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Potentially inappropriate medication in long-term care wards of a veteran hospital in Taiwan: Investigation using a spreadsheet-based rapid assessment tool

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Abstract

Background: Multimorbidity and polypharmacy increase in the aging population and are accompanied by the use of potentially inappropriate medications (PIMs) and adverse drug events (ADEs). This study developed a rapid assessment tool to investigate PIM use among patients in long-term care wards.

Methods: We retrospectively collected the data of patients in long-term care wards of a veteran hospital in Taiwan between July 2019 and June 2020. The patients with chronic diseases and medications were selected. The data, including gender, age, diagnosis, and medications, were deidentified. Nonchronic disease diagnosis and short-term and topical use medications were excluded. We used Microsoft Excel (Microsoft Corporation, Redmond, Washington, USA) and the 2019 version of the Beers Criteria to establish a rapid assessment tool. The correlations between the prevalence of PIM use and age, the number of diagnoses, and the number of medications were analyzed using SPSS version 23.

Results: A total of 176 patients were included in this study, of which 76.7% (n = 135) were male and 23.3% (n = 41) were female. The average age of men was 82.1 years and that of women was 83.4 years. The average number of diagnoses for men was 5.5, and that for women was 7.3. The average number of medications for men was 5.8, and that for women was 6.5. The prevalence of PIM use was 59.1% (n = 104). Logistic regression revealed that the prevalence of PIM use may be associated with the number of medications ($p < 0.001$; odds ratio = 1.378). Decision tree analysis revealed that patients who simultaneously used more than four medications exhibited a higher risk of PIM.

Conclusion: PIM use is a key factor causing ADEs among older adults. Therefore, comprehensive assessment of PIM use is necessary. This study designed a rapid assessment tool to simultaneously integrate and evaluate medications. Future studies may investigate the effectiveness of the proposed assessment tool.

Keywords: Adverse drug events; Beers Criteria; Long-term care; Potentially inappropriate medication

1. INTRODUCTION

Population aging is a global trend. The United Nations reported that the global older population will increase to more than 16% of the total population by 2050, including in Taiwan, in which the aging population prevalence is expected to exceed 20%, rendering it a super-aged society by 2025. As the population ages, older adults experience multimorbidity and polypharmacy. This phenomenon notably increases the prevalence of potentially inappropriate medications (PIMs) and adverse drug events (ADEs).[1]

Marengoni et al[2] discovered that 55%-98% of older adults (people aged more than 65 years) experience multimorbidity. King et al[3] reported that multimorbidity has been increasing year on year in the USA. Furthermore, in 2018, up to 91% of older adults who were aged more than 65 years exhibited multimorbidity. Kantor et al[4] discovered that the prevalence of polypharmacy in the USA in 2015 exceeded 15% and was more than 39% among older adults aged more than 65 years. The more the number of concomitant drug items, the higher the probability of PIM use. Several studies have reported that PIM use is closely related to increased incidence of ADEs, higher hospitalization rates, higher mortality, and higher medical costs.[1,5–9] PIMs are defined as medications that should be avoided, and whose negative outcomes (eg, ADEs, hospitalization, disability, and economic burden) may outweigh their expected clinical benefits.[10–13] A systematic review conducted by Opondo et al[14] revealed a 20.5%

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prevalence of PIM prescriptions among older adults aged more than 65 years. Clyne et al[15] reported that when the number of drugs increased to two, the probability of ADEs was 13%; when the number of drugs increased to five, the probability of ADEs increased to 58%; and if more than seven drugs were consumed, the probability of ADEs was as high as 82%. Gurwitz et al[16] reported that ADEs were common among patients in long-term care facilities; 42% of those ADEs should have been avoided. Caitriona revealed that between 2007 and 2009, 265 802 older adults in the USA presented at the emergency department each year with ADEs; 37.5% of the patients required hospitalization. In Europe, 10% to 20% of older patients required hospitalization for ADEs. Many studies have investigated the relationship between PIM use and treatment outcomes and have developed assessment criteria and detection tools to reduce PIM use.[17]

