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Original Research

Prevalence and factors associated with potentially inappropriate medication and medication complexity for older adults in the emergency department of a secondary teaching hospital in Indonesia

Khusnul Fitri Hamidah , Mahardian Rahmadi , Farah Meutia , Prihatma Kriswidyatomo , Firman Suryadi Rahman , Zamrotul Izzah , Bambang Subakti Zulkarnain , Leopold N. Aminde , Christopher Paul Alderman , Yulistiani , Budi Suprapti 

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Abstract

Background: Older adults experience progressive decline in various organs and changes in pharmacokinetics and pharmacodynamics of the drugs in the body which lead to an increased risk of medication-related problems. Potentially inappropriate medications (PIMs) and medication complexity are key factors contributing to adverse drug events in the emergency department (ED). **Objective:** To estimate the prevalence and investigate the risk factors of PIMs and medication complexity among older adults admitted to the ED. **Methods:** A retrospective observational study was conducted among patients aged > 60 years admitted to the ED of Universitas Airlangga Teaching Hospital in January - June 2020. PIMs and medication complexity were measured using the 2019 American Geriatrics Society Beers Criteria® and Medication Regimen Complexity Index (MRCI), respectively. **Results:** A total of 1005 patients were included and 55.0% (95% confidence interval [CI]: 52 – 58%) of them received at least one PIM. Whereas, the pharmacological therapy prescribed to older adults had a high complexity index (mean MRCI 17.23 + 11.15). Multivariate analysis showed that those with polypharmacy (OR= 6.954; 95% CI: 4.617 – 10.476), diseases of the circulatory system (OR= 2.126; 95% CI: 1.166 – 3.876), endocrine, nutritional, and metabolic diseases (OR= 1.924; 95% CI: 1.087 – 3.405), and diseases of the digestive system (OR= 1.858; 95% CI: 1.214 – 2.842) had an increased risk of receiving PIM prescriptions. Meanwhile, disease of the respiratory system (OR = 7.621; 95% CI: 2.833 – 15.150), endocrine, nutritional and metabolic diseases (OR = 6.601; 95% CI: 2.935 – 14.847), and polypharmacy (OR = 4.373; 95% CI: 3.540 – 5.401) were associated with higher medication complexity. **Conclusion:** In our study, over one in every two older adults admitted to the ED had PIMs, and a high medication complexity was observed. Endocrine, nutritional and metabolic disease was the leading risk factors for receiving PIMs and high medication complexity.

Keywords: beers criteria; elderly; medication regimen complexity index; medication-related problem; polypharmacy

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INTRODUCTION

Potentially inappropriate medication (PIM) is one of the factors causing medication-related problems in older adults.¹⁻³ PIM is a drug with a risk of adverse effects more significant than its benefits when used by older adults, especially if safer alternative therapies are available and provide the same effectiveness.⁴ PIM prescriptions in older adults are a recognized problem for health services, contributing to the increased prevalence of morbidity, hospitalization, and costs.¹

The most frequently used approach to identify the presence of PIM in patients' therapy is the American Geriatrics Society (AGS) Beers Criteria[®], an interdisciplinary consensus-based approach that lists drugs categorized as PIM in older adults. The Beers Criteria[®] is continuously updated and an important measurement tool in identifying PIM to improve the quality and safety of the therapy. Moreover, the Beers Criteria[®] can be used in various service areas.^{2,5,6}

Older adults experience a progressive decline in various systems and organs. These contribute to increase the prevalence of disease and susceptibility to receive more medications. They receive more than two types of drugs and polypharmacy occurs in 20-50% of these elderly patients.^{5,7} As a consequence, it may put them at high risk of drug-related problems and lead to hospital admission.

Globally, the number of older patients admitted to hospital emergency departments (ED) increase significantly annually, which is in line with the growth in ageing populations and increasing life expectancy.⁸ In 2015, about 13 million patients came to the ED with a history of diabetes in America, 59% of them were older adults.⁹ In Indonesia, almost 25% of people aged > 65 years visit the ED at least once a year, and 8% undergo repeat visits.¹⁰ On the other hand, the ED is a high-risk service area for the occurrence of medication errors in the hospital. Some contributing factors include: (1) patients in emergency conditions; (2) patients of various ages; (3) high use of high alert drugs; (4) treatment is carried out simultaneously on patients; (5) and the lack of ability of health workers to communicate with patients due to the density of services.¹¹

In 2003–2012, the prevalence of PIM in older adults identified by the Beers Criteria[®] increased from 5.6% to 26% in European and Asian countries.¹² Even though older patients get medications in a single dose and for a short time in the ED, some drugs can cause serious side effects. Another study in the United States showed that at least 7% of patients presenting with myocardial infarction required dose adjustment because of actual side effects. In older patients who require more therapy, it is necessary to consider the risk of PIM use and drug interactions¹¹⁻¹³.

