ORIGINAL ARTICLE

Exploring Potentially Inappropriate Medications for Elderly Thai Patients in an Outpatient Setting at a Tertiary Care Hospital: an Analysis Based on the 2023 American Geriatrics Society Beers Criteria

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Objective: Potentially Inappropriate Medications (PIMs) in older patients are prevalent and possess the potential for modification. It is linked to several detrimental health outcomes. The extent of research pertaining to PIMs in Thailand remains restricted. The primary aim of the present study was to determine the prevalence of PIMs, employing the Beers criteria from 2023. The secondary objective focused on the identification of factors correlated with PIMs within this population.

Materials and Methods: A retrospective electronic medical record of older patients at outpatient clinics of Srinagarind Hospital during November 2021 and November 2022 was reviewed. Patient demographic data were collected and analyzed. The Beers criteria (version 2023) were employed for identifying PIMs. Logistic regression analysis was used to determine contributing to the occurrence of PIMs.

Results: Of the 23,758 patients enrolled, 49.03% were found to have at least one PIM. The factors that exhibited associations were age (odds ratio [OR] 1.01), polypharmacy (≥5 medications) (OR 6.29), dementia (OR 1.84), osteoarthritis (OR 1.40), chronic kidney disease (OR 1.29), hypertension (OR 1.15), dyslipidemia (OR 0.87), diabetes mellitus (OR 0.84), gastritis/gastrointestinal reflux disease/peptic ulcer disease (OR 0.59), and peripheral vascular disease (OR 0.29).

Conclusion: The present study highlights the high prevalence of PIMs among elderly outpatients. Factors associated with PIMs were identified, it is possible to develop and implement targeted strategies aimed at reducing the use of PIMs in order to mitigate the negative clinical consequences associated with PIMs in these populations.

Keywords: Beers criteria; Older adults; Elderly; Outpatient; Potential inappropriate

Older individuals tend to be prescribed a greater number of medications in comparison to their younger counterparts owing to the fact that they frequently experience the presence of at least one persistent ailment, namely hypertension, diabetes, or cardiovascular disease. The physiological alterations that occur with age, specifically in relation to pharmacokinetics and pharmacodynamics, can potentially lead to unfavorable responses in the elderly population as a result of their utilization of medication[1,2]. Potentially inappropriate medications (PIMs) refer to medications which should be avoided or used cautiously in the elderly population due to the increased probability of adverse reactions and/or the lack of empirical evidence regarding their advantages when safer and equally or more effective therapeutic alternatives are accessible[3]. Adverse clinical consequences are associated with PIMs, leading to a subsequent rise in morbidity, mortality, extended hospital stays, admission rates, and healthcare expenditure, especially among high-risk populations. For instance, elderly individuals with diabetes and chronic kidney disease[4].

Identifying PIMs among the prescriptions provided to elderly patients holds significant

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importance. A variety of assessment instruments have been developed and made accessible, including the Beers criteria, the Screening Tool of Older Persons' Potentially Inappropriate Prescriptions (STOPP), the European List of Potential Inappropriate Medications (EU [7]–PIM) list, and the Potentially Inappropriate Medications In The Elderly (PRISCUS) list, serving the purpose of identifying PIMs[5,6]. The prevalence of PIMs in older adults has been reported varies from 25% to 95%, depending on identification tools and study settings[7-9]. At a tertiary care hospital in Thailand, the prevalence of PIMs ascertained through the Beers criteria and STOPP was determined to be 19.2% and 31.5%, respectively[10]. In India, the prevalence of PIMs usage, as defined by the Beers criteria for the years 2015 and 2019, was found to be 60.1% and 61.9% correspondingly[11]. In primary care in Thailand, the prescription of PIMs was significantly influenced by the presence of chronic diseases, individuals aged 75 years and older, and the co-occurrence of polypharmacy[12]. In Chinese, female, advanced age, and polypharmacy were positively associated with PIMs use in older adults[13]. Among the PIMs identified, benzodiazepines, antipsychotics[14], first-generation antihistamines, and sulfonylurea[15] were found to be the most frequently prescribed medications.

