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ORIGINAL RESEARCH

Potentially inappropriate medications in hospitalized older patients: a cross-sectional study using the Beers 2015 criteria versus the 2012 criteria

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Aim: Polypharmacy and potentially inappropriate medications (PIMs) are prominent prescribing issues in elderly patients. The purpose of the study was to investigate the prevalence of PIMs identified by the Beers 2015 and 2012 criteria in older patients in China and identify the correlates of PIMs.

Methods: This retrospective, cross-sectional study was conducted at Peking University First Hospital. The Beers 2015 and 2012 criteria were applied to evaluate PIMs among hospitalized patients. The associations between PIM use and independent variables were analyzed by logistic regression. The differences between PIM use according to Beers 2012 and 2015 criteria were calculated using chi-squared and kappa tests.

Results: A total of 456 patients were analyzed; 244 (53.5%) and 204 (44.7%) patients had at least one PIM identified by the Beers 2015 and 2012 criteria, respectively. The most frequent PIMs were proton-pump inhibitors (PPIs), benzodiazepines, and benzodiazepine receptor agonists according to the Beers 2015 criteria. PIMs identified by the Beers 2015 criteria were associated with excessive polypharmacy (OR 1.864, 95% CI 1.210–2.871), a Barthel index ≤60 (OR 1.935, 95% CI 1.056–3.546), and the length of stay (OR 1.066, 95% CI 1.037–1.097). PIM use increased significantly between two criteria (chi-squared test, $P<0.001$), but good accordance was found between the previous and updated criteria (kappa test 0.782, $P<0.001$).

Conclusion: Our study showed a high prevalence of PIM use in China, which was associated with various correlates. The Beers 2015 criteria detected significantly more PIMs than the 2012 criteria due to the inclusion of PPIs.

Keywords: Beers criteria, inappropriate prescription, polypharmacy

Introduction

The physiological alterations related to aging, such as changes in body composition and reductions in kidney and liver function, can significantly change pharmacokinetic and pharmacodynamic properties. Alteration of age-related pharmacokinetics and pharmacodynamics predisposes older adults to drug-related problems, such as adverse drug reactions (ADRs), drug–drug interactions, and drug–disease interactions.[1] Potentially inappropriate medications (PIMs) can be defined as drugs for which use among older adults should be avoided due to the high risk of adverse reactions for this population and/or insufficient evidence of their benefits when safer and equally or more effective therapeutic alternatives are available.[2] Inappropriate medication prescribing in older adults has become a public health concern due to its high prevalence,[3] associated negative outcomes, including ADRs, morbidity, hospitalization, health services use, and increased costs.[4–9]

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To prevent PIM use, experts have begun to address this issue and devise screening tools to assess the extent of PIMs and guide clinical practice in older adults. One of the first consensuses of experts was achieved by Beers et al in the USA in 1991,[10] which was proposed by an expert panel using the Delphi method. The American Geriatrics Society Beers Criteria for PIM Use in Older Adults is an explicit list of PIMs that should be avoided in older adults in general and in people with certain diseases or syndromes, prescribed at a reduced dosage or used with caution or careful monitoring.[11] The Beers criteria are one of the most frequently consulted sources and were updated in 2003 and 2012. The changes in the 2015 update were not as extensive as those of the previous updates; the following two major components were added: 1) drugs for which dose adjustment is required based on kidney function and 2) drug–drug interactions.[12] With the increasing use of the Beers criteria as a quality-of-care measure, a need exists to strengthen the predictive validity of the Beers criteria in all health care settings.[13]

However, to our knowledge, no data have shown the prevalence of PIMs identified by the updated version of the Beers criteria in China and no studies have compared the 2012 and 2015 versions to detect PIMs. Therefore, the objectives of the present study were 1) to assess the prevalence of PIMs using the Beers 2012 and 2015 criteria; 2) to explore related risk factors for PIMs according to the 2015 criteria; and 3) to compare the prevalence of differences and the accordance of PIMs between the 2012 and 2015 criteria.

