



Potentially Inappropriate Medication (PIM) Prescribing According to Beers Criteria among Elderly Outpatients at Pasar Minggu Hospital, Jakarta

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ABSTRACT

Elderly patients generally have physiological changes that cause multipathological conditions, so they require several drugs to treat these conditions, it is necessary to evaluate the use of drugs to optimize the treatment of geriatric patients. Beers Criteria 2019 is a criteria that is commonly used to present Potentially Inappropriate Medication (PIM). This study aimed to examine the inaccuracy of prescription drugs in the elderly using Beer's criteria 2019. This research is an observational analytic study with a cross-sectional descriptive design. The Beer's 2019 criteria classify PIM into five categories. Data were taken retrospectively as many as 847 prescriptions met the inclusion criteria at the Pasar Minggu Hospital Outpatient Polyclinic. Data were analysed by Univariate and Bivariate. The results showed that from 847 prescriptions for geriatric patients, there are 160 prescriptions for geriatric patients who experienced PIM (18.89%). Percentage of PIM incidents by category; namely, category 1 was 29.17%, category 2 was 6.77%, category 3 was 44.79%, category 4 was 16.67%, and category 5 was 2.60%. The results of the analysis showed that there was a significant relationship between the number of drugs and Heart Failure and CAD with the incidence of PIM with a p value of 0.000 and 0.035. DM and Heart Failure are 2 diseases that significantly influence the incidence of PIM. This study concludes that the elderly are at risk for receiving potentially inappropriate medications.

Keywords: Outpatient; Potentially Inappropriate Medication; Elderly; Geriatric; Beers Criteria

INTRODUCTION

As a result of sustainable development, the elderly population continues to increase, both in terms of number and proportion. Improvements in the fields of health, access to education, employment, quality of life, and various other socio-economic aspects have had an impact on reducing mortality rates and increasing life expectancy. By 2030, it is

estimated that at least 1 in 6 of the world's population will be elderly.¹ The number of world residents aged 60 years and over is expected to increase from 1.4 billion in 2020 to 2.1 billion in 2050. Since 2021, Indonesia has entered an elderly population structure, where around 1 in 10 residents are elderly. Susenas data for March 2022 shows that 10.48% of the population is elderly.²

As they age, elderly people naturally experience a decline in physiological and cognitive function, making them vulnerable to various complex health problems which are usually called geriatric syndromes. Common conditions in the elderly include hearing loss, cataracts and refractive errors, back and neck pain and osteoarthritis, chronic obstructive pulmonary disease, diabetes, depression, and dementia.³ As seniors get older, they are more likely to experience several medical conditions at the same time. So that, Elderly patients use a lot of medication (polypharmacy). Polypharmacy makes elderly patients more susceptible to Potentially Inappropriate Medication (PIM) events, which can lead to an increased risk of ADEs, polypharmacy, and ADRs plus not yet the existence of adequate specific guidelines for the treatment of comorbidities in geriatric patients causes Geriatric patients have the potential to experience PIM. The incidence of PIM in geriatrics is a serious public health problem because it is intrinsically associated with increased morbidity, mortality and health costs³. Therefore, while there are certain drugs or classes of drugs that have a high risk of ADRs and do not have sufficient evidence of benefit, in some cases, safer or more effective therapies may exist for the same clinical condition.⁴

Research has shown that ADEs in the elderly can cause increased visits to the emergency room or inpatient visits, resulting in increased health insurance costs and health care costs.³ The risk of drug-related side effects increases exponentially with the amount of drug used. To date, studies investigating drug-drug interactions in the elderly population are rare. Seeing these projections, there needs to be development in the field of elderly services so that the elderly feel comfortable and safe, both physically and psychologically. Regular evaluation of drug prescriptions is an important component in the treatment of elderly patients. This evaluation can lead to

changes in therapy such as stopping therapy if there is no indication, replacing therapy with safer drugs, reducing or increasing drug doses or adding new drugs so that treatment of elderly patients can be more optimal.⁵

A number of criteria have been published to assist prescribers in detecting potentially inappropriate prescribing events. The Beers Criteria is one of the most commonly used explicit criteria because it is the simplest to apply, easy to follow, the data obtained is reproducible, has strong evidence, is cheap and can clearly identify potential inappropriate drug use.⁶

Research previously by Wulansari et al (2021) regarding PIM with Beer's 2019 criteria in inpatient geriatric patients at RSUD Dr. H. Moch. Ansari Saleh Banjarmasin showed that the prevalence percentage of PIM using Beer's 2019 criteria was 89 patients (63.1%) out of a total of 141 patients. The results of the analysis show that there is a significant relationship between the number of drugs and length of stay with the incidence of PIM in the Inpatient Installation of Dr. RSUD. H. Moch. Ansari Saleh Banjarmasin with p values of 0.03 and 0.00.⁷

Therefore, researchers are interested in specializing research on BPJS/general geriatric patients who receive outpatient treatment because it is based on the fact that the increasing prevalence of geriatric category patients in Indonesia and in the world has led to an increase in the use of prescription and non-prescription drugs in geriatric patients who can leading to increased polypharmacy, ADEs and ADRs. There were 98,273 outpatient visits during the period April 2022 - September 2022 at Pasar Minggu Regional Hospital. Patients over 61 years of age had 29,368 visits. There were 375 geriatric patients during April - September 2022.

Outpatient geriatric patients at Pasar Minggu Regional Hospital tend to receive chronic medication, if for example ADR/ADEs occur while the geriatric patient lives alone at home they will be more at risk. Be Based on the above, it is necessary to conduct research on the

incidence of PIM based on the 2019 Beers criteria in geriatric outpatients at Pasar Minggu District Hospital as an evaluation of drug use in geriatric patients which can be used as a basis for making guidelines/guidelines for drug use in geriatric patients in hospitals and as a direction. for clinicians in hospitals regarding what laboratory tests are important to carry out and to be able to assist pharmacists in carrying out drug therapy monitoring (PTO) so that PIM incidents can be avoided and treatment therapy in geriatric patients becomes better. This study aims to identify the incidence of PIM on geriatric outpatient prescription sheets using the 2019 Beers Criteria at Pasar Minggu Hospital, Jakarta.