Besides PIM, medication regimen complexity also plays a role in drug-related problems and the incidence of readmissions and hospitalizations in elderly patients. Therefore, hospital pharmacists should pay attention to the medication complexity in older patients. The medication regimen complexity index (MRCI) is a validated instrument that can be used to describe

the complexity of medications, including drug dosage forms, dosing frequency, and additional directions.^{5,14,15}

To the best of the authors knowledge, there is limited information regarding PIM and medication complexity among the Indonesian population. Previous studies were performed using the 2015 Beers Criteria[®] and no recent study in Indonesia has been conducted with the updated 2019 version.^{1,16-18} Therefore, to complement this knowledge gap, studies on PIM and medication complexity in older adults visiting the hospital ED in Indonesia are needed to improve patient safety. Moreover, the study results can be utilized to identify older patients at risk of adverse drug events or who require supervision from specialist medical personnels.¹⁴

METHODS

Study design and setting

A retrospective observational study was conducted at the ED of Universitas Airlangga (UNAIR) Teaching Hospital in Indonesia, located in Surabaya, East Java Province, which receives 80-120 emergency patients daily. A clinical pharmacist together with a hospital pharmacist and seven pharmacy technicians provide pharmacy services in the ED, such as reviewing prescribed medicines, drug reconciliation, working collaboratively with physicians and nurses to control patients with intoxication.¹⁹

Data were extracted from patient medical records admitted to the ED during January to June 2020 (Figure 1). The study protocol was approved by the Ethics committee of UNAIR Teaching Hospital (Approval certificate no.177/KEP/2020) prior to the commencement of the study.

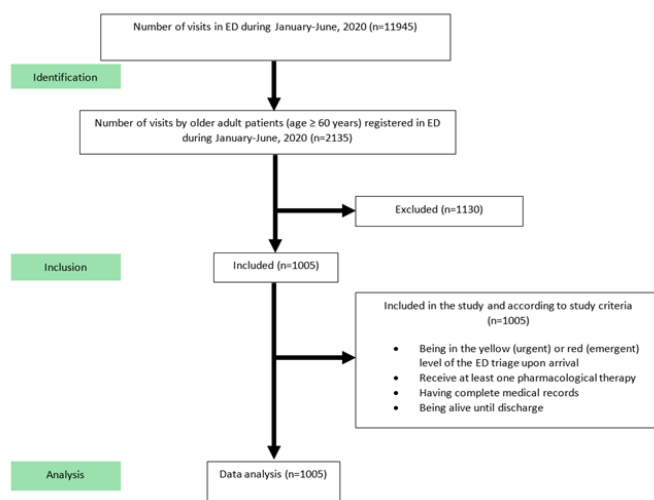


Figure 1. Study enrolment flowchart

Data collection

Data were recorded on the data collection sheet and kept confidential during collection. Data collection included demographic (gender, year of birth or age, occupation), clinical characteristics (triage level, underlying diseases or diagnosis, comorbidities), laboratory and supporting examinations (serum



electrolytes, creatinine, blood glucose, full blood count), and prescribed medications (active substance, strength, dosage form, route of administration, dosing frequency, and additional instructions, if applicable).

Diseases classification and comorbidity

A classification of diseases was carried out using the International Classification of Diseases and Related Health Problems, tenth revision (ICD-10).²⁰ In addition, the comorbidity index was calculated using the validated Charlson Comorbidity Index (CCI).¹⁶ The prevalence of each disease group and comorbid index were further calculated.

Potentially inappropriate medications assessment

The primary outcome of this study was the prevalence and risk factors for PIMs in older adult patients in the ED. PIMs were analyzed based on the 2019 AGS Beers Criteria[®]. We summarised the PIM assessment in our study population in a tabular format according the type and number of PIMs in each category.

