

# Potentially inappropriate medication in elderly patients in outpatient clinics

HM Ma<sup>1</sup> MBChB (CUHK), CM Lum<sup>1</sup> FRCP (Edin), FHKAM (Med),  
LK Dai<sup>2</sup> FRCP (Glas, Ireland, Lond), FHKAM (Med), CYT Kwok<sup>2</sup> FRCP,  
FHKAM (Med), J Woo<sup>1,2</sup> MD, FHKAM (Med)

## ABSTRACT

**Objective.** To determine the prevalence and factors associated with potentially inappropriate medication (PIM), in elderly patients attending medical specialist outpatient clinics.

**Methods.** A 1-week cross-sectional survey was conducted in the general medical and geriatric specialist outpatient clinics of a regional hospital under the Hospital Authority. Elderly patients, aged 65 years or older, were included in the study. Regular prescription and non-prescription medications and diagnoses were reviewed through the electronic patient record. Those with prescriptions for less than 4 weeks of treatment were excluded. Beers criteria (2003 version), both independent of and in consideration of the diagnosis were employed to determine the appropriateness of each medication.

**Major outcome measure.** Prevalence of PIM and associated factors.

**Results.** A total of 312 patients were recruited in the study, of whom 53 (19%) were in receipt of at least one PIM. The most common agents involved in PIMS were methyl dopa (33%), doxazosin (26%), antihistamines (12%) and amiodarone (10%). Constipation was the only condition identified in which calcium channel blockers were inappropriately used. Logistic regression analysis showed that polypharmacy was an independent risk factor (odds ratio [OR], 10.01; 95% confidence interval [CI], 1.17-85.59). Males (OR, 6.25; 95% CI, 1.07-36.47) were six times more likely to be in receipt of PIMs.

**Conclusion.** Receipt of PIMs in elderly patients attending the general medical and geriatric specialist outpatient clinics is common. Further research is warranted to study consequential adverse drug reactions and health outcomes in these elderly, as well as to provide a more comprehensive view on the local epidemiology and pattern of inappropriate prescribing.

**Key words:** Aged; Medication errors; Outpatients

<sup>1</sup> Department of Medicine and Geriatrics, Shatin Hospital

<sup>2</sup> Department of Medicine and Therapeutics, Prince of Wales Hospital, Chinese University of Hong Kong

Correspondence to: Dr HM Ma, Department of Medicine and Geriatrics, Shatin Hospital.  
E-mail: hmma@cuhk.edu.hk

## INTRODUCTION

Elderly patients commonly have multiple pathologies leading to polypharmacy, and altered pharmacokinetics and pharmacodynamics, and are prone to adverse drug reactions from inappropriate

medication.<sup>1</sup> Their drug-related problems are important reasons for acute hospital admission.<sup>2</sup> Physicians caring for the elderly should always aim to optimise drug use among this high-risk group. Optimal drug use includes prescription of appropriate medications as well as avoidance of under-treatment,

over-treatment and drug-drug and drug-disease interactions. Overseas studies showed that about 11.5 to 14.0% of community living elderly were using at least one inappropriate medication.<sup>3,4</sup> A local survey conducted 10 years ago at a specialist geriatric clinic reported that 8% of the elderly were prescribed inappropriate medications.<sup>5</sup> In reality, geriatric clinics cannot cope with the entire elderly population and many elderly patients are in other specialist medical clinics. Thus, this survey provided historic data based on a restricted sample. It is essential to have up-to-date data on potentially inappropriate medications (PIMs) among the elderly, so that remedial actions can be taken. The objectives of the current study were to study: (1) the prevalence of PIMs in elderly patients attending medical specialist clinics, and (2) factors associated with such PIMs, with a view to correct them.

