

# Potentially Inappropriate Medication Prescribing in Elderly Hypertensive Patients in the Primary Care Unit

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**Background:** Pharmacotherapy is necessary in the treatment of chronic diseases. However, potential inappropriate medication (PIM) prescriptions are associated with adverse events, especially in the elderly.

**Objective:** To quantify the prevalence and classify the type of PIM prescribing in elderly patients with hypertension, in a primary care unit (PCU) of a tertiary hospital, as well as to study factors associated with PIM prescription.

**Materials and Methods:** A retrospective medical record review was conducted in elderly patients followed up for treatment of hypertension at the PCU, between January 1 and December 31, 2018. Beers criteria were used to identify PIM. Factors associated with PIM prescription were analyzed using generalized estimating equation (GEE) modeling analysis.

**Results:** Nine hundred sixty-six subjects were included in the present study with 61.4% female and a median age (Q1, Q3) of 72.5 (68.5, 78.0) years. The prevalence of PIM was 66.9%. Most common PIM were diuretics (28.9%), aspirin (10.2%), and benzodiazepines (9.1%). The associated factors of PIM prescription were being female, visiting the PCU with an acute illness only, and the number of drugs prescribed [adjusted OR (95% CI): 1.60 (1.24 to 2.06), 2.32 (1.45 to 3.70), and 1.73 (1.61 to 1.86), respectively].

**Conclusion:** The prevalence of PIM prescription among elderly hypertensive patients was high, especially female patients, patients with a high number of medications prescribed, and patients visiting the OPD with acute illnesses. Appropriate medication prescribing can reduce preventable adverse drug events from PIM prescription. Using explicit criteria for prescription is one such useful method.

**Keywords:** Inappropriate medications prescription; Hypertension; Elderly; Primary care unit

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The number of elderly people in the world is continuously growing, including those in Thailand. The report shows 56.0% of elder, Thai adults have at least two underlying diseases, with the most common chronic diseases diagnosed being hypertension, diabetes mellitus, and dyslipidemia<sup>(1)</sup>. The treatments of these chronic diseases consist of lifestyle modifications and medications. All medications have associated risks. A medication is considered a potentially inappropriate medication (PIM) when the potential harm is greater than

the potential benefit among a particular group<sup>(2)</sup>. Many studies have documented that PIM is one of the major medication-related problems causing adverse drug events (ADEs) such as, increased risk of falls, hip fractures, emergency department visits, hospitalization, and mortality in older adults<sup>(2-4)</sup>. Half of the medications that can cause ADEs, could be prevented by physicians<sup>(4)</sup>. Nowadays, multiple explicit criteria, such as Beers criteria<sup>(5)</sup>, STOPP/START criteria<sup>(6)</sup>, and the Thai criteria for high-risk medication use<sup>(7)</sup> can help physicians avoid prescribing PIMs to elderly patients. Beers criteria is one of the popular tools in assessing PIM, which is regularly updated, following the new evidence. The Beer criteria, 2015 version<sup>(5)</sup>, divided PIM into five groups. They are medications to avoid for many or most older adults, medications for older adults with specific diseases or syndromes to avoid, medications to be used with caution, drug-drug interactions, and medications to avoid or dosages that should be adjusted based on kidney function.

From the Thai people's health survey in 2014<sup>(8)</sup>, hypertension is the most common chronic disease in

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elderly adults and more than half of them (53.2%) were diagnosed with hypertension. Changes in vessel capacity, caused by aging<sup>(9)</sup>, requires the elderly to take more anti-hypertensive medications for the control of blood pressure (BP) when compared with the adult group. Some of them are included in the PIM checklist<sup>(5,6)</sup>, such as diuretics. Furthermore, many common medications used in elderly hypertensive patients are also potentially inappropriate prescriptions, such as non-steroidal anti-inflammatory drugs (NSAIDs), which may increase the risk of exacerbation of hypertension<sup>(5,6)</sup>.