The recently used tools to detect PIM use among older adults can be categorized according to two types of criteria: implicit criteria and explicit criteria. The Beers Criteria, which are globally used criteria, are explicit criteria developed in 1991 by the American geriatrician Mark H. Beers. He, along with his team of experts, used communication questionnaires, quintiles, and Delphi method to establish this set of criteria. The Beers Criteria were first employed in nursing homes and nursing care units to reduce the prevalence of PIM use among older adults. After several revisions, the 2019 version of the criteria is currently used, and it has been approved by the American Geriatrics Society.[18]

Only a few hospitals established a computerized alert system to prevent PIM use.[19,20] It is not widely applied in Taiwan. The veteran hospital has no medication evaluation system for long-term care wards also. The present study designed a tool for the simple and rapid detection of PIM use. This tool was used to investigate the current status and underlying factors of PIM use in long-term care wards of a veteran hospital in Taiwan.

2. METHODS

This study was performed between April 2021 and December 2021 and has been reviewed and approved by the Institutional Review Board (3) of Taipei Veteran General Hospital under approval number IRB-TPEVGH: 2021-04-014CC. The study involved two steps: designing a PIM assessment tool and using the assessment tool to evaluate and analyze PIM use. The research process is illustrated in Fig. 1.

2.1. Step I: Designing a PIM assessment tool

To ensure the popularity and convenience of the detection tool, this study used the common spreadsheet program Microsoft Excel (Microsoft Corporation, Redmond, Washington, USA) as the basic tool. The 2019 version of the Beers Criteria was used as the evaluation standard for PIM, and automatic detection was implemented. The PIM assessment tool was divided into three parts: Drug Database, PIM Database, and PIM Assessment Chart, which were constructed in the following order (Fig. 2):

1. Establishing the Drug Database: The drug code, trade name, and generic name were selected from the drug list of a veteran hospital in Taiwan. Then, the data were imported to the spreadsheet or entered manually. The total number of samples related to the "Drug Database" was 399.
2. Establishing the PIM Database: The database was established based on the table of the 2019 version of the Beers Criteria. The table listed the drugs potentially inappropriate in older adults and included organ systems, therapeutic categories, drug names, rationale, recommendation, quality of evidence, and strength of recommendation. The drug names, rationale, and recommendations were selected and manually entered into the spreadsheet. The total number of drugs related to the "PIM Database" was 115.
3. Establishing the PIM Assessment Chart: This chart is divided into four parts: basic information, diagnosis, medication record, and suggestion. Medication record include drug code, brand name, generic name, rationale, and recommendations.
4. Setting the assessment function: The function (1) IFERROR (VLOOKUP (A7,'Drug Database'!$A$1:$C$681,2,0),"") entered in the B row of the PIM Assessment Chart. The function (2) IFERROR (VLOOKUP (A7,'Drug Database'!$A$1:$C$681,3,0),"") entered in the C row of the PIM Assessment Chart. The function (3) IFERROR (VLOOKUP (C7, 'PIM Database'!$A$1:$C$116,2,0),"") entered in the D row of the PIM Assessment Chart. (4) IFERROR (VLOOKUP (C7,'PIM Database'!$A$1:$C$116,3,0),"") entered in the E row of the PIM Assessment Chart. The setting was, thus, complete. A7 and C7 were the drug code and generic name of the Drug Database and PIM Assessment Chart shown in Fig. 2. For example, entering the drug code "ALPR" in Cell A7, Cell B7, C7, D7, and E7 will automatically bring up the brand name "Alpraline 0.5 mg", the generic name "Alprazolam", words of PIM rationale and words of recommendation.