## METHODS

A 1-week cross-sectional survey was conducted in the general medical and geriatric specialist outpatient clinics of a regional hospital under the Hospital Authority. This hospital has 300 medical beds and serves a population of 1.3 million. All elderly patients, aged 65 years or older, who attended the clinics in that week were recruited into the study. Regular medications, both prescription and non-prescription, were reviewed through the electronic patient record (e-PR) system. Prescription medications were those prescribed in the medical or geriatric clinic at the index consultation. 'Non-prescription medications' were those not prescribed in the medical or geriatric clinics under study. Only medications prescribed for at least 4 weeks and to be taken on a regular basis were included in this survey. This caveat was based on the assumption that prescribing labelled as a PIM might have been 'appropriately' prescribed for a short course with close monitoring. The underlying diagnoses and other demographic data were also reviewed through the e-PR system.

The latest version (2003) of Beers criteria<sup>6</sup> was used to label PIMs explicitly. The criteria comprise two parts. The first consists of 48 individual or classes of medications to be generally avoided in persons 65 years or older because either they are ineffective or pose unnecessarily high risk when safer alternatives are available. The second describes 20 diseases or conditions in which some medications should

be avoided. The Beers criteria were used because according to our literature search they were the most up to date, applicable to both community and residential living elderly (aged 65 years more), and had been used extensively in other studies.<sup>7-13</sup>

Microsoft Office Excel 2003 was used to perform descriptive statistical analysis and STATA (version 9.1) for logistic regression analysis to determine factors associated with inappropriate prescribing. Odds ratios (OR) and 95% confidence interval (CI) were calculated for factors associated with PIMs. A p value of <0.05 was considered statistically significant.

## RESULTS

A total of 341 elderly patients attended the general medical and geriatric specialist outpatient clinics of the regional hospital during the study period. Of these, 312 patients (92%) were included and 29 were excluded because they were less than 65 years old. **TABLE 1** describes the baseline characteristics of this sample.

Fifty-nine patients (19%) received at least one potentially inappropriate medication (PIM). Of these, 53 (90%) received only one while 6 (10%) received two, and none received three. Forty-eight patients (81%) received PIMs independent of their diagnosis, 8 (14%) took the diagnosis into consideration, and 3 (5%) entailed both. Thirty-six of 62 PIMs (58%) were classified as high severity. **TABLE 1** describes the characteristics of the patients and **TABLE 2** summarises the types of PIM.

Logistic regression analysis was performed to determine the risk factors associated with PIMs and corresponding results are summarised in **TABLE 3**. The analysis on each stratum (1-5) of the total number of medications was not performed, because of collinearity. Instead, comparison was made between the groups with polypharmacy ( $\geq 6$  drugs) and without (1-5 drugs). Polypharmacy (OR, 10.01; 95% CI, 1.17-85.59) was an independent risk factor associated with inappropriate prescribing and males (OR, 6.25; 95% CI, 1.07-36.47) were six times more likely to receive PIMs. Age and the nature of the clinics (general medical versus geriatrics) had no significant association with inappropriate medication use. The logistic regression model was statistically significant ( $\chi^2=15.73$ ;  $p<0.05$ ).

**TABLE 1**  
**Characteristics of sample population and subgroups of patients with potentially inappropriate medications (PIMs)**

Patient characteristics	No. of patients (%)	
	Sample	PIMs
Gender		
Male	141 (45)	33 (56)
Female	171 (55)	26 (44)
Age (years)		
65-74	101 (32)	13 (22)
75-84	153 (49)	31 (53)
≥85	58 (18)	15 (25)
Nature of clinic visit		
General medical	238 (76)	41 (70)
Geriatric	74 (24)	18 (31)
Total No. of medications (both prescription and non-prescription medications)		
1	19 (6)	0 (0)
2	33 (11)	4 (7)
3	21 (7)	3 (5)
4	35 (11)	6 (10)
5	46 (15)	4 (7)
≥6 (poly-pharmacy)	158 (51)	42 (71)