METHODS

This research is an observational analytical research. Data are all drug prescriptions from geriatric outpatients who meet the inclusion and exclusion criteria during the period April 2022 - September 2022. Data collection was carried out retrospectively. Identification of PIM incidents uses guidelines that are commonly used in the world, namely the 2019 Beers Criteria.

Data was obtained from prescription reports at the Pharmacy installation and tracing patient medical records through the Hospital Management Information System (SIMRS). Sampling was taken using total sampling technique. The data will be analyzed using statistical analysis. Data analysis by Univariate was carried

out to see the prevalence of PIM in geriatric outpatients. Bivariate analysis was carried out to determine the relationship between the incidence of PIM in terms of the number of drugs and type of disease using the nonparametric chi square test. Multivariate analysis uses logistic regression to see the diseases that influence the incidence of PIM. Data was analysed using SPSS V. 23. This Research has ethical research from Pasar Minggu Hospital with Number: 39/KEPK/RSUDPM/X/2022.

RESULTS AND DISCUSSION

This research was carried out retrospectively by taking a total sample, namely all drug prescriptions from outpatient geriatric patients who sought treatment and took medication at the Pharmacy Installation of Pasar Minggu Hospital in the period April 2022 to September 2022. Based on the research that had been carried out, 847 patient drug prescriptions were obtained. geriatricians who meet the inclusion criteria. All data taken and analyzed are listed as follows:

Characteristics of research subjects

This research involved more of the age group 70 -79 years or middle elderly, of the 847 prescription sheets, 430 prescriptions (50.77%) were obtained from the 70 - 79 year age group, followed by the 61 - 69 year old age group or young elderly as many as 307 prescriptions (36.25%) and finally in the age group > 80 years or the elderly there were 110 prescriptions (12.99%).

Table 1. Characteristics of prescriptions for geriatric outpatients at Pasar Minggu regional hospital

Characteristics	Based on Number of Recipes				
	n = 374	%	n = 847	%	
Age					
61-69 years old	Young Elderly	165	44.12	307	36.25
70-79 years old	Middle Elderly	153	40.91	430	50.77
> 80 years	Old Elderly	56	14.97	110	12.99
Gender					
Man		187	50	467	55.1
Woman		187	50	380	44.9

This data shows that the 70 - 79 year age group tends to get a lot of prescriptions because at this age comorbid diseases begin to appear, so patients need other drugs.

The results of this research are in line with research conducted by Fauziah H, Mulyana R, Martini RD (2020) stated that the age group that received the most prescriptions was the middle elderly.⁵

Based on gender, as table 1 shows that the number of prescriptions for male geriatric patients is greater than for female geriatric patients. There were 380 prescriptions for female geriatric patients (44.86%) and there were more prescriptions for male patients with 467 prescriptions (55.14%). This is in line with research conducted by Bhagavathula AS *et al* (2021) showed that male patients hospitalized received more prescriptions.⁸ This is also in line with research conducted by Handayani U (2018) which confirmed that the high prevalence of degenerative diseases in male geriatric patients is due to unhealthy lifestyles, such as smoking habits, drinking alcohol, eating habits, obesity, excessive physical activity. lack, and environmental pollution. These risk factors can cause 2 times more in male patients, making it easier to trigger other degenerative diseases.⁹ Research conducted by Rumi A, Tahir MT and Ilham M (2023) also shows that the gender characteristic of most patients is male.¹⁰

Research conducted by Sasfi SM, Untari EK and Rizkifani S (2022) shows that the prevalence of men being found to experience disease is caused by their activities or living habits and daily habits. Men have general traits such as freedom, competition, aggression, and so on. These characteristics show that men prefer to act freely without any rules or anything binding. This is different from women, where women have characteristics such as dependency, caring and sensitivity. Apart from that, women have a higher level of obedience or obedience compared to men. These female characteristics cause women to be more obedient and obedient to things that are considered important, including taking medicines or taking care of things related to health.¹¹

Use of medication in outpatient geriatric patients

Table 2 shows that the most prescription sheets were obtained from the internal medicine clinic with 362 prescriptions (42.7%), then the heart polyclinic with 180 prescriptions (21.3%), the neurology polyclinic with 95 prescriptions (11.2%), the pulmonary polyclinic. as many as 60 prescriptions (7.1%), and the urology clinic 60 prescriptions (7.1%).

Table 2. Prescription origin polyclinic for geriatric patients

No	Poly Name	Number of Recipes	Percentage (%)
1	Internal Medicine Poly	362	42.7
2	Heart Poly	180	21.3
3	Neuro Poly	95	11.2
4	Lung Poly	60	7.1
5	Urology Poly	60	7.1
6	Skin and Genital Poly	35	4.1
7	Medical Rehabilitation Poly	24	2.8
8	Orthopedic Poly	12	1.4
9	Psychiatric Poly	9	1.1
10	General Surgery Poly	8	0.9
11	Neurosurgery Poly	1	0.1
12	Midwifery Poly	1	0.1
Grand Total		847	100

Based on this research data, most prescriptions came from internal medicine clinics (42.7%). These results are in accordance with the literature which states that decreased physiological function due to increasing age can cause elderly people to more easily suffer from more than one or multipathological disease. Decreased immune system in the elderly is a cause of degenerative disease problems.¹²

The results of this study are in line with research conducted by Fixen DR (2019) which states that geriatric patients have multipathological characteristics, low physiological reserves, atypical clinical symptoms and signs, decreased functional status, and nutritional disorders.¹³

Table 3. Number of medications received by geriatric patients

Number of Drugs	n	Percentage (%)
≤ 5 drugs	578	68.2
≥ 6 drugs	269	31.8
Total Patients	847	100

Table 3 shows that the average number of geriatric patients receiving medication prescriptions ≤ 578 drugs (68.2%), and those who received ≥ 6 were 269 types of medication prescriptions (31.8%). Based on this research data, the highest number of drugs prescribed by geriatric patients is ≤ 5 medication (68.2%). This is because Pasar Minggu Regional Hospital validates and reviews prescriptions based on the national formulary. So drugs that do not comply with BPJS restrictions cannot be given.