Methods

Setting and sample

This retrospective, cross-sectional study was conducted at Peking University First Hospital, a 1,500 bed tertiary care teaching hospital in China. The Department of Geriatrics cares for aging patients and patients with age-related diseases (such as cardiocerebral vascular disease, respiratory disease, and digestive disease). Hospitalized patients in the geriatric department aged ≥65 years were enrolled from May 2015 to December 2015. If a patient had more than one visit for a prescription refill within the study period, only the first occurrence was used in the analyses. Patients without any medications were excluded. The study protocol was approved by the Ethics Committee of Peking University First Hospital. Each participant provided written informed consent to be included in the study.

Data collection and measures

Data including age, gender, primary diagnosis, comorbidities, prescribed drugs and precise dosages, length of stay, ADRs, Barthel index, estimated glomerular filtration rate (eGFR), and prognosis (discharge or death) were extracted from patient medical records. The eGFR was calculated using the modified, abbreviated Modification of Diet in Renal Disease equations based on Chinese patients. The Charlson Comorbidity Index (CCI) was calculated for each patient. The Beers 2015 and 2012 criteria were adopted to determine the use of PIMs in the study patients.

Statistical analysis

All analyses were conducted using SPSS version 23.0; a two-tailed value of $P<0.05$ was considered statistically significant. Continuous data are expressed as the mean ± SD, nonparametric variables are expressed as the median and interquartile range (IQR), and categorical data are expressed as frequencies. The patients were divided into PIM (at least one PIM) and non-PIM (without any PIMs) groups. A chi-squared test was applied to compare dichotomous variables between groups, and Fisher's exact test was used when expected cell counts were below five. Student's *t*-test or a nonparametric test was applied to compare the mean or median, respectively, of continuous variables. Multivariate logistic regression was used to examine factors related to PIMs according to the Beers 2015 criteria. The chi-squared test and kappa test were used to evaluate the prevalence of differences and accordance of the two criteria, respectively.

Results

Demographics of participants

Table 1 describes the characteristics of the study population. A total of 611 participants aged 65 years or older were included in the present study. Of these, 140 participants were excluded for being repeatedly admitted to the hospital and 15 participants were excluded as no medication was prescribed during hospitalization. Among the remaining 456 patients, the average age was 81.8±7.8 years (range 65–103 years) and 334 (73.2%) patients were male. A total of 70 patients (15.4%) had a Barthel index of ≤60, which indicated physical disability. The prevalence of elderly patients who were regularly prescribed ≥10 drugs was 37.9%. The median length of hospital stay and CCI were 14 days (IQR 9–21) and two points (IQR 1–3), respectively. Of all patients, 13 ADRs occurred, and four events were due to PIMs. Long-term usage of zolpidem tartrate tablets that leads to abnormal behavior and sleep disorders, taking dabigatran that leads to gastrointestinal bleeding, taking amiodarone that leads to elevated transaminase levels, and taking diuretics that caused orthostatic hypotension and falls during hospitalization were the four ADRs.

Table 1 Baseline and clinical characteristics of 456 older adults as identified by the Beers criteria of 2015 and 2012