2.2. Step II: Assessing PIM

The research data were the retrospectively collected data of 352 patients in long-term care wards of a veteran hospital in

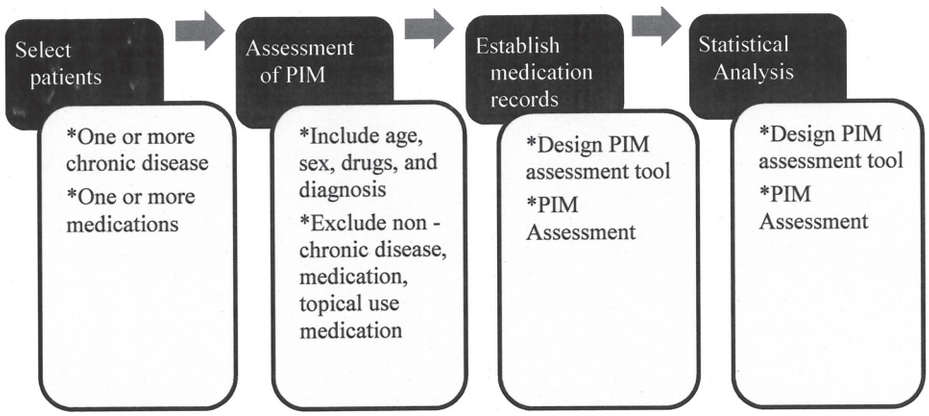

Fig. 1 Study flowchart. PIM = potentially inappropriate medication.

	A	B	C
1	Code	Trade Name	Generic Name
2	GLUC	GlucoBAY 50mg	Acarbose
3	TONE	Tonec 100mg	Aceclofenac
4	ACEM6	Acemet 60mg	Acemetacin
5	ALPR	Alpraline 0.5mg	Alprazolam
6	SCA	Depyretin (Scanol)500mg	Acetaminophen
7	DIA	Acetazolamide 250mg	Acetazolamide

Sheet A. Drug Database

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	A	B	C	D	E
1	Potentially Inappropriate Medication Evaluation Chart				
2	Basic information:				
3					
4	Diagnosis:				
5	Medication Record:				
6	Code	Brand Name	Generic Name	PIM Rationale	Recommendation
7	alpr	Alpraline 0.5mg	Alprazolam	Older adults have increased sensitivity to benzodiazepines and decreased metabolism of long- acting agents; in general, all benzodiazepines increase risk of cognitive impairment, delirium, falls, fractures, and motor vehicle crashes in older adults May be appropriate for seizure disorders, rapid eye movement sleep behavior disorder, benzodiazepine withdrawal, ethanol withdrawal, severe generalized anxiety disorder, and periprocedural anesthesia	Avoid
8	VEN	Benamine (Vena) 50mg	Diphenhydramine	Highly anticholinergic; clearance reduced with advanced age, and tolerance develops when used as hypnotic; risk of confusion, dry mouth,constipation, and other anticholinergic effects or toxicity.Use of diphenhydramine in situations such as acute treatmen	Avoid
9	CORD	CorDARONE 200mg	Amiodarone	Amiodarone is effective for maintaining sinus rhythm but has greater toxicities than other antiarrhythmics used in atrial fibrillation; it may be reasonable first-line therapy in patients with concomitant heart failure or substantial left concomitant hear	Avoid as first-line therapy for atrial fibrillation unless patient has heart failure or substantial left ventricular hypertrophy
10	Suggestion:				

Sheet B. PIM Assessment Chart

❸ ❹

	A	B	C
1	Drug	Rationale	Recommendation
2	Alprazolam	Older adults have increased sensitivity to benzodiazepines and decreased metabolism of long- acting agents; in general, all benzodiazepines increase risk of cognitive impairment, delirium, falls, fractures, and motor vehicle crashes in older adults May be appropriate for seizure disorders, rapid eye movement sleep behavior disorder, benzodiazepine withdrawal, ethanol withdrawal, severe generalized anxiety disorder, and periprocedural anesthesia	Avoid
3	Amiodarone	Effective for maintaining sinus rhythm but has greater toxicities than other antiarrhythmics used in atrial fibrillation; may be reasonable first-line therapy in patients with concomitant heart failure or substantial left ventricular hypertrophy if rhythm control is preferred over rate control	Avoid as first-line therapy for atrial fibrillation unless patient has heart failure or substantial left ventricular hypertrophy