**TABLE 2**  
**Types of potentially inappropriate medications (PIMs)**

Medications	Frequency (%)	Severity rating
Independent of diagnosis		
Methyldopa	17 (33)	High
Doxazosin	13 (26)	Low
Antihistamines	6 (12)	High
Amiodarone	5 (10)	High
Non-cyclo-oxygenase-selective non-steroidal anti-inflammatory drugs	4 (8)	High
Ferrous sulphate (>325 mg/day)	3 (6)	Low
Amitriptyline	3 (6)	High
Propoxyphene	2 (4)	Low
Long-acting benzodiazepines	1 (2)	High
Digoxin (>125 mcg/day)	1 (2)	Low
Total	51 (100)	
Considering diagnosis		
Constipation (calcium channel blocker)	11 (100)	Low
Total	11 (100)	

## DISCUSSION

### Prevalence of potentially inappropriate medication

Our survey showed that nearly one in five (19%)

of elderly patients received at least one PIM. The result was in keeping with the findings from other studies using the Beers criteria (16.3-22.0%),<sup>8-13</sup> but much higher than the 7.7% as reported by Ko et al.<sup>5</sup> This apparent difference may be due to the use of different criteria; in Ko's study, the Stuck criteria<sup>3</sup>

**TABLE 3**  
**Results of logistic regression analysis\***

Parameter	Odds ratio	95% CI	P value
Gender			
Male	6.25	1.07-36.47	0.042
Female	1.00	Reference	
Age (years)			
65-74	1.00	Reference	
75-84	4.36	0.49-39.07	0.188
≥85	2.45	0.13-46.67	0.551
Nature of clinic visit			
General medical	1.00	Reference	
Geriatric	0.91	0.13-6.36	0.925
Total No. of medications			
1-5 <sup>†</sup>	1.00	Reference	
≥6 (poly-pharmacy)	10.01	1.17-85.59	0.035

\* The overall model significance:  $X^2=15.73$ ,  $p<0.05$

<sup>†</sup> The analysis on each stratum of number of medications (1-5) was dropped because of collinearity

were used. With advances in medical knowledge and development of new drugs, new criteria should be adopted. The use of the latest version of the Beers criteria allows adjustment for up-to-date information and enables international comparison.

### Types of potentially inappropriate medications

Among those with PIMs, the great majority received only one (90%). Methylodopa, doxazosin, antihistamines and amiodarone accounted for 80% of all PIMs, which should in general be avoided in elderly persons (≥65 years), irrespective of comorbidities. Taking diseases or conditions into account, calcium channel blockers (CCBs) were identified as inappropriately used in patients with constipation.

Methylodopa is a centrally acting anti-adrenergic antihypertensive. It reduces the central sympathetic outflow, cardiac output and heart rate,<sup>14</sup> apart from causing bradycardia and aggravating depression in the elderly.<sup>7</sup> Although methylodopa is a long-standing anti-hypertensive, it is no longer recommended as a first-line treatment because of its side-effects and the availability of alternatives. The common use of methylodopa in our locality may be due to its low cost and prescribing habits. Alternative anti-hypertensive drugs such as thiazide diuretics and beta-blockers should be considered if there are no

contraindications.

Doxazosin is a selective alpha-blocker and used in relieving the lower urinary tract symptoms in benign prostatic hyperplasia. Orthostatic hypotension is a common side-effect; others include dizziness, asthenia and ejaculatory problems.<sup>15</sup> A randomised controlled trial showed that compared to standard doxazosin, doxazosin GITS (slow release) had a lower incidence of all-cause adverse effects, including postural hypotension (1.2% vs 2.2%).<sup>16</sup> It is suggested that other selective alpha-blockers, such as terazosin and prazosin or specific preparations of doxazosin (doxazosin GITS) are safer alternatives in the elderly.

Antihistamines (H<sub>1</sub> blockers) are commonly used in the treatment of allergic rhinitis and common cold. Older antihistamines, such as chlorpheniramine, promethazine and diphenhydramine, are sedating and may cause psychomotor impairment, including eye-hand dys-coordination. Their anti-cholinergic (muscarinic) effects result in visual disturbance, urinary retention and constipation.<sup>17</sup> However, it is unusual for patients to require long-term regular antihistamine treatment. For which reason both the indications and duration of treatment should be reviewed.