Characteristics	Total (n=456)	Beers 2015 criteria		*P*-value	Beers 2012 criteria		*P*-value
		PIM (n=244)	Non-PIM (n=212)		PIM (n=204)	Non-PIM (n=252)	
Instances of PIM per person (mean ± SD)		1.7±0.9			1.5±0.8		
Age, years (mean ± SD)	81.8±7.8	83.2±7.7	80.3±7.6	<0.001	83.6±7.7	80.4±7.5	<0.001
Gender							
Male, N (%)	334 (73.2)	170 (69.7)	164 (77.4)		142 (69.6)	192 (76.2)	
Female, N (%)	122 (26.8)	74 (30.3)	48 (22.6)	0.064	62 (30.4)	60 (23.8)	0.114
Barthel score							
≤60, N (%)	70 (15.4)	52 (21.3)	18 (8.5)		46 (22.5)	24 (9.5)	
>60, N (%)	386 (84.6)	192 (78.7)	194 (91.5)	<0.001	158 (77.5)	228 (90.5)	<0.001
Prescribed medications							
<10, N (%)	283 (62.1)	125 (51.2)	158 (74.5)		99 (48.5)	184 (73.0)	
≥10, N (%)	173 (37.9)	119 (48.8)	54 (25.5)	<0.001	105 (51.5)	68 (27.0)	<0.001
Length of stay in hospital, days, median (IQR)	14 (9–21)	17 (11–24)	11 (8–18)	<0.001	17 (11–24)	12 (8–19)	<0.001
eGFR (mean ± SD)	69.1±23.7	67.3±24.2	71.1±23.1	0.081	67.1±24.9	70.7±22.6	0.090
CCI (points), median (IQR)	2 (1–3)	2 (1–4)	2 (1–3)	0.008	2 (1–4)	2 (1–3)	0.177
Adverse drug reaction, N (%)	13 (2.8)	8 (3.3)	5 (2.4)	0.771	7 (3.4)	6 (2.4)	0.503
Fall in hospital, N (%)	1 (0.2)	1 (0.4)	0 (0.0)	1.000	0 (0.0)	1 (0.4)	1.000
Death in hospital, N (%)	4 (0.9)	2 (0.8)	2 (0.9)	1.000	1 (0.5)	3 (0.2)	0.632

Abbreviations: CCI, Charlson Comorbidity Index; eGFR, estimated glomerular filtration rate; IQR, interquartile range; PIM, potentially inappropriate medication; SD, standard deviation.

PIM use

According to the Beers 2015 criteria, our study identified 244 of the 456 patients using PIMs. Table 2 shows that 407 medications were detected, resulting in 1.7±0.9 PIMs per patient. The distribution of PIMs in our sample according to the Beers 2015 criteria was as follows: 265 cases were identified in which patients were using medications that should be avoided in older patients; the most frequent PIMs were proton-pump inhibitors (PPIs) (111/265, 41.9%), benzodiazepines (79/265, 29.8%), and benzodiazepine receptor agonist hypnotics (22/265, 8.3%). These three PIMs accounted for 80% of the medications that should be avoided. Additionally, 13 patients were taking medications to be avoided in older adults with certain diseases and syndromes that the drugs can exacerbate and 122 patients were taking drugs to be used with caution, mostly including diuretics (89/122, 73.0%) and dabigatran (25/122, 20.5%). Spironolactone (2/6, 33.3%) and famotidine (4/6, 66.7%) were drugs to be avoided for patients with reduced kidney function. One case of antidepressant use combined with ≥2 central nervous system-active drugs was detected as a drug–drug interaction.

Thirteen ADRs occurred in our participants. Of these, four events were due to PIMs, including digoxin (1), zolpidem (2), and dabigatran (1). Other ADRs were due to aspirin, zoledronate, iodine contrast medium, chemotherapeutics, antibiotics, and angiotensin-converting enzyme inhibitors.

Beers criteria of 2012 versus 2015

A total of 204 patients were identified as using PIMs according to the Beers 2012 criteria. Table 3 shows 18 PIMs detected by the 2012 criteria that were removed from the 2015 criteria. In addition, 111 PIMs were added to the Beers 2015 criteria that were not included in the classification of the 2012 criteria. Notably, these were nearly all PPIs. Benzodiazepines were replaced by PPIs as the most frequent PIMs.

The use of Beers 2015 criteria yielded significantly higher PIM use within our sample than the 2012 criteria (55.3 versus 44.7%, respectively, $P<0.001$), as shown in Table 4. A kappa test showed good accordance among the previous and updated criteria (kappa >0.7, $P<0.001$).

Our findings suggest that the differences between the 2012 and 2015 criteria were due to PPIs, a new list of drugs to be avoided or reduced according to kidney function and PIMs resulting in drug–drug interactions.