Some studies in Thailand explored the prevalence and associated factors of PIM prescription in an elderly group of patients. However, the results were varied<sup>(10-12)</sup>. On the other hand, few studies have been conducted in elderly patients with chronic disease, especially hypertension<sup>(3,13-15)</sup>. Hence the present study aimed to quantify the prevalence and associated factors of PIM prescription in elderly patients with hypertension, in a primary care unit (PCU) of a tertiary care hospital in Southern Thailand.

## Materials and Methods

### Study design

A retrospective medical record review was conducted in the PCU of Songklanagarind Hospital, which is a tertiary care and medical school, with residency training, and a referral center in the South of Thailand.

### Study sample and sampling

The authors included patients aged 65 years and older, diagnosed with essential hypertension, confirmed by their physicians before September 30, 2018, having had at least three months of consecutive visits to the PCU of Songklanagarind Hospital, and having had at least one drug prescribed. The authors excluded patients receiving drugs that should be avoided, or dosage adjustment based on kidney function, but did not have kidney function test within the past year. The sample size was calculated based on both objectives of the present study. For the first objective, the authors used the infinite population proportion formula that considered the prevalence of PIM to be 40.4%<sup>(10)</sup>, 95% confidence interval, and a precision error of 5%, which was  $n = (Z^2sd^2)/d^2 = 370$ . For the second objective, to find the factors associated with PIM prescription, the authors used G\*power (version 3.1.9.4) that considered an odds ratio 1.87 for polypharmacy<sup>(11)</sup>, with alpha error probability 0.05, power 80%, and adjusted effect of other variables

20%. The result was 546 patients. The present study enrolled all patients who were compatible with the eligibility criteria.

### Variables

The primary outcome was PIM prescription assessed by criteria, which was developed from the Beers criteria 2015<sup>(5)</sup>. Independent variables included characteristics of the patients, which the previous studies found to be associated with PIM prescription<sup>(10-14,16-18)</sup>.

### Data collection

All prescriptions were reviewed by the researcher from the hospital information system of Songklanagarind Hospital. Patients who received at least one PIM in the study year were documented as a PIM prescription. The details of PIM for each prescription were listed, including types, names, and the number of PIM.

### Data management and analysis

Data were entered in EpiData (version 3.1, Denmark), with double entry basis and analyzed using the R program (R Core Team 2021, Vienna, Austria). Descriptive statistics were used to analyze the baseline characteristics, and characteristic of PIM prescription. Categorical data were presented in terms of percentage, and the continuous data were presented in median (Q1, Q3). Generalized estimating equation (GEE) was used for multivariable-adjusted analysis of the associated factors of PIM prescribing, with model variables in the final model obtained from Akaike information criterion (AIC) values in a backward stepwise algorithm. Statistical significance was considered as p-value less than 0.05.

### Ethics statement

The present study protocol was approved by the Office of Human Research Ethics Committee (HREC), Prince of Songkla University (REC 62-006-9-4). Informed consent forms were not required, due to the retrospective medical record review study design.

### Results

There were 966 elderly hypertensive patients continuously visiting the PCU during the present study period, baseline characteristics of these are summarized in Table 1. More than half of them were female, and the median age was 72.5 years. The number of underlying diseases ranged from 1

**Table 1.** Characteristics of the participants (n=966)

Characteristic	
Sex; n (%)	
Female	593 (61.4)
Male	373 (38.6)
Age (year); median (Q1, Q3)	72.5 (68.5, 78.0)
Number of underlying diseases; median (Q1, Q3)	3.0 (2.0, 4.0)
Number of visits; median (Q1, Q3)	4.0 (3.0, 5.0)
Types of comorbidities; n (%)	
Dyslipidemia	863 (89.3)
Diabetes mellitus	350 (36.2)
Gout	139 (14.4)
Osteoarthritis	113 (11.7)
Chronic kidney disease	87 (9.0)

**Table 2.** Number of PIM prescript per each prescription (n=3,999)

Number of PIMs	n (%)
1	1,243 (58.1)
2	587 (27.4)
3	218 (10.2)
4	68 (3.2)
5	20 (0.9)
6	1 (0.1)
7	2 (0.1)

PIMs=potentially inappropriate medications

to 8, with the most common comorbidities being dyslipidemia (89.3%).