Prevalence of 2019 Beers PIM criteria incidents

Polypharmacy increases the chance or possibility of having drugs included in the Beers Criteria list.^{14,15} The 2019 Beers Criteria is a standard for drug use in geriatric patients which contains a list of drugs that should not be used or avoided

in geriatric patients. Drugs included in the Beers criteria can play a large role in reducing the incidence of ADRs because the Beers criteria contain a list of potentially inappropriate drugs, and the inclusion of a drug in this list does not mean that it should not be used in elderly patients. This list is intended as a guide to identify medications whose risks may outweigh the benefits in older patients. The prescriber's clinical assessment of each patient's needs should always be considered.¹⁶

Table 4 shows that in this study, of the 847 geriatric outpatient prescriptions, there were 160 prescriptions for patients (18.89%) who experienced PIM from various types of PIM that occurred and 687 prescriptions for patients who did not have PIM (81.11%). Based on this data, it can be concluded that the incidence of PIM at Pasar Minggu Regional Hospital is not much (18.89%). This is because pharmacists and pharmacy officers review prescriptions when validating prescriptions. For chronic prescriptions based on BPJS restrictions and for non-chronic drugs following INA-CBGs. Prescriptions that do not match the patient's clinical diagnosis will be immediately confirmed by the prescriber as a consideration when prescribing medication to the patient.

This result is in line with the number of drugs received by patients, namely <5 drugs (Table 3) so that the incidence of PIM at Pasar Minggu Regional Hospital is not high. In research conducted by Isnaini RD, Darmawan E and Dewi FY (2022), it was concluded that polypharmacy was the main causal factor in the incidence of PIM and was in accordance with the findings of previous researchers including Bhagavathula AS *et al* (2021), stating that polypharmacy was the main factor associated with the incidence of PIM ($p = 0.024$).^{16,8}

Table 4. PIM events per recipe sheet based on 2019 Beers criteria

	n	Percentage (%)
Prescriptions with drugs in the 2019 Beers Criteria	160	18.89
Prescription without medication in the 2019 Beers Criteria	687	81.11
TOTAL	847	100.00

The results of this research are in line with research by Sasfi SM, Untari EK and Rizkifani S in 2022 showing the incidence of PIM was 18.3% and this research is in line with research by Isnaini RD, Darmawan E and Dewi FY in 2022 which also showed that there was a PIM incidence of 38.9%.^{11,16}

Table 5. PIM based on gender

Gender	n	Percentage (%)
Man	84	52.50
Woman	76	47.50
TOTAL	160	100.00

As can be seen in table 5 based on gender, men experienced more incorrect prescriptions with 84 prescriptions (52.50%) while women had 76 prescriptions (47.50%). Most of the prescriptions who experienced PIM at the Pasar Minggu Regional Hospital were male because almost all of the elderly male patients visited follow-up polyclinics/were referred to other polyclinics for examination of other complaints.

These results are in line with research by Sasfi SM, Untari EK and Rizkifani S (2022), men experience PIM more often than women because men have a 2-fold higher risk of degenerative diseases compared to women. This degenerative disease can be caused by a bad lifestyle, such as smoking, drinking alcohol, diet, lack of physical activity and obesity. However, women also have a risk of PIM because women will experience menopause, resulting in a decrease in the production of the hormones estrogen and progesterone. A decrease in the production of this hormone will affect the distribution of body fat unfavorably. Poor distribution of body fat can disrupt the body's

metabolic system and make the body vulnerable to degenerative diseases.¹¹

Based on table 6, it shows the types of PIM that occur in geriatric outpatients. Of the 847 prescription sheets for geriatric patients with the highest scores, they are category 3 with a total of 86 (44.79%), category 1 with a total of 56 (29.17%), category 4 with a total of 32 (16.67%), category 2 with a total of 13 (6.77%), and the smallest value category 5 with a total of 5 (2.60%). PIM often occurs in category 3, namely the use of diuretic drugs in heart failure patients. This is because almost all diuretic drugs at Pasar Minggu Regional Hospital actually cause a risk of SIADH. So it is best to reduce the dose of diuresis medication and be accompanied by monitoring sodium levels in the blood, or it could also be accompanied by non-pharmacological therapy such as a combination of foods or limiting the use of salt.

These results are in line with research conducted by Viviandhari D, Nurhasnah N, Sakinah RN and Wulandari D (2022) that the highest incidence of PIM found using the Beers Criteria was found in criterion 3, namely the use of furosemide with 46 incidents, followed by spironolactone with 33 incidents.¹⁷

Research conducted by Rumi A, Tahir MT and Ilham M (2023) showed that category 3 had the most PIM incidents with category 1 namely alprazolam (2.75%), diazepam (1.83%), diclofenac sodium (8.27%) , mefenamic acid (7.34%), meloxicam (4.59%), ketoprofen (2.75%), ketorolac (19.27%), and glimepiride (0.92%). Category 2 is ketoprofen (0.92%), and meloxicam (0.92%). Category 3 is furosemide (34.86%), tramadol (1.83%), and acetylsalicylic acid (1.83%). Category 4 is corticosteroid interactions with NSAIDs (5.5%), and opioid interactions with

benzodiazepines (1.83%). Category 5 is ranitidine (3.67%), and ciprofloxacin (0.92%).¹⁰

Research conducted by Cahyaningsih I and Amaliya N (2019) showed that the incidence of PIM which is included in the category of drugs used with caution in

geriatric patients, the highest percentage is furosemide with 37 uses (71.2) followed by mannitol 13.5%, chlorpromazine (5.8%), haloperidol (3.8%), while spironolactone, fluoxetine and amitriptyline were 1.9% each.¹⁸