Medication regimen complexity assessment

As the secondary outcome, the medication regimen complexity was measured using the validated MRCI,¹⁴ which includes 65 assessment items categorized. The complexity index was assessed for each therapy received by older adult patients based on predetermined parameters and values, namely: (1) dosage forms; (2) dosing frequency; and (3) additional directions.¹³ Then, the values obtained in each subgroup were summed, tabled and classified to get the mean of MRCI as a cut-off point for high complexity category. A higher MRCI score indicates higher complexity.

Statistical analysis

Descriptive analysis was done by summarising the categorical variables as counts with percentages and continuous variables as means with standard deviation. Continuous variables checked using the Kolmogorov-Smirnov test. The prevalence of PIM was estimated by dividing the number of older patients by the total study population. We conducted univariate binary logistic regression analyses to investigate factors associated with PIM use and MRCI. The following factors were tested: diseases groups by ICD-10 classification, comorbidities, and the number of prescribed medications. To determine factors that were independently associated with PIM use and high medication complexity, all factors that were statistically significant in the univariate analyses were used to build a multivariate logistic regression model. All statistical analyses were carried out in the Statistical Package for the Social Sciences (SPSS) version 25 with a significance level of $\alpha = 0.05$.

RESULTS

General characteristics

In this study, a total of 1005 emergency visits of patients aged ≥ 60 years with a yellow or red triage and received at least one

therapy were included. The mean age was 69.2 ± 7.2 years and 50.7% were female. More than half (59.1%) of the participants had comorbidities and nearly one-third (29.2%) of visits had polypharmacy. Demographic and clinical characteristics of study population can be seen in Table 1.

Variable	n (%)
No. of visits	1005
Gender	
Male	495 (49.3)
Female	510 (50.7)
Age (years)	
60 – 64	314 (31.2)
65 – 69	283 (28.2)
70 – 74	189 (18.8)
≥ 75	219 (21.8)
ED triage	
Yellow	746 (74.2)
Red	259 (25.8)
Charlson Comorbidity Index	
No comorbidity (0)	411 (40.9)
Mild (1 – 2)	559 (55.6)
Moderate (3 – 4)	32 (3.2)
Severe (≥ 5)	3 (0.3)
Disease groups (ICD-10)	
Diseases of the respiratory system	194 (19.3)
Diseases of the digestive system	177 (17.6)
Symptoms, signs and abnormal clinical and laboratory findings, not elsewhere classified	155 (15.4)
Diseases of the circulatory system	107 (10.6)
Diseases of the nervous system	94 (9.4)
Endocrine, nutritional and metabolic diseases	94 (9.4)
Diseases of the genitourinary system	61 (6.1)
Injury, poisoning and certain other consequences of external causes	37 (3.7)
Certain infectious and parasitic diseases	32 (3.2)
Diseases of musculoskeletal system and connective tissue	23 (2.3)
Diseases of the skin and subcutaneous tissue	13 (1.3)
Neoplasms	10 (1.0)
Diseases of the blood and blood-forming organs	5 (0.5)
Disorders of gallbladder, biliary tract and pancreas	3 (0.3)
Number of prescribed medications	
< 5	712 (70.8)
≥ 5 (polypharmacy)	293 (29.2)
Condition after ED visit	
Hospitalization	652 (64.9)
Discharge	353 (35.1)

Potentially inappropriate medications

Based on visit cases, at least one PIM was prescribed in more than half patients (55.0%, 95% confidence interval [CI]: 52 – 58%) and 62.3% of those were potentially inappropriate use in most older adults PIM criteria. The prevalence and classification of PIM are shown in Table 2. The list of top ten drugs categorized as PIM received by elderly patients in the ED is shown in Table 3. Metoclopramide was the most prescribed PIM (16.6%), followed by omeprazole (10.4%).



