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# Incidence and risk of potential adverse drug interactions in the emergency room

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## Abstract

**Objective:** To determine the incidence and risk factors of potential adverse drug interactions occurring in patients in the emergency department. **Design:** Survey of a random sample of medical records of elderly persons and other adults seeking care at an emergency department. The interactions were determined by a computer programme, reviewed using explicit criteria, and excluded if of uncertain or trivial clinical significance. **Setting:** University Hospital Medical Emergency Department. **Patients:** A total of 423 randomly selected adults seeking care at a university hospital emergency department. Attendances made by 195 persons over age 60 and 228 younger adults were evaluated. All subjects were treated on an outpatient basis. **Main outcome measures:** Seventy percent of attendances led to the prescription of an added medication. In 5.4% of the attendances in which at least one medication was added, the new medication introduced a potential adverse interaction. The number of medications used at attendance was the best predictor of whether a potential interaction would occur. Additional medications prescribed in the emergency department that accounted for most of the added interactions were theophylline, macrolid antibiotics, digitalis glycosides, nonsteroidal anti-inflammatory agents, angiotensin converting-enzyme inhibitors and calcium antagonists. **Conclusions:** Potential adverse drug interactions were more common in elderly patients because of the higher number of concurrent medications rather than age-based factors. Safeguards need to be introduced to prevent patients from receiving medications in the emergency departments that have the potential to cause adverse interactions. © 2001 Elsevier Science Ireland Ltd. All rights reserved.

**Keywords:** Drugs; Prescription; Medication

## Resumo

**Objetivo:** Determinar a incidência e risco de potenciais interacções medicamentosas adversas que ocorram em doentes no departamento de emergência. **Método:** Analise de uma amostra aleatória de registos médicos de doentes idosos e outros adultos que procuraram cuidados médicos num departamento de emergência. As interacções foram determinadas por um programa de computador, submetidas a revisão utilizando critérios explícitos e excluídas se o seu significado clínico fosse trivial ou equívoco. **Local:** Departamento de Emergência Médica de um Hospital Universitário. **Doentes:** Um total de 423 adultos seleccionados de forma aleatória entre os que procuraram cuidados médicos num departamento de emergência dum hospital universitário. Foram avaliadas as observações realizadas a 195 doentes com mais de 60 anos e a 228 adultos de idade inferior. Todos os doentes foram tratados em ambulatório. **Resultados finais principais:** Setenta por cento das observações resultaram na prescrição de medicação adicional. Em 5.4% das observações em que foi adicionado pelo menos um novo medicamento, este introduziu um potencial de interacção adversa. O número de medicamentos em utilização na altura da observação foi o melhor factor predictivo da ocorrência de uma interacção potencial. Os medicamentos adicionais prescritos no departamento de emergência responsáveis pela-

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maioria das interacções introduzidas foram a teofilina, antibióticos macrólidos, digitálicos, anti-inflamatórios não esteróides, inibidores de enzima conversora da angiotensina e antagonistas dos canais de cálcio. *Conclusões:* As interacções medicamentosas potencialmente adversas foram mais frequentes nos doentes idosos devido ao elevado número de medicamentos administrados em simultâneo e menos correlacionadas com factores relacionados com a idade. No departamento de emergência são necessárias medidas de salvaguarda para prevenir a administração de medicamentos ou associações de medicamentos com risco potencial de causar interacções adversas. © 2001 Elsevier Science Ireland Ltd. All rights reserved.

*Palavras chave:* Medicamentos; Prescrição; Medicação

## 1. Introduction

Clinicians, administrators and policymakers have become interested in the system factors that contribute to adverse drug reactions and how prescribing practice can be improved [1]. Adverse drug reactions are common and expensive [2]. In the outpatient setting, rates of adverse drug reactions range from 2 to 50% [3].