Table 6. PIM Incidence per Category Based on 2019 Beers Criteria

PIM Category	Medicine name	QoE	SoR	n	Percentage (%)
Category 1	Alprazolam Tablets	Moderate	Strong	2	1.04
	Amitriptyline Tablets	High	Strong	1	0.52
	Diazepam Tablets	Moderate	Strong	6	3.13
	Glimepiride Tablets	High	Strong	35	18.23
	Lorazepam Tablets	Moderate	Strong	2	1.04
	Risperidone Tablets	Moderate	Strong	1	0.52
	Hyosin Tablets	Moderate	Strong	6	3.13
	Trihexylpenidil Tablets	Moderate	Strong	3	1.56
Sub-Total				56	29.17
Category 2	Dementia - Antipsychotics (risperidone)	Moderate	Strong	1	0.52
	Dementia - Benzodiazepime (lorazepam)	Moderate	Strong	1	0.52
	Kidney Failure - NSAIDs (diclofenac)	Moderate	Strong	2	1.04
	Heart Failure - NSAIDs (diclofenac)	Moderate	Strong	4	2.08
	Heart Failure - NSAIDs (ibuprofen)	High	Strong	2	1.04
	Heart Failure - Thiazolidine (Pioglitazone)	Moderate	Strong	3	1.56
	Sub-Total				13
Category 3	Furosemide Tablets	Moderate	Strong	40	17.70
	Hydrochlorthiazide (HCT) Tablets	Moderate	Strong	25	11.06
	Spirinolactone Tablets	Moderate	Strong	21	9.29
Sub-Total				86	44.79
Category 4	Antidepressant x Benzodiazepime X Antiepileptic	Moderate	Strong	17	8.85
	Corticosteroid X NSAID	Moderate	Strong	11	5.73
	RAS	Moderate	Strong	3	1.56
	Warfarin X NSAID	Moderate	Strong	1	0.52
Sub-Total				32	16.67
Category 5	Gabapentin Capsules*	Moderate	Strong	1	0.52
	Spirinolactone Tab*	Moderate	Strong	4	2.08
Sub-Total				5	2.60
Total				192	100

Category 1

Category 1 PIM incidents, which are drugs that must be avoided in elderly patients, occurred at Pasar Minggu Regional Hospital, namely the drugs Alprazolam, Amitriptyline, Diazepam, Glimepiride, Lorazepam, Risperidone, Hyosine, and Triheksipenidil.

Alprazolam, Diazepam and Lorazepam is category 1 benzodiazepine drugs Beers Criteria 2019 with respective percentages of 1.04%, 3.13% and 1.04%. Alprazolam, diazepam and lorazepam should be avoided based on the 2019 Beers Criteria because they can increase the risk of cognitive impairment, delirium, falls and bone fractures in the elderly.¹⁶ The risk of falls and broken bones in the elderly is a side effect of benzodiazepine drugs, such as dizziness, weakness and drowsiness, which can also reduce concentration and balance in elderly patients.¹⁹

The Beers Criteria have identified short-acting and long-acting benzodiazepines as potentially inappropriate for elderly patients due to the risk of cognitive impairment, falls, and fractures. Short-term use of benzodiazepines has been considered clinically appropriate and is commonly prescribed for minimal sedation use in dentistry. For elderly patients it is best to reduce the dose below the clinical range, considering that elderly patients have increased sensitivity and slower metabolism of benzodiazepines. Drugs with a long half-life, such as diazepam, should be avoided. Hepatic metabolism of diazepam produces the active metabolite, desmethyldiazepam, which prolongs its half-life and elimination effects. Lorazepam is a shorter-acting benzodiazepine, without active metabolites, and is safer for elderly patients who require.²⁰

Amitriptyline is a TCA class drug that pThe percentage of prescriptions at Pasar Minggu Regional Hospital reached 0.52%. Patients at Pasar Minggu Regional Hospital use this drug as an antidepressant and pain reliever. This drug works in the central nervous system which are effective in

depressed patients but are associated with potential side effects are not recommended for use in the elderly.²¹ Based on the 2019 Beers Criteria, amitriptyline should be avoided because the use of amitriptyline in the elderly carries a high risk. Amitriptyline may cause substantial anticholinergic effects, sedation, and orthostatic hypotension¹³. Side effects of anticholinergics on the central nervous system include cognitive impairment, confusion, hallucinations, and delirium. Anticholinergics also affect the peripheral nervous system, including causing dry mouth, dry eyes, and constipation.²² If amitriptyline needs to be used in the elderly, it should be given in low doses to reduce side effects.²⁰

Glimepiride. The percentage of Glimepiride prescriptions for the elderly at Pasar Minggu Regional Hospital reached 18.23%. Glimepiride at Pasar Minggu Regional Hospital is used as an antidiabetes mellitus type 2. This is because some DM patients do not want to use this type of insulin preparation while the provision of DM medication at Pasar Minggu Regional Hospital does not have many choices. UseLong-term glimepiride in type 2 diabetes patients can prolong the risk of hypoglycemia, this occurs because it is in accordance with the mechanism of action of the sulfonylurea group, namely stimulation of pancreatic beta cells to increase insulin production which can reduce blood glucose levels. According to Criteria Beers 2019, the use of glimepiride should be avoided because it has a high risk of causing long-term hypoglycemia in the elderly.¹³ Because the effects of hypoglycemia, which in fatal cases, can reduce the patient's consciousness.²³ Short-acting second generation sulfonylureas such as glipizide are recommended for treating diabetes mellitus in the elderly because they have the lowest risk of hypoglycemia.¹⁹

Risperidone. The percentage of Risperidone prescriptions for the elderly at Pasar Minggu Regional Hospital reached 0.52%, mis an antipsychotic drug. Risperidone at Pasar Minggu Regional

Hospital is given to dementia patients. This is not appropriate according to the 2019 Beers Criteria as use in dementia patients should be avoided unless non-pharmacological options have failed or are no longer possible. This is because risperidone can increase the risk cardiovascular mortality in elderly patients.¹³ Risperidone is effective in reducing aggressive behavior as well as paranoid and delusional behavior in elderly psychotic patients but is known to induce EPS symptoms at low doses (1-2 mg daily) in elderly patients, especially patients with a previous diagnosis of dementia. The maximum recommended dose of Risperidone in the elderly is 2-3 mg/day. The use of Risperidone in low doses has been shown to be associated with increased tremor and rigidity. Quetiapine may be the most appropriate choice as a replacement for risperidone but reports of clinical use are limited.²²

Hyoscyamine. The percentage of hyoscyamine prescriptions for the elderly at Pasar Minggu Regional Hospital reached 3.13%, as an antispasmodic for the elderly. The use of hyoscyamine at Pasar Minggu Regional Hospital as a pain reliever/stomach spasm. According to the 2019 Beers Criteria, the use of hyoscyamine should be avoided due to uncertain effectiveness, the quality of the evidence is moderate and the strength of recommendation is strong. Hyoscyamine has very strong cholinergic effects and is rarely used in European countries.^{13,15} Hyoscyamine should be used with a comprehensive clinical assessment of the patient taking into account the patient's history and physical examination, laboratory assessment, and assessment of gait and balance.⁷