In the current study, 10% of PIMs were attributed to the use of amiodarone, a Class 3 anti-arrhythmic

drug. Its clinical efficacy has been established in the management of ventricular and other arrhythmias. However, its role in the rhythm control of patients with atrial fibrillation is debatable. A recent study comparing rate and rhythm control of atrial fibrillation showed no significant difference in 5-year mortality between patients with rate control and rhythm control group (21.3% and 23.8% respectively,  $p=0.08$ ).<sup>18</sup> Rate control is effective with beta-blockers, CCBs or digoxin. It is well known that the pharmacokinetics of amiodarone are complex and unpredictable, and the risk of drug-drug interactions with other cardiac drugs is high.<sup>19</sup> Isolated observational studies suggested that 34 to 93% patients encounter adverse drug reactions during courses of treatment.<sup>20</sup> Thus use of amiodarone for either rhythm or rate control should generally be avoided, and if really necessary, patients should be closely monitored. In our study, details for the indication of prescribing amiodarone were not examined, and it is possible that such prescribing was to counter life-threatening ventricular arrhythmia. This may have contributed to the excessive use of 'inappropriate' amiodarone prescribing we encountered.

CCBs are classified as dihydropyridines (nifedipine, amlodipine and felodipine) and non-dihydropyridines (verapamil and diltiazem), which are commonly used in the treatment of hypertension and tachyarrhythmias respectively. Common side-effects include flushing, headache, hypotension, constipation and pedal oedema.<sup>21</sup> There is a possible drug-disease interaction between CCBs and patients with constipation. Beta-blockers can be considered alternatives if there are no contra-indications. However, in view of the clinical efficacy of CCBs as anti-hypertensive agents, they may continue to be used, because the elderly may have multiple co-morbidities restricting the use of alternatives (beta blockers or angiotensin converting enzyme inhibitors). Nevertheless, one should be aware of potential side-effects in the elderly so that the most appropriate drug is prescribed.

Psychotropic medications (anti-depressants, anti-anxiety and hypnotic/sedatives) were low down in the list in this study, accounting for 8% of total PIMs. This is in contrast to the 27% in another study,<sup>10</sup> suggesting that inappropriate prescribing of psychotropic medications is not common among local elderly. This is probably due to the pattern of

use of psychotropic medications in Chinese and Caucasian populations.

Previous studies showed that propoxyphene accounted for about 7% of PIMs<sup>11</sup> and its use in the elderly is associated with adverse outcome (OR, 2.39; 95% CI, 1.54-3.71).<sup>22</sup> The low prevalence of propoxyphene PIMs (4%) in our study may be because it is usually taken as needed, and short-term and intermittent users may have been missed as per our definition of a PIM.

### Predictors of inappropriate prescribing

In this study, male gender and polypharmacy were risk factors associated with inappropriate prescribing. The higher risk of inappropriate prescribing in male elderly was compatible with the finding that doxazosin was responsible for the second commonest PIM. In contrast, Beers showed that women were more likely to receive PIMs (OR, 1.6-1.96) associated with the use of psychotropic medications and pain-relievers.<sup>7</sup> In our study, fewer patients had PIMs with these agents. This may explain why women were not identified as more liable to inappropriate prescribing in our series.

This study demonstrated that polypharmacy is associated with an increased risk of inappropriate prescribing, which was in keeping with the findings from other reports (OR, 1.14-1.91).<sup>12, 22</sup> However, the cause-effect relationship between polypharmacy and PIMs is unclear. Conceivably, the first PIM could cause adverse effects for which secondary drugs are prescribed to alleviate side-effects of the first drug, thus perpetuating a prescription cascade. Alternatively, after balancing the risk and benefits, the complexity of the patient's condition may make PIMs necessary, whilst also resulting in polypharmacy. Detailed clinical studies that include the sequencing of drug treatment are required to clarify these issues. Nevertheless, review of treatment medications is advisable in patients subjected to polypharmacy ( $\geq 6$  medications), with a view to avoid over-prescribing and untoward side-effects.

