ผลของการบริบาลทางเภสัชกรรมต่อความเหมาะสมในการสั่งใช้ยาสำหรับผู้ป่วยสูงอายุ: การศึกษาเชิงทดลองแบบสุ่ม
Effects of Pharmaceutical Care on Appropriateness of Medication Prescribing for Elderly Patients: A Randomized Controlled Trial

นิพนธ์ต้นฉบับ

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บทคัดย่อ

วัตถุประสงค์: เพื่อประเมินผลของการให้บริบาลทางเภสัชกรรมต่อความเหมาะสมในการสั่งใช้ยาสำหรับผู้ป่วยสูงอายุ **วิธีการศึกษา:** การศึกษาทางคลินิกแบบสุ่มและมีกลุ่มควบคุมโดยใช้ Screening tool of older people's prescriptions (STOPP) criteria version 2 และ American Geriatrics Society (AGS) Beers Criteria หรือ Beers criteria 2015 เพื่อใช้พิจารณารายการยาที่อาจไม่เหมาะสม (potentially inappropriate medications; PIMs) ในผู้ป่วยสูงอายุที่มีโรคเรื้อรังและรับยาต่อเนื่องที่คลินิกโรคเรื้อรัง โรงพยาบาลอุตรดิตถ์ จำนวน 234 ราย ถูกสุ่มเข้าไปในกลุ่มทดลองซึ่งได้รับการบริบาลทางเภสัชกรรมหรือกลุ่มควบคุมที่ได้รับการบริการตามแนวทางปกติ เปรียบเทียบโอกาสในการเกิด PIMS โดยสถิติ multilevel logistic regression ระหว่างกลุ่มทดลองและกลุ่มควบคุมโดยทดสอบตัวแปรที่อาจรบกวนผลลัพธ์ด้วย **ผลการศึกษา:** ผู้ป่วยในกลุ่มทดลองมีโอกาสได้รับรายการยา PIMs น้อยกว่ากลุ่มควบคุมเป็น 0.22 เท่า (adjusted OR = 0.22, 95% CI: 0.06 - 0.78, *P*-value = 0.019) เมื่อเปรียบเทียบกับกลุ่มควบคุม **สรุป :** การบริบาลทางเภสัชกรรมต่อความเหมาะสมในการสั่งใช้ยาสำหรับผู้ป่วยสูงอายุที่เข้ารับการรักษาต่อเนื่องในโรงพยาบาลอุตรดิตถ์โดยใช้ Beers criteria 2015 และ STOPP criteria version 2 ทำให้สามารถค้นหาและลดการสั่งใช้ยาที่เป็น PIMs ได้

คำสำคัญ: การสั่งยาที่ไม่เหมาะสม, ผู้สูงอายุ, Beers criteria, STOPP criteria, การบริบาลทางเภสัชกรรม

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Original Article

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Abstract

Objective : To assess the effects of pharmaceutical care on appropriateness of medication prescribing for elderly patients. **Methods:** In this rndomized controlled trial, Screening Tool of Older People's Prescriptions (STOPP) version 2 and American Geriatrics Society (AGS) Beers Criteria 2015 (Beers criteria 2015) were used a tools to perform pharmaceutical care by identifying potentially inappropriate medications (PIMs). 234 elderly patients with chronic diseases attending chronic disease clinics at Uttaradit hospital were included and randomized to either the test group (pharmaceutical care) or control group (usual care). Multilevel logistic regression adjusted for potential confounders was used to analyze the likelihood of PIMs. **Result:** The likelihood of experiencing PIMs among patients in the test group was 0.22 times of that in the control group (adjusted OR = 0.22, 95% CI: 0.06 - 0.78, *P*-value = 0.019). **Conclusion:** Pharmaceutical care toward appropriateness of medication prescribing for elderly patients using Beers criteria 2015 and STOPP criteria version 2 resulting in identifying and reducing the prescription of PIMs.