In Thailand, the amount of research on PIMs remains limited. Prior studies on PIMs were conducted at the same study site in 2013 and were based on the Beers criteria version from 2003[10]. However, it is important to note that these criteria were last updated in 2023[16]. Furthermore, there has been an increase in the prevalence of PIMs among older Chinese adults over time, with a rise from 71% in 2016 to 73.4% in 2018[13]. This trend highlights the continued significance of PIMs in the prescription of medications for the elderly, necessitating efforts to prevent such occurrences for the sake of safety. Consequently, the primary objective of the present study was to determine the prevalence of PIMs by utilizing the Beers criteria for 2023. The secondary objective aimed to identify factors associated with PIMs in this particular population.

Materials and Methods

The present study was a part of a retrospective analysis, specifically a subsidiary exploration within the project titled "Prevalence and factors linked to drug-drug interactions among elderly patients at Srinagarind Hospital". It was carried out at Srinagarind Hospital, situated in Khon Kaen, which serves as both a tertiary

care and university hospital within the northeastern region of Thailand. Further details of the study design have been described elsewhere[17]. Briefly, the study gathered all prescriptions for individuals from the outpatient clinics from November 2021 to November 2022. Individuals aged 65 years or older who were consuming at least one medication were included in this examination. Topical medications, including inhalers, creams, ointments, patches, and sprays, were excluded from this analysis. Patient data were obtained from the hospital information system with the utmost caution taken to ensure patient anonymity and data confidentiality. The investigation (reference number HE661074) obtained authorization from the Institutional Review Board of Khon Kaen University, with a waiver for individual consent for this observational evaluation.

The study acquired information from electronic medical records, which covered patient demographics including age, gender, number of prescribed medications, main diagnosis, and comorbidities.

Definition of PIMs in older adults

The identification of PIMs in the present study was conducted using the American Geriatrics Society (AGS) Beers criteria 2023. The Beers criteria are explicit and are composed of five general categories. These categories encompass medications that are considered potentially inappropriate, medications that may be inappropriate for patients with specific diseases or syndromes, medications that require caution when used, drug-drug interactions that are potentially inappropriate, and medications that necessitate dosage adjustment based on renal function[16].

Statistical analysis

Descriptive statistics were used in order to depict the attributes of the study sample. Mean values with a standard deviation (SD) were utilized to express continuous variables such as age while categorical variables including gender, and the presence of polypharmacy (it is defined as the utilization of five or more medications)[12], and disease were presented as the count of participants accompanied by a percentage. The factors that were associated with PIMs were evaluated through both univariate and multivariate regression analysis. The outcomes were subsequently demonstrated by presenting the crude odds ratios (OR) for univariate analysis and adjusted OR for multivariate analysis, along with a respective 95% confidence interval (CI). Factors with a p-value of less than 0.2 or those that were discovered to possess

clinical significance in previous reports were included in a multivariate model. Then, a p-value of less than 0.5 deemed to indicate statistically significant differences. The imputation method was used to deal with missing data. All statistical analyses were carried out using STATA version 10.0 (StataCorp, College Station, Texas).

Results

There were a total of 23,758 elderly individuals who participated in this study, in which potentially inappropriate medications (PIMs) were detected in 11,648 out of the 23,758 participants, amounting to 49.03%. Table 1 demonstrated demographic information of the studied sample. The mean age was 73.2 years, with a higher representation of the female gender. The average numbers of prescribed medications were 4.6. Polypharmacy was found nearly 40% of the participants. The three most prevalent diseases were hypertension, dyslipidemia, and diabetes.