There were 3,999 prescriptions from 966 patients, with an average of  $4.4 \pm 2.3$  medications per prescription, with a maximum of 16 medications for two prescriptions. More than half of the patients (66.9%) and prescriptions (53.5%) were found as having had at least one PIM prescribed. For prescriptions that had at least one PIM, the number of PIM per prescription is shown in Table 2. More than half of them received one PIM, with more than a quarter of them receiving two PIMs and 0.1% of them receiving seven PIMs, simultaneously. The present study found 3,421 PIMs, types and names of PIM prescription are shown in Table 3. Common types of PIM were drugs that should be used with caution (38.9%), and drugs to be avoided independent of condition (37%). The most common prescribed PIM were diuretics (28.9%), aspirin (10.2%), and benzodiazepines (9.1%).

Table 4 shows the multivariable analysis, with GEE analysis between PIM prescription and associated factors. The authors found that female

**Table 3.** Types and names of PIM prescription (n=3,421)

Drug type and list	n (%)
1. Drugs to be avoided in elderly	1,276 (37.3)
Benzodiazepines	313 (9.1)
First generation antihistamine	195 (5.7)
PPI >8 weeks	177 (5.2)
Loop diuretic	142 (4.2)
Antidepressants	157 (4.6)
Long acting sulfonylurea	86 (2.5)
Peripheral alpha-1 blockers	79 (2.3)
CNS stimulants	49 (1.4)
Muscle relaxant	51 (1.5)
Other	27 (0.8)
2. Drug-disease interaction	751 (22.0)
NSAIDs and HT	288 (8.4)
BBs and DM	212 (6.2)
HCTZ and gout	139 (4.1)
ACEIs/ARBs - hyperkalemia	75 (2.2)
HCTZ and hypokalemia or hyponatremia	25 (0.7)
Tricyclics antidepressants and glaucoma	5 (0.1)
BBs and symptomatic bradycardia/heart block	5 (0.1)
COX-2 NSAIDs and cardiovascular disease	1 (0.03)
Thiazolidinedione and heart failure	1 (0.03)
3. Drug used with precaution in the elderly	1,345 (39.3)
Diuretics	989 (28.9)
Aspirin for primary prevention myocardial infarction	349 (10.2)
Vasodilators	7 (0.2)
4. Drug-drug interaction	24 (0.7)
Benzodiazepines and $\geq 2$ others CNS active drugs	19 (0.6)
Antidepressant and $\geq 2$ others CNS-active drugs	2 (0.06)
Anticholinergic and anticholinergic	2 (0.06)
Aspirin and NSAIDs without PPI	1 (0.03)
5. Drug avoid in chronic kidney diseases	25 (0.7)
Metformin (eGER <30)	16 (0.5)
NSAIDs (eGFR <50)	9 (0.3)

PPI=proton pump inhibitor; CNS=central nervous system; NSAIDs=non-steroidal anti-inflammatory drugs; HT=hypertension; BBs=beta blockers; DM=diabetes mellitus; HCTZ=hydrochlorothiazide; ACEIs=angiotensin-converting enzyme inhibitors; ARBs=angiotensin receptor blockers; eGFR=estimated glomerular filtration rate

gender, visiting the PCU with an acute illness only, and a greater number of drugs received were significantly associated with increasing of PIM prescribing [adjusted OR (95% CI): 1.60 (1.24 to 2.06), 2.32 (1.45 to 3.70), and 1.73 (1.61 to 1.86), respectively].