### Controversy over explicit criteria on prescribing

This survey's results should be interpreted with caution. The notion that one fifth of our elderly were given medication inappropriately is not necessarily

valid. It is acknowledged that development of explicit criteria is an important means of boosting physician awareness of special issues about prescribing medications, especially for elderly patients who are prone to age- and disease-related pharmacokinetic and pharmacodynamic changes.<sup>23,24</sup> This is the basis of explicit PIMs criteria, which are useful for clinical practitioners, and especially those who are inexperienced and junior. However, explicit criteria should never limit the physician's freedom to prescribe, appropriate clinical evaluation of benefits against risks being of paramount importance in every instance.

### Limitations

Several limitations of this survey should be noted. First, as noted above, though explicit criteria constitute a useful reference, a patient's condition may vary what may be regarded as a PIM by definition is not so in reality. Accordingly, our 19% PIM rate may be an over-estimate of 'inappropriate of prescriptions'. Second, the residential status of the participants was not documented, which may have a bearing on the prevalence and pattern of inappropriate prescribing; elderly persons living in nursing homes differ from those in the community with respect to co-morbidities and the medications they take. Further studies are needed to evaluate the differences in inappropriate prescribing among community and residential care elderly residents. Third, possible drug-drug interactions were not examined, e.g. concomitant use of verapamil or diltiazem and warfarin may cause over-anticoagulation. Similarly, some side-effects may be dose-dependent and this too was not explored. Fourth, electronic record systems have inaccuracies with respect to documenting current and past medical histories, as well as the rationale for prescribing or not prescribing a particular medication. This may introduce errors into analysing and interpreting data. Furthermore, the elderly commonly take over-the-counter medications and those prescribed by the general practitioners, which may not have been recorded in this study. Finally, the wide confidence interval of risk factors for inappropriate prescribing implies an inadequate sample size; a larger sample could have improved statistical accuracy.

### CONCLUSION

This study serves to remind physicians of the

side-effects of commonly prescribed medications when treating elderly patients. Explicit criteria should never be regarded as absolute prescribing guidelines, as physicians always have the freedom to choose the most appropriate medications for their patients. Moreover, the Beers criteria may not suit our local elderly patients, in view of different drug pharmacokinetics and pharmacodynamics in Chinese and Caucasian populations. Ideally a group of local experts in geriatric care and pharmacology need to prepare explicit criteria for local elderly patients in a bid to avoid unnecessary adverse drug reactions.

### Acknowledgements

We would like to thank Dr CC Chow, COS of Department of Medicine and Therapeutics of Prince of Wales Hospital, for granting access to data for analysis and Professor LK Hung, Department of Orthopedics and Traumatology of Chinese University of Hong Kong, for reviewing the manuscript.

### References

1. Chan TY, Wang AY, Woo J, Critchley JA. Adverse drug reactions in the elderly – the local scene. *J Hong Kong Med Assoc* 1991;43:200-4.
2. Chan TY, Critchley JA. Drug related problems as a cause of hospital admission in Hong Kong. *Pharmacoepidemiol Drug Saf* 1995;4:165-70.
3. Stuck AE, Beers MH, Steiner A, Aronow HU, Rubenstein LZ, Beck JC. Inappropriate medication use in community-residing older persons. *Arch Intern Med* 1994;154:2195-200.
4. Lindley CM, Tully MP, Paramsothy V, Tallis RC. Inappropriate medication is a major cause of adverse drug reaction in elderly patients. *Age Ageing* 1992;21:294-300.
5. Ko CF, Ko PS, Tsang ML. A survey on polypharmacy and use of inappropriate medication in a geriatric out-patient clinic. *J Hong Kong Geriatr Soc* 1996;7:28-31.
6. Fick DM, Cooper JW, Wade WE, Waller JL, Maclean JR, Beers MH. Updating the Beers criteria for potentially inappropriate medication use in older adults: results of a US consensus panel of experts. *Arch Intern Med* 2003;163:2716-24.
7. Beers MH, Ouslander JG, Fingold SF, Morgenstern H, Reuben DB, Rogers W, et al. Inappropriate medication prescribing in skilled-nursing facilities. *Ann Intern Med* 1992;117:684-9.
8. Goulding MR. Inappropriate medication prescribing for elderly ambulatory care patients. *Arch Intern Med* 2004;164:305-12.
9. Fu AZ, Liu GG, Christensen DB. Inappropriate medication use and health outcomes in the elderly. *J Am Geriatr Soc* 2004;52:1934-9.
10. Curtis LH, Ostbye T, Sendersky V, Hutchison S, Dans PE, Wright A, et al. Inappropriate prescribing for elderly Americans in a large outpatient population. *Arch Intern Med* 2004;164:1621-5.
11. Simon SR, Chan KA, Soumerai SB, Wagner AK, Andrade SE, Feldstein AC, et al. Potentially inappropriate medication use by elderly persons in US Health Maintenance Organizations, 2000-2001. *J Am Geriatr Soc* 2005;53:227-32.

