

Potentially inappropriate medication use among geriatric patients in primary health care centers by applying the list of risk drugs for Thai elderly criteria

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ABSTRACT

Potentially inappropriate medications (PIM) are medications having a risk greater than benefit, leading to a high risk of adverse drug reactions and mortality in elderly patients. The List of Risk Drugs for Thai Elderly (LRDTE) was the criteria used for identifying PIM in Thai elderly. This study aimed to examine the prevalence of PIM use in primary care centers (PHCs) using the LRDTE and identify factors associated with PIM use. A retrospective, cross-sectional descriptive study was conducted in 2017 at eight PHCs in Thailand. Secondary data of eligible elderly patients aged 60 years and older were retrieved from the Health Data Center database. Descriptive statistics and multivariate logistic regression were used to identify patient characteristics and health service utilization variables of PIM use. A total of 20,671 prescriptions were included for analysis. The prevalence of PIM prescription was 45.7%. The top three PIMs were Anticholinergic drugs (40.5%), Non-steroidal anti-inflammatory drugs (7.5%) and Proton Pump Inhibitors (3.4%). Three severity levels of PIM (mild, moderate and severe) were identified by age group. We found 35.8% of elderly participants aged 60–74 years received mild PIM, while 16.1% of elderly participants aged 75 years and over were prescribed moderate PIM. The percentages of elderly participants aged 60–74 years and 75 years and older that were prescribed severe PIM were 0.03% and 0.02%, respectively. The likelihood of using PIM increased significantly in elderly patients aged 75 years and older [adjusted OR 1.3 95% CI 1.2-1.4] along with polypharmacy [adjusted OR 1.7; 95% CI 1.6-1.9]. The statistically significant factors associated with having PIM prescriptions were diabetes mellitus, hypertension, dyslipidemia, upper respiratory tract infection, dizziness, and muscle strain. Therefore, these factors should be addressed, and the PIM knowledge of health professionals in PHCs is important to avoid PIM prescription in elderly patients.

Key words: potentially inappropriate medications, primary health care center, elderly

INTRODUCTION

The number of people aged 60 and over in Thailand in 2017 stands at about 11.2 million, accounting for 17.1% of the population. The next four years, Thailand is expected a full-fledged ageing society.¹ The growing numbers of older people associated with the increasing burden of non-communicable diseases (NCDs). Almost Thai elderly who have at least one chronic disease and they have been continuously prescribed the polypharmacy. This problem related to the increase risk of adverse drug reaction (ADR) and greater risks for potentially inappropriate medication (PIM) use.²

PIMs are medications having a risk greater than benefit and the medication use inappropriate dose and duration.³ This issue is a major healthcare problem, leading to a high risk of adverse drug reactions, morbidity, mortality and greater healthcare expenditure of elderly patients around the world.⁴ Presently, there are many screening tool for identifying PIM to improve drug safety in elderly. Several international countries have developed PIMs criteria with the hope that the criteria will decrease the occurrence of medication side effects, enhance the quality of care, and decrease the cost of additional health care.⁵ Therefore, explicit checklists to identify PIM need to revise for the specific countries. The original criteria most widely used are the Beers and Screening Tool of Older Persons' potentially inappropriate Prescriptions (STOPP) criterias.^{6,7} Beers criteria was created in the United States and have been regularly updated with a current version.⁶ The update version emphasized the effect of kidney function. For STOPP criteria was created in Europe and updated in 2015. The medication list was organized by the physiological organ system.⁷ The List of Risk Drugs for Thai Elderly

(LRDTE) was developed and updated from the Beers criteria and STOPP criteria. The medication lists were categorized by age and severity of PIM. The advantage of the LRDTE covered Thai standard treatment guidelines and hospital formularies.⁸ Several countries showed the PIM prevalence ranged from 23% - 63% by using Beer and STOPP criteria.⁹⁻¹¹ A previous study examined the prevalence of PIMs in a primary health care centers was found 67% using Beers criteria and 34 % using STOPP criteria.¹² In primary health care centers (PHCs), 52 % of patients had PIM prescription using the Beers criteria.¹³ Applying the LRDTE in secondary care hospitals found that 80 % of elderly patients was prescribed PIMs. The factors showed that a strong effect on PIM use were comorbidities, polypharmacy and physician characteristics.¹⁴ Those factors were similar to most previous studies and highly associated with PIM use in Ireland, Utah, and Japan.¹⁵⁻¹⁷ However, the prevalence of PIM using the LRDTE has not been determined in Thai primary health care centers. The primary objective of this study was to examine the prevalence of PIM use in PHCs by using the LRDTE. The secondary objective was to identify factors associated with PIM use. The outcomes of this study lead to the prevention and reduction of PIM prescription in PHCs.