Keywords: potentially inappropriate medications, elderly, Beers criteria, STOPP criteria, pharmaceutical care

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Introduction

The rising of elderly population has been a worldwide phenomenon. As estimated by the World Health Organization, populations who are 65 years or older have been increasing.[1] Thailand has entered aging society since 2001.[2] More illnesses and medications in the elderly bring more problems. With physiological changes, the elderly are more likely to receive more potentially inappropriate medications (PIMs). More PIMs increase the risk of adverse drug events, hospitalization and illnesses.[3] The burden of PIMs is of great concern and needs tools to detect and prevent PIMs.

There have been a few criteria which have been developed and tested in assessing PIMs in the elderly. These tools include screening tool of older people's prescriptions (STOPP) criteria[4] and American Geriatrics Society (AGS) Beers Criteria or Beers criteria.[5] These criteria evaluate medications listed as problematic and their use should be avoided or cautious in the elderly. These criteria also list medications requiring dose adjustment in renal impaired patients and those with potential drug interactions.[4,5] Previous studies showed that Beers criteria and STOPP criteria could identify PIMs[6-9] in the elderly. They have been used in various healthcare services including pharmaceutical care.[6,10,11]

Pharmacists in various hospitals identify PIMs listed in Beers criteria and/or STOPP criteria as information

recommended to physicians for appropriate drug regimen modification for the elderly patients. Studies to show performance of Beers criteria and STOPP criteria in Thailand have been limited.[8] All previous studies focused on incidence of PIMs including that in Thailand. No studies used the two criteria as an intervention tool in alleviating inappropriate drug use. In this present interventional study, we used STOPP criteria version 2 and Beers criteria 2015 as additional tools in our pharmaceutical care to identify inappropriate medications in the elderly. This study aimed to determine beneficial effects of pharmaceutical care with the use of STOPP criteria version 2 and Beers criteria 2015 in identifying inappropriate drug use among the elderly patients compared with the usual care. We also aimed, among patients in the test group, to determine rate of acceptance on the PIMs management solutions recommended to the physician. We hypothesized that the elderly patients receiving pharmaceutical care with the use of STOPP criteria version 2 and Beers criteria 2015 (test group) had lower incidence of inappropriate drugs when compared with those receiving the usual care (control group). It was also hypothesized that proportion of accepted recommendations after visit 2 was higher than that after visit 1.

Methods

In this randomized controlled trial (RCT), we recruited the patients receiving regular care at the out-patient department of Uttaradit Hospital, Uttaradit, Thailand. Study sample was patients aged 60 years old or older, receiving care at diabetes clinic, hypertension clinic and coronary heart disease clinic. We excluded patients with cancer, terminal illness, dementia or psychosis. Patients who did not complete their consecutive visits were also excluded.

The sample size was estimated based on the randomized controlled trial with binary outcome using n4Studies software program. Based on the incident rate of PIMs identified by STOPP version 2 and Beers criteria 2015 of 0.37 and 0.56 in the pharmaceutical care group and the usual care group, respectively, found in the study of Frankenthal and colleagues[6], a type I error of 5% and a type II error of 20%, a sample size of 234 participants was required.

With stratified and block randomization, the participants were assigned to receive pharmaceutical care with the use of STOPP criteria version 2 and Beers criteria 2015 (test group) or the usual care (control group), stratified by number of medications (2- 5 vs. 6 or more medications) and a block size of 4. In both groups, at each visit, participants met the pharmacist (P. Ketweerapong) after seeing the physician. Participants in both grop met the physician at 3 consecutive visits from November 1, 2018 to April 19, 2019.

Intervention and data collection process

The test group

Data of demographic characteristics (gender, age, and insurance payment scheme), medical history (chronic illnesses, number of medications prescribed, and renal function as creatinine clearance), and data from each visit including physical examinations (signs and symptoms), laboratory investigations, medications prescribed, adverse drug events obtained from the patient and their caregivers and from medical records were recorded in the data collection form. The pharmacist used signs, symptoms and laboratory results to evaluate the possibility of drugs causing adverse events using Naranjo algorithm.

In terms of pharmaceutical care service in this study, the pharmacist (P. Ketweerapong) evaluated medication prescribing of the physician for the elderly patients for appropriateness, redundant medications, and drug interactions using the Beers criteria 2015 and/or STOPP criteria version 2. The pharmacist also provided physician with recommendation with supporting evaluation on issues mentioned previously, as well as management solutions.