Sheet C. PIM Database

Fig. 2 Assessment rule of the PIM assessment chart. ❶ Entering "alpr" in A7 of sheet B will automatically link the drug code of sheet A, ❷ and bring in the "Alpraline 0.5mg" and "Alprazolam" in B7 and C7 of sheet B. ❸ The "Alprazolam" in C7 of sheet B will automatically be compared with the drug name in sheet C. ❹ If compared, the rationale and recommendation will fill into D7 and E7 of sheet B. PIM = potentially inappropriate medication.

Taiwan between July 2019 and June 2020. The patients with chronic diseases and prescribed medications were selected. Then, data on gender, age, chronic disease diagnosis, and medications were collected. A total of 176 cases were selected for analysis; the corresponding medication records were established. The diagnosis of nonchronic diseases was excluded.

The drugs used for acute illnesses and topical use were also excluded.

The medication records were entered into the PIM Assessment Chart. The drug code was entered in column A of the PIM Assessment Chart and was automatically linked to the drug code cell in column A of the Drug Database (shown in Fig. 2 step 1). Then, the brand name and generic name were filled in column B and column C, respectively (shown in Fig. 2 step 2). The generic name cell in column C was automatically linked to the drug name cell in column A of the PIM Database (shown in Fig. 2 step 3). If the same drug name was compared, the drug was regarded as a PIM. The PIM rationale and recommendation in columns B and C of the PIM Database were automatically filled into columns D and E of the PIM Assessment Chart (shown in Fig. 2 step 4). If the name of the drug could not be compared, the drug was regarded as a non-PIM, and columns D and E were left blank. After collecting the evaluation data, we performed the statistical analysis of PIM data.

We performed descriptive statistics, logistic regression, and decision tree analysis using statistical software SPSS version 23 (IBM, Armonk, NY). Logistic regression was used to explore the relationship between the prevalence of PIM use and age, the number of diagnoses of chronic disease, and the number of medications. We used the decision tree analysis to find the burst nodes between the correlation factor and PIM use. The correlation factor was divided into two different parts by the node. We could select the node to make the best strategy for PIM use.

3. RESULTS

We selected patients with chronic diseases and the use of associated medications. This study included 176 patients in long-term care wards of a veteran hospital in Taiwan who were diagnosed with chronic diseases and used more than one drug. Among the 176 patients, 135 were male (76.7%), and 41 were female (23.3%). The average age of men was 82.1 years, and the average age of women was 83.4 years. The average number of chronic disease diagnoses for men was 5.5, and that for women was 7.3. The average number of medications prescribed to men was 5.8, and that prescribed to women was 6.5. The overall prevalence of PIM use among 176 patients was 59.1% (n = 104). Furthermore, 79 of the 135 men used one or more PIMs, with a prevalence of 58.5%; and 25 of 41 women used one or more PIM, with a prevalence of 61.0% (Table 1). Logistic regression revealed that the prevalence of PIM use was not significantly correlated with age and the number of chronic disease diagnoses. However, the prevalence of PIM use had a significant positive correlation with the number of medications ($p < 0.001$; odds ratio = 1.378) (Table 2). Then, we used a decision tree to analyze the correlation between the prevalence of PIM use and the number of medications. The results indicated that patients who were simultaneously administered more than four medications were at a higher risk of PIM use (Fig. 3).