METHODS

Study Design and Population

A retrospective, cross-sectional descriptive study was conducted in 2017 to examine a PIM use among elderly patients at PHCs. All 80 PHCs, those PHCs were divided by a geographic location into four regions: Northern, Central, Southern, and Northeastern. Each region was selected by simple random sampling that picked up two PHCs. A list of the number of health centers

within these clusters was selected by stratified sampling. Then we used simple random sampling to get the eligible eight PHCs. Participating PHCs agreed to provide the required information in the health data database of elderly patients. The eligible patients were Thai elderly aged 60 years and older by basing on the classification of the age group in the LRDTE. In addition, those visited at outpatients in PHCs between January and December 2017, and had at least one pharmacy claim. The incomplete and error data of patient characteristics and health service utilization were excluded.

Data Source and Variables

Secondary data of eligible patients were retrieved from the Health Data Center database of PHCs, which recorded patient information including personal data, clinical data, diagnoses, prescriptions, and types of health care services. According to a literature review, possible risk factors for PIM use were selected: gender (male or female), age (60–74 or ≥ 75 years) by basing on the LRDTE criteria^{9,8} and health insurance schemes (the Universal Coverage Scheme (UCS, as the National Health Security Program) and non-UCS (including Civil Servant Medical Benefit Scheme, CSMBS and the Social Security Scheme, SSS).^{14,18} Diagnoses were classified according to the 10th revision of the International Statistical Classification of Disease and Related Health Problems (ICD-10).^{14,19} Diagnoses were divided into two groups: The first group was non-communicable diseases (NCDs), which were the chronic diseases for long periods of time and progress slowly such as diabetes mellitus (DM), hypertension (HT), dyslipidemia (DLP), asthma, and gout.¹⁴ The second group was acute diseases, which included any diseases that developed quickly, were intense or severe and last a relatively short period of time such as upper respiratory tract infection (URI), headache,

dizziness, dental problems, dyspepsia, muscle strain, rash, and abdominal pain.¹⁴ For health service utilization data, we selected the date of hospital visits and medication dispensation characteristics, including the generic or brand name, strength, dosage, number of medications, and date of dispensation. Medicines were coded according to the Anatomical Therapeutic Chemical (ATC) classification system recommended by the World Health Organization.^{14,20} For Screening of Potentially Inappropriate Medicines, PIMs were assessed by using the LRDTE criteria, the new explicit criteria to identify PIM for Thai elderly was developed from the 2015 Beers criteria and STOPP version 2. The LRDTE criteria consisted of 76 medications and eight medication classes: anticholinergic, antithrombotic, anti-infective, cardiovascular, central nervous system, endocrine, gastrointestinal, and pain management. The medication lists were categorized by age and severity of PIM. Age was divided into two categories, 60–74 years and 75 years and older. Medicine was categorized into three severity levels, 1) mild level (medicine use within short term use or with intensive monitoring), 2) moderate level (avoid by using alternative choices) and 3) severe level (not recommended and no benefit). The advantage of the LRDTE covered by Thai standard treatment guidelines and hospital formularies.⁸

Data Analysis

The main objective of this study was to explore the prevalence of PIMs use among Thai elderly patients based on the LRDTE. The prevalence of PIM prescriptions was calculated as the number of elderly patients who received at least one PIM were divided by the number of elderly patients receiving any treatment at the eight PHCs. The t-test and the chi-square test were used to analyze variables of the patients with PIM and without PIM. Multiple logistic regression analysis was used to determine

the factors including age group, gender, polypharmacy, health insurance schemes, diseases and the number of medicine that were associated with PIMs. The odds of PIM use associated with various risk factors were described by using adjusted and unadjusted odds ratios (ORs) and 95% confidence intervals (CIs). A p-value less than .05 was considered statistically significant. All analyses were carried out using STATA software version 13 (Stata, College Station, TX, USA).

The study was approved by the Human Research Ethics Committee of Thammasat University, Thailand. No.1, Faculty of Medicine (MTU-EC-CF-1-185/60) on January 23, 2018. Access to the data was officially approved by eight PHCs and HDC.