Medications of participants in the test group were identified for any PIMs using the STOPP criteria version 2 and/or Beers criteria 2015 at every visit. Pharmacist note about the evaluation of PIMs, adverse drug events, and management recommendation was provided to the physician. Recommendation to the physician could be followed up. All of this information provided to the physician and the acceptance of the physician was also recorded in the data collection form.

The control group

Patients in the control group were provided with regular pharmacy service by practicing pharmacist at each visit. Drug use advice was provided to the patient as necessary. In contrast with the test group, medications of participants in the control group were retrospectively identified for any PIMs using the STOPP criteria version 2 and Beers criteria 2015

after the 3rd visit was completed. Data collection was similar to that of the test group.

Outcomes

All medications identified as PIMs by STOPP version 2 and/or Beers criteria 2015 at each visit in individual patients (prospectively in the test group and retrospectively in the control group) were identified and recorded.

In each group, the number of patients with at least one PIM from each visit and all three visits combined was recorded and respective proportion (percentage) in relation to the total number of patient in each group was calculated. We also classified number of PIMs according to each of the two tools.

In the test group, number of patients with recommendation to the physician after visits 1 and 2 was recorded and respective proportion (percentage) in relation to the total number of patients was calculated. Similarly, of those patients with recommendation to the physician after visits 1 and 2, patients with recommendation accepted by the physician were recorded and respective proportion (percentage) in relation to the total number of patients with recommendation was calculated.

In addition, individual medications identified as PIMs by the STOPP criteria version 2 and/or Beers criteria 2015 were counted. Medications most identified by each of the two tools were reported separately.

Ethical considerations

This study was approved by the Ethics Committee for Human Study of the Faculty of Pharmacy, Chiangmai University (approval number: 036/2561, approval date: October 16, 2018) and the Ethics Committee for Human Study of Uttaradit Hospital (approval number: 03/2561). The researcher provided prospective participants with information about objectives, process, benefits and risk of participating the study. With voluntary nature of the study, participants were able to withdraw from the study at any time with no impact on the care they received from the hospital. Once they agreed to participate, written informed consent was obtained.

Statistical data analysis

Demographic and clinical characteristics were presented as descriptive statistics including mean with standard deviation (SD) and frequency with percentage. Differences of these characteristics between the two groups were tested using independent t-test for continuous variables with normal distribution or Mann-Whitney U test (for those not normally distributed) as appropriate, and chi-square test for categorical variables.

Based on the patients from both groups, the risk of having at least PIMs from visits 2 or 3 controlling for occurrence of PIMs at visit 1 (baseline) was analyzed using the multilevel binary logistic regression. In our study, the three measurements were nested under the individual patients which were nested under their respective group (either test or control group). We used the multilevel binary logistic regression to quantify the likelihood of occurrence of PIMs at visits 2 and 3 combined, and at visit 3 alone. In addition, to differences of baseline characteristics, numbers of PIMs in test and control groups at visit 1 (baseline) were compared using chi-square test. If any baseline characteristics and PIMs at baseline were significantly different, they were controlled for in the multilevel binary logistic regression. Both analyses were presented as adjusted odds ratio with 95% confidence interval (95% CI).

Among patients in the test group, proportions of patients with recommendation for PIMs management that were provided to the physician after visits 1 and 2 were tested using McNemar test. Among patients that their PIMs management recommendations were provided to the physician, proportions of accepted recommendations after visits 1 and 2 were also tested using McNemar test. Significance for all statistical analyses was set at type I error of 5% or *P*-value < 0.05. All statistical analyses were performed using the STATA version software program.

Results

Of a total of 236 patients recruited, there were 118 patients in each group. At the end of the study, one patient in each group did not complete their three consecutive visits, leaving 117 patients in each group. Patients in the two groups were comparable in demographic and health status characteristics except for renal function (Table 1). Mean creatinine clearance of patients in the test group (58.41 ml/min) was significantly higher than that in the control group (50.87 ml/min) (*P*-value = 0.013). However, mean creatinine clearances in both groups were in CKD stage 3 (i.e., 30 – 59 ml/min).