Trihexylpenidyl. The percentage of THP prescriptions for the elderly at Pasar Minggu Regional Hospital reached 1.56%, which is an antiparkinsonian agent. The use of THP at Pasar Minggu Regional Hospital is given to Parkinson's and ischemic stroke patients. The use of THP according to the 2019 Beers Criteria is not

recommended for the elderly with a recommendation level to avoid, the quality of evidence is moderate level and the strength of recommendation is strong.¹³ Trihexylpenidil should be used with a comprehensive clinical assessment of the patient taking into account the patient's history and physical examination, laboratory assessment, and assessment of gait and balance.⁷

Category 2

Drugs in category 2 should be avoided if there is a history of certain diseases or if they can cause interactions between the disease and the drug that can worsen the disease condition. Some of the drugs used in the elderly at Pasar Minggu Regional Hospital in this category include Risperidone, Lorazepam, Diclofenac, Ibuprofen, and Pioglitazone. Total aThe incidence of PIM category 2 was 6.77%. This is due to the condition of elderly patients who like to experience complaints of pain, either neurotropic pain or pain in each joint, so they often receive concocted painkillers.

Dementia – Antipsychotics (Risperidone), Benzodiazepime (Lorazepam)

The incidence of PIM category 2 for dementia with antipsychotic drugs (risperidone) & benzodiazepines (lorazepam) is 0.52% each. The use of risperidone at Pasar Minggu Regional Hospital is used in dementia patients. According to the 2019 Beers Criteria, avoid chronic use of antipsychotics in elderly dementia patients due to adverse CNS effects unless nonpharmacologic options (e.g., behavioral interventions) fail or are impossible and the geriatric patient threatens substantial harm to self or others. Antipsychotics are associated with a greater risk of causing more severe cerebrovascular side effects (stroke) and mortality in dementia patients.¹³

The use of benzodiazepines in patients with dementia should be avoided because of the adverse central nervous system (CNS) side effects, namely somnolence.

The relationship between benzodiazepine use and dementia has been the subject of several studies, with mixed results. There is research that provides evidence of a relationship between the use of benzodiazepines and cognitive decline in elderly patients. In addition to the potential for cognitive decline, the use of benzodiazepines is also associated with an increased risk of falls, fractures, delirium, and accidents when using motor vehicles which can increase morbidity and mortality in the geriatric population.²⁴

Research conducted by Toombs AR, Jung JY and White ND (2018), data shows that patients who are informed about the potential risks of benzodiazepine are more likely to stop using benzodiazepine therapy. Informed patients will try lifestyle modifications to manage insomnia. Therapists should be familiar with the nonpharmacologic approaches recommended for elderly patients. Such as sleep hygiene, sleep restriction, sleep compression, and cognitive behavioral therapy for insomnia (CBT-I). If benzodiazepine therapy is deemed necessary, it should be initiated cautiously, with the lowest effective dose for the shortest possible duration under careful monitoring.²⁴

Kidney Failure - NSAIDs (Diclofenac)

The incidence of PIM category 2 for kidney failure with NSAID drugs is 1.04%. Because pain is a common problem that has been shown to negatively impact quality of life, and both pain and its treatment can cause a variety of morbidities, especially in the CKD population, prompt recognition and appropriate management of pain in this population is essential.

NSAID drugs are included in category 2 because these drugs can worsen the condition of kidney failure in patients elderly. NSAIDs can worsen kidney failure due to inhibition of prostaglandin synthesis. Use of NSAIDs can also increase sodium retention. In research conducted by Roy PJ, Weltman M, Dember LM, Liebschutz J, Jhamb M and HOPE C (2020), group prescription of NSAIDs for elderly

patients with renal failure reached 1.5% for diclofenac sodium. Paracetamol is the safest non-narcotic analgesic for elderly patients with kidney failure.²⁵ However, you must be aware that using high doses can cause chronic nephrotoxicity. Paracetamol or in combination with low potency opioids does have mild anti-inflammatory properties and has been shown to be effective in acute and chronic inflammatory conditions.

Pain management with non-pharmacological interventions, for acute pain, topical thermal therapy can be applied to the painful area in addition to pharmacological therapy. While superficial heat is thought to be helpful in reducing local muscle spasm and pain in the acute phase of injury, cryotherapy (i.e. ice packs) has been suggested to reduce local metabolism, acute inflammation, and pain. Physiological studies, however, suggest that compared with heat therapy, cryotherapy offers greater restorative and therapeutic effects, while topical heat limits its benefits to palliative effects. In many chronic pain conditions, rehabilitation options include exercise programs along with the use of physical modalities included *Transcutaneous Electrical Stimulation* (TENS), topical thermal therapy or ultrasound may be considered. Studies involving animal models of inflammation have revealed that TENS use can modulate pain perception through changes in the peripheral nervous system as well as the spinal cord and descending inhibitory pathways. While TENS has been proposed to be beneficial for both acute and chronic pain, it is most effective for post-operative pain, osteoarthritis and chronic musculoskeletal pain.²⁵

Heart Failure - NSAIDs (Diclofenac, Ibuprofen)

The incidence of PIM category 2 for heart failure with NSAID drugs is 3.13%. The use of NSAIDs at Pasar Minggu Regional Hospital is used to treat pain and arthritis in elderly patients. NSAIDs work by inhibiting phosphodiesterase 3, causing an increase in cAMP concentrations,

resulting in inhibition of prostate platelet aggregation.¹⁹ Diclofenac Sodium, Ibuprofen, is a class of drugs NSAIDs (Non Steroid Anti-Inflammatory Drugs) selective non-cyclooxygenase. The mechanism of action of the NSAID group is by inhibits the enzymes cyclooxygenase-1 and 2 (COX-1 and COX-2). Inhibition of COX enzyme action results in decreased production of prostaglandins (PGE2) and prostacyclin (PGI2) which is an inflammatory mediator.²⁶

Based on the 2019 Beers Criteria, NSAIDs should be avoided for long-term use in the elderly because they can cause perforation. Perforation is a hole or wound in the wall of organs such as the stomach, esophagus, small intestine and large intestine. This drug may increase the risk of gastrointestinal bleeding or stomach ulcers in high-risk age groups (>75 years). Elderly patients are advised to take gastroprotective drugs such as misoprostol to reduce the risk of gastrointestinal bleeding if taking NSAIDs.¹³

Heart Failure - Thiazolidine (Pioglitazone)