Prevalence of PIM Prescriptions by Using LRDTE

Table 1 Characteristics of the elderly patients at 8 Public Health Centers in Thailand in 2017 (n=20,671)

Characteristics	All Patients (n=20,671)		PIM use (n=9,451; 45.7%)	p
	Numbers	(%)		
Age, Mean ± SD	71± 8.2		71.8± 8.2	<.001 [§]
60-74 years	14,344	(69.4)	6,265	(43.7)
≥ 75 years	6,327	(30.6)	3,186	(58.4)
Female	13,239	(64.0)	6,106	(46.1)
Health insurance schemes				
UCS	18,836	(91.1)	8,685	(46.1)
Non-UCS	1,835	(8.9)	766	(41.7)
^a Non-communicable diseases (NCDs)				
Hypertension	7,185	(34.8)	1,924	(26.8)
Diabetes mellitus	2,776	(13.4)	1,537	(55.4)
Dyslipidemia	1,752	(8.5)	1,035	(59.1)
^b Acute diseases				
Dyspepsia	7,235	(35.0)	3,963	(54.8)
URI	1,026	(5.0)	630	(61.4)

RESULTS

Patients' Characteristics

A total of 20,671 prescriptions were included between January to December 2017. Table 1 showed the patients' characteristics. The mean age and standard deviation was 71 years ± 8.2 and 64.0 % of participants were female. Most of them received Universal Health Coverage (UHC) was approximately 91.1%. The top three NCDs were HT, DM, and DLP. For the acute diseases, dyspepsia, upper respiratory tract infection, dizziness and muscle strain were the most common diagnoses. In addition, the average number of medications and standard deviation was 3.5 medications ± 2.5 (range 1-26).

Table 1 Characteristics of the elderly patients at 8 Public Health Centers in Thailand in 2017 (n=20,671) (Cont.)

Characteristics	All Patients (n=20,671)		PIM use (n=9,451; 45.7%)	p
	Numbers	(%)		
Dizziness	609	(2.9)	368 (60.4)	<.001*
Muscle strain	535	(2.6)	319 (59.6)	<.001*
Numbers of medications, Mean ± SD	3.5 ± 2.5		3.9 ± 2.9	.030§
1-4 medicines	15,195	(73.5)	6,285 (41.4)	<.001*
≥ 5 medicines	5,476	(26.5)	3,166 (57.8)	

Abbreviations: PIMs = potentially inappropriate medications, UCS= Universal Coverage scheme, URI = Upper Respiratory Tract Infection,

* Statistically significant at $p < .05$, chi-square test

§ Statistically significant at $p < .05$, t-test

^{a,b} Elderly patients had more than one comorbidity, total was more than 100%.

The prevalence of PIM prescription was 45.7% (Table 1). More elderly patients aged 75 years and older were prescribed PIMs than those aged 60-74 years. Female patients received more PIMs than male patients. The majority of PIM users received UCS (46.1%). Among patients with NCDs, the highest prevalence of PIM use in NCDs was found among patients

with DLP (59.1%) and with DM (55.4%). For patients with acute disease, elderly patients who had URI (61.4%) had high PIM prevalence. Moreover, PIM prescriptions were found more frequently among patients receiving polypharmacy (≥ 5 medicines) compared to patients receiving < 5 medications. ($p < .05$)

Table 2 The frequently prescribed PIMs at 8 Public Health Centers in Thailand in 2017 identified using the List of Risk Drug for Thai Elderly (LRDTE)(n=20,671)

Medication ^c	ATC code	PIM level		Total (%)
		60-74 years	≥75 years	
Anticholinergic drugs				7,896 (38.2)
Chlorpheniramine	R06AB04	L 1 (Mild)	L 2 (Moderate)	5,869 (28.4)
Hydroxyzine	N05BB01	L 1 (Mild)	L 2 (Moderate)	1,842 (8.9)
Dimenhydrinate	R06AA02	L 1 (Mild)	L 2 (Moderate)	978 (4.7)
Hyoscine butylbromide	A03BB01		L 3 (Severe)	11 (0.1)

Table 2 The frequently prescribed PIMs at 8 Public Health Centers in Thailand in 2017 identified using the List of Risk Drug for Thai Elderly (LRDTE)(n=2 0 ,671) (Cont.)