Factors associated with PIM use

According to the Beers 2015 criteria, the PIM group exhibited significant differences regarding age ($P<0.001$), a Barthel index of ≤60 ($P<0.001$), 10 or more prescribed medications ($P<0.001$), length of hospital stay ($P<0.001$), and CCI points ($P=0.008$) compared to the non-PIM group.

In the multivariate logistic regression model, based on the Beers 2015 criteria, PIM use was associated with

excessive polypharmacy (≥10 prescribed medications) (OR 1.864, 95% CI 1.210–2.871), a Barthel index of ≤60 (OR 1.935, 95% CI 1.056–3.546), and length of hospital stay (OR 1.066, 95% CI 1.037–1.097), as shown in Table 5.

Table 2 Most commonly encountered PIMs according to the Beers 2015 criteria

Beers 2015 criteria PIMs (N=407)			
Drugs that should be avoided		**n=265**	**%**
Anticholinergics	Chlorpheniramine	3	1.1
	Promethazine	1	0.4
Antispasmodics	Belladonna alkaloids	2	0.8
Cardiovascular	Doxazosin	14	5.3
	Terazosin	14	5.3
	Digoxin	8	3.0
	Amiodarone	4	1.5
Antipsychotics	Olanzapine	4	1.5
Benzodiazepines	Alprazolam (1), estazolam (63), lorazepam (10), clonazepam (4), and diazepam (1)	79	29.8
Benzodiazepine receptor agonist hypnotics	Eszopiclone (4) and zolpidem (18)	22	8.3
Gastrointestinal	Metoclopramide	2	0.8
	Proton-pump inhibitors	111	41.9
NSAIDs	Ibuprofen	1	0.4
Drug–disease or drug–syndrome interaction		**n=13**	**%**
Dementia or cognitive impairment	Estazolam	3	23.1
	Zolpidem	5	38.5
History of falls or fractures	Midazolam	1	7.7
	Diazepam	1	7.7
History of gastric or duodenal ulcers	Ibuprofen	2	15.4
	Lysine acetylsalicylate	1	7.7
Drugs that should be used with caution		**n=122**	**%**
	Aspirin for primary prevention of cardiac events	1	0.8
	Dabigatran	25	20.5
	Diuretics	89	73.0
	Carbamazepine	1	0.8
	Mirtazapine	4	3.3
	Olanzapine	1	0.8
	Carboplatin	1	0.8
Drugs that should be avoided or reduced with impaired kidney function		**n=6**	**%**
	Spironolactone	2	33.3
	Famotidine	4	66.7
Drug–drug interactions that should be avoided		**n=1**	**%**
	Flupentixol/melitracen, paroxetine with zolpidem, and olanzapine	1	100

Abbreviations: NSAIDs, nonsteroidal anti-inflammatory drugs; PIM, potentially inappropriate medications.

Table 3 Medication changes in Beers 2015 criteria since Beers 2012 criteria

Removed		**Number of drugs (N)**
Antiarrhythmic drugs as first-line treatment for atrial fibrillation	Propafenone	4
Chronic constipation	Diltiazem (3), chlorpheniramine (1), diphenhydramine (1), belladonna (2), and hyoscyamine (1)	8
Lower urinary tract	Inhaled anticholinergic drugs	6
Added		**N**
Proton-pump inhibitors	Proton-pump inhibitors	111

Discussion

The present study compared the prevalence of PIMs and their association with related factors between two versions of the Beers criteria in elderly inpatients in China. The major findings were as follows: 1) relatively high PIM prevalence rates were detected, 53.5 and 44.7%, by the Beers 2015 and 2012 criteria, respectively; 2) the prevalence of PIM use identified according to the previous criteria and the updated criteria exhibited significant differences but had good concordance; 3) benzodiazepines were replaced by PPIs as the most frequent PIMs; and 4) according to the Beers 2015 criteria, PIM use was associated with excessive polypharmacy, a Barthel index of ≤60, and the length of the hospital stay.