12. Fialova D, Topinkova E, Gambassi G, Finne-Soveri H, Jonsson PV, Carpenter I, et al. Potentially inappropriate medication use among elderly home care patients in Europe. *JAMA* 2005;293:1348-58.
13. Zhan C, Sangl J, Bierman AS, Miller MR, Friedman B, Wickizer SW, et al. Potentially inappropriate medication use in the community-dwelling elderly: findings from the 1996 Medical Expenditure Panel Survey. *JAMA* 2001;286:2823-9.
14. Fisher ND, William GH. Hypertensive vascular disease. In: Braunwald K, Hauser F, Jameson L, editors. *Harrison's principles of internal medicine*, 16th ed. McGraw-Hill; 2005:1463-81.
15. McNaughton-Collins M, Barry MJ. Managing patients with lower urinary tract symptoms suggestive of benign prostatic hyperplasia. *Am J Med* 2005;118:1331-9.
16. Kirby RS, Andersen M, Gratzke P, Dahlstrand C, Hoyer K. A combined analysis of double-blind trials of efficacy and tolerability of doxazosin-gastrointestinal therapeutic system, doxazosin standard and placebo in patients with benign prostatic hyperplasia. *BJU Int* 2001;87:192-200.
17. Austen KF. Allergies, anaphylaxis, and systemic mastocytosis. In: Braunwald K, Hauser F, Jameson L, editors. *Harrison's principles of internal medicine*, 16th ed. McGraw-Hill; 2005:1947-56.
18. Van Gelder IC, Hagens VE, Bosker HA, Kingma JH, Kamp O, Kingma T. A comparison of rate control and rhythm control in patients with recurrent persistent atrial fibrillation. *N Engl J Med* 2002;347:1834-40.
19. Yamreudeewong W, DeBisschop M, Martin LG, Lower DL. Potentially significant drug interactions of class III antiarrhythmic drugs. *Drug Saf* 2003;26:421-38.
20. Wilson JS, Podrid PJ. Side effects from amiodarone. *Am Heart J* 1991;121:158-71.
21. Eisenberg MJ, Brox A, Bestawros AN. Calcium channel blockers: an update. *Am J Med* 2004;116:35-43.
22. Perri M 3rd, Menon AM, Deshpande AD, Shinde SB, Jiang R, Cooper JW, et al. Adverse outcomes associated with inappropriate drug use in nursing homes. *Ann Pharmacother* 2005;39:405-11.
23. Lau DT, Kasper JD, Potter DE, Lyles A, Bennett RG. Hospitalization and death associated with potentially inappropriate medication prescriptions among elderly nursing home residents. *Arch Intern Med* 2005;165:68-74.
24. Mangoni AA, Jackson SH. Age-related changes in pharmacokinetics and pharmacodynamics: basic principles and practical applications. *Br J Clin Pharmacol* 2004;57:6-14.