Drug interactions are an example of inappropriate use of medication that may endanger patients' health and this may be avoided by more careful prescribing [4,5]. The clinical impact of the interaction may be most significant at the time of initial exposure. Awareness of potential drug interactions may permit development of clinical strategies to prevent their occurrence. Careful follow-up and monitoring help avoid toxicity. Adverse interactions between drugs prescribed in the emergency department are particularly worrisome, because there is often no follow-up, and those follow-up visits which do not occur are usually with a physician different from the original prescriber of the additional medication [6–8]. These problems are particularly relevant in elderly patients [9] because of the clinical complexity of their care [10] and because the common adverse events are preventable.

The potential for introducing drug interactions was reported previously in a few single centre studies on a total of ~1200 attendances at emergency departments in the United States with frequencies ranging from 3 to 47% (mean 13.1%) [11–14]. Since health care systems differ widely, even within the western world, these studies have limited general application. To our knowledge, no systematic data are available on the likelihood of introducing potential drug interactions during the care delivered by hospital emergency departments in Europe.

For this paper, our specific aims were to determine the frequency of potentially adverse drug interactions in an emergency department of a European university hospital, the medications prescribed in the emergency department that most commonly lead to interactions, and whether the department staff were more cautious when prescribing medications to persons at higher risk of side effects, such as the elderly and persons who were currently taking several medications.

## 2. Materials and methods

### 2.1. Study design

For analysis of potential adverse drug interactions we collected data retrospectively on 528 adults who sought care at one university hospital emergency department. Data sources included the complete emergency department records including the registration form, the emergency room physician's record, and the written instructions given to the patient.

### 2.2. Study setting and population

Data were collected on two populations, one over 60 and one ≤ 60 years of age. We sampled all subjects over the age of 60 who attended the emergency department for care during a 12-month period from June 1998 to May 1999 and who were not admitted to the hospital. Patients were selected through simple random sampling. A list of eligible patients was created and the random sample was drawn using a random number generator. We also collected data on adult attendances by people 60 years of age and below; each of these records was randomly selected from attendances on the same day as an elderly subject included in the study. The attendances were not matched in any way other than by date; ~7% of the records were included. We excluded records of both age groups if the patient was transferred to another hospital for possible admission or further evaluation, if the record was unreadable, if the patient was dead on arrival, or if the medication history was noted as incomplete in the physician's record. One-hundred and five cases were excluded; 423 subjects were included in our analysis. The most common diagnoses on discharge were hypertension, syncope, bronchitis, arrhythmia, dyscardia, and diarrhoea.

All patients seen in the emergency department have a medication history taken by a physician on duty and recorded on the emergency department record. All patients are given written instructions describing medication changes. The emergency department is staffed by house officers and supervised by senior registrars. It is a

seven-bed unit in which more than 12 000 patients are seen each year, and more than 30% of these patients are over 60 years of age. Approximately 38% of emergency department attendances result in admission to the hospital.

### 2.3. Study protocol

We included all of the information on medication use that was available to the prescribing physician and recorded in the physician's note. The physician's orders and written instructions given to the patient provided information on the additional and discontinued medications. Based on this information, we compiled three lists: medications used at presentation, medications added by the emergency department, and medications discontinued by the emergency department. We entered these lists into a computer using a programme that determines drug interactions (Micromedix, Interaction Profiles, Drug Evaluation 3/2000).

The computer programme describes all potential interactions, states whether information is available on specific drugs within a class of drugs, briefly indicates the clinical relevance of the interaction and whether the interaction has been well established in the literature, and gives literature citations. Using the computer programme, we determined all of the potential drug interactions existing before the patient attended and after the changes had been made in the emergency department visit. In determining potential interactions, we took into consideration both the medications added and discontinued.

To exclude clinically insignificant or questionable interactions, we developed explicit exclusion criteria before revision. These criteria were interactions relating to a drug in the same class but not established for the specific drug prescribed, interactions substantiated only by a case report, interactions with negligible clinical significance, interactions that were rare, and interactions

that were related to hypokalemia if potassium supplements were being given or were added. These criteria led to the exclusion of 40% of the interactions described by the computer programme.