The prevalence of PIMs in this study was apparently higher than that found in studies conducted in other countries. In a study conducted in a psychiatric hospital in the Netherlands, which was more likely to detect PIMs with psychotropic drugs, a low prevalence of PIMs (47%) was found in elderly patients evaluated by the Beers 2012 criteria.[11] Another noteworthy study was a US retrospective cohort study that included 38,250 inpatients and reported that the prevalence of PIMs evaluated by the Beers 2012 criteria decreased from 37.6% in 2007 to 34.2% in 2012.[14] A cross-sectional analysis that included 567 Belgian patients aged

Table 4 Beers 2015 and 2012 criteria concordance

	Beers 2015 listed		**Total**	***P*-value**
	PIM patients	**Non-PIM patients**		
Beers 2012 listed				
PIM patients	199 (43.6%)	5 (1.1%)	204 (44.7%)	<0.001[a]
Non-PIM patients	45 (9.9%)	207 (45.4%)	252 (55.3%)	<0.001[b] (Kappa =0.782)
Total	244 (53.5%)	212 (46.5%)	456	

Notes: [a]Based on the chi-squared test. [b]Based on kappa test.
Abbreviation: PIM, potentially inappropriate medication.

Table 5 Multivariate analysis of variables independently associated with potentially inappropriate medication use according to the Beers 2015 criteria

Variables	OR	95% CI	*P*-value
Excessive polypharmacy (prescribed medications ≥10)	1.864	(1.210–2.871)	0.005
Barthel index ≤60	1.935	(1.056–3.546)	0.033
Length of stay	1.066	(1.037–1.097)	<0.001

80 years and older reported that PIMs classified as drugs to avoid according to the Beers 2012 were used in 32% of the patients and PIMs labeled to be used with caution were found in 45% of the patients.[15]

The Beers criteria have been very widely used in China. The prevalence of PIMs in this study was comparable to that found in other studies conducted in China. One study that evaluated 1,796 hospitalized Chinese elderly patients reported that 53.2% of patients used at least one PIM according to the 2012 Beers criteria.[16] Another study completed by the same research team evaluated 6,337 hospitalized Chinese elderly patients and reported that the prevalence of PIMs detected by the Beers 2012 criteria was 72.48%.[17]

The possible reasons for the higher prevalence of PIMs in China may be as follows: 1) older Chinese patients are unwilling to try nondrug methods of therapy, such as exercise and psychological approaches; 2) physicians in China, even geriatricians, lack necessary knowledge of polypharmacy and PIMs in elderly adults; and 3) a lack of intervention by clinical pharmacists based on efficient screening tools.[14,18]

The 2015 revision of Beers criteria aimed to provide a comprehensive systematic review and grading of evidence regarding drug-related problems and ADRs in older adults. Notable changes included drug–drug interactions and medications that require dose reduction or avoidance with renal impairment.[11] In our study, spironolactone and famotidine were to be used with caution or avoided in patients with reduced kidney function. Patients with a creatinine clearance of <30 mL/min are recommended to avoid using spironolactone, which may increase potassium levels. Spironolactone is a potassium-sparing diuretic that increases serum potassium levels, as it blocks the potassium secreting effect of aldosterone in the distal tubulus. Spironolactone is widely used in China, and hyperkalemia is a severe and even fatal consequence.[19] A standard dose of spironolactone poses a great risk to patients with renal insufficiency.[20]

Consistent with most studies, the most common PIMs identified by the 2012 criteria were benzodiazepines. According to the Beers 2015 criteria, the most frequently prescribed PIMs were PPIs. The use of PPIs for >2 months is not recommended except in specific circumstances when long-term acid suppression therapy is indicated. This was a new addition to the Beers criteria, and 111 related cases were detected in our study. PPIs are generally well tolerated with short-term treatment, but prolonged exposure to PPIs can cause *Clostridium difficile*-associated diarrhea[21] and has also been associated with falls and fractures.[22] Additional concerning risks of PPIs treatment in the elderly, although not as well supported through clinical evidence, include chronic kidney disease, acute interstitial nephritis, vitamin B12 deficiency, rhabdomyolysis, anemia, thrombocytopenia, and hypomagnesemia.[23,24] Our study analyzed medications during hospitalization, which was often <2 months. PIM use of PPIs was defined as using PPIs in the hospital and recommendations to continue use after discharge from the hospital without specific indications. This may be a possible reason for the high prevalence of PIM use of PPIs. The high prevalence of PPIs' use in the elderly must be considered. Clinicians should value opportunities to reduce doses or deprescribe PPIs for long-term care, particularly among those with risk factors for unnecessary medication use.