The pharmacological categories of frequently used PIMs are benzodiazepines (26.6%), antipsychotics (24.9%), proton-pump inhibitors (17.8%), alpha-1 blockers of hypertension (7.1%), and first-generation antihistamines (4.7%), which accounted for approximately 80%. The other categories were antiparkinsonism medications (3.6%), nonbenzodiazepine (3.6%), antidepressants (1.8%), noncyclooxygenase-selective non-steroidal anti-inflammatory drugs (NSAIDs) (1.8%), and sulfonylureas (1.8%). The most commonly used PIMs were quetiapine (16.6%), omeprazole (13.0%), clonazepam (8.9%), estazolam (6.5%), lorazepam (6.5%), doxazocin (4.7%), olanzapine (4.1%), hydroxyzine (4.1%), lansoprazole (4.1%), and trihexyphenidyl (3.6%). These medications included three benzodiazepines (clonazepam, estazolam, and lorazepam), two antipsychotics (quetiapine and olanzapine), two proton-pump inhibitors (omeprazole and lansoprazole), one alpha-1 blocker (doxazocin), one first-generation antihistamines (hydroxyzine), and one antiparkinsonian (trihexyphenidyl).

4. DISCUSSION

We designed and used a tool to assess PIM use among patients in long-term care wards. The study involved two steps: designing an assessment tool and investigating the status of PIM use using the tool. According to the evaluation regulations, long-term care institutions should have pharmacists to perform drug evaluations. The veteran hospital selected in this study had no medication evaluation system for long-term care wards, and all medication information and evaluations were manually recorded. Patients in long-term care institutions may receive medications from different hospitals. In addition, doctors can only review the medicines prescribed at the time of assessment; thus, it may easily duplicate or manipulate the medicines or drug–drug interactions. Therefore, pharmacists cooperating with long-term care units (or institutions) should integrate and analyze medication records to determine the prevalence of PIM use. In Taiwan, pharmacists are required to perform medication evaluation in long-term care institutions every 3 months. Manually integrating and evaluating medication records are time-consuming, and effectively and accurately identifying PIM is challenging. The present study designed a rapid tool for assessing PIM use. The evaluation was considered complete when the medications are inputted or imported into the PIM Assessment Chart. Thus, pharmacists can use this tool to quickly and accurately identify PIM use.

Allowing every long-term care institute to customize their own health-care system is not feasible. We selected the most accessible and extensively used spreadsheet program Microsoft Excel as the assessment tool. Further, we used the Beers Criteria to design a low-cost and easy-to-use tool for assessing PIM use.

Table 1

Patient and prevalence of PIM use characteristics (n = 176)

	Men (n = 135)				Women (n = 41)			
Patient	**Min**	**Max**	**Mean**	**SD**	**Min**	**Max**	**Mean**	**SD**
Age	45.0	103.0	82.1	13.9	57.0	100.0	83.4	8.2
No. of diagnoses	1.0	14.0	5.5	3.0	15.0	3.0	7.3	3.0
No. of medications	1.0	15.0	5.8	3.2	1.0	12.0	6.5	2. 5
Prevalence of PIM use	N (%)		Effective %	Cumulative %	N (%)		Effective %	Cumulative %
Without PIM	56 (41.5)		41.5	41.5	16 (39.0)		39.0	39.0
With PIM	79 (58.5)		58.5	100.0	25 (61.0)		61.0	100.0

PIM = potentially inappropriate medication.

Table 2

Results of logistic regression

Predictor	B	SE	Wald	df	Sig.	Exp(B) (odds ratio)
Age	0.001	0.013	0.001	1	0.975	1.000
No. of medications	0.321	0.075	18.306	1	0.001*	1.378
No. of diagnoses	−0.003	0.065	0.002	1	0.963	0.997
Constant	−1.421	1.171	1.471	1	0.225	0.242

Sig. = significance.

Sensitivity = 0.837, specificity = 0.514, area under the curve = 0.729 (p-value ≤ 0.001; 95% CI, 0.654-0.804), Nagelkerke R Square = 0.216.

*$p < 0.05$.

The proposed tool can be used in more hospitals or long-term care institutions to improve the efficiency of PIM assessment. The tool can be adjusted according to the needs of each medical or long-term care institution. For example, the basic information of patients, such as height, weight, age, and nasogastric feeding, can be customized. Users can simply enter the drug code to view the PIMs identified through automatic screening and can then make recommendations and print or email them to the physician.