Medication ^c	ATC code	PIM level		Total (%)	
		60-74 years	≥75 years		
Non-steroidal anti-inflammatory drugs (NSAIDs)				1,551	(7.5)
Diclofenac	M01AB05	L 1 (Mild)		1,038	(5.0)
Naproxen	M01AE02	L 1 (Mild)		213	(1.0)
Ibuprofen	M01AE01	L 1 (Mild)		68	(0.3)
Gastrointestinal medicines (Proton Pump Inhibitors ;PPIs)					
Omeprazole	A02BC01	L 1 (Mild)		701	(3.4)
Central Nervous System				482	(2.3)
Lorazepam	N05BA06	L 1 (Mild)	L 2 (Moderate)	349	(1.7)
Amitriptyline	N06AA09	L 2 (Moderate)		133	(0.6)
Pain management (Antigout)					
Colchicine	M04AC01	L 1 (Mild)		232	(1.1)
Endocrine medicine					
Pioglitazone	A10BG03	L 2 (Moderate)		252	(1.2)
Pioglitazone	A10BG03	L 2 (Moderate)		252	(1.2)

Abbreviations: ATC = the Anatomical Therapeutic Chemical

^cElderly patients receive PIM more than one.

PIM levels : 1) mild medicine use within short term use or with intensive monitoring; 2) moderate - avoid by using alternative choices; and, 3) severe - not recommended and has no benefit.

Table 2 showed the prevalence of the commonly prescribed PIMs by LRDTE criteria, the top three PIMs were anticholinergic drugs (38.2%), non-steroidal anti-inflammatory drugs; NSAIDs (7.5%) and Proton Pump Inhibitors; PPIs (3.4%). Figure 1 presented the severity of PIM by age, 35.8% of elderly patients aged 60–74 years old received mild PIM. 16.1% of elderly patients aged 75 years old and over were prescribed moderate PIM. Elderly patients aged 60-74 years old and those aged 75 years and older were still prescribed severe PIM (0.03%, 0.02%, respectively).

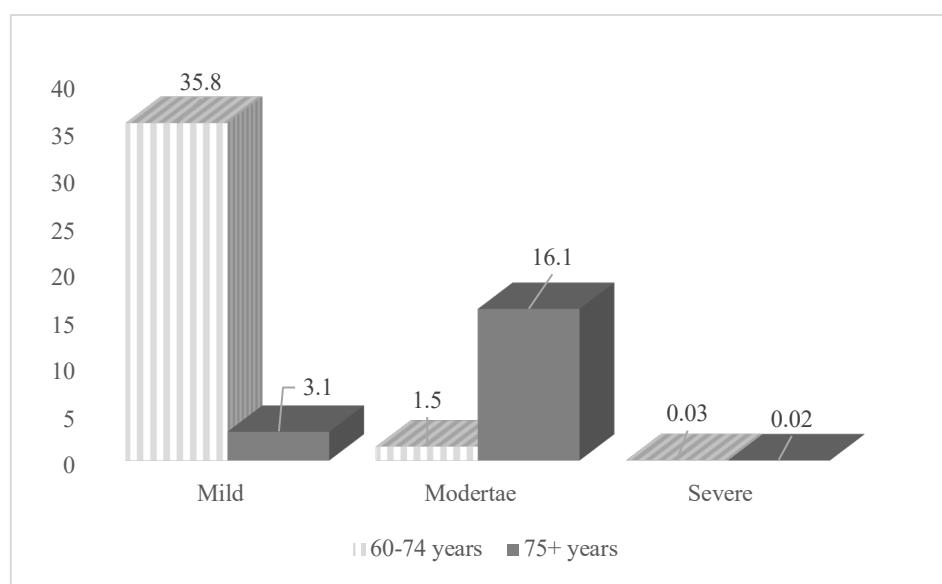


Figure 1 Percentages of elderly received PIM by age group (60-47 years old; 75+ years old)
PIM levels: 1) mild medicine use within short term use or with intensive monitoring;
2) moderate - avoid by using alternative choices; and, 3) severe - not recommended
and has no benefit.

Factors Associated with PIM in Elderly Patients

Table 3 Factors that associated with Potentially Inappropriate Medication (PIM) use among elderly patients at 8 Public Health Centers in Thailand in 2017, after adjusted for age and gender

Variable	Unadjusted OR (95%CI)	Adjusted OR (95%CI) ¹
Age		
60-74 years	1 (Reference)	1 (Reference)
≥ 75 years	1.3 (1.2-1.4)	1.3 (1.2-1.4)*
Female	1.04 (1.0-1.1)	0.95 (0.9-1.0)
Numbers of medications		
1-4 medicines	1 (Reference)	1 (Reference)
≥ 5 medicines	1.4 (1.3-1.4)	1.7 (1.6-1.9)*
Health insurance schemes		
UCS	1 (Reference)	1 (Reference)
Non-UCS	0.8 (0.8-0.9)	0.9 (0.8-1.0)
Comorbidities		
Diabetes mellitus	1.6 (1.4-1.7)	1.5(1.4-1.7)*
Hypertension	1.3(1.2-1.4)	1.2(1.2-1.4)*

Table 3 Factors that associated with Potentially Inappropriate Medication (PIM) use among elderly patients at 8 Public Health Centers in Thailand in 2017, after adjusted for age and gender (Cont.)

