribution	2009	ICU	3	1	6.6
Shaughnessy & D'Amico ^[15] (before and after feedback)	Prescribing	Before 691 After 921	Gen med	—	3	Before 14.4 After 6.0
Schumock et al. ^[16]	Prescribing	294	Gen med	—	3	5.8
Lesar et al. ^[17]	Prescribing	3 903 433	Hospital	—	3	0.3
Bates et al. ^[18]	Prescribing and distribution	10 070	Gen med ICU	?	2/3/4	5.3
Hartwig et al. ^[19]	Prescribing and distribution	279 818	Hospital	?	2	0.04
Lacasa et al. ^[20]	Prescribing and distribution	839	Hospital	1	1/3	6.8

a Defined as the total number of doses ordered plus any un-ordered doses given (distribution errors) or the total number of prescriptions (prescribing errors).

b 1 = unit-dose system; 2 = ward-based pharmacy system with daily ward visits by pharmacists; 3 = floor-stock system without regular visits by pharmacists.

c 1 = disguised-observation technique; 2 = spontaneous reporting; 3 = review of prescriptions; 4 = patient chart review.

gen med = general medical ward; **gen surg** = general surgical ward; **ger** = geriatric ward; **ICU** = intensive care unit; **med surg** = medical–surgical ward; **rehab** = rehabilitation ward; **resp** = respiratory ward; **urol** = urology ward.

Table III. Frequencies of adverse drug reactions (ADRs) in hospitalised patients

Study	No. of patients	Setting	Method ^a	Frequency (%) or no. (n)
Schumock et al. ^[21]	160	General medical	2 vs 5	8.8 vs 2.5
Classen et al. ^[22,23]	36 653	Hospital	4	1.8
Lindley et al. ^[24]	416	Geriatric/medical	2	27
Wodtke & Generali ^[25]	?	Hospital	1 vs 5	n = 25 vs n = 136
Madsen ^[26]	30 057	Hospital	3 vs 5	1.7 vs 3.1
van Kraaij et al. ^[27]	105	General medical	2	37.3
Nazario et al. ^[28]	12 229	Hospital	1/3	2.2
Chan & Critchley ^[29]	430	General medical	1/2	10.2
Bowman et al. ^[30]	1024	Internal medicine	1/2/3	23.1
Pearson et al. ^[31]	10 587	Hospital	1	1.9
Vandel et al. ^[32]	3809	Psychiatric ward	1/2	3
Johnstone et al. ^[33]	110 ^b	Hospital	3 vs 5	n = 25 vs n = 101
Sacilotto et al. ^[34]	?	Hospital	1 (nurses vs doctors)	n = 164 vs n = 1498
Hall et al. ^[35]	?	Hospital	1 (nurses vs doctors)	n = 100 vs n = 28
Orsini et al. ^[36]	24 500 vs 25 530	Hospital	1 (before and after improvement)	0.4 vs 1.3
Cosentino et al. ^[37]	50	Psychiatric hospital	1/4	16
Lin Wu et al. ^[38]	666	General medicine	1	2.7
Smith et al. ^[39]	20 695	General medicine	1	6.9
Classen et al. ^[40]	91 574	Hospital	4	2.4
Vargas et al. ^[41]	2093	Cardiology/general medicine	2	11.1
Lee et al. ^[42]	?	Several hospitals	1 (without vs with pharmacists)	n = 360 vs n = 482
Moore et al. ^[43]	329	Internal medicine	2	6.4
Azaz-Livshits et al. ^[44]	153	General medicine	4 vs 5	16.3 vs 24.8
Gholami et al. ^[45]	370	Hospital	2	16.8
Van den Bemt et al. ^[46]	620	General medicine paediatric patients	1, 2 (nurses vs doctors vs patients)	29

a 1 = spontaneous reporting; 2 = intensive surveillance (patient review during ward visits, regular chart review); 3 = using indicators for ADRs (targeted drug orders, abnormal serum drug concentrations, etc.); 4 = computerised surveillance; 5 = medical record retrospective reporting.

b Inclusion limited to patients with adverse drug reactions.

3.3 Adverse Drug Events

Many studies look at adverse drug events as a whole. The results of these studies can be found in table IV.^[50-58] Rates of adverse drug events reported in these studies are between 0.7 and 6.5%. The low rate of 0.7% is probably due to the strict definition of adverse events in the Harvard Medical Practice Study (HMPS) [events that prolonged hospitalisation and/or caused disability]. In the studies that looked at preventability,^[51-58] 28 to 56% of adverse drug events were found to be pre-

ventable. Preventable adverse drug events are those events that are the result of an error.