Table 1 Demographic and clinical characteristics of participants (N = 234).

Characteristics	Test group (n = 117)	Control group (n = 117)	*P*-value
Gender			
Female	61 (52.1)	69 (59.0)	0.293*
Male	59 (47.9)	48 (41.0)	
Age (years)			
60 - 65	38 (32.5)	37 (31.6)	0.643*
66 - 70	34 (29.1)	27 (23.1)	
71 - 75	19 (16.2)	20 (17.1)	
> 75	26 (22.2)	33 (28.2)	
Mean age ± SD	69.6 ± 7.5	70.9 ± 7.5	0.164‡
Insurance payment scheme			
Universal coverage	72 (61.5)	78 (66.7)	0.746$
Civil servant medical benefit scheme	39 (33.3)	32 (27.4)	
Social security scheme	4 (3.4)	4 (3.4)	
Government enterprise employee medical benefit scheme	2 (1.7)	3 (2.6)	
Chronic illness co-morbidity			
Hypertension	109 (93.2)	106 (90.6)	0.473*
Hyperlipidemia	95 (81.2)	100 (85.5)	0.380*
Diabetes mellitus	57 (48.7)	58 (49.6)	0.896*
Coronary heart disease	24 (20.5)	15 (12.8)	0.144*
Chronic kidney disease	12 (10.3)	20 (17.1)	0.128*
Others	63 (53.85)	54 (46.15)	0.239*
Charlson Comorbidity Index, median (interquartile range)	3 (3 - 4)	3 (3 - 4)	0.557†
Number of medications			
2 – 4	22 (18.8)	14 (12.0)	0.485*
5 – 7	51 (43.6)	51 (43.6)	
8 - 10	33 (28.2)	39 (33.3)	
> 10	11 (9.4)	13 (11.1)	
Creatinine clearance (CrCl) (ml/min) (Cockcroft-Gault equation)			
≥ 60	53 (45.3)	43 (36.8)	0.013*
45 – 59	36 (30.8)	23 (19.7)	
30 – 44	17 (14.5)	33 (28.2)	
< 30	11 (9.4)	18 (15.4)	
Mean CrCl, median (interquartile range)	58.41 (46.1 - 74.41)	50.87 (37.11 - 69.14)	0.013†

† Mann-Whitney U test.

* Chi-squared test.

$ Fisher's exact test.

At visit 2, the incidence of PIMs in the test group slightly increased from visit 1 (37.6% to 39.3%), then substantially decreased to 28.2% at visit 3 (Table 2). In contrast, incidence of PIMs in the control group decreased slightly over time, from 58.1% to 58.1%, and 56.9%, respectively. At visit 1 (baseline), number of PIMs in test and control groups were difference (*P*-value = 0.002), therefore proportion of PIMs at baseline was controlled for in the multilevel binary logistic regression. For renal function, since the mean creatinine clearance of both groups were in CKD stage 3 (i.e., 30 – 59 ml/min) (58.41 and 50.87 ml/min, in test and control groups, respectively), reatinine clearance level was not controlled for in the regression even though statistically significant. After controlling for the PIMs occurrence at baseline, patients in the test group were significantly less likely to experience PIMs at the second and/or third visits. Specifically the odds of PIMs in the test group was 0.22 times of that in the control group (adjusted OR = 0.22, 95%CI: 0.06-0.78, *P*-value = 0.019). In addition, patients in the test group were 0.34 times to experience PIMs at the third visit when compared with those in the control group with statistical significance (adjusted OR = 0.34, 95%CI: 0.17-0.68, *P*-value = 0.002). Both analyses were controlled for the occurrence of PIMs at the 1st visit.

Table 2 Incidence of potentially inappropriate medications (PIMs) and risk of PIMs of the intervention compared with control (N = 234).

