Eur J Clin Pharmacol (2003) 59: 157–162
DOI 10.1007/s00228-003-0600-8

PHARMACOEPIDEMIOLOGY AND PRESCRIPTION

**Graziano Onder · Francesco Landi
Matteo Cesari · Giovanni Gambassi
Pierugo Carbonin · Roberto Bernabei
on behalf of investigators of the GIFA Study**

Inappropriate medication use among hospitalized older adults in Italy: results from the Italian Group of Pharmacoepidemiology in the Elderly

Received: 23 September 2002 / Accepted: 28 March 2003 / Published online: 7 May 2003

Abstract *Objective*: To determine the prevalence of inappropriate medication use among hospitalized older adults and to identify predictors of this use.
Methods: A total of 5734 patients (mean age 79 years) admitted to geriatric and internal medicine wards participating in the study in 1995 and 1997 were included in this analysis. Inappropriate medication use was defined on the basis of the criteria published by Beers in 1997. Only medications used during hospital stay were considered for the present study.
Results: During hospital stay, 837 (14.6%) patients received one or more medications classified as inappropriate based on Beers criteria. Ticlopidine ($n = 346$; 6.0% of the study sample) was the most frequently used medication among those in Beers' list, followed by digoxin ($n = 174$; 3.0%) and amytriptyline ($n = 113$; 2.0%). The multivariate analysis showed that age [75–84 years vs 65–74 years, odds ratio (OR) 0.85, 95% confidence interval (CI) 0.71–1.00; ≥85 years vs 65–74 years, OR 0.58, 95% CI 0.46–0.73], cognitive impairment (OR 0.77, 95% CI 0.64–0.94), Charlson co-morbidity index (≥2 vs 0–1, OR 1.20, 95% CI 1.02–1.40) and overall number of medications used during hospital stay (5–8 medications vs < 5 medications, OR 2.20, 95% CI 1.72–2.82; ≥9 medications vs < 5 medications, OR 3.68, 95% CI 2.86–4.73) were significantly associated with use of inappropriate medications.
Conclusions: Inappropriate medication use was common among hospitalized older adults. The most important determinant of risk of receiving an inappropriate medication was the number of drugs being taken. Older age and cognitive impairment were associated with a reduced likelihood of using an inappropriate medication.

Keywords Elderly · Inappropriate medication use · In-hospital patients

G. Onder (✉) · F. Landi · M. Cesari · G. Gambassi
P. Carbonin · R. Bernabei
Centro Medicina dell'Invecchiamento,
Università Cattolica del Sacro Cuore,
Policlinico A. Gemelli,
L.go Francesco Vito 1, 00168
Roma, Italy
E-mail: graziano_onder@rm.unicatt.it
Tel.: +39-06-30154341
Fax: +39-06-3051911

G. Onder · M. Cesari
Section of Gerontology and Geriatrics,
Wake Forest University,
Baptist Medical Center,
Winston Salem, NC, USA

Introduction

In Western countries, adverse drug reactions are an important medical problem, resulting in 3–5% of all hospital admissions, accounting for 5–10% of in-hospital costs and being associated with a substantial increase in morbidity and mortality [1, 2, 3, 4, 5]. Older patients are particularly vulnerable to drug-related illnesses because they are usually on multiple drug regimens, and age is associated with changes in pharmacokinetics and pharmacodynamics [6, 7].

The use of inappropriate medications, defined as medications in which the risk outweighs the benefit, is a major factor influencing the likelihood of adverse drug events among the elderly. Since 1991, Beers and colleagues have developed a comprehensive set of explicit criteria for inappropriate medication use, with the intent of providing a useful tool for assessing the quality of prescribing in older persons [8, 9, 10]. Despite these criteria not representing substitutes for careful clinical consideration by physicians, they may be used in drug utilization review, as the basis for educational materials and in assessing the quality of prescribing. In addition, the identification of factors related to inappropriate drug consumption can be used to design and implement effective drug utilization programs aimed at influencing prescribing patterns [10, 11].