4. Costs and Increased Length of Hospital Stay

4.1 Medication Errors

Information regarding the costs associated with medication errors is not readily available. However, the costs related to preventable adverse events in the HMPS were estimated to be \$US739 million (1984 values) in 1 year.^[53] As 10% of all prevent-

able adverse events in this study were caused by medication errors, one might estimate the costs related to medication errors to be \$US74 million (1984 values) in 1 year in the 51 hospitals of the HMPS. Furthermore, Bates et al.^[59] give information on costs associated with preventable adverse drug events (according to their definition these preventable events can be called medication errors).^[59] They estimate that 1 preventable adverse drug event leads to an excess cost of \$US4685 (1993 values). Annually, the costs for a 700-bed teaching hospital would be \$US2.8 million (1993 values). Each preventable adverse drug event was associated with an increase in length of hospital stay of 4.6 days.

4.2 Adverse Drug Reactions

Classen et al.^[40] determined the excess cost attributable to one adverse drug reaction to be \$US2013 (1993 values) and the increased length of stay to be 1.7 days in their 520-bed hospital. With the incidence of adverse drug reactions reported in their study this would add up to a total of \$US1.1 million (1993 values) in 1 year. Vargas et al.^[60] showed that each adverse drug reaction in an intensive care unit increased the length of stay by 1.8 days.^[60]

4.3 Adverse Drug Events

Finally, Schneider et al.^[61] report the costs that are associated with adverse drug events occurring in their university hospital (number of beds not mentioned). These were \$US1.5 million (1993 values) in 1 year.^[61]

5. Possible Causes and Methods for Prevention

5.1 Medication Errors

In our review we found that medication errors were divided into 4 main categories, namely prescribing errors, transcription/interpretation errors, dispensing errors and administration errors. The last 3 categories can also be called 'distribution er-

rors' (as in table II). Hartwig et al.^[19] describe the results of a voluntary reporting system for medication errors: 45% of all reported errors were administration errors, 32% were transcription errors, 13% were dispensing errors and 4% were prescribing errors. In another study by Leape et al.,^[57] 39% of medication errors were found to be prescribing errors, 38% were administration errors, 12% transcription errors and 11% dispensing errors.^[57]

5.1.1 Prescribing Errors

Prescribing errors involved prescription of a wrong drug (indication error), right drug to wrong patient (contraindication, known allergy, drug-drug interaction), wrong dose (dosing error) or wrong dosage form (e.g. tablets prescribed for a patient unable to swallow).^[8] In a study by Tully and Tallis,^[50] 34% of patients admitted to an elderly care unit experienced one or more adverse drug reactions and drugs considered unnecessary were prescribed in 20% of the patients. These drugs accounted for a third of all adverse drug reactions.^[50] Tully and Tallis were also involved in a larger study among 416 elderly patients admitted to a teaching hospital. Almost half of all adverse drug reactions were associated with drugs that were absolutely contraindicated and/or deemed unnecessary.^[24] Vargas et al.^[41] found a relationship between the number of adverse drug reactions and the number of potential drug-drug interactions. Preventable adverse drug reactions in hospitalised patients were associated with dosing and previous allergy to the drug, as Seeger et al.^[62] showed. Lesar et al.^[63] found an error rate of 4 errors per 1000 medication orders. Of the errors with potential for adverse patient effects, 13.9% were due to decline in renal or hepatic function requiring alteration of drug therapy, 12.1% to known drug allergy, 11.4% to using the wrong drug name, dosage form or abbreviation, 11.1% to incorrect dosage calculations and 10.8% to incorrect dosage frequency.

Causes for errors in prescribing were lack of knowledge about the prescribed drug,^[64] unfamiliarity with the patient^[64,65] and mental slips due to distraction^[66] or calculation errors.^[67] In the study

by Lesar et al.,^[63] 30% of errors were due to lack of knowledge of the drug, 29% to lack of knowledge regarding patient factors and 17.5% to dose calculations.

Prevention of Prescribing Errors

Different approaches were described in the literature to prevent prescribing errors. These approaches included improving education with respect to drugs and patient characteristics important for drug therapy,^[64] using a pharmacy computer for medication order entry^[68-70] and by using computerised physician order entry.^[71,72] One of the actions Hartwig et al.^[68] took in response to the number of allergic reactions reported in their hospitals, was the upgrading of the pharmacy computer system to facilitate capture of allergy information. In Salt Lake City in the US, the Health Evaluation through Logical Processing (HELP) system was developed.^[22,23,69] In this pharmacy-based computer system, all medication orders were entered as well as information regarding known drug allergies and appropriate drug administration rates. As the computer also uses laboratory information on patients and orders for specific 'tracer' drugs (antidotes), alerts for potential adverse drug events can be sent to physicians. Evans et al.^[69] showed that prospective surveillance for known drug allergies, and appropriate drug administration rates, can reduce the number of adverse drug events. Furthermore, they showed that early notification of physicians of potential adverse drug events allowed for modifications of drugs and/or dosages that could reduce the progression of mild adverse drug events to more serious conditions.