## Discussion

The problem of PIM prescription was high among elderly hypertensive patients in the PCU of a tertiary care hospital in Southern Thailand. Female

**Table 4.** Factor associated with PIM prescription, multivariable GEE analysis

Variables	Adjust OR (95% CI)	p-value (Wald's test)
<b>Sex</b>		
Male	1	
Female	1.60 (1.24 to 2.06)	<0.001
Number of underlying diseases	0.91 (0.80 to 1.02)	0.108
<b>Types of comorbidities</b>		
Diabetes mellitus	1.02 (0.77 to 1.35)	0.906
Dyslipidemia	0.86 (0.62 to 1.20)	0.372
Gout	0.74 (0.55 to 1.12)	0.181
Chronic kidney disease	1.39 (0.92 to 2.11)	0.122
<b>Diagnosis</b>		
Visit with follow up only	1	
Visit with both follow up and acute illness	1.09 (0.86 to 1.38)	0.468
Visit with acute illness only	2.32 (1.45 to 3.70)	<0.001
<b>Prescribing doctors'</b>		
Family medicine staff	1	
Family medicine resident	0.83 (0.68 to 1.00)	0.052
Intern	0.79 (0.49 to 1.25)	0.311
Number of drugs prescribed	1.73 (1.61 to 1.86)	<0.001

OR=odds ratio; CI=confidence interval

patients, the high number of medications received, and visiting the PCU with an acute illness were associated with increased risk of PIM prescription.

In the present study, the number of females was twice the number of males, similar to the previous studies<sup>(3,10-12)</sup>. The average age of the patients was also similar to the previous studies that used 65 years or older in their eligible criteria<sup>(3,11-15)</sup>, according to Beers criteria, which is intended for use in all ambulatories for populations aged 65 and older<sup>(5)</sup>.

The prevalence of PIM prescription in elderly hypertensive patient was 66.9%. Comparing the results of the present study to the other previous studies was challenging, because of the prevalence of PIM prescription varying, depending on the definition of PIM, study designs, and settings as well as different study populations. However, the prevalence of PIM in the present study was higher than the study that examined hypertensive, non-institutionalized African-American adults (46.0%)<sup>(3)</sup>. This may be due to the difference in the setting of study. The present study was conducted in a tertiary hospital that deals with more complicated diseases than that of a community unit. When considering the details of PIM types, according to the Beer criteria 2015<sup>(5)</sup>, it was found that actually two from five types of PIMs were not incorrect. These being 1) drug-disease interaction,

such as, NSAIDs used may raise BP, so they should be avoided in uncontrolled hypertensive patients, and 2) drugs used with precaution but not to be avoided, such as diuretics used in the elderly may cause unwanted adverse drug reaction. However, diuretics are one class of medication recommended to be used as the initial medication for treatment of hypertension<sup>(19,20)</sup>. Removing the two types of PIM that the physician can use with caution would significantly decreased the prevalence of PIM to 401 patients (41.51%), and 1,037 prescriptions (25.93%).

The commonly prescribed PIM in the present study were diuretics, aspirin, and benzodiazepines, which are the same as the previous studies<sup>(10-13,15-18)</sup>. Diuretics are described above. Aspirin stayed in the group of drugs that should be used with caution in the elderly<sup>(5)</sup>. This was the same as diuretics, so physicians can prescribe aspirin to elder patients, if it was assessed that the benefits are greater than the harm such as, for secondary prevention of cardiovascular disease. Prescribing a low-dose aspirin as a primary prevention in the elderly should be avoided, due to a higher risk of major hemorrhages, without any usefulness against a lower risk of cardiovascular prevention<sup>(21)</sup>. For the last one, both short- and long-acting benzodiazepines were commonly prescribed to elder patients to treat insomnia and other psychological disorders, which is often found in this age group. All benzodiazepines stayed in the group of drugs that should be avoided in the elderly, because it increased the risks of cognitive impairment, delirium, falls, fractures, and motor vehicle crashes<sup>(5)</sup>. To minimize these adverse events, physicians should advise non-pharmacologic therapy before prescribing these medications. Beside Benzodiazepines, more than one-third of PIMs in the present study stayed in the group of “drugs to be avoided in elderly”. Therefore, the physician should avoid them by either using non-pharmacotherapy or alternative, safer drugs such as, second generation antihistamine instead of first-generation antihistamine, and short-acting sulfonylurea or other hypoglycemic agents instead of long-acting sulfonylurea. Furthermore, the physician should conduct a medication review before prescribing new medications to avoid drug-drug interaction problems. This should also include a periodic follow up of kidney function in elderly patients, and then adjusting drug dosages according to renal function, to avoid some medications in chronic kidney diseases.