Previous studies have documented widespread inappropriate medication use in the community, nursing homes, board and care facilities, physician office practices, and homebound elderly with a prevalence ranging from 12% to 40% [8, 9, 11, 12, 13, 14, 15, 16, 17, 18]. However, the use of inappropriate medications among in-hospital patients has rarely been evaluated [19, 20]. Hospitalized older adults are usually 'frail' and present with acute diseases, which may increase their susceptibility to adverse medication effects and raise the severity of drug-related illnesses [2]. Moreover, in-hospital patients, who often have a genuine need for many drugs, are usually victims of a "prescribing cascade", which leads to an increased likelihood of receiving inappropriate drug therapy [21].

Therefore, the aims of the present study were (a) to determine the prevalence of inappropriate medication use in a hospitalized elderly population and (b) to identify predictors of this use. To accomplish this issue, we used data from the study of the Italian Group of Pharmacoepidemiology in the Elderly (GIFA), which has been designed to explore drug use and quality of in-hospital care in Italy. Nationwide, continuous data acquisition has led to the creation of a database, containing information on a large, and representative population of elderly patients admitted to acute care hospitals.

Methods

GIFA database

The GIFA is a group of investigators operating in community and university-based hospitals throughout Italy. The GIFA periodically surveys drug use, occurrence of adverse drug reactions, and quality of hospital care. The methods of the GIFA study have been described in detail elsewhere [4, 22]. Briefly, all patients admitted to 81 geriatric and internal medicine wards participating in the study were enrolled and followed until discharge. The study periods were the following: 1 May to 30 June and 1 September to 31 December 1988; 15 May to 15 June 1991; and 1 May to 30 June and 1 September to 31 October in 1993, 1995, 1997 and 1998.

For each participant, a questionnaire was completed at admission and updated daily by a study physician who received specific training. Data recorded included socio-demographic characteristics, indicators of physical function and cognitive status, clinical diagnoses on admission and at discharge, medications taken prior to admission, during hospital stay, and those prescribed at discharge.

Inappropriate medication use

To identify inappropriate medication use, we adopted the criteria developed and published by Beers in 1997, which identify patterns of medication use that unnecessarily place older persons at risk of adverse drug reactions [10]. These criteria were developed with the intent to be generalizable to any population of persons older than 65 years, regardless of their level of frailty or their place of residence. We used 25 of the 26 criteria for inappropriate medication use independent of diagnosis. These are listed in Table 1. We did not apply the criterion for cough and cold preparations containing antihistamines because our system for drug coding did not specifically identify this class of drugs. Only medications used during hospital stay were considered for the present study.

Table 1 Prevalence of inappropriate medication use based on Beers' criteria. Propoxyphene, trimethobenzamide, meperidine, doxepin were not available on the market in Italy during the surveys periods. Phenylbutazone, meprobamate, methyldopa and were not used by any patient. The criterion for cough and cold preparations containing antihistamines was not used because the system for drug coding did not specifically identify this class of drugs

Inappropriate medication	*n*	%
Any inappropriate medication	837	14.6
Ticlopidine	346	6.0
Digoxin >125 mg/day[1]	174	3.0
Amitriptyline	113	2.0
Chlordiazepoxide	91	1.6
Diazepam	91	1.6
Indomethacin	63	1.1
Iron >325 mg/day	33	0.6
Dipyridamole	29	0.5
Chlorpropamide	17	0.3
Flurazepam	10	0.2
High dose short-acting benzodiazepines[2]	10	0.2
Muscle relaxants[3]	7	0.1
GI antispasmodic drugs[4]	5	0.1
Pentazocine	4	0.1
Disopyramide	3	0.1
Barbiturates except phenobarbital[5]	1	<0.1
Ergot mesyloids	1	<0.1
Reserpine	1	<0.1

[1]Except for patients with atrial arrythmias
[2]Daily doses exceeding: lorazepam, 3 mg; oxazepam, 60 mg; alprazolam, 2 mg; temazepam, 15 mg; zolpidem, 5 mg; triazolam, 0.25 mg
[3]Including methocarbamol, carisoprodol, oxybutynin, chlorzoxazone, metaxalone and cyclobenzaprine
[4]Including dicyclomine, hyosciamyne, propantheline, belladonna alkaloids, clidinium-chlordiazepoxide
[5]Except when used to control seizures

Covariates

Cognitive performance was assessed at hospital admission using the Hodkinson abbreviated mental test (AMT) [23]. This test has proven to be reliable for detecting both mild cognitive impairment and dementia in older populations, and has previously been adopted in epidemiological surveys [24, 25]. A score below 7 was used to identify patients cognitively impaired [25].