Variable	Unadjusted OR (95%CI)	Adjusted OR (95%CI) ¹
Dyslipidemia	1.8 (1.6-2.0)	1.7 (1.6-1.9)*
URI	1.9 (1.7-2.2)	2.6 (2.2-2.9)*
Dizziness	1.85 (1.6-2.2)	2.2 (1.8-2.6)*
Muscle strain	1.8 (1.5-2.1)	2.5 (2.1-3.0)*

Abbreviations: PIMs = potentially inappropriate medications, UCS = Universal Coverage scheme,

URI = Upper respiratory tract infection

¹ Adjusting for age and gender of patient, *Statistically significant at $p < .05$

The multivariate logistic regression models identified independent significant risk factors of PIM use in Table 3. The likelihood of having PIM increased significantly in elderly patients aged 75 years and older [adjusted OR 1.3 95% CI 1.2-1.4] compared to those aged 65-74 years old.

There was also a higher likelihood of having PIM for patient with polypharmacy [adjusted OR 1.7; 95% CI 1.6-1.9] compared to those with < 5 medications. Specific diagnoses had statistically significant associations with PIM use DM, HT, DLP, URI, dizziness, and muscle strain. The OR of having PIM was 1.5, 1.2, 1.7, 2.6, 2.2 and 2.5 for DM, HT, DLP, URI, dizziness and muscle strain, respectively.

DISCUSSIONS

This study explored the prevalence of PIM prescriptions and factors associated with PIM prescriptions among elderly patients in PHCs by using the LRDTE criteria. Which was developed from the Beers and STOPP criteria but the medication list of LRDTE criteria differed from those criteria. In addition, the LRDTE

covered Thai standard treatment guidelines and Thai hospital formularies. Hence, the LRDTE was reflected clinical practice in Thailand^{8,14}

In this study, the prevalence of PIM prescriptions among elderly patients was 45.7 % of elderly patients. Refer to Thai study examining the prevalence of PIMs in PHCs, the study reported a similar PIM prevalence when using STOPP criteria.^{13,21} To compare with the prevalence of PIM prescriptions in our study was higher than prior studies using the previous version of STOPP criteria found that 35% of elderly patients in Netherland²² and 34% of elderly patients in Brazil.²³

Our study reported that the prevalence of PIM was lower than another study (59%) by using the 2015 Beers criteria.¹³ The prevalence of PIM in this study was unable to directly compare with other studies due to the setting, hospital formularies and the particular PIM screening tools were different. According to the previous Thai PIM study in the secondary care hospitals by using LRDTE criteria, showed that 79% of elderly patients used PIM.¹⁴ Thus, the prevalence of PIM in PHCs in our study (45.7%) was lower than the prevalence of prescribed PIM in the secondary care hospitals. The prevalence of

PIM in PHC was lower than the secondary hospital because there were limited number of medicine lists in hospital formulary, the number of patients and diseases. In Thailand, public hospitals have medicines on the National List of Essential Medicines (NLEM) and non NLEM but PHCs have only NLEM. Most of patients who visited PHCs were having a basic disease in contrast with patients who have chronic and complication diseases visited at the secondary hospital.²⁴ Therefore, hospital formulary in PHCs should be revised and PIM knowledge is important for health professionals to avoid PIM prescription.

The top three most common PIMs prescribed to elderly patients aged 60 years and older were anticholinergic drugs (38.2%), NSAIDs (7.5%), and PPIs (3.4%). Anticholinergic drugs in this study included chlorpheniramine, hydroxyzine and dimenhydrinate. According to a PIM study in Ireland which used the STOPP version 2 criteria, the most common PIMs were anticholinergic drugs, NSAIDs, and PPIs.⁹ The anticholinergic drugs in LRDTE criteria was divided as mild to severe of PIM level by considering the age and adverse drug reaction.⁸ This medicine group will increase the occurrence of the side effects in the elderly, which include drowsiness, blurred vision, urinary retention and confusion. According to the recommendation of Beers and STOPP criteria stated that the elderly patients should avoid the first generation of anticholinergic drugs by using alternative choices^{6,7} Therefore, alternative medicines should be provided for PHCs to reduce the risk of drug-induced problems in elderly patients. For NSAIDs, Beers 2019 criteria and STOPP version 2 have different recommendation. Beers 2019 allows a short-term use of NSAIDs for acute conditions, while STOPPS version 2 suggests to avoid NSAIDs in some conditions or patients with specific medications such as antiplatelet agents.^{6,7}