The research on PIM revealed that 104 of the 176 people used one or more PIMs in long-term care wards attached to a veteran hospital. The prevalence of PIM use was as high as 59.1%, indicating that three out of every five residents used PIMs. The results of the present study are consistent with those of an Indian study that also used the Beers Criteria. The study included 380 patients with an average age of 65.4 years, and 65% of the prescriptions included one or more PIMs.[21] Pattani

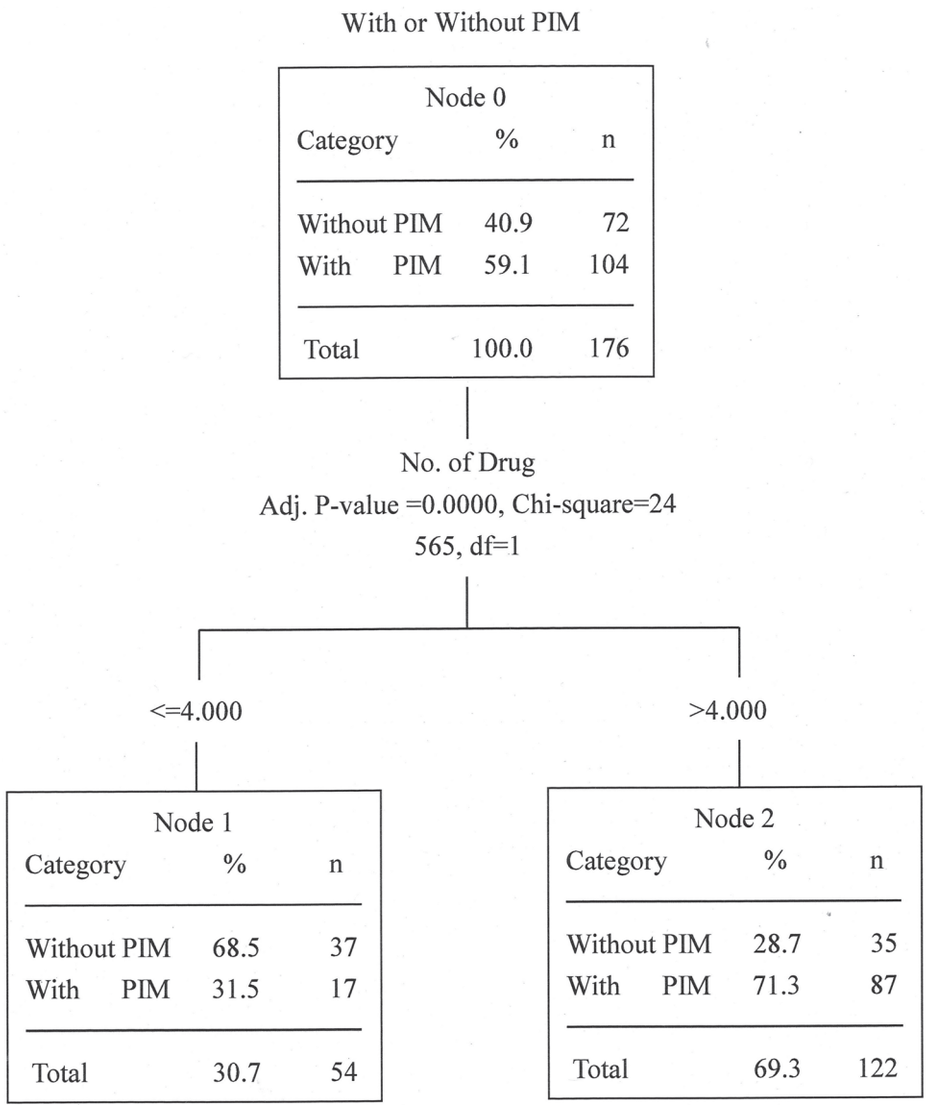

Fig. 3 Results of decision tree. PIM = potentially inappropriate medication.

et al[22] reported similar results; 200 hospitalized older adults had a PIM use prevalence of 53%.