	Incidence of PIMs at each visit, n of patients with MIPs out of 117 patients in each group				Adjusted OR*	95% CI	*P*-value*
	Overall	Visit 1	Visit 2	Visit 3			
Occurrence of PIMs at visits 2 and/or 3							
Test group	54 (46.2)	44 (37.6)	46 (39.3)	33 (28.2)	0.22	(0.06 - 0.78)	0.019
Control group	81 (69.2)	68 (58.1)‡	68 (58.1)	66 (56.9)	1.00	Reference	
Occurrence of PIMs at visit 3†					0.34	(0.17 - 0.68)	0.002
					Reference		

* Multilevel binary logistic regression controlling for occurrence of PIMs at visit 1 (baseline).

† Data were similar to those for occurrence of PIMs at visits 2 and/or 3.

‡ At visit 1 (baseline), number of PIMs in test and control groups were difference (*P*-value = 0.002, chi-square test).

The most found medications at all 3 visits in both groups by Beers criteria 2015 were lorazepam, omeprazole and doxazosin. These three medications were also the most repeatedly prescribed in the next visit. On the other hand, medications most found by STOPP criteria version 2 in the control group were central nervous acting benzodiazepines (diazepam and clonazepam) and first generation antihistamine (hydroxyzine). In the test group, PIMs were hydroxyzine and omeprazole which were found in one patient for each drug.

Physician's acceptanace for the recommendations

Among patients in the test group, proportions of patients with recommendation for PIMs management that were provided to the physician after visits 1 and 2 were relative comparable (37.6% and 39.3%, respectively, *P*-value = 0.637) (Table 3). Among patients that their PIMs management recommendations were provided to the physician, proportion of accepted recommendations after visit 2 (41.3%) was significantly higher than that after visit 1 (20.5%) (*P*-value = 0.041).

In terms of recommendations to the physician after visits 1 and 2 about PIMs, most were for PIM discontinuation, and dose reduction and shortened duration of treatment as recommended solutions. PIMs with repeated or continued

prescriptions were lorazepam, doxazosin, tramadol and omeprazole. These PIMs were prescribed by physicians different from the previous ones.

Adverse drug events

No differences of adverse drug events between patients in the test and control groups. In the control group, there were one case of glipizide-related hypoglycemia, losartan-related hyperkalemia, and hydrochlorothiazide-related hypokalemia. In the test group, a case of amlodipine-related ankle edema and a case of enalapril-related hyperkalemia. These adverse drug events are not listed as PIMs by STOPP version 2 or Beers criteria 2015.

Discussions and Conclusion

In this randomized controlled trial, appropriatenesss of prescribing medications for the elerly in outpatient clinics had been monitored and recommendations had been provided tp the physician for 3 visits by pharmaceutical care with the use of Beers criteria 2015 and STOPP criteria version 2 compared with the usual pharmacy service. Pharmaceutical care with Beers criteria 2015 and STOPP criteria version 2 was able to identify potentially inappropriate medications (PIMs) and reduce the incidence of PIMs prescribed at visits 2 and 3 combined significantly when compared with the usual service as presented as adjusted OR = 0.22 (95% CI 0.06 - 0.78, *P*-valye = 0.019). Such lower incidence with the intervention when compared with the usual care was also evident when considered only the incidence of PIMs at visit 3 (adjusted OR = 0.34, 95%CI: 0.17-0.68, *P*-value = 0.002).

Our finding was consistent with the study of Frankenthal and colleagues in 2014.[6] They used START/ STOPP criteria version 1 to identify PIMs in hospitalized patients in Israel and found that the intervention could reduce number of PIMs and monthly expense when compared with no intervention significantly. The intervention also resulted in fewer falls but with no statistical significance.[6] This beneficial findings were also consistent with other previous studies[10-13] which indicate that Beers criteria and/or STOPP criteria could help identify and reduce the number of PIMs prescribed.

We found that among the recommendations on PIMs provided to the physician, the longer the intervention was conducted, the more acceptance was found (acceptance rate of 20.5% after visit to 41.3% after visit 2). We found that some of physicians who accepated the recommendations were those regularly on the study clinics. Based on the preferable continuing care idea, this is consistent with the fact that care could be improved if the patients meet the same physician.