Potentially Inappropriate Medications among geriatric outpatients using the 2023 American Geriatrics Society Beers Criteria

Table 2 reveals a compilation of commonly encountered medications that are deemed potentially inappropriate. The medications with the highest

prevalence included benzodiazepines at 13.99%, ASA for primary prevention of cardiovascular disease at 10.75%, the long-term usage of proton-pump inhibitors in patients who were not considered high risk, accounting for 6.67%, antidepressant with strong anticholinergic activity at 6.38% of cases, and first-generation antihistamine at 4.87%. Table 3 illustrates common medications that were

Table 2. Common medications considered as potentially inappropriate

Organ system, Therapeutic category, Drug(s)	Recommendation	n (%)
Benzodiazepine: alprazolam, clobazam, clonazepam, clorazepate, diazepam, lorazepam	Avoid	3,323 (13.99)
Aspirin for primary prevention of cardiovascular disease	Avoid initiating aspirin for primary prevention of cardiovascular disease.	2,554 (10.75)
Proton-pump inhibitors: dexlansoprazole, esomeprazole, lansoprazole, omeprazole, pantoprazole, rabeprazole	Avoids scheduled use for >8 weeks unless of high-risk patients (e.g. oral corticosteroids or chronic NSAID use), erosive esophagitis, Barrett's esophagitis, pathologic hypersecretory condition, or demonstrated need for maintenance treatment	1,607 (6.67)
Antidepressant with strong anticholinergic activity, alone or in combination: amitriptyline, imipramine, nortriptyline, paroxetine	Avoid	1,515 (6.38)
First-generation antihistamine: chlorpheniramine, cyproheptadine, dimenhydrinate, Hydroxyzine	Avoid	1,156 (4.87)

Sulfonylurea group included patients who received sulfonylureas as first- or second-line monotherapy, not include add-on therapy due to the limitation of study design

Table 1. Demographic information of the participants

Demographic variables	n=23,758
Age (years); mean (SD)	73.2 (6.6)
Male, n (%)	10,480 (44.1)
Numbers of medication, mean (SD)	4.6 (3.8)
Polypharmacy, n (%)	9,129 (38.4)
Diagnosis, n (%)	
- Hypertension	7,138 (30.0)
- Dyslipidemia	5,645 (23.8)
- Diabetes mellitus	5,191 (21.8)
- Chronic kidney disease	2,399 (10.1)
- Cerebrovascular disease	1,346 (5.7)
- CAD/ heart failure	1,509 (6.4)
- PVD	182 (0.8)
- Osteoporosis	1,670 (7.0)
- Osteoarthritis	2,409 (10.1)
- Dementia	973 (4.1)
- Hepatitis/cirrhosis	826 (3.5)
- Gastritis/GERD/PUD	1,799(7.6)

SD=standard deviation; n=total number of populations; CAD=coronary artery disease; PVD=peripheral vascular disease; GERD=gastroesophageal reflux disease; PUD=peptic ulcer disease

Table 3. Common medications potentially inappropriate in patients with certain diseases or syndrome

Disease or syndrome	Drug(s)	n (%)
Dementia or cognitive impairment	- Antipsychotics: chlorpromazine, haloperidol, perphenazine, aripiprazole, clozapine, lurasidone, olanzapine, paliperidone, quetiapine, risperidone.	376 (1.58)
	- Benzodiazepines	228 (0.96)
	- Anticholinergics: antidepressants, antihistamines, antimuscarinics, antiparkinsonian agents, antipsychotics, antispasmodics, skeletal muscle relaxants	116 (0.49)
History of fall or fracture	- Anticholinergics	113 (0.43)
	- Antidepressants: SNRIs, SSRIs, tricyclic antidepressants	50 (0.21)

SNRI=duloxetine, desvenlafaxine, and venlafaxine; SSRI= escitalopram, paroxetine fluoxetine, and sertraline

potentially inappropriate for patients with specific diseases or syndromes. These medications encompass antipsychotics, benzodiazepines, and anticholinergics for patients with dementia or cognitive impairment, as well as anticholinergics and antidepressants for patients who have a history of falls or fractures. Moving forward, Table 4 provides a comprehensive list of medications that should be administered with caution. Amongst these, mirtazapine and SNRIs are the most prevalently prescribed antidepressants. Lastly, Table 5 and Table 6 present commonly prescribed medications that may result in potentially inappropriate drug-drug interactions and medications whose dosages should be adjusted based on renal function, respectively.