Drugs were coded according to the Anatomical Therapeutic and Chemical codes [26]. Diagnoses were coded according to the International Classification of Diseases, Ninth Edition, Clinical Modification codes [27]. Co-morbidity was quantified using the Charlson co-morbidity index by adding scores assigned to specific discharge diagnoses, as illustrated in the original publication [28]. For analytical purposes, we computed a variable for heart disease, which includes diagnoses of ischemic heart disease, atrial fibrillation and congestive heart failure. ADL disability was defined as need of assistance to perform one or more of the following tasks: eating, dressing, bathing, transferring, and toileting. Alcohol use was defined as consumption of any amount of alcohol before hospital admission. Three levels of variables for number of drugs used during hospital stay and length of hospital stay were computed based on tertiles.

Data analysis

To reduce the variability in medication use related to changes in drug availability on the market and to select a uniform sample of patients, we limited the analyses to participants aged 65 years or older hospitalized in 1997 or 1998 according to surveys of those years. Therefore, from the initial sample of 32,181 patients, we excluded those enrolled in the study between 1988 and 1995 ($n = 24837$), and those younger than 65 years ($n = 1610$). In order to identify independent predictors of use of any inappropriate medication during hospital stay, a multivariate analysis was performed in the resulting sample of 5734 patients. From bivariate comparisons, variables associated with the use of any inappropriate medication at a P level ≤ 0.10 were selected and entered into a logistic regression model adjusted for age and gender.

To compare characteristics of participants receiving and not receiving inappropriate medications, we used the Chi-square test for categorical variables. Differences between continuous variables were assessed using analysis of variance (ANOVA) comparisons for normally distributed parameters; alternatively, the Kruskal-Wallis test was adopted. A value of P below 0.05 was considered statistically significant. All analyses were performed using SPSS for Windows version 10.0.

Results

In the 1997–1998 period, a total of 5734 patients aged 65 years or older were enrolled in the study. The principal characteristics of the population are illustrated in Table 2. Mean age ± SD was 79.0 ± 7.5 years; males and females were equally represented. During hospital stay, 837 (14.6% of the study sample) patients received one or more medications classified as inappropriate based on Beers criteria. More specifically, 697 (12.2%) patients used one inappropriate medication and 140 (2.4%) two or more. As shown in Table 1, ticlopidine ($n = 346$; 6.0% of the study sample) was the most frequently used medication, among those in Beers' list, followed by digoxin ($n = 174$; 3.0%), amytriptyline ($n = 113$; 2.0%), chlordiazepoxide ($n = 91$; 1.6%) and diazepam ($n = 91$; 1.6%).

At the bivariate analyses, subjects receiving an inappropriate medication were younger, had a lower prevalence of cognitive and functional impairment and were more likely to be enrolled in a 1998 survey than other participants (Table 2). In addition, these subjects had a higher co-morbidity index, consumed a higher number of drugs during hospital stay and had a longer length of hospital stay than participants not receiving inappropriate medications (Table 2). Entering these variables in a logistic regression model, age and cognitive impairment were associated with a reduced likelihood of receiving an inappropriate medication. In contrast, Charlson co-morbidity index and overall number of medications used during hospital stay were associated with a higher use of inappropriate medications (Table 3).

Since ticlopidine was responsible for about one-third of the cases of the inappropriate medication use, we repeated the analysis excluding this drug from the list elaborated by Beers. Based on these revised criteria, 527 participants (9.2% of the study sample) received an inappropriate medication. However, the results of the multivariate analysis showed that the inverse association of inappropriate medication use with age [75–84 years vs 65–74 years, odds ratio (OR) 0.72, 95% confidence interval (CI) 0.59–0.89; ≥85 years vs 65–74 years, OR 0.58, 95% CI 0.45–0.77] and cognitive impairment (OR 0.75, 95% CI 0.59–0.95) was confirmed. In addition, the number of medications used during hospital stay (5–8 medications vs < 5 medications, OR 2.42, 95% CI 1.73–3.40; ≥9 medications vs < 5 medications, OR 4.97, 95% CI 3.55–6.96) still showed a significant direct relationship with the outcome, while no association was