### 2.4. Statistical analysis

We report the rates of potential adverse drug interactions for elderly and non-elderly patients. Data are presented as percent, mean and standard deviation. Group comparisons were performed using the Fisher exact test, Chi-Square test or Mann Whitney-U-test as appropriate. Logistic regression analysis was performed to determine multivariate associations of premedication, medication given in the emergency room and the patients age with potential adverse drug interactions.  $P$ -values  $< 0.05$  were considered statistically significant.

## 3. Results

The study population comprised 423 adults (mean age,  $57 \pm 21$  years; range, 17–95) with 195 subjects over 60 years and 228 subjects 60 years of age or below. The sample included 186 men and 237 women. The population used  $2.4 \pm 2.55$  (range, 0–13) medications on average at presentation to the emergency department; younger adults used  $1.1 \pm 1.64$  medications and older adults used  $3.8 \pm 2.66$  ( $P < 0.001$ ). Most frequently used agents were antiplatelets, angiotensin converting-enzyme inhibitors, antianginals and benzodiazepines. Table 1 describes the frequency of medication use in young and old subjects.

At the time of presentation to the emergency department, 6.4% of the subjects (2.2%  $< 60$  years, 11.3%  $> 60$  years;  $P < 0.001$ ) used medications known to have potential interactions. In decreasing order, the substances were theophylline, digitalis, calcium antagonists, benzodiazepines and loop diuretics. Without more data on the

Table 1  
Frequency of medication use

Number of medications used	All patients (n = 423)	Patients over 60 years of age (n = 195)	Patients 60 years of age and below (n = 228)
	Percent		
0	32	9	51
1	17	14	20
2	13	13	13
3	10	13	8
4	9	16	3
5	6	9	3
6	5	10	1
7	3	5	1
8	3	7	0
9	2	3	0
10 and more	1	2	0

**Table 2**  
Comparison of younger and older patients

Variable	All patients	Patients over 60 years of age	Patients 60 years of age or under
Sample size, <i>n</i>	423	195	228
Medication use (mean $\pm$ S.D.)	2.36 $\pm$ 2.55	3.79 $\pm$ 2.66	1.13 $\pm$ 1.64 <sup>a</sup>
At least one medication prescribed, %	69.5	74.9	64.9 <sup>b</sup>
An interaction introduced, %	3.8	6.6	1.3 <sup>c</sup>
In those prescribed at least one medication, an interaction introduced, %	5.4	8.9	2.0 <sup>d</sup>

<sup>a</sup>  $P < 0.001$ .<sup>b</sup>  $P = 0.034$ .<sup>c</sup>  $P = 0.004$ .<sup>d</sup>  $P = 0.01$ .

**Table 3**  
Comparison of low users and high users of medication

Variable	All patients	Patients on three or more medications	Patients on less than three medications
Sample size, <i>n</i>	423	160	263
Age; mean $\pm$ standard deviation	56.6 $\pm$ 21.2	69.9 $\pm$ 16.3	48.5 $\pm$ 19.7 <sup>a</sup>
At least one medication prescribed, %	69.5	72.2	63.7 <sup>b</sup>
An interaction introduced, %	3.8	8.8	0.8 <sup>c</sup>
In those prescribed at least one medication, an interaction introduced, %	5.4	12.2	1.1 <sup>d</sup>

<sup>a</sup>  $P < 0.001$ .<sup>b</sup>  $P = 0.089$ .<sup>c</sup>  $P < 0.001$ .<sup>d</sup>  $P < 0.001$ .

**Table 4**  
Frequency of emergency room medication

Number of medications given in ER	Patients	Percent of patients
1	156	53.1%
2	82	27.9%
3	39	13.3%
4	14	4.8%
5	3	1.0%
Total	294	100%

duration of therapy, drug dosage, or other variables from the emergency department record, we could not assess their clinical significance.