	n (%)
Number of PIM	
Visit without PIM	452 (45.0)
Visit with PIM	553 (55.0)
1	359 (35.7)
2	141 (14.0)
3	40 (4.0)
4	10 (1.0)
5	2 (0.2)
6	1 (0.1)
PIM Criteria	
PIM use in older adults	512 (62.3)
PIM use in older adults due to drug-disease or drug-syndrome interactions that may exacerbate the disease or syndrome	48 (5.8)
PIM to be used with caution	192 (23.4)
PIM that should be avoided due to drug interactions	18 (2.2)
PIM that should be avoided or require dose adjustment due to decreased renal function	52 (6.3)
Therapeutic category	
Gastrointestinal medications	352 (43.1)
Diuretics	123 (15.1)
Nonsteroidal anti-inflammatory drugs	103 (12.6)
Endocrine medications	92 (11.3)
Antiplatelet aggregation	74 (9.1)
Benzodiazepines	20 (2.40)
Antispasmodic	17 (2.1)
Cardiovascular medications	15 (1.8)
Corticosteroid	7 (0.9)
Anticoagulant	3 (0.4)
Antihistamine	2 (0.2)
Narcotic analgesics	1 (0.1)
Antidepressants	1 (0.1)
Central nervous system and analgesics drugs	1 (0.1)
AGS American Geriatric Society, PIM potentially inappropriate medication	

Factors associated with PIM use

From the univariate analysis, we found that having diseases of the respiratory system, digestive system, presence of symptoms, signs and abnormal clinical and laboratory findings, circulatory system, endocrine, nutritional and metabolic diseases, genitourinary system, presence of neoplasms and patients with polypharmacy had p-values < 0.25 and were considered candidate variables for inclusion in the multivariable model.

Our multivariate analysis showed that those with circulatory system diseases (OR = 2.126; 95% CI: 1.166–3.876), endocrine, nutritional and metabolic diseases (OR = 1.924; 95% CI: 1.087–3.405), and digestive system diseases (OR = 1.858; 95% CI: 1.214 – 2.842) had increased likelihood of being prescribed PIMs compared to their counterparts, while those with diseases

Drugs listed as PIM	n (%)	Criteria for inappropriate use
Metoclopramide	167 (16.6)	It may cause extrapyramidal effects, including tardive dyskinesia; the risk may be greater in frail elderly and prolonged exposure
Omeprazole	105 (10.4)	Risk of infection <i>Clostridium difficile</i> , bone loss, and fractures
Furosemide	83 (8.3)	It may exacerbate or cause SIADH or hyponatremia
Rapid/short acting insulin	80 (8.1)	Higher risk of hypoglycaemia; avoid insulin regimens containing only short or rapid-acting insulin and dosed according to current blood glucose levels without co-administration of basal or long-acting insulin
Acetylsalicylic acid	78 (7.7)	The risk of acute bleeding from ASA increases markedly in the elderly
Ketorolac	55 (5.5)	It increases the risk of gastrointestinal bleeding/peptic ulcer disease and acute kidney disease in the elderly
Ranitidine	49 (4.9)	Potential to cause changes in mental status in elderly patients with creatinine clearance < 50 mL/min
Metamizole	46 (4.6)	Potential to increase fluid retention and worsen heart failure
Spirolactone	39 (3.9)	May worsen or cause SIADH or hyponatremia, potentially cause increased potassium levels in elderly patients with creatinine clearance < 30 mL/min.
Lansoprazole	26 (2.6)	Risk of infection <i>Clostridium difficile</i> , bone loss, and fractures
AGS American Geriatric Society, ASA acetylsalicylic acid, PIM potentially inappropriate medication, SIADH syndrome of inappropriate antidiuretic hormone		

of the respiratory system (OR = 0.183; 95% CI: 0.112–0.302), symptoms, signs, and abnormal clinical and laboratory findings (OR = 0.668; 95% CI: 0.430 – 1.036) had lower odds of being prescribed PIMs compared to their counterparts who did not have these conditions. Table 4 depicts our regression results for factors associated with the use of PIMs in elderly patients in the ED.

Medication regimen complexity

The mean of MRCI scores was 17.23 ± 11.15 with cut-off upper quartile, thus the scores were categorized into two groups: high complexity with MRCI score ≥ 24 and low with MRCI score < 24. Our multivariate analysis showed that those with respiratory system disease (OR = 7.621; 95% CI: 2.833–5.150), and endocrine, nutritional and metabolic diseases (OR = 6.601; 95% CI: 2.935–14.847) were highly correlated with MRCI scores, while those with musculoskeletal system and connective tissue disease (OR = 1.974; 95% CI: 0.175 – 22.209), nervous system disease (OR = 1.746; 95% CI: 0.530 – 5.746), and symptoms,