Medication order entry in a pharmacy computer system, was also used in the study by Raschke et al.^[70] This computer system generated primary prevention alerts (e.g. linking aminoglycoside dosage to creatinine clearance of the patient and thus recommending dosage adjustment) and secondary prevention alerts (laboratory values and use of 'tracer' drugs in order to detect adverse drug events at an early stage). Computerised physician order entry eliminates the need for transcription of orders by nursing staff and for interpretation of orders by

pharmacy staff. Anderson et al.^[71] showed that computerised physician order entry could result in a 21% reduction in prescribing errors. The computer system Bates et al.^[72] used in their study on the effect of computerised physician order entry, provided the physician with a menu of medications from the formulary and default dosages. For a number of medications, relevant laboratory test results were displayed on the screen at the time of ordering. Furthermore, the computer provided a limited drug-allergy check, drug-drug interaction check and drug-laboratory check (e.g. potassium levels in patients receiving potassium). Physician order entry using this computer system resulted in a 55% decreased rate of non-intercepted serious medication errors.^[72]

In a more recent study, Bates et al.^[73] report an increased sophistication of the physician order entry. They thus found a larger reduction in medical errors; from 142 per 1000 patient-days to 26.6 per 1000 patient-days.^[73]

Another strategy for the prevention of prescribing errors is the use of pharmacy services. Leape et al.^[74] have shown that the presence of a pharmacist on rounds in a medical intensive care unit was associated with a lower rate of prescribing errors (3.5 prescribing errors per 1000 patient-days with a pharmacist, compared with 10.4 prescribing errors per 1000 patient-days without a pharmacist). In a study by Bond et al.,^[75] it was shown that increased staffing for clinical pharmacists was associated with lower drug costs. Better patient care is mentioned by the authors as one of the reasons for this cost reduction.

5.1.2 Transcription/Interpretation Errors

Many drug distribution systems rely on transcription of physician orders by nursing staff, which offers substantial opportunity for error. Handwritten orders (either directly written by physician or after transcription by nurses) need to be interpreted by pharmacy personnel and translated into the dispensing of the right drug at the right dosage. West et al.^[76] have found verbal medication orders to be associated with a lower rate of errors, mainly due to a smaller rate of transcription

errors. These results are not in line with other studies, as verbal orders are generally perceived to be associated with a high rate of errors.^[77,78] Illegible handwriting and the use of abbreviations and decimal points are especially associated with erroneous interpretation.^[78]

Prevention of Transcription/Interpretation Errors

Prevention of this category of errors can best be achieved by computerised physician order entry, which eliminates the need for both transcription and interpretation.

5.1.3 Dispensing Errors

Errors can occur even after a correct interpretation of the medication order in the pharmacy. These errors can be subdivided into 4 categories: calculation errors, preparation errors, dispensing errors and distribution errors.^[79]

Prevention of Dispensing Errors

Possibilities for prevention of dispensing errors are the use of bar-coding, the use of strict preparation procedures and the use of double-checks. The unit-dose system provides the possibility for double-checking.^[79,80] By using an automated dispensing system, Klein et al.^[81] showed that the error rate could be reduced from 0.84 to 0.65%. More studies are needed on the impact of this technology.

5.1.4 Administration Errors

Administration errors occur in the last part of the distribution process, when the drug is administered to the patient. The errors that can occur in this stage involve the 5 'rights': giving the right drug to the right patient at the right dose by the right route at the right time. A common classification includes wrong patient, wrong dose, wrong time, omissions, wrong drug, extra dose, improper route or method, wrong rate of flow, un-ordered drug and duplication of a drug.^[82]

Look-alike packages, lack of education on drugs, lack of double-checking, unclear medication orders (e.g. illegible handwriting, verbal orders) and under-staffing are common causes for these errors.^[82]

Prevention of Administration Errors

Preventive measures should include computerised physician order entry, the use of computer lists for administration (including printed drug names, dosages and routes and times of administration), the education of nurses and the introduction of double-checks.^[82] Furthermore, automated cart filling^[81] and bar-coding may also be of use in this stage.^[82]

5.2 Adverse Drug Reactions

Adverse drug reactions are not caused by errors and therefore preventive measures to avoid them are not as easy to implement as for medication errors. However, as with medication errors, early detection of adverse drug reactions can result in the prevention of further harm to the patient. A computerised alert system (e.g. the HELP system^[22,23,69]) could be used for this early detection. Because such a computerised system can only aid in the detection of previously known adverse drug reactions, it needs to be complemented by a voluntary reporting system. This will allow previously unknown adverse drug reactions to be detected as early as possible.