Based on Beers criteria 2015 and STOPP criteria version 2 and various clinical guidelines, PIMs most found were similar to those reported in previous studies. For example, lorazepam was prescribed for insomnia which was inappropriate for the elderly according to Beers criteria 2015 and STOPP criteria version 2, the Rational Drug Use policy in hospitals in Thailand[1 4], and other recommendations for insomnia treatment for the elderly.[15-18] The presciprion of lorazepam in the elderly has been a long-time problem in Uttaradit Hospital. This could be due to no report of adverse events from these benzodiazepines to raise awareness among physicians. It also could be attributable to no specialists taking care of the elderly patients, therefore medications were prescribed for them based on clinical guidelines for general patients.

For the performance, Beers criteria 2015 were able to identify more PIMs than STOPP criteria version 2. This finding was consistent with the study of Vishwas and co-workers in 2012 revealing that Beers criteria 2003 identified more PIMs than STOPP criteria version 1[19] as well as the study of Li and colleagues in 2017.[9] The discrepancy that Beers criteria 2015 allows more PIMs to be identified than STOPP criteria version 2 could be due to a larger set of PIMs listed in. In Beers criteria 2015, a total of 86 PIMs include medications that should be avoided in the elderly, PIMs in various illnesses or disease, medications that need caution in use, medications that should be avoided or their doses should be adjusted in kidney impaired patients, and medications that should not be used together because of potential drug interactions. In STOPP criteria version 2, 80PIMs are classified as 13 medications in cardiovascular diseases, 14 in central nervouse system, and 5 in respiratory system. In addition, some medications listed as PIMs in Beers criteria because of the duration of use. In our study, the most found PIMs based on Beers criteria 2015 and STOPP criteria version 2 were lorazepam, omeprazole and doxazosin.

For adverse drug events, they were rare and not different between the two groups. With only five adverse drug events found, these events were not caused by PIMs. The study of Dvora and colleagues in 2014 also found that in test and control groups, only one benzodiazepine related fall in the elderly was found based on STOPP criteria version 1.[6]

Rare adverse events in our study could be attributable to a lack of knowledge among patients and caregivers to be able to observe the events and to report the physician. It could also be that the physician might have used open-ended question that made it difficult for the patient and caregiver to recall the events. Therefore, the patient and caregiver should be provided with how to recognize signs and/or symptoms of adverse drug events. In addition, healthcare providers should also be encouraged to understand PIMs in the elderly and their related adverse events so that they can ask the patient about specific signs and symptoms of frequent adverse events.

It is recommended that more thorough guidelines for the use of medications in the elderly should be implemented. For example, the use of lorazepam in the elderly should be detailed for appropriate use. Not only to be consistent with Beers criteria 2015 and STOPP criteria version 2, more importantly the Rational Drug Use policy in hospitals in Thailand is complied.[14,15] These guidelines and policies all suggest the restricted use of benzodiazepines in the elderly aged over 65 years old for their insomnia where lifestyle modification is the first option, and medications as the complementary modality.[16-18] List of benzodiazepines should be made and communicated to raise awareness among physicians, if adequate number of geriatric specialists is not available. To provide more comprehensive care for the elderly, more studies on the use of PIMs in outpatient and inpatient department by the multidisciplinary team should also be conducted.

This study had certain limitations. During the study period, prescription system in the Uttaradit Hospiotal was changed and communications between pharmacist and physician for PIMs recommendation could be difficult. Since no specialists at diabetes and hypertension clinics, most patients were treated with different physicians for different visits. This could cause disrupted care. In addition, since medications the patient acquired from other places such as drugstores, such as non-steroidal anti-inflammatory drugs, were not taken into account, PIMs could be found less than expected. For potential confounding effects on PIMS, multilevel logistic regression adjusted for potential confounders could have lessened such bias.

In conclusion, pharmaceutical care with the use of Beers criteria 2015 and STOPP criteria version 2 could reduce prescribing potentially inappropriate medications (PIMs). More effective and safer medication use could be expected.