Table 4. Factors associated with potentially inappropriate medications use among elderly patient visits in the ED of Universitas Airlangga Teaching Hospital, Indonesia, 2020						
Variable	PIM prescription		Univariate analysis**		Multivariate analysis***	
	Yes n (%)	No n (%)	Odds ratio (95% CI)	p-value	Odds ratio (95% CI)	p-value
Disease group*						
Diseases of the respiratory system						
Yes	61 (11.0)	133 (29.4)	0.297	0.000	0.183	0.000
No	492 (89.0)	319 (70.6)	(0.213 – 0.415)		(0.112 – 0.302)	
Diseases of the digestive system						
Yes	115 (20.8)	62 (13.7)	1.652	0.004	1.858	0.004
No	438 (79.2)	390 (86.3)	(1.178 – 2.315)		(1.214 – 2.842)	
Symptoms, signs and abnormal clinical and laboratory findings, not elsewhere classified						
Yes	63 (11.4)	92 (20.4)	0.503	0.000	0.668	0.071
No	490 (88.6)	360 (79.6)	(0.355 – 0.713)		(0.430 – 1.036)	
Diseases of the circulatory system						
Yes	87 (15.7)	20 (4.4)	4.033	0.000	2.126	0.014
No	466 (84.3)	432 (95.6)	(2.438 – 6.671)		(1.166 – 3.876)	
Diseases of the nervous system						
Yes	49 (8.9)	45 (10.0)	0.879	0.553	-	-
No	504 (91.1)	407 (90.0)	(0.575 – 1.345)			
Endocrine, nutritional and metabolic diseases						
Yes	70 (12.7)	24 (5.3)	2.585	0.000	1.924	0.025
No	483 (87.3)	428 (94.7)	(1.597 – 4.183)		(1.087 – 3.405)	
Diseases of the genitourinary system						
Yes	42 (7.6)	19 (4.2)	1.873	0.027	1.669	0.117
No	511 (92.4)	433 (95.8)	(1.073 – 3.269)		(0.879 – 3.166)	
Injury, poisoning and certain other consequences of external causes						
Yes	17 (3.1)	20 (4.4)	0.685	0.261	-	-
No	536 (96.9)	432 (95.6)	(0.354 – 1.324)			
Certain infectious and parasitic diseases						
Yes	16 (2.9)	16 (3.5)	0.812	0.562	-	-
No	537 (97.1)	436 (96.5)	(0.401 – 1.642)			
Diseases of musculoskeletal system and connective tissue						
Yes	14 (2.5)	9 (2.0)	1.278	0.700	-	-
No	539 (97.5)	443 (98.0)	(0.548 – 2.982)			
Diseases of the skin and subcutaneous tissue						
Yes	6 (1.1)	7 (1.5)	0.697	0.520	-	-
No	547 (98.9)	445 (98.5)	(0.233 – 2.090)			
Neoplasms						
Yes	8 (1.4)	2 (0.4)	3.303	0.132	3.327	0.147
No	545 (98.6)	450 (99.6)	(0.698 – 15.631)		(0.656 – 16.878)	
Diseases of the blood and blood-forming organs						
Yes	3 (0.5)	2 (0.4)	1.227	0.823	-	-
No	550 (99.5)	450 (99.6)	(0.204 – 7.377)			
Disorders of gallbladder, biliary tract and pancreas						
Yes	2 (0.4)	1 (0.2)	1.637	0.668	-	-
No	551 (99.6)	451 (99.8)	(0.148 – 18.112)			
Charlson Comorbidity Index						
No comorbidity (0)	209 (37.8)	202 (44.7)	-	-	-	-
Mild (1 – 2)	320 (57.9)	239 (52.9)	0.517	0.592	-	-
			(0.047 – 5.750)			
Moderate (3 – 4)	22 (4.0)	10 (2.2)	0.669	0.744	-	-
			(0.060 – 7.426)			
Severe (≥ 5)	2 (0.4)	1 (0.2)	1.100	0.941	-	-
			(0.089 – 13.592)			



Table 4. Factors associated with potentially inappropriate medications use among elderly patient visits in the ED of Universitas Airlangga Teaching Hospital, Indonesia, 2020