Another possibility to prevent adverse drug reactions lies in the identification of risk factors that contribute to the development of adverse drug reactions. Certain drugs can then be avoided in patients with those risk factors. Age is generally considered to be a risk factor for adverse drug reactions,^[83,84] but some argue that it is not an independent risk factor. They consider the increase of adverse drug reactions with increasing age to be the result of an increased number of drugs used by the patient and of the health status of the patient.^[85,86] This immediately reveals 2 more risk factors: number of drugs used and comorbidity.^[85,86] Another risk factor is the female gender,^[87,88] although this may be caused by the fact that women live longer than men and by their increased use of drugs.

Table IV. Frequencies of adverse drug events (ADEs) in hospitalised patients

Study	No. of patients	Setting	Method ^a	Frequency (%) or no. (n)
Tully & Tallis ^[50]	100	Geriatric	2	27.0% (ADEs) 9.0% as a result of inappropriate prescribing
Brennan et al. ^[51] Leape et al. ^[52-53]	30 121	Several hospitals	5	0.7% (ADEs) 45.2% of ADEs preventable
Bates et al. ^[54]	420	Hospital	1/2	6.4% (ADEs) 56.0% of ADEs preventable 11.0% medication errors without patient harm
Cullen et al. ^[55]	?	Medical/surgical ICU	1/2	n = 54 (ADEs) 28% of ADEs preventable
Bates et al. ^[56] Leape et al. ^[57]	4031	Medical/surgical	1/2	6.5% (ADEs) 28.8% of ADEs preventable 5.5% medication errors without patient harm
Cullen et al. ^{[58]b}	4031 (in total)	Medical/surgical vs ICU	1/2	10 events ^c per 1000 patient days vs 19 events per 1000 patient days

a 1 = voluntary reporting; 2 = intensive surveillance (patient review during ward visits, regular chart review); 3 = using indicators for ADRs (targeted drug orders, abnormal serum drug concentrations etc.); 4 = computerised surveillance; 5 = medical record retrospective reporting.

b Publication on basis of data from study of Bates et al.^[56]

c 'Events' defined as a combination of preventable ADEs and potential ADEs (i.e. medication errors leading to patient harm combined with medication errors without patient harm).

ICU = intensive care unit.

5.3 Adverse Drug Events

Bates et al.^[89] have studied risk factors for adverse drug events (both preventable and non-preventable) in hospitalised patients. After controlling for level of care and length of hospitalisation, few risks emerged. They conclude from their analysis that prevention strategies should focus on improving medication systems.

6. Conclusion

Medication errors and adverse drug reactions are relatively common in hospitalised patients and can result in patient morbidity and mortality and thus in increased costs. Our review shows a wide variety of incidences of both medication errors and adverse drug reactions. This wide variety can be largely explained by the different study methods and by the different definitions used. Therefore, one can only conclude that drug-related problems are an important problem in hospitalised patients.

The exact magnitude of the problem remains difficult to estimate from these studies, but the frequency of medication errors is many times the frequency of adverse drug reactions.

These adverse consequences of drug therapy may be averted by using preventive measures. Several possibilities for prevention exist, especially for the prevention of medication errors. Introduction of the unit-dose system has resulted in substantial decreases in error rates in many hospitals. The implementation of computerised physician order entry can result in a major reduction in the number of medication errors. Furthermore, clinical pharmacists can contribute to the reduction of medication errors. The use of automated dispensing systems and of bar-coding may further reduce the error rates. Other measures are the avoidance of look-alike packages, education of personnel involved in the drug distribution process and introducing systems for early detection of adverse drug events.

More studies are needed on the effects of such preventative measures.

Early detection is important in the prevention of adverse drug reactions and thus each hospital should have a system for the detection of adverse drug reactions. Identifying risk factors that contribute to the development of adverse drug reactions, may also aid in the prevention of these reactions, although the effect of a focus on risk factors is likely to be smaller than the effect of a focus on medication systems improvements.

In summary, drug-related problems are an important problem in hospitalised patients, although the exact magnitude of the problem is difficult to estimate from the studies presented in our review. Drug-related problems result in increased morbidity and mortality, so hospitals should introduce or further improve quality systems for the safe use of drugs.

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