The incidence of PIM category 2 for heart failure with the drug pioglitazone was 1.56%. Use of the drug pioglitazone at Pasar Minggu Regional Hospital for patients with type 2 diabetes mellitus. According to the 2019 Beers Criteria, this drug should be used with "caution" in asymptomatic heart failure patients and should be avoided in symptomatic heart failure patients.¹³ Pioglitazone works by binding to PPAR-gamma to increase sensitivity to insulin.¹⁹ The use of pioglitazone in heart failure patients can increase fluid retention which can worsen heart failure.¹³

Category 3

Category 3 are drugs that should be used with "caution." The prescription for category 3 elderly people with the most incidence of PIM in Pasar Minggu Regional Hospital (44.79%) is a class of diuretics used for heart failure patients. Diuretic drugs in the incidence of PIM in this category were 20.83% for furosemide,

13.02% for spironolactone, and 10.94% for hydrochlorothiazide (HCT). Diuretic drugs work to increase the excretion of sodium, water and chloride, which then reduces blood volume and extracellular fluid. Diuretic drugs must be given with "caution" because they can cause hyponatremia or SIADH (Syndrome of Inappropriate Antidiuretic Hormone Secretion).¹⁹ The use of diuretic drugs in the elderly must be followed by monitoring sodium levels.¹³

A study conducted by Astuti R and Susanti R (2022) showed that diuretics were widely prescribed in elderly patients (21.18%).¹⁹ Research conducted by Cahyaningsih I and Amaliya N (2019) shows that for the category of medicines that must be used with caution, the highest frequency of use of the diuretic drug furosemide was 37 uses (71.2%) followed by mannitol with 7 uses (13.5%) followed by with chlorpromazine (5.8%) while haloperidol, spironolactone and amitriptyline were 1.9% each.¹⁸ According to research conducted by Isnaini RD, Darmawan E and Dewi FY (2022) furosemide is a class of strong diuretic drugs. Its use is indicated in edema conditions due to heart, liver and kidney disease, apart from that as additional therapy in acute pulmonary edema and brain edema where it is hoped that a rapid onset of therapy will occur.⁶ Administration of the drug furosemide can cause hyponatremia so that when using it, sodium levels must be monitored closely when starting or changing the dose in geriatric patients.¹³

Category 4

Drugs in category 4 should be avoided because they can cause drug-disease interactions. There were 4 types of interactions at Pasar Minggu Hospital with 32 incidents (16.67%) occurring, namely, interactions between using antidepressants in combination with 3 other antidepressants (antidepressants x benzodiazepim x antiepileptics), interactions between corticosteroids and NSAIDs, interactions between

combinations of RAS drugs with other RAS, and Interaction of Warfarin with NSAIDs.

Antidepressants-Other Antidepressants (Antidepressants x Benzodiazepines x Antiepileptics)

The incidence of PIM in the Antidepressant x Benzodiazepim x Antiepileptic group reached 8.85%. In this study, there were several combinations of drug use that affected the central nervous system because there was a prescription concocted by Pasar Minggu Hospital which contained a combination of these drugs which were used to relieve pain. Simultaneous use of central nervous system drugs with more or less a combination of > 3 classes of drugs that affect the central nervous system (antidepressants, benzodiazepines, antiepileptics) simultaneously can cause severe sedation, respiratory depression, coma, and death.¹³

Based on the drugs.com drug interaction application, use with the drugs amitriptyline, diazepam and gabapentin can increase side effects such as dizziness, drowsiness, confusion and difficulty concentrating. Elderly patients can experience problems in thinking, judgment and motor coordination. The level of drug interactions is moderate.

Corticosteroids - NSAIDs

The incidence of PIM in the corticosteroid-NSAID group reached 5.73%. Use of concurrent drugs with corticosteroids - NSAIDs at Pasar Minggu Regional Hospital to reduce pain. According to the 2019 Beers Criteria, corticosteroids-NSAIDs should be avoided. Concomitant use of corticosteroids and NSAIDs may increase the risk of gastrointestinal side effects such as gastric ulcers, dyspepsia, gastrointestinal bleeding, and gastritis.¹³ The potential for gastrointestinal disorders due to the combination of NSAIDs with corticosteroids is only caused by the COX-1 enzyme. This effect can occur due to the corticosteroid mechanism which inhibits arachidonic acid by phospholipase so that

prostaglandins are not formed. Prostaglandins function as protectors of the digestive tract, so if the formation of prostaglandins is inhibited, it can increase the potential for gastrointestinal disorders. Prescription of COX-2 selective NSAIDs is recommended if the prescription must be combined with corticosteroids.²⁷ If the use of corticosteroids-NSAIDs cannot be avoided, it is recommended to take drugs that can protect the digestive tract.¹³

In research by Isnenia I in 2020, it was stated that the use of corticosteroids and NSAIDs can result in an increased risk of ulcers in the digestive tract because both of them work not selectively on cox-1 so that the stomach's natural protection is reduced.²⁸ Likewise, research conducted by Rumi A, Tahir MT and Ilham M in 2023 resulted in category 4, namely the interaction of corticosteroids with NSAIDs of (5.5%).¹⁰

Based on the drugs.com drug interaction application, use with drugs dexametasone with diclofenac is generally not recommended with the level of interaction being moderate. Combining these drugs may increase the risk of gastrointestinal side effects such as inflammation, bleeding, ulceration, and rarely, perforation. Gastrointestinal perforation is a potentially fatal condition and medical emergency in which a hole forms along the stomach or intestines.

RAS

The incidence of PIM in the RAS x RAS group reached 1.56%. Candesartan, Captopril, Ramipril and Sprinolactone are Renin Angiotensin System (RAS) drugs. The use of RAS at Pasar Minggu Regional Hospital is for hypertension and CHF patients, which according to AGS Beers 2019 if used together will cause an increased risk of hyperkalemia so it is recommended to avoid routine use in elderly patients with ckg stage 3a or above.¹³

Based on the drugs.com drug interaction application, use with drug spironolactone with candesartan can increase potassium levels in the blood.

High potassium levels can cause hyperkalemia, which in severe cases can lead to kidney failure, muscle paralysis, irregular heart rhythm, and heart attack.