Variable	PIM prescription		Univariate analysis**		Multivariate analysis***	
	Yes n (%)	No n (%)	Odds ratio (95% CI)	p-value	Odds ratio (95% CI)	p-value
Number of prescribed medications						
<5	325 (58.8)	387 (85.6)	-	-	-	-
≥ 5 (polypharmacy)	228 (41.2)	65 (14.4)	4.177 (3.056 – 5.709)	0.000	6.954 (4.617 – 10.476)	0.000
*Disease groups according to the ICD-10						
**p-value < 0,05; 95% CI (univariate analysis)						
***p-value < 0,25; 95% CI (multivariate analysis candidate)						

signs and abnormal clinical findings (OR = 1.502; 95% CI: 0.588 – 3.836) were not associated with MRCI score. Table 5 depicts our regression results for factors associated with high complexity use among elderly patients in the ED.

DISCUSSION

PIM is one of the most common drug-related problems encountered in older adults and negatively impacts patients' health and quality of life and also susceptible to medication complexity, contributing to adverse drug effects and elevated risk of unplanned hospitalization.^{15,21-23} This study revealed that over half of the elderly patients in the ED of UNAIR Teaching Hospital received PIMs. Over a third of them received at least one PIM and about two-thirds of PIM use was within the 'PIM use in older adults' category of the 2019 AGS Beers Criteria[®]. Our results are consistent with research conducted by Sharma et al. on the prevalence of PIM in 323 elderly patients at Guru Gobind Singh Medical College and Hospital, Punjab using the 2019 Beers Criteria[®], which demonstrated that 61.9% of prescriptions were PIMs.²⁴ Previous studies have estimated the prevalence of PIMs using the 2015 Beers Criteria[®] albeit in varied health care settings and found similar results to ours, such as in Jordan (49.2% to 62.5% among older patients),^{25,26} Saudi Arabia (61% geriatrics),²⁷ and comparatively lower prevalence was found Japan (47.9% elderly patients),²⁸ and Pennsylvania (35.8% elderly patients).²⁹ Recent studies using the 2019 Beers Criteria[®] conducted in the United Arab Emirates found that 34.7% and in China, about 74.1% of elderly patients had at least one PIM, which is more than double the finding in our study.^{30,31}

This study showed that the most common group of diseases among older adults in the ED was digestive system disorders. In addition, the most widely used PIMs came from the gastrointestinal therapeutic class (43.1%), diuretics (15.1%), and nonsteroidal anti-inflammatory drugs (12.6%). This finding is in line with a study conducted in Qatar, which showed that the most commonly used PIMs were drugs listed in gastrointestinal (84.2%) and analgesics (49.9%).³² Although PIMs prescriptions generally occur in chronic therapy, our

study showed that PIMs could also happen in acute therapy. We found that gastrointestinal drugs (i.e., metoclopramide and omeprazole) were the most common PIM. Metoclopramide was reported to reach 25% extrapyramidal effects.³³ Another study conducted in Brazil reported that 41% of elderly patients received metoclopramide.³⁴ Jeon et al. also showed that in 79,552 elderly patients in South Korea, metoclopramide was one of the most frequently used PIMs (22%).³⁵ On the other hand, omeprazole poses a risk of *Clostridium difficile* infection especially in long-term use.^{4,36} A study in Brazil showed that about a third of the elderly patients received for omeprazole. They further reported that 63% of the omeprazole prescriptions were not indicated.³⁴ Omeprazole, a proton pump inhibitor (PPI) is used for treating gastric acid disorders.³⁷

Some patient-related factors make older adults more susceptible to receiving PIMs in the ED. Our multivariate analyses showed that patients with circulatory system disorders had the highest probability, that is, compared to their counterparts, were two times as likely to get PIMs. Although diseases of the circulatory system were not the most common disease group, the therapeutic profile of cardiovascular patients put them at high risk of receiving PIM in the ED. In Pakistan, a prior study showed that nearly three-quarters of elderly patients with cardiovascular diseases had at least one PIM.³⁸ Furthermore, a European study using the START/STOPP screening criteria found similar results, where 61.5% of elderly patients with cardiovascular disorders received PIM.³⁹ Sheikh-Taha and Dimassi also reported that 87.4% of elderly patients visiting the USA cardiology unit received at least one PIM.⁴⁰ These findings suggest a need for close monitoring and caution in treating patients with cardiovascular disorders.