In the present study, among the pharmacological categories, benzodiazepines (26.63%) were the most commonly used; this is consistent with the findings of previous studies on PIM use.[22–24] These results indicated that the use of benzodiazepines was common among older adults, who have increased sensitivity to benzodiazepines and decreased metabolism of long-acting agents such as clonazepam. All benzodiazepines are associated with increased risks of cognitive impairment, delirium, falls, fractures, and motor vehicle crashes among older adults. The second most used category was antipsychotics (24.9%), which can increase the incidence of cerebrovascular accidents, cognitive decline among dementia patients, and mortality.[25] Antipsychotics should be avoided, except in cases of schizophrenia, bipolar disorder, or short-term use as antiemetics during chemotherapy. Antipsychotics should also be avoided for behavioral conditions such as dementia or delirium unless nonpharmacological options have failed or are not possible.

In the present study, proton-pump inhibitors (17.8%) were the third most used PIM. The proton-pump inhibitors will increase the risks of Clostridium difficile infection, bone loss, and fractures. The use of proton-pump inhibitors for more than 8 weeks should be avoided unless steroids or NSAIDs are used to treat erosive esophagitis or Barrett's esophagus in the long term, except in patients with inflammation and other diseases.[18] Alpha-1 blockers (7.1%) are not recommended as long-term antihypertensive drugs for older adults because of the risk of postural hypotension. Furthermore, first-generation antihistamines (4.7%) may accumulate because of reduced drug clearance, thereby resulting in confusion, dry mouth, constipation, and anticholinergic toxicity. Quetiapine (16.6%) is the first used PIM to alleviate agitation in patients who were could not calm down at night even after appeasement. However, quetiapine increases the risk of adverse outcomes of the central nervous system among older adults, for example, syncope and impaired psychomotor performance. Furthermore, it causes cognitive impairment, falls, and increased risk of cerebrovascular accidents and death. Quetiapine should be avoided unless other effective treatments are unavailable.

Logistic regression revealed that the prevalence of PIM use was not significantly correlated with age or the number of chronic disease diagnoses but had a significant positive correlation with the number of medications ($p < 0.001$). For each additional medication, the prevalence of PIM use increased by 1.378 times. The results obtained using the decision tree indicated that when the number of medications was less than or equal to four, the prevalence of PIM use was 31.5%. When the number of medications exceeded four, the prevalence of PIM use increased to 71.3%. An increase in the prevalence of PIM use indicated an increase in the incidence of ADEs. These results are similar to the findings of Clyne et al[15] that the incidence of ADEs was 58% when patients used five drugs.

The Beers Criteria are a common globally used tool for identifying PIMs. Several medical and long-term care facilities use the Beers Criteria to assess PIM use. A retrospective study in 2021 reported that hospitals can effectively reduce PIM use by applying various evaluation criteria. Most hospitals use explicit criteria for evaluation. Therefore, medical institutions and healthcare institutions should apply such evaluation criteria to reduce the prevalence of PIM use and improve the outcomes of care.[26]

As the population ages and the number of long-term care facilities increases, the quality of care in long-term care facilities becomes crucial. Many studies have suggested that the prevalence of PIM use in long-term care facilities is approximately 60%.[24] PIM use is an important factor that drives the development of ADEs among older adults and other health outcomes. Evaluating PIM use can reduce ADEs and the incidence of hospitalization among older adults.[27]

The current approach used to manually assess PIM use is time-consuming and difficult to be generalized. The rapid assessment tool designed in this study may enable pharmacists to rapidly screen PIMs during the implementation of medication integration. The proposed tool is convenient and cost-effective for medical institutions or long-term care institutions. Future studies are warranted to evaluate the applicability and benefits of the tools used for assessing PIM use. Besides, this study explored that the number of drugs is positively related to PIM use. The incidence of PIM will be increased markedly by taking more than four drugs contemporarily. Therefore, we can use it as a management strategy for PIM use for future research.

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