NSAID induced gastrointestinal side effects such as ulcers and bleeding.²⁵ Specifically in the elderly, NSAIDs have become a leading cause of hospitalization and may increase the risk of death from ulceration more than 4-fold.²⁶ Moreover, NSAIDs may increase risk of the kidney malfunction.²⁷ Short-term use and monitoring are key to prevent adverse drug events of NSAIDs for older adults. Long term treatment of omeprazole increased the risk of a number of adverse effects including the reduction of calcium absorption, fractures, Clostridium difficile infection, community-acquired pneumonia, kidney disease, and dementia. Omeprazole as PPIs was commonly prescribed to prevent potential adverse effects from NSAID toxicity. Therefore, elderly patients should be continuously monitored.^{28,29}

When classifying the severity of PIM by age, 35.7% of elderly participants aged 60–74 years old received mild PIM. 16.1% of elderly participants aged 75 years old and over were prescribed moderate PIM. The benefits of those medicines are outweighed by risk, so older patients should be intensely monitored by their health care providers to prevent long term prescription.⁸

Hyoscine butylbromide as severe PIM was the only one antispasmodic drug which associated with strong anticholinergic effects and serious adverse drug effects in elderly patients with underlying cardiac disease but it was included in hospital formulary at PHCs. This medicine should be avoided by using alternative medications.²⁴ However, due to the restrictions of the hospital formulary in PHCs, health care providers at PHCs do not have alternative medicines to prescribe. Therefore, the hospital formulary in PHCs should be revised.¹⁴

The factors positively associated with PIM use in this study were older age, polypharmacy and comorbidity. Those predictors were similar to the previous

studies in other countries, in which those factors also showed a strong effect on risk of PIM prescription.^{30,31,32} Elderly people who continuously received polypharmacy were associated with an increased likelihood of PIM use.^{33,34} Nevertheless, avoiding polypharmacy in the elderly is difficult because of their health conditions and complications from diseases.³⁵ Having comorbidities were also positively related to having PIM prescription. An increased number of comorbidities in a patient, either identified by Charlson Comorbidity Index or Cumulative Illness Rating Scale for Geriatrics, are significantly associated with PIMs. There were many diseases in strong positive factors of PIM use such as diabetes mellitus, hypertension, dyslipidemia, URI, dizziness, and muscle strain. Those diseases were commonly found in older patients. The physiologic changes that occur, elderly people were often treated for multiple diseases and received polypharmacy. Those important factors should be addressed by avoiding PIMs prescription and using deprescribing process to reduce unnecessary medicines in elderly patients.³¹⁻³³ The UCS variable found that there was not statistically significant association because almost elderly patients used UCS. Consistently, the previous studies were not found significant differences between the health insurance schemes regarding PIM prescriptions.¹⁴ The drug policy promoted the use of medication list on the NLEM for all patients and health insurances as first line treatment so this health insurance scheme was not associated with PIM use.^{14, 24}

The limitation of this study was the clinical data and other health services data could not be collected in the electronic medical records and prescription data source. For example, the constipation symptom in patients who used amlodipine were included in LRDTE criteria but this data was without in the health data in the

hospital database. Hence, the results of PIM use might be unexpectedly underestimated or overestimated.

RECOMMENDATIONS

PIM and LRDTE criteria are the new knowledge for Thai medical staff so the training of PIM is important for health professionals to avoid PIM prescription in PHCs. The revision of hospital formulary is necessary to improve elderly patient safety, avoid the side effect of medication and improve the quality of life for older people. In addition, Computerized PIM detection and alerts for medical providers may also be effective in the prevention and reduction of PIM use.

CONCLUSION

The prevalence of PIM use in this study according to LRDTE criteria was 45.70% in Thai elderly patients. The most common PIM prescription were anticholinergic drugs, NSAIDs, and omeprazole. The factors associated with having PIM prescriptions were older age, polypharmacy, diabetes mellitus, hypertension, dyslipidemia, upper respiratory tract infection, dizziness, and muscle strain. Further research on the deprescribing process should be conducted to improve polypharmacy, PIMs prescription, and drug safety.

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