This study revealed that the most common PIMs were benzodiazepines, according to the Beers 2012 criteria, which ranked only second to PPIs' use according to the Beers 2015 criteria. This is consistent with other studies of hospitalized older patients.[17,25] A potential reason for the high prevalence of benzodiazepine use is that with aging, a greater number of older adults are troubled with insomnia and depression. To solve this problem, psychoactive drugs are more frequently prescribed to older adults by physicians, thereby causing PIM use. Benzodiazepines and benzodiazepine receptor agonists are known to increase the risk of falls and hip fractures, especially in individuals with a prior history of falls. Nonpharmacological options are recommended to treat insomnia initially, including sleep hygiene combined with behavioral interventions.[26] Even if nonpharmacological therapy is difficult to perform in hospitalized patients, avoiding long-term use of benzodiazepines and conducting rehabilitation of sleep in community health institutions should be applied. Recently, some authors have focused on reducing benzodiazepine prescriptions. Direct-to-consumer education by physicians or pharmacists has been confirmed as being more effective than usual care for reducing the overuse of benzodiazepines.[27]

A significant factor associated with PIMs was the regular prescription of ≥10 medications, even after adjusting for confounding variables. A strong association between polypharmacy and PIMs has been reported in many studies. However, no consensus exists on the minimum number of regular medications

that need to be prescribed to be considered polypharmacy. The majority of studies have used ≥5 prescribed drugs as the threshold for polypharmacy, and ≥10 drugs are considered excessive polypharmacy.[28] Increasing the number of combinations of medications increases the risk of inappropriate prescriptions and ADRs.[29] A systematic review[30] using the Beers criteria as an instrument to assess the appropriateness of prescriptions indicated that approximately one in five prescriptions for elderly persons in primary care is inappropriate.

Deprescribing is a complex process that is required for the safe and effective cessation of inappropriate medications.[31] Systematic reviews of medication withdrawal trials (deprescribing) show that reducing specific classes of medicines, especially psychotropic and anticholinergic drugs, may decrease adverse events and improve the quality of life.[32] Shared decision-making should be an integral part of the deprescribing process.[33]

The present study demonstrates that a Barthel index of ≤60, rather than age, increased the odds of receiving a potentially inappropriate prescription. The Barthel index is the most widely used scale to evaluate activities of daily living and is scored from 0 to 100 points; scores <60 points indicate moderate-to-severe physical impairment.[34] Older disabled adults, who often have complex comorbidities that require the prescription of multiple medications, may be highly susceptible to PIM use. Yang PJ et al[35] revealed a high frequency of PIMs (94/141, 66.7%) detected by the Beers 2012 criteria in disabled (Barthel index ≤60) older patients, which was higher than the prevalence rates reported in previous studies. Benzodiazepines and hypnotics were the most commonly prescribed PIMs in disabled older patients.

Several limitations should be noted in the present study. First, it was a retrospective, single-center study. Second, only hospitalized patients were included and they were not representative of older, community-dwelling patients. Finally, the consequences of PIMs were not analyzed.

Conclusion

Our study described a high prevalence of polypharmacy and PIMs in hospitalized older patients. PIMs defined by the Beers 2015 criteria were shown to be associated with excessive polypharmacy, a Barthel index of ≤60, and length of the hospital stay. The Beers 2015 criteria detected significantly more PIMs than the 2012 criteria due to the inclusion of PPIs. The updated Beers criteria provide a valuable tool to guide prescription in older adults.

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Disclosure

The authors report no conflicts of interest in this work.

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