Table 2 Bivariate comparison of principal characteristics of the population ($n = 5734$) according to use of inappropriate medications

	Inappropriate medication use ($n = 837$)	No inappropriate medication use ($n = 4897$)	P value
Age (years)			< 0.001
65–74	39.7	32.0	
75–84	43.7	42.9	
≥85	16.6	25.1	
Gender (male)	49.8	47.2	0.159
Alcohol users[1]	46.7	46.6	0.951
Current smokers	8.4	8.5	0.915
Cognitive impairment[2]	25.6	33.8	< 0.001
ADLs disability[3]	35.6	42.7	< 0.001
Charlson co-morbidity index ≥2	55.0	48.0	< 0.001
Number of medications used during hospital stay			< 0.001
< 5	11.4	28.4	
5–8	35.4	38.4	
≥9	53.3	33.3	
Length of hospital stay			< 0.001
< 8 days	19.2	26.9	
8–12 days	33.6	36.1	
≥13 days	47.2	37.0	
Geriatric ward	72.3	72.8	0.737
Enrolled in 1997	46.0	51.0	0.001

[1]Consumers of any amount of alcohol before hospital admission

[2]Defined as Hodkinson abbreviated mental test < 7

[3]Defined as need of assistance to perform one or more of the following tasks: eating, dressing, bathing, transferring, and toileting

Table 3 Factors associated with inappropriate medication use. Results form the multivariate analysis. All the variables were simultaneously entered in the logistic regression model. The likelihood ratio test, assessing the statistical significance of fit improvement resulting from the addition of the variables to the model, was 248,566 ($P < 0.001$)

	Odds ratio	95% Confidence interval
Age (years)		
65–74	1	–
75–84	0.85	0.71–1.00
≥85	0.58	0.46–0.73
Gender (male)	1.01	0.87–1.18
Cognitive impairment[1]	0.77	0.64–0.94
ADLs disability[2]	0.86	0.72–1.03
Charlson co-morbidity index ≥2 (vs 0–1)	1.20	1.02–1.40
No. of medications used during hospital stay		
< 5	1	–
5–8	2.20	1.72–2.82
≥9	3.68	2.86–4.73
Length of hospital stay		
< 8 days	1	–
8–12 days	1.01	0.82–1.26
≥13 days	1.16	0.94–1.44
Enrolled in 1998 (vs 1997)	1.10	0.93–1.28

[1]Defined as Hodkinson abbreviated mental test < 7
[2]Defined as need of assistance to perform one or more of the following tasks: eating, dressing, bathing, transferring, and toileting

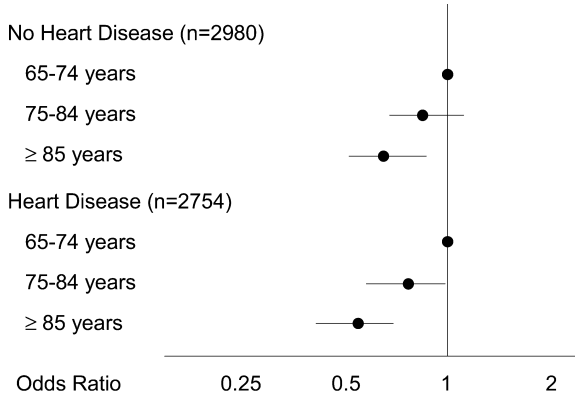

Fig. 1 Odds ratio and 95% confidence interval of inappropriate medication use by age groups, in subjects with and without heart disease. Heart disease includes diagnoses of ischemic heart disease, atrial fibrillation and congestive heart failure. Analyses are adjusted for gender, cognitive impairment, ADL disability, Charlson co-morbidity index, number of medications used during hospital stay, length of hospital stay and year of survey

observed for the Charlson co-morbidity index (≥2 vs 0–1, OR 0.99, 95% CI 0.82–1.20).