Factors associated with potentially inappropriate medications

Factors associated with potentially inappropriate medications in the present study were identified

Table 4. Common medication to be used with caution

Drugs	n (%)
Antidepressants: mirtazapine, SNRIs, SSRIs, TCAs	1,480 (6.32)
Tramadol	1,302 (5.48)
Diuretics	1,115 (4.69)
Antipsychotics	739 (3.11)
SGLT2 inhibitors: canagliflozin, dapagliflozin, empagliflozin	603 (2.54)

SNRI=duloxetine, desvenlafaxine, and venlafaxine; SSRI=escitalopram, paroxetine fluoxetine, and sertraline; TCAs=tricyclic antidepressants, SGLT2=sodium-glucose co-transporter-2

Table 5. Commonly prescribed potentially inappropriate drug-drug interactions

Object drug or class	Interaction drug or class	n (%)
Antiepileptics (including gabapentinoids)	Any combination >3 of these CNS-active drugs	1,776 (7.48)
Antidepressants (TCAs, SSRIs, and SNRIs)		
Antipsychotics		
Benzodiazepines		
Nonbenzodiazepine (i.e., Z-drugs)		
Opioids		
Skeletal muscle relaxants		
Anticholinergics	Anticholinergics	841(3.54)
Opioid	Benzodiazepine	597(2.51)

CNS=central nervous system; SNRI=duloxetine, desvenlafaxine, and venlafaxine; SSRI=escitalopram, paroxetine fluoxetine, and sertraline; TCAs=tricyclic antidepressants; SGLT2=sodium-glucose co-transporter-2

using univariate and multivariate analysis, as shown in Table 7. The univariate analysis revealed that all variables, except for gender, cerebrovascular disease, and osteoporosis were significant factors (with a p-value of less than 0.2). Following the assessment for multicollinearity, factors with a p-value of less than 0.2 were included in the multivariate analysis model. The subsequent factors exhibited an association with the presence of potentially inappropriate medications (with a p-value of less than 0.05); these factors encompassed age, the presence of polypharmacy, underlying conditions of dementia, osteoarthritis, chronic kidney disease, hypertension, dyslipidemia, diabetes mellitus, gastritis/GERD/peptic ulcer disease, and peripheral vascular disease.

Discussion

Applying the 2023 American Geriatrics Society Beers Criteria[16], the current study revealed a prevalence of 49.03% for at least one PIM which was comparable to the previous reports which found ranging from 48.6% and 63.6% such as, it was 49.3% in Jordan[17], 55.0% in Indonesia[18], and 57.2 to 63.6% in Saudi Arabia[19]. In comparison to the prevalence of PIMs in the same setting in 2010 using the Beers criteria 2003, the prevalence of PIMs was 19.2%[11]. However, the previous investigation solely examined the prevalence of PIMs within the internal medicine department, where the physicians exhibited a propensity for prescribing medications more frequently than other departments[10]. Another study conducted in Ireland demonstrated that the prevalence of PIMs escalated from 39.7% to 45.6% over a five-year monitoring period[20]. It appears that PIMs continue to pose a substantial healthcare concern for older individuals.

In our research, the most commonly used PIMs were basically consistent to the prior reports which were benzodiazepines, aspirin for primary prevention

Table 6. Common medication whose dosages should be adjusted based on renal functions

Drug	CrCl (mL/min) at which action is required	n (%)
Gabapentin	<60	137 (0.58)
Colchicine	<30	119 (0.50)
Ciprofloxacin	<30	81 (0.34)
Tramadol	<30	80 (0.3)
NSAIDs, COX-2 inhibitors	<30	32 (0.13)

CrCl=creatinine clearance; NSAIDs=nonsteroidal anti-inflammatory drugs; COX-2=cyclooxygenase-2