Warfarin x NSAIDs

PIM incident at Pasar Minggu Regional Hospital in the group Warfarin x NSAIDs reached 0.52%. Warfarin was used to treat the heart, but the patient also had OA, so he used NSAIDs to treat the pain. According to the 2019 Beers Criteria, concurrent use of Warfarin and NSAIDs can increase the risk of bleeding resulting in use. This must be accompanied by close monitoring.¹³

Based on the drugs.com drug interaction application, use Mefenamic acid drugs together with warfarin can cause easy bleeding. Care must be taken to adjust the dose based on prothrombin time or International Normalized Ratio (INR).

Category 5

Category 5 are drugs that should be avoided, or the dose should be reduced according to the creatinine clearance (CrCl) value. Category 5 experienced 5 PIM incidents (2.60%). The measure of kidney function used in the 2019 Beers Criteria is creatinine clearance and is reported in mL/minute. Some of the category 5 drugs used in the elderly at Pasar Minggu Regional Hospital are Spirinolactone and Gabapentin.

Spirinolactone

Percentage of prescriptions spironolactone in patients with CrCl < 30 mg/ml among the elderly at Pasar Minggu Hospital reached 2.08%. Spironolactone is used at Pasar Minggu Regional Hospital as a potassium-saving diuretic hypertension drug. Spirinolactone has a mechanism of action in the distal tubule of the kidney, inhibiting the reabsorption of sodium and water ions and retaining potassium ions. Based on the 2019 Beers Criteria, the use of spirinolactone should be avoided in patients with creatinine clearance levels <30 mL/minute because it can increase

potassium levels. So special monitoring is needed for elderly patients, because according to research by Viviandhari et al (2022) elderly patients are at higher risk of experiencing hyperkalemia.¹⁷

Gabapentin

Percentage of prescriptions Gabapentin in patients with CrCl < 60 mg/mL among the elderly at Pasar Minggu Regional Hospital reached 0.52%. The use of gabapentin at Pasar Minggu Regional Hospital to reduce neurotrophic pain or diabetic polyneuropathy. The 2019 Beers Criteria indicate that the dose of gabapentin should be reduced in patients with creatinine clearance levels <60 mL/minute because it can cause CNS side effects.

Gabapentin is excreted entirely by the kidneys, and so the risk of use is highest in people with chronic kidney disease.²⁹ In addition, elderly patients tend to experience decreased clearance due to decreased kidney function, so it is recommended to use gaba by reducing the dose. The recommended dose is 300-1200 mg three times a day when the creatinine clearance level is 60 mL/minute. Meanwhile, when the creatinine clearance level is >30-59 mL/minute, a dose of 200-700 mg twice a day is recommended.³⁰

The relationship of the amount of medication with the incident of PIM

Based on the output table 7, the Asymp value is known. Sig (2-sided) in the Pearson Chi-Square test is 0.000. Because the sig (2-tailed) significance value is smaller than 0.05, it means that H0 is rejected and H1 is accepted. Thus it can be interpreted that there is a relationship between the amount of medication and the event PIM on geriatric outpatients at Pasar Minggu District Hospital, Jakarta. With the information 0 cells (0.0%) have expected count less than 5, this means that the assumption of using the chi square test in this research has met the requirements.

Table 7. Relationship between the amount of medication and the incidence of PIM

Independent Variable	PIM n (%)		Total	P value
	YES	No		
Number of Drugs	< 6 Medication	70	508	0,000
	> 5 Medications	90	179	
Total		160	687	847

This is also in accordance with what was done by Wulansari A, Wiedyaningsih C and Probosuseno P (2021) that the results of research analysis conducted at RSUD Dr. H. Moch. Ansari Saleh Banjarmasin showed that there was a significant relationship between the amount of medication and the incidence of PIM with a p value of 0.03.⁷ Likewise, research conducted by Darmawan E, Ahmad H, Perwitasari DA and Kusumawardani N (2020) stated that the results of bivariate analysis (Fisher's Exact Test) showed that the number of drugs prescribed was significantly related to the use of PIMs (p=0.049). Patients who are prescribed 10 or more types of drugs (polypharmacy) are 11 times more likely to be prescribed PIMs than those who are prescribed <10 types of drugs.⁶ This is also in accordance with research conducted by Bhagavathula AS (2021) which states that the number of drugs prescribed (polypharmacy) is the main predictor factor associated with PIMs in geriatric patients (p=0.024).⁸ Research conducted by Almeida TA et al (2019) states that polypharmacy is associated with PIMs (p<0.001).⁴

The relationship of the number of diseases and the incident of PIM

To see the relationship between disease and the incidence of PIM, researchers used bivariate chi square analysis. You can see in table 8 and 9 the relationship between disease and the incidence of PIM.

Based on the output table for sufferers of DM, Neurotrophic Pain, Hypertension, Dementia and CVD SI, each Asymp value is known. The Sig (2-sided) on the Pearson Chi-Square test is 0.089, 0.848, 0.099, 0.887, and 0.188. Because the sig (2-tailed)

significance value is greater than 0.05, it means that H0 is accepted and H1 is rejected. Thus it can be interpreted that nothere is a relationship between the sufferersDM, Neurotrophic Pain, Hypertension, Dementia and CVD SI with events PIM ongeriatric outpatients at Pasar Minggu District Hospital, Jakarta. With the information 0 cells (0.0%) have expected count less than 5, this means that the assumption of using the chi square test in this research has met the requirements.

Meanwhile for Suffering from heart failure and CAD, the Asymp value is known. Sig (2-sided) in the Pearson Chi-Square test is 0.000 and 0.035 respectively. Because the sig (2-tailed) significance value is smaller than 0.05, it means that H0 is rejected and H1 is accepted. Thus it can be interpreted that there is a relationship between suffererheart failure and CAD with events PIM on geriatric outpatients at Pasar Minggu District Hospital, Jakarta. With the information 0 cells (0.0%) have expected count less than 5, this means that the assumption of using the chi square test in this research has met the requirements.