Finally, to confirm the inverse relationship between age and inappropriate medication use, and in consideration of the fact that the two drugs most frequently responsible for inappropriate use (ticlopidine and digoxin) are usually prescribed in subjects with heart disease, we repeated the multivariate analysis in participants with and without this disease. Overall, 2754 participants (48% of the study sample) had heart disease (which includes diagnoses of ischemic heart disease or atrial fibrillation or congestive heart failure). As expected, compared with other participants, subjects with heart disease had a higher likelihood of receiving an inappropriate medication (16.9% vs 12.5%; $P < 0.001$). However, as shown in Fig. 1, in the multivariate analyses, the inverse association of age groups with inappropriate drug use was confirmed in both groups of subjects with and without heart disease.

Discussion

In this study, we showed that among hospitalized older adults inappropriate drug use was common, and about 15% of participants were receiving at least one of the medications listed in the 1997 Beers criteria. In this sample, age and cognitive impairment were inversely associated with inappropriate drug use, while a direct relationship was observed for a number of drugs used during hospital stay and Charlson co-morbidity index.

Beers criteria have been criticized, since they do not identify all causes of potentially inappropriate prescribing and sometimes identify appropriate prescribing as inappropriate [29, 30]. However, these criteria represent a widely used and standardized tool for pharmacological research, despite the fact that they can not be used as a substitute for careful clinical judgement [10]. In this context, we did not apply diagnoses-related criteria for inappropriate medication use. Indeed, the high co-morbidity rate observed in this 'frail' population may have required careful adjustments of pharmacological regimens based on individual needs of each patient, leading to use of medications contraindicated for a certain disease to treat a coexisting one.

The prevalence of inappropriate medication use in this population was lower than those reported from other studies conducted in the United States [8, 9, 11, 12, 13, 14, 15, 16, 17], but in line with a previous observation in a European population [18]. This result may be explained by differences in pharmaceutical market among countries. Several of the drugs on Beers' list are not available in Italy. For example, propoxyphene, which appeared to be one of the most frequently prescribed inappropriate medications in the United States [11, 12], is not available on the market in Italy. Similarly, the fact that clopidogrel was not available on the market in Italy during the surveys periods, may have been responsible for the elevated consumption of ticlopidine as an alter-

native to aspirin. In this context, differences between the USA and Italy in indications to use of medications may have influenced our results. For example, Italian guidelines to anti-thrombotic treatment in the elderly, considered as appropriate the use of ticlopidine in subjects with ischemic heart disease intolerant to aspirin [31].

Finally, the characteristics of this study population may have influenced the prescribing pattern. For example, the elevated rate of heart disease observed in this sample, may explain the high consumption of ticlopidine and digoxin, which accounted for about 50% of any inappropriate medication use.

In contrast with other studies [9, 11, 14], we found that age was inversely related to the likelihood of receiving an inappropriate medication. We believe that this finding may be explained by the fact that older hospitalized adults in this population were 'frail' and at high risk of experiencing drug-related illnesses [2]. In this context, physicians may have been cautious in prescribing high-risk medications in this vulnerable population and they may have preferred to use medications with a safe profile. An alternative explanation is that older patients, compared with other participants, had a higher need of 'life-saving' medications with indubitable positive effects to treat acute severe conditions. This, by converse, may have reduced the use of other medications, which were not clearly beneficial for the patient.

Similarly, cognitive impairment may represent a marker of frailty. Therefore, the fact that, compared with other participants, cognitively impaired patients were less likely to use inappropriate medications probably reflected, among these clinically complex patients, a careful choice by physicians of medications whose risks do not outweigh benefits. Interestingly, the different use of inappropriate medications related to cognitive status may partially explain the inverse association between cognitive impairment and drug-related illnesses we have previously documented [32].

The most important factor predicting the probability of inappropriate medication use was the total number of prescription medications. The most likely hypothesis is that each prescription had a certain probability of being inappropriate, thus proportionally increasing a subject's probability of being on an inappropriate therapy with each additional medication. Similarly, the direct association between co-morbidity and inappropriate medication use may be explained by the fact that the elevated number of medications needed to treat multiple coexistent conditions increased a patient's likelihood of receiving an inappropriate prescription.