This research also pointed out that number of medications received by older adults had a significant effect on the prevalence of PIMs in the ED ($p < 0.005$). Elderly patients who received polypharmacy had a risk of experiencing PIM by 6.954 times than older adults who received fewer medications. Alhawassi et al. signified that elderly patients who received polypharmacy were 7.79 times more likely to receive PIM.⁴¹ Other studies conducted in Turkey and Sweden also stated that there was a significant effect of polypharmacy on the number



of PIM ($p < 0.001$).^{42,43}

Aside from potentially inappropriate prescribing, medication complexity also plays a role in drug-related problems. Research conducted by Wimmer et al. supported this finding that comorbidities lead the patients to be treated with more complex medication.¹⁵ In terms of disease groups, elderly patients have a reasonably varied MRCI score. For example, patients' endocrine diseases are more likely to receive additional directions for diabetes management. These likely contribute to increasing the prevalence of complex therapy, as observed in our study. This finding is supported by a prior study which stated that 60% of patients with diabetes mellitus received medications with high complexity (MRCI >16.5).⁴⁴

Regarding the number of medications, 77.1% of older adults received polypharmacy with high medication complexity (MRCI ≥ 24). This finding follows the results of the study of Ferreira et al., where 74.2% of patients who received polypharmacy had high MRCI values (MRCI > 13.0). Another study also showed that 37.5% of elderly patients with polypharmacy had at least

an MRCI > 16.5.⁴⁴ Moreover, dosage form, dosing frequency, and specific drug instructions also contribute to the MRCI value. In this study, the dosage form contributed to the highest average complexity value compared to dosing frequency and additional directions for drug use. Pantuzza et al. reported that among the three components of the medication regimen complexity assessment in two primary healthcare units, the dosing frequency contributed the highest average complexity value with an average MRCI lower than the results of our study. The findings from our study differ from previous studies in part because of differences in the study setting. Most of the medicines prescribed in the ED were for parenteral use, which requires sufficient knowledge (route and time of administration) to avoid medication administration errors. As a result, we found that the dosage form had the highest MRCI values.⁴⁵

Furthermore, our study showed disease of respiratory system and endocrine, nutritional and metabolic diseases had a strong association with MRCI value in the disease group, while the rest were very weak associated (Table 5).

Table 5. Factors associated with high complexity use among elderly patient visits in the ED of Universitas Airlangga Teaching Hospital, Indonesia, 2020

Variable	MRCI mean \pm SD	MRCI		Univariate analysis		Multivariate analysis	
		Low (<24) n (%)	High (≥ 24) n (%)	Odds ratio (95% CI)	p-value	Odds ratio (95% CI)	p-value
MRCI assessment							
Dosage forms	10.95 \pm 6.401						
Dosing frequency	5.51 \pm 4.980						
Additional instructions	0.78 \pm 1.440						
Disease group							
Diseases of the respiratory system							
Yes		99 (13.3)	95 (36.8)	3.815	0.000	7.621	0.000
No		648 (86.7)	163 (63.2)	(2.743 – 5.305)		(3.833 – 15.150)	
Diseases of the digestive system							
Yes		154 (20.6)	23 (8.9)	0.377	0.000	2.911	0.009
No		593 (79.4)	235 (91.1)	(0.237 – 0.599)		(1.312 – 6.459)	
Symptoms, signs and abnormal clinical and laboratory findings, not elsewhere classified							
Yes		142 (19.0)	13 (5.0)	0.226	0.000	1.502	0.395
No		605 (81.0)	245 (95.0)	(0.126 – 0.407)		(0.588 – 3.836)	
Diseases of the circulatory system							
Yes		78 (10.4)	29 (11.2)	1.086	0.720	-	-
No		669 (89.6)	229 (88.8)	(0.691 – 1.707)		-	
Diseases of the nervous system							
Yes		85 (11.4)	9 (3.5)	0.282	0.000	1.746	0.359
No		662 (88.6)	249 (96.5)	(0.139 – 0.568)		0.530 – 5.746	
Endocrine, nutritional and metabolic diseases							
Yes		52 (7.0)	42 (16.3)	2.599	0.000	6.601	0.000
No		695 (93.0)	216 (83.7)	(1.683 – 4.012)		(2.935 – 14.847)	