Table 7. Factors associated with potentially inappropriate medications

Factors	Univariate			Multivariate		
	Crude OR	95%CI	p-value	Adjusted OR	95% CI	p-value
Age (years)	1.02	(1.01 to 1.02)	<0.05	1.01	(1.001 to 1.01)	<0.05
Male	1.01	(0.96 to 1.06)	0.84	-		
Polypharmacy	6.15	(5.80 to 6.52)	<0.05	6.29	(5.90 to 6.72)	<0.05
Principal diagnosis						
- Dementia	2.19	(1.91 to 2.51)	<0.05	1.84	(1.58 to 2.14)	<0.05
- Osteoarthritis	1.35	(1.24 to 1.47)	<0.05	1.40	(1.22 to 1.47)	<0.05
- CAD/ heart failure	2.25	(2.01 to 2.52)	<0.05	1.39	(1.23 to 1.58)	0.06
- Chronic kidney disease	1.94	(1.78 to 2.12)	<0.05	1.29	(1.17 to 1.43)	<0.05
- Hypertension	1.56	(1.48 to 1.65)	<0.05	1.15	(1.08 to 1.24)	<0.05
- Hepatitis/cirrhosis	1.12	(0.97 to 1.28)	0.12	1.00	(0.86 to1.17)	0.99
- Dyslipidemia	1.24	(1.17 to 1.31)	<0.05	0.87	(0.80 to 0.93)	<0.05
- Diabetes mellitus	1.62	(1.53 to 1.73)	<0.05	0.84	(0.78 to 0.91)	<0.05
- Gastritis/GERD/PUD	0.88	(0.80 to 0.97)	<0.05	0.59	(0.53 to 0.66)	<0.05
- PVD	0.50	(0.36 to 0.68)	<0.05	0.29	(0.21 to 0.41)	<0.05
- Cerebrovascular disease	1.07	(0.95 to 1.19)	0.26	-		
- Osteoporosis	0.95	(0.86 to 1.04)	0.27	-		

OR=odds ratio; CI=confidence interval; CAD=coronary artery disease; PVD=peripheral vascular disease; GERD=gastroesophageal reflux disease; PUD=peptic ulcer disease

for cardiovascular disease, and proton inhibitors use for a period longer than 8 weeks in patients with low risk of bleeding[3,5,21]. Antipsychotics, benzodiazepines, and anticholinergics were the most common prescription in syndrome associated with PIMs in our finding, aligning well with a study conducted in Korea[22]. Furthermore, our study identified antidepressants, tramadol, and diuretics as medications that should be prescribed with caution. This finding was comparable to studies carried out in Qatar and Saudi Arabia, where diuretics were the most frequently prescribed medications[23,24]. The most common drug-drug interactions were observed between CNS-active drugs and anticholinergics. This finding aligned with a previous study conducted at our research site, which highlighted CNS-active drugs as a prevalent source of drug-drug interactions[25]. Anticholinergics are widely prescribed for various clinical conditions in older adults. Interestingly, most medications commonly prescribed to older individuals are not routinely acknowledged as having anticholinergic properties and can be readily obtained without a prescription. Examples of such medications include first-generation antihistamines, tricyclic antidepressants, antiparkinsonian agents, antispasmodics, and skeletal muscle relaxants[26]. The medication whose dosages should be adjusted based on renal functions found minimal (<1%) in our findings where the underrecognition of gabapentin

toxicity in patients with CrCl less than 60 ml/min was the most commonly identified, in agreement with the situation in Jordan[26]. It implied that a significant number of physicians were greatly concerned about this matter.

Our results revealed that age, presence of polypharmacy, and underlying diseases of dementia, osteoarthritis, chronic kidney disease and hypertension were significant factors associated with PIMs whereas dyslipidemia, diabetes mellitus, gastritis/ GERD/PUD, and peripheral vascular disease and were protective factors. A systematic review reported that the risk for receiving PIMs increased with advancing age[27]. The possible explanations are likely due to multiple factors including the vulnerability of this population to experiencing polypharmacy, changes in both pharmacokinetics and pharmacodynamics, as well as the frequent presence of multiple comorbidities that subsequently increase the chances of encountering PIMs[28]. Polypharmacy served as another contributing factor that supported the previous research findings[29,30]. Since the use of multiple medications is linked to the increase of the complexity of medication regimens, risk of adverse drug reactions, inadequate monitoring of drug efficacy or possible side effects, and risk of drug-drug interactions[31,32]. The presence of dementia, osteoarthritis, chronic kidney disease or hypertension has been found to be associated with an increased