An important limitation of this study relates to generalizability of the results. Our findings, which are based on a hospitalized population cannot be extrapolated to subjects living in the community. Moreover, as we mentioned above, as consequence of differences in the pharmaceutical market among countries, the results of this study should not be compared with those of previous observations in the United States or other European countries [33]. In addition, the measurement of some predictors of inappropriate medication use may not have been accurate. For example, data on alcohol intake were self-reported and, therefore, subject to misclassification, and information on type of alcoholic beverage and duration of alcohol use were not gathered. Finally, this study is only assessing the problem of use of potentially harmful medications, not exploring the issue of underuse of beneficial therapies. Such underuse problem has been identified in the management of a broad range of chronic conditions in elderly patients, including cardiovascular disease, hypertension, osteoporosis and pain management [34, 35, 36, 37, 38] and it deserves the same level of attention and scrutiny given to problems of overuse of drug therapies.

In conclusion, the present study showed that inappropriate medication use is common among hospitalized older adults in Italy. The most important determinant of risk of receiving an inappropriate medication was the number of drugs being taken. Older age and cognitive impairment were associated with a reduced likelihood of using an inappropriate medication. We believe that the understanding of the factors associated with inappropriate prescribing may be valuable in designing and implementing effective drug utilization programs to influence prescribing patterns and they can be incorporated into medication use control programs.

Acknowledgements The GIFA study was partially supported by a grant from the National Research Council (no. 94000402) and by Neopharmed.

References

1. Einarson TR (1993) Drug-related hospital admissions. Ann Pharmacother 27:832–840
2. Onder G, Pedone C, Landi F, Cesari M, Della Vedova C, Bernabei R, Gambassi G (2002) Adverse drug reactions as cause of hospital admissions: results from the Italian Group of Pharmacoepidemiology in the Elderly (GIFA). J Am Geriatr Soc 50:1962–1968
3. Bordet R, Gautier S, Le Louet H, Dupuis B, Caron J (2001) Analysis of the direct cost of adverse drug reactions in hospitalised patients. Eur J Clin Pharmacol 56:935–941
4. Carbonin P, Pahor M, Bernabei R, Sgadari A (1991) Is age an independent risk factor of adverse drug reactions in hospitalized medical patients? J Am Geriatr Soc 39:1093–1099
5. Lazarou J, Pomeranz BH, Corey PN (1998) Incidence of adverse drug reactions in hospitalized patients: a meta-analysis of prospective studies. JAMA 279:1200–1205
6. Everitt DE, Avorn J (1986) Drug prescribing for the elderly. Arch Intern Med 146:2393–2396
7. Bates DW (1998) Drugs and adverse drug reactions: how worried should we be? JAMA 279:1216–1217
8. Beers MH, Ouslander JG, Rollingher I, Reuben DB, Brooks J, Beck JC (1991) Explicit criteria for determining inappropriate medication use in nursing home residents. UCLA Division of Geriatric Medicine. Arch Intern Med 151:1825–1832
9. Stuck AE, Beers MH, Steiner A, Aronow HU, Rubenstein LZ, Beck JC (1994) Inappropriate medication use in community-residing older persons. Arch Intern Med 154:2195–2200
10. Beers MH (1997) Explicit criteria for determining potentially inappropriate medication use by the elderly. An update. Arch Intern Med 157:1531–1536