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References

1. National Institute on Aging (NIA), National Institutes of Health (NIH). Global health and aging, Report No.: HHSN263200700991P. Geneva, Switzerland. World Health Organization, 2011.
2. Center for Information technology and Communication. Thai elderly: present and future, 1st ed. Bangkok. The Office of Permanent Secretary, Ministry of Social Development and Human Security, 2014. (in Thai)
3. Davies EA, O'Mahony MS. Adverse drug reactions in special populations - the elderly. *Br J Clin Pharmacol* 2015;80(4):796-807.
4. O'Mahony D, Gallagher P, Ryan C, et al. STOPP & START criteria: A new approach to detecting potentially inappropriate prescribing in old age. *Eur Geriatr Med* 2010;1(1):45-51.
5. American Geriatrics Society Beers Criteria Update Expert Panel. American geriatrics society 2015 updated beers criteria for potentially inappropriate medication use in older adults. *J Am Geriatr* Soc 2015;63(11):2227-2246.
6. Frankenthal D, Lerman Y, Kalendaryev E, Lerman Y. Intervention with the screening tool of older persons potentially inappropriate prescriptions/ screening tool to alert doctors to right treatment criteria in elderly residents of a chronic geriatric facility: a randomized clinical trial. *J Am Geriatr Soc* 2014;62(9):1658-1665.
7. Lim YJ, Kim HY, Choi J, et al. Potentially inappropriate medications by Beers criteria in older outpatients: Prevalence and risk factors. *Korean J Fam Med* 2016;37(6):329-333.
8. Thavornwattanayong W, Anothayanon J, Reungsakul N, Sriphiromrak P, Chomjan R. High-risk medication use in Thai elderly patients: Case study in Wangtaku subdistrict, Nakhonpathom. *J Health Syst Res* 2011;5(2):187-194. (in Thai)
9. Li H, Pu S, Liu Q, et al. Potentially inappropriate medications in Chinese older adults: The Beers criteria compared with the screening tool of older persons' prescriptions criteria. *Geriatr Gerontol Int* 2017;17(11):1951-1958.
10. Frankenthal D, Israeli A, Caraco Y, et al. Long-term outcomes of medication intervention using the screening tool of older persons potentially inappropriate prescriptions screening tool to alert doctors to right treatment criteria. *J Am Geriatr Soc* 2017;65(2):e33-e38.
11. Kimura T, Ogura F, Yamamoto K, et al. Potentially inappropriate medications in elderly Japanese patients: effects of pharmacists' assessment and intervention based on screening tool of older persons' potentially inappropriate prescriptions criteria ver.2. *J Clin Pharm Ther* 2017;42(2):209-214.
12. Kovacevic SV, Simisic M, Rudinski SS, et al. Potentially inappropriate prescribing in older primary care patients. *PLoS One* 2014;9(4):e95536.
13. Herawati F, Maharjana IBN, Kuswardhani T, Susilo AP. STOPP-START medication review: A non-randomized trial in an Indonesian tertiary

hospital to improve medication appropriateness and to reduce the length of stay of older adults. *Hosp Pharm* 2020:0018578720942227. (doi: https://doi.org/10.1177/0018578720942227)

14. Committee of Rational Drug Use. Rational drug use hospital manual. Bangkok. The Agricultural Co-operative Federation of Thailand Printing, 2015. (in Thai)
15. Jongtrakul P. How to teach RDU: 100 teaching issues. Conference on health science learning on rational drug use. 2019. June 21, 2019. Nonthaburi. Rational Drug Use Committee, 2019. (in Thai)
16. Patel D, Steinberg J, Patel P. Insomnia in the elderly: a review. *J Clin Sleep Med* 2018;14(6):1017-1024.
17. Krystal AD, Prather AA, Ashbrook LH. The assessment and management of insomnia: an update. *World Psychiatry* 2019;18(3):337-352.
18. Reynolds AC. Treatment of sleep disturbance in older adults. *J Pharm Pract Res* 2019;49(3):396-304.
19. Vishwas HN, Harugeri A, Parthasarathi G, Ramesh M. Potentially inappropriate medication use in Indian elderly: comparison of Beers' criteria and Screening Tool of older persons' potentially inappropriate prescriptions. *Geriatr Gerontol Int* 2012;12(3):506-514.