likelihood of PIMs in this study. These results were not unexpected, as older patients with these conditions often experience polypharmacy, complicated treatment regimens, and multiple comorbidities[33]. Specifically, individuals with dementia, particularly those with behavioral and psychological symptoms of dementia (BPSD), tended to be prescribed medications that could adversely affect their cognitive function, including benzodiazepines, anticholinergics, and antipsychotics. Despite the recommendation of non-pharmacological interventions, the implementation of these interventions is often insufficient[22,34,35]. In contrast, the current study found that the presence of dyslipidemia, diabetes mellitus, gastritis/GERD/PUD, and peripheral vascular disease were protective factors, which differed from the preceding studies[36,37]. The potential reasons for this could be the limitation of the study design. For example, the identification of PIMs using the criteria for sulfonylurea in this particular study solely encompassed patients who received it as a monotherapy. Furthermore, there are available Thai national guidelines specifically intended for the geriatric population, which possibly mitigate the risk of PIMs[38].

According to our research findings, the global findings were comparable to previous reports, thus revealing a substantial occurrence of PIMs worldwide. However, it should be noted that there were variations in the contexts and definition of PIMs. Despite the development of multiple guidelines such as Beers criteria, Screening Tool of Older Persons' Prescriptions (STOPP), and Screening Tool to Alert to Right Treatment (START)[16,32,33,39], it is evident that there is a lack of comprehension among physicians regarding the principles of prescribing medications for geriatric patients. An example of this can be seen in the case of benzodiazepines, which possess extensive data highlighting their unfavorable long-term consequences including dependence, withdrawal symptoms, cognitive impairment, and falls[40], and the use of aspirin for this indication is not routinely recommended in many guidelines[41,42]. However, certain medications, classified as PIMs in Beers 2023, continue to be suggested as first-line drugs in Thailand, such as tricyclic antidepressants for patients suffering from neuralgia. Additionally, pharmacists can play a major role in improving the appropriateness of medications use. Healthcare professionals should expand in order to take the necessary precautions when managing older adult conditions to avoid PIMs and adverse events. The prescription of PIMs may not always be unsuitable, if PIMs prescription is unavoidable, physicians and pharmacists should closely monitor patients for drug-related problems and deprescribe PIMs when they are no longer indicated[12]. Furthermore, it is of utmost importance that specialists from various disciplines collaborate in order to incorporate updated evidence with healthcare policy makers, thereby formulating a national guideline that can be effectively implemented in clinical practice especially for at-risk conditions including atherosclerotic disorders, dementia, and osteoarthritis.

The present study has some limitations. Firstly, it was a retrospective study, and the analysis was predicated upon data recorded via electronic medical records, potentially leading to an underestimation of PIMs. Secondly, non-prescription medications from other sources were not considered within the dataset. Lastly, certain criteria from the Beers criteria (2023) may not have been fully incorporated into this analysis owing to the study's design limitations, such as the utilization of sulfonylureas as an adjunctive therapy in patients with other variables which were unable to be included in the present study.

Conclusion

Inappropriate medications were found half among geriatric outpatients of tertiary care hospital, Thailand. This finding heightens awareness among healthcare professionals. Factors associated with PIMs were identified, it is possible to develop and implement targeted strategies aimed at reducing inappropriate medication and preventing negative clinical outcomes.

What is already known on the topic?

The presence of Potentially Inappropriate Medications (PIMs) is widespread among older patients and is associated with several negative health consequences. Currently, there is a scarcity of up-to-date information on the prevalence of PIMs within the outpatient department of a tertiary care facility, where patients tend to have more complicated medical conditions.

What this study adds?

The prevalence of potentially inappropriate medications (PIMs) among elderly individuals attending the outpatient clinic of a tertiary care hospital was approximately 50%. Among these medications, benzodiazepine was the most commonly prescribed and was considered to be potentially inappropriate. Dementia or cognitive impairment was found to be the most frequent syndrome associated with the use of

PIMs. The occurrence of PIMs was found to be related to factors such as advancing age, polypharmacy, and specific medical conditions.

Conflicts of interest

The authors declare no conflicts of interest.

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