11. Aparasu RR, Mort JR (2000) Inappropriate prescribing for the elderly: beers criteria-based review. Ann Pharmacother 34:338–346
12. Willcox S, Himmelstein D, Woolhandler S (1994) Inappropriate drug prescribing for the community-dwelling elderly. JAMA 272:292–296
13. Beers MH, Ouslander JG, Fingold SF, Morgenstern H, Reuben DB, Rogers W, Zeffren MJ, Beck JC (1992) Inappropriate medication prescribing in skilled-nursing facilities. Ann Intern Med 117:684–689
14. Spore D, Mor V, Larrat P, Hawes C, Hiris J (1997) Inappropriate drug prescriptions for elderly residents of board and care facilities. Am J Public Health 87:404–409
15. Aparasu R, Fliginger S (1997) Inappropriate medication prescribing for the elderly by office-based physicians. Ann Pharmacother 31:823–829
16. Aparasu R, Sitzman S (1999) Inappropriate prescribing for elderly outpatients. Am J Health Syst Pharm 56:433–439
17. Golden A, Preston R, Barnett S, Llorente M, Hamdan K, Silverman MA (1999) Inappropriate medication prescribing in homebound older adults. J Am Geriatr Soc 47:948–953
18. Pitkala KH, Strandberg TE, Tilvis RS (2002) Inappropriate drug prescribing in home-dwelling, elderly patients: a population-based survey. Arch Intern Med 162:1707–1712
19. Grant RL, Batty GM, Aggarwal R, Lowe D, Potter JM, Pearson MG, Oborne A, Jackson SH (2002) National sentinel clinical audit of evidence-based prescribing for older people: methodology and development. J Eval Clin Pract 8:189–198
20. Elliott RA, Woodward MC, Oborne CA (2001) Improving benzodiazepine prescribing for elderly hospital inpatients using audit and multidisciplinary feedback. Intern Med J 31:529–535
21. Rochon PA, Gurwitz JH (1997) Optimising drug treatment for elderly people: the prescribing cascade. BMJ 315:1096–1099
22. Onder G, Landi F, Della Vedova C, Pedone C, Atkinson H, Cesari M, Bernabei R, Gambassi G (2002) Moderate alcohol consumption and adverse drug reactions among older adults. Pharmacoepidemiol Drug Saf 11:385–392
23. Hodkinson HM (1972) Evaluation of a mental test score for assessment of mental impairment in the elderly. Age Ageing 1:233–238
24. Gomez de Caso JA, Rodriguez-Artalejo F, Claveria LE, Coria F (1994) Value of Hodkinson's test for detecting dementia and mild cognitive impairment in epidemiological surveys. Neuroepidemiology 13:64–68
25. Rocca WA, Bonaiuto S, Lippi A, Luciani P, Pistarelli T, Grandinetti A, Cavarzeran F, Amaducci L (1992) Validation of the Hodkinson abbreviated mental test as a screening instrument for dementia in an Italian population. Neuroepidemiology 11:288–295
26. Pahor M, Chrischilles EA, Guralnik JM, Brown SL, Wallace RB, Carbonin PU (1994) Drug data coding and analysis in epidemiological studies. Eur J Epidemiol 10:405–411
27. PHS-HCFA (1980) International classification of diseases, 9th rev. Public Health Service-Health Care Financing Administration, Washington
28. Charlson ME, Pompei P, Ales KL, Mackenzie CR (1987) A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. J Chron Dis 40:373–383
29. Avorn J (2001) Improving drug use in elderly patients: getting to the next level. JAMA 286:2866–2868
30. Gurwitz JH, Rochon P (2002) Improving the quality of medication use in elderly patients: a not-so-simple prescription. Arch Intern Med 162:1670–1672
31. Cerbone AM, Tufano A, Di Minno G (2000) Linee Guida di terapia antitrombotica nel paziente anziano. Giorn Geront 48:419–433
32. Onder G, Gambassi G, Scales CJ, Cesari M, Della Vedova C, Landi F, Bernabei R (2002) Adverse drug reactions and cognitive function among hospitalized older adults. Eur J Clin Pharmacol 58:371–377
33. Lawson DH, Jick H (1976) Drug prescribing in hospitals: an international comparison. Am J Public Health 66:644–648
34. Gambassi G, Forman DE, Lapane KL, Mor V, Sgadari A, Lipsitz LA, Bernabei R (2000) 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 139:85–93
35. Onder G, Gambassi G, Landi F, Pedone C, Cesari M, Carbonin PU, Bernabei R (2001) Trends in antihypertensive drugs in the elderly: the decline of thiazides. J Hum Hypertens 15:291–297
36. Berlowitz DR, Ash AS, Hickey EC, Friedman RH, Glickman M, Kader B, Moskowitz MA (1998) Inadequate management of blood pressure in a hypertensive population. N Engl J Med 339:1957–1963
37. Onder G, Pedone C, Gambassi G, Landi F, Cesari M, Bernabei R (2001) Temporal patterns in medical treatment of osteoporosis among elderly patients in Italy. Eur J Clin Pharmacol 57:599–604
38. Bernabei R, Gambassi G, Lapane K, Landi F, Gatsonis C, Dunlop R, Lipsitz L, Steel K, Mor V (1998) Management of pain in elderly patients with cancer. SAGE Study Group. Systematic assessment of geriatric drug use via epidemiology. JAMA 279:1877–1882