Additional medication was prescribed during the emergency room visit for 69.5% of the patients. Tables 2 and 3 summarize the differences between the younger and older patients and between the low (fewer than three medications) and high (three or more medications) users of medication, respectively. There was no statistical difference between prescribing to younger and older patients (65% compared with 75%) or between patients using three or more medications and those using less than three (64% compared with 72%).

Five-hundred and eight prescriptions were given during the 423 patient attendances (range, 0–5 prescriptions per visit) (Table 4). The most commonly prescribed medications were nonsteroidal anti-inflammatory agents, gastrointestinal therapy, mineral products, antianginals and angiotensin converting-enzyme inhibitors. A medication was discontinued by the emergency room physician in 31 cases (7.3%).

Potential drug interactions were introduced by the changes made during the emergency department visit for 3.8% of the subjects; however, for the 69.5% of the sample that was given at least one medication, a potential interaction was introduced in 5.4% of cases. Regression analysis revealed, that age was not a significant predictor ( $P = 0.277$ ); only the number of medications that the subject was using at presentation ( $P = 0.001$ ) and the number of medications prescribed by the emergency department physician ( $P = 0.005$ ), were significant predictors of a potential interaction. Six categories of medications prescribed by the emergency department accounted for most of the added interactions. These medications were theophylline, macrolid antibiotics, digitalis glycosides, nonsteroidal anti-inflammatory agents, angiotensin converting-enzyme inhibitors and calcium antagonists.

## 4. Discussion

Our data confirm that a visit to an emergency department is likely to result in the prescription of a medication and that the prescription often has pharmacological interactions with other medications, interactions that could potentially lead to adverse clinical consequences.

### 4.1. Comparison with other studies

Our data suggests that, even when the medication history is available, emergency department physicians do not screen for potential drug interactions routinely. Groups at higher risk of drug complications, the elderly and those taking multiple medications, may receive more cautious care. However, in a previous study on the incidence and risk factors of clinically relevant adverse drug interactions occurring in emergency department patients, all potential drug interactions were brought to the attention of the attending emergency physician, their subsequent interactions were noted, and clinically relevant interactions were determined [13]. The resulting incidence of clinically relevant interactions was 3.1% [13], which is only slightly below the frequency of potential adverse interactions of 3.8% observed in this retrospective analysis, where no particular attention was paid to potential interactions when prescribing or administering drugs. A slightly higher incidence of potential adverse interactions of 4.7% was observed in another retrospective analysis that had a comparable study design [11]. In comparison with the literature available, data suggest that additional on-site information on potential drug interactions for prescribing emergency physicians may reduce but not eliminate adverse interactions. Other relevant system factors need to be identified that further reduce adverse interactions. Such factors may be related to patient monitoring and follow-up after discharge [6,7].

Nearly four (3.8%) of emergency department attendances resulted in medication changes associated with a potentially harmful drug interaction and, in those cases in which an additional medication was prescribed, over five (5.4%) of attendances introduced a potentially harmful interaction. If a patient's advanced age or multiple medication use caused physicians to be more restrained in prescribing, fewer medications would have been given to the elderly and to high medication users; this was not the case. In fact, the elderly were most likely to have an interaction added, simply because they used more medication.

### 4.2. Limitations of study

Hancock et al. [12] reported an average of three medications in elderly (>65 years of age) patients

attending the emergency department. This is close to number observed in our study population. The rate of a potentially significant drug interaction between a newly prescribed medication in the emergency department and current medications in the previous study was 3.4% [12]. In the present survey, an incidence of 6.6% of potentially significant drug interaction was observed in adults >60 years. The reasons for this higher incidence may be related to differences in the study population and to the definition of 'clinically significant interactions'. However, in the study by Hancock et al., the number of medications the patient 'forgot' was 1.3, and there was an upward trend that correlated with an increased chance for an incomplete medication history as the total number of current medications increased [12]. Even though we tried to exclude patients who gave incomplete medication histories, it is possible that some such records were still included and that the real number of medications used may have been underestimated, particularly in the elderly. In a similar context, the population we studied, particularly by the older adults, used somewhat more medication than has previously been reported by others [11]. Our study group may have included less ambulatory elderly and more institutionalized elderly who tried to use larger numbers of medications [15]. Thus, other groups of elderly persons who use less medication might have a smaller risk of potential drug interactions from an emergency department visit.