Table 8. Number of Diseases

Number of Diseases	Number of Recipes
0	279
1	271
2	188
3	83
4	18
5	7
6	1
Grand Total	847

Table 9. Relationship Between Disease and PIM Incidence

Independent Variable		PIM n (%)		Total	Asymp. Sig (2-sided)
		YES	No		
DM	Yes	62	218	280	0.089
	No	98	469	567	
Heart failure	Yes	45	77	122	0,000*
	No	115	610	725	
Neurotrophic Pain	Yes	18	81	98	0.848
	No	142	606	748	
Hypertension	Yes	52	179	231	0.099
	No	108	508	616	
CAD	Yes	43	133	176	0.035*
	No	117	554	671	
Dementia	Yes	5	23	28	0.887
	No	155	664	819	
CVD SI	Yes	18	55	73	0.188
	No	142	632	774	

Note: * $p < 0.05$, DM: Diabetes Mellitus, CAD: Coronary Artery Disease, CVD SI: *Cardio Vascular Disease-Ischemic Stroke*

Factors influencing the incident of PIM in outpatient geriatric patients

Statistical analysis in the form of logistic regression was carried out to determine the factors that influence the incidence of PIM in geriatric outpatient prescriptions. Logistic regression analysis was carried out after obtaining the results of the bivariate analysis, then a multivariate analysis was carried out to determine the independent variables that influenced the incidence of PIM. In the initial stage of the analysis, several determinant factors were determined as independent variables that influence the incidence of PIM as the dependent variable. These independent variables include:

1. Patient factors include age and gender
2. Origin of Polyclinic
3. Number of drugs obtained
4. Types of Disease (DM, Heart Failure, Neuropathic Pain, Hypertension, CAD, Dementia and CVDSI).

Multivariate analysis, only variables that have a significance value <0.25 at the bivariate stage are included in the logistic

regression model. However, here the researcher includes all variables that have determining factors in the incidence of PIM.

In table 10, the dependent variable code is displayed, namely Yes, PIM occurrence and No PIM occurrence in the logistic regression analysis process.

Table 10. Dependent Variable Encoding

Original Value	Internal Value
PIM	0
No PIM	1

In table 11 Multivariate analysis test results of multiple logistic regression method Backward Stepwise (Conditional). The results of the multivariate logistic regression analysis test using the Backward Stepwise (Conditional) method can be seen as to what determinant factors have the most dominant influence on the incidence of PIM.

Table 11. Multivariate Test Results

Disease Variables	Sig.	Exp(B)
Poly Origin	0.004*	1,215
Gender	0.965	1,009
Age	0.761	0.941
Number of Drugs	0,000*	0.301
Diabetes mellitus	0.316	1,257
Heart failure	0,000*	3,308
Neuropathic Pain	0.331	0.752
Hypertension	0.119	1,437
CAD	0.753	0.932
Dementia	0.730	1,203
CVDSI	0.205	0.681

Note: *p < 0.05 Sig. = Significance, Exp (B) = Odd Ratio (OR)

Where in step 8 the variables in the equation in the attachment can be interpreted as follows:

1. Origin Variable Poly has a Sig value. (P Value) of 0.04 (<0.05), concluding that poly origin has a partial effect on the incidence of PIM with Exp (B) of 1.215.
2. Variable The amount of medicine has a Sig value. (P Value) of 0.000 (< 0.05), concluding that the amount of medication has a partial effect on the incidence of PIM with Exp (B) of 0.301.
3. Disease Variables Heart Failure has a Sig value. (P Value) of 0.000 (< 0.05), concluding that heart failure partially influences the incidence of PIM with Exp (B) of 3.308.
4. Variable Hypertension has a Sig value. (P Value) was 0.102 (> 0.05), concluding that hypertension had no significant effect in the multivariate analysis on the incidence of PIM with Exp (B) of 1.461.

So it can be concluded that the disease variables with the most dominant influence are:

1. Polyclinic Origin Variable with an Odd Ratio of 1.215 and a sig value. (P-Value) of 0.04 (< 0.05)
2. Variable Number of Drugs with an Odd Ratio of 0.301 and a sig value. (P-Value) of 0.000 (< 0.05)

3. The variable heart failure has an Odd Ratio of 3.308 and a sig value. (P-Value) of 0.000 (< 0.05)
4. Hypertension variable with an Odd Ratio of 1.461 and a sig value. (P-Value) is 0.102 (> 0.05), so it can be concluded that the hypertension variable has no significant effect in the multivariate analysis. (see step 8 in the Variables in the Equation table)
5. CVDSI variable with an Odd Ratio of 0.690 and a sig value. (P-Value) is 0.220 (> 0.05), so it can be concluded that the CVDSI disease variable has no significant effect in the multivariate analysis (see step 8 in the Variables in the Equation table).
6. Neuropathic Pain Variable with an Odd Ratio of 0.752 and a sig value. (P-Value) is 0.331 (> 0.05), so it can be concluded that the variable Neuropathic Pain has no significant effect in the multivariate analysis (see step 8 in the Variables in the Equation table).
7. DM variable with an Odd Ratio of 1.257 and a sig value. (P-Value) is 0.316 (> 0.05), so it can be concluded that the DM variable has no significant effect in the multivariate analysis (see step 8 in the Variables in the Equation table).
8. Dementia variable with an Odd Ratio of 1.200 and a sig value. (P-Value) is 0.734 (> 0.05), so it can be concluded that the Dementia disease variable has no significant effect in the multivariate analysis (see step 8 in the Variables in the Equation table).
9. Age variable with an Odd Ratio of 0.941 and a sig value. (P-Value) is 0.761 (> 0.05), so it can be concluded that the age variable has no significant effect in the multivariate analysis (see step 8 in the Variables in the Equation table).
10. Gender variable with an Odd Ratio of 1.009 and a sig value. (P-Value) is 0.965 (> 0.05), so it can be concluded that the Gender variable has no significant effect in the multivariate analysis (see step 8 in the Variables in the Equation table).
11. CAD variable with an Odd Ratio of 0.931 and a sig value. (P-Value) is 0.748

(> 0.05), so it can be concluded that the CAD variable has no significant effect in the multivariate analysis (see step 8 in the Variables in the Equation table).

CONCLUSION

The results of the analysis showed that there was a significant relationship between the number of drugs, Heart Failure and CAD with the incidence of PIM with a p value of 0.000 and 0.035. DM and Heart Failure are 2 diseases that significantly influence the incidence of PIM. This study concludes that the elderly are at risk for receiving potentially inappropriate medications.

Conflict of Interest

The authors declare no conflict of interest.

Authors' Declaration

The authors hereby declare that the work presented in this article is original and that any liability for claims relating to the content of this article will be borne by them.

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