A factor significantly associated with PIM prescription was female gender, similar to the

previous studies<sup>(10,13,16-18)</sup>, because females have a higher prevalence of hypertension and a higher rate of awareness<sup>(22)</sup>. More prescriptions can increase the chance to receive more PIMs, as shown in the previous studies<sup>(10-13,16-18)</sup>. Visiting the outpatient department (OPD) with only acute illnesses was also a risk factor of PIM prescribing, similar to other studies<sup>(10,14)</sup>. This may be due to acute illnesses leading to the requirement of more medications being prescribed, resulting in an increased chance of PIMs prescribing.

While the present study was being conducted, the American Geriatrics Society (AGS) released a new version of Beers criteria 2019<sup>(23)</sup>. The difference between the two versions were the removal of several medications and the addition of some medications. However, these changes do not affect the results of the present study, as medications that were documented as PIM in the present study were also potentially inappropriately assessed by the new version of Beers criteria<sup>(23)</sup>.

The strengths of the present study were that this study is one of the few studies in Thailand that used the explicit criteria for PIM prescription in specific conditions. Additionally, the present study accumulated data over a period of 12 months, which may have decreased any seasonal influence. The present study also had limitations. Firstly, this study was a retrospective electronic medical record review only. Therefore, the authors did not include over-the-counter medications, or medications from other health care providers that might contain more PIMs. This may have caused an underestimated prevalence of PIM. On the other hand, physician may not record their reasons for prescribing medications, or show that they use high-risk medications with caution. These may have caused an overestimated prevalence of PIM. Secondly, the present study was conducted in a single, tertiary care hospital, so the results might not apply to other hospital settings or populations.

## Conclusion

Prevalence of PIM prescription among elderly hypertensive patients was high, especially for female patients, patients with a high number of medications received, and patients visiting the OPD with acute illnesses. Explicit criteria such as the Beer criteria, is one useful tool to help health care providers in avoiding PIM prescriptions.

## What is already known on this topic?

Previous studies on the prevalence of PIM

prescription and its associated factors were done in various countries, including Thailand<sup>(10-12)</sup>. Most of the previous studies were done in whole elderly group of patients.

## What this study adds?

This study used the Beers criteria to assess PIM prescription in a specific group of elderly, the elderly with hypertension, which is one of the most common diseases worldwide. The results showed a high prevalence of PIM, even after excluding two types of PIM, which may be used in the elderly with caution. Details of PIM types can be used in planning interventions, for reducing PIM prescribing, such as setting up hospital systems to have ‘warning pop-ups’ when prescribing PIM for the elderly. For example, when a physician orders benzodiazepines, they should be alerted as “this drug should be avoided in the elderly”, or “this drug should be avoided when eGER is less than 30” when ordering metformin.

## Suggestions

From the results of the high prevalence of PIM prescription in hypertensive elderly patients, it is time to recognize and resolve this problem. This might start with a review of the medications at every visit, both from this hospital and medications received from the other health care providers, including over-the-counter medication. Physicians can help reduce PIM prescription by stopping unnecessary drugs and being aware of “drug-drug interaction” and “drug-disease interaction” problems when prescribing new medication. Explicit criteria is one useful tool for avoiding PIM prescription within the limited time of OPD visits. The authors suggest that future studies should explore other groups of elderly patients, other health care settings, and include a prospective study design.

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## Conflicts of interest

The authors declare no conflict of interest.

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