We used a computer programme to identify drug interactions. Because the programme may have described interactions that are not clinically significant or have not been well substantiated, we reviewed all of the interactions. We rejected nearly half of the interactions using explicit criteria and included only the interactions that appeared to have reasonable clinical relevance. Nonetheless, from our data, we were only able to determine potential adverse interactions and could not detect whether those interactions actually led to complications.

## 5. Conclusions

We found that clinically relevant interaction between both current and emergency department-initiated medication was associated with a patient history of being on multiple medications prior to arrival at the emergency department. It is important that medical staff in the emergency department be made aware of the need to screen for potential drug interactions, especially when prescribing drugs to elderly and other patients who are taking several medications. Better safety measures are needed to avoid introducing adverse interactions. These

include a careful check of medication lists and screening for potential interactions with special computer programmes. System factors for preventing adverse drug interactions may also include medication records with useful visual charts, frequent review of medication and discussion with the patient, and better monitoring and follow-up after discharge involving primary care.

## References

- [1] Leape LL, Bates DW, Cullen DJ, Cooper J, Demonaco HJ, Gallivan T, et al. Systems analysis of adverse drug events. *JAMA* 1995;274:35–43.
- [2] Bates DW, Spell N, Cullen DJ, Burdick E, Laird N, Petersen LA, et al. The costs of adverse drug events in hospitalized patients. *JAMA* 1997;277:307–11.
- [3] Nolan L, O'Malley K. Prescribing for the elderly. Part 1: Sensitivity of the elderly to adverse drug reactions. *J Am Geriatr Soc* 1988;36:142–9.
- [4] Avery GS. Drug interactions that really matter: a guide to major important drug interactions. *Drugs* 1977;14:132–46.
- [5] Rizack MA, Hillman CD. The Medical Letter Handbook of Drug Interactions. New Rochelle, New York, Medical Letter, 1987. p. 6–124.
- [6] Lauck BW, Bigelow DA. Why patients follow through on referrals from the emergency room and why they don't. *Nurs Res* 1983;32:186–7.
- [7] Straus JH, Orr ST, Charney E. Referrals from an emergency room to primary care practices at an urban hospital. *Am J Public Health* 1983;73:57–61.
- [8] Hamaker JB, Baker BK, Weinbarger M, Neill PJ. The emergency room and the hypertensive patient. Improving linkage to clinical care. *Med Care* 1984;22:755–9.
- [9] Chin MH, Wang LC, Jin L, Mulliken R, Walter J, Hayley DC, et al. Appropriateness of medication selection for older persons in an urban academic emergency department. *Acad Emerg Med* 1999;6:1232–42.
- [10] Thomas EJ, Brennan TA. Incidence and types of preventable adverse events in elderly patients: population based review of medical records. *Br Med J* 2000;320:741–4.
- [11] Beers MH, Storrie M, Lee G. Potential adverse drug interactions in the emergency room. An issue in the quality of care. *Ann Intern Med* 1990;112:61–4.
- [12] Hancock D, Kennington JM, Beckner RR, Quick G. Emergency department medication and drug interaction evaluation. *Hosp Pharm* 1992;27:129–32.
- [13] Herr RD, Caravati EM, Tyler LS, Iorg E, Linscott MS. Prospective evaluation of adverse drug interactions in the emergency department. *Ann Emerg Med* 1992;21: 1331–6.
- [14] Goldberg RM, Mabee J, Chan L, Wong S. Drug-drug and drug-disease interactions in the ED: analysis of a high-risk population. *Am J Emerg Med* 1996;14:447–50.
- [15] Ostrom JR, Hammarlund ER, Christensen DB, Plein JB, Kethley AJ. Medication usage in an elderly population. *Med Care* 1985;23:157–64.