Diseases of the genitourinary system								
Yes		42 (5.6)	19 (7.4)	1.334	0.314	-	-	
No		705 (94.4)	239 (92.6)	(0.761 – 2.339)				
Injury, poisoning and certain other consequences of external causes								
Yes		29 (3.9)	8 (3.1)	0.792	0.566	-	-	
No		718 (96.1)	250 (96.9)	(0.357 – 1.756)				
Certain infectious and parasitic diseases								
Yes		21 (2.8)	11 (4.3)	1.540	0.255	-	-	
No		726 (97.2)	247 (95.7)	(0.732 – 3.239)				
Diseases of musculoskeletal system and connective tissue								
Yes		22 (2.9)	1 (0.4)	0.128	0.045	1.974	0.582	
No		725 (97.1)	257 (99.6)	(0.017 – 0.956)			0.175 – 22.209	
Diseases of the skin and subcutaneous tissue								
Yes		10 (1.3)	3 (1.2)	0.867	0.829	-	-	
No		737 (98.7)	255 (98.8)	(0.237 – 3.175)				
Neoplasms								
Yes		6 (99.2)	4 (98.4)	1.945	0.306	-	-	
No		741 (0.8)	254 (1.6)	(0.544 – 6.947)				
Diseases of the blood and blood-forming organs								
Yes		4 (0.5)	1 (0.4)	0.723	0.772	-	-	
No		743 (99.5)	257 (99.6)	(0.080 – 6.496)				
Disorders of gallbladder, biliary tract and pancreas								
Yes		3 (0.4)	0 (0.0)	0.000	0.999	-	-	
No		774 (99.6)	258 (100.0)	(0.000 –)				
Charlson Comorbidity Index								
No comorbidity (0)		325 (79.1)	86 (20.9)	-	-	-	-	
Mild (1 – 2)		402 (71.9)	157 (28.1)	0.132 (0.012 – 1.476)	0.100	-	-	
Moderate (3 – 4)		19 (59.4)	13 (40.6)	0.195 (0.018 – 2.169)	0.184	-	-	
Severe (≥ 5)		1 (33.3)	2 (66.7)	0.342 (0.028 – 4.176)	0.401	-	-	
Number of prescribed medications								
<5		680 (95.5)	32 (4.5)	4.011	-	4.373	-	
≥ 5 (polypharmacy)		67 (22.9)	226 (77.1)	(3.345 – 4.809)	0.000	(3.540 – 5.401)	0.000	
<i>MRCI</i> medication regimen complexity index								

This study also found that polypharmacy had a strong correlation with the MRCI value. This is in line with previous studies, which denoted that the number of medications and changes in the dosing frequency associated with the MRCI value ($p < 0.001$).⁴³ Additionally, Advinha et al. described that MRCI value would increase by increasing therapy⁴⁵ and greater MRCI scores are predictive of readmission to hospital.⁴⁷

This study has several limitations. First, we did not assess all drugs listed on the 2019 AGS Beers Criteria[®] available due to hospital formulary at the research site and this single-center study limits the generalizability of the findings beyond the

catchment area served by the study center. Nevertheless, our relatively large number of visits increases the power of the study and limits the possibility of type 1 error.

Moreover, to our knowledge, this study is the first to be conducted in Indonesia to assess the prevalence and risk factors for PIM (using the 2019 AGS Beers Criteria[®]) and medication complexity (using MRCI) among older adults. In addition, the study was conducted in the ED, which has a specificity of the intervention in services. Therefore, our findings will serve as a benchmark for future studies exploring other determinants of PIM use and the medication regimen complexity in Indonesia.



There are no studies that state the cut-off value of MRCI, which can be a reference for categorizing high treatment complexity. Based on the data we collected, it is suggested that future research is needed with varied backgrounds (country, service setting, disease, and number of drugs) and need for some validation and reliability study on the MRCI to be able to determine a universally acceptable cut-off value to define medication complexity are high, moderate or low. Hopefully, after knowing the complexity threshold, PIM and high medication complexity can be controlled to improve patient safety and develop health intervention strategies.

CONCLUSION

Our study found that more than half of older adults admitted

to the ED had PIMs, and a high medication complexity was observed. Patients with disease of Endocrine, nutritional and metabolic disease was risk factors for both PIMs and medication regimen complexity. A strict monitoring and vigilance are needed on PIMs and medication regimen complexity in the elderly with disease groups mentioned in this research to prevent the potential adverse impacts on vulnerable patients and improve the health system.

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