ASSOCIATION BETWEEN BEERS' CRITERIA-BASED ASSESSMENT OF MEDICATION USE AT DISCHARGE AND UNPLANNED HOSPITAL READMISSIONS OR EMERGENCY DEPARTMENT VISITS AMONG OLDER PATIENTS

BY

WATCHARASAK SOMBUT

A THESIS SUBMITTED IN PARTIAL FULFILLMENT OF THE REQUIREMENTS

FOR THE DEGREE OF MASTER OF SCIENCE

(PHARMACEUTICAL AND HEALTH SCIENCES)

FACULTY OF PHARMACY

THAMMASAT UNIVERSITY

ACADEMIC YEAR 2025

Ref. code: 25686518030066AYF

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ENTITLED

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was approved as partial fulfillment of the requirements for

the degree of Master of Science (Pharmaceutical and Health Sciences)

on November ๑๗, 2025

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Thesis Title	ASSOCIATION BETWEEN BEERS' CRITERIA-BASED ASSESSMENT OF MEDICATION USE AT DISCHARGE AND UNPLANNED HOSPITAL READMISSIONS OR EMERGENCY DEPARTMENT VISITS AMONG OLDER PATIENTS
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Academic Year	2025

ABSTRACT

Background: Evidence on the association between potentially inappropriate medications (PIMs) and adverse outcomes after hospital discharge remains limited and contradictory. This study aimed to determine the prevalence, predictors, and impact of PIMs at discharge on early unplanned readmissions and emergency department (ED) visits in older adults.

Methods: This retrospective cohort study analyzed electronic medical records of older patients discharged from a tertiary-care hospital to home. Prevalence of PIMs was determined with the 2023 Beers’ criteria. Predictors were determined with logistic regression. Patients were followed for 90 days to assess unplanned readmissions and ED visits. Multiple Cox regression and parametric survival analysis determined the association between PIMs and early readmissions/ED visits.

Results: Among 4,012 older patients, 2,299 (57.3%) were discharged with at least one PIM. Factors independently associated with PIM use included a higher Charlson Comorbidity Index (OR 1.08, 95% CI 1.01–1.15, p=0.02), longer hospital stay (OR 1.01, 95% CI 1.00–1.02, p=0.01), and a greater number of discharge medications (OR 1.26, 95% CI 1.24–1.29, p<0.001). Within 90 days post-discharge, unplanned readmissions or ED visits occurred in 183 of 2,299 (7.96%) patients with PIMs and 89 of 1,713 (5.20%) without PIMs. In multivariable Cox regression, PIM use was associated with a non-significant increase in the risk of unplanned readmissions and ED visits (HR 1.15, 95% CI 0.87–1.51, p = 0.32), a finding consistent across parametric survival models using Weibull, exponential, lognormal, and log-logistic distributions.

Conclusion: PIMs were highly prevalent in older patients at discharge, with comorbidity burden, the duration of hospital stays, and polypharmacy as significant predictors. However, PIMs were not significantly associated with early unplanned readmissions or unplanned readmissions and ED visits.

Keywords: Early readmission; Potentially inappropriate medications; PIMs; Older adults; Unplanned visits.

Ref. code: 25686518030066AYF

ACKNOWLEDGEMENTS

I wish to extend my profound gratitude to all those whose support and contributions have made the completion of this master's thesis possible.

In particular, I am especially indebted to my thesis advisor, Assoc. Prof. Dr. Arom Jedsadayanmata, whose steadfast guidance, insightful feedback, and expert advice have been instrumental in shaping and refining this research.

I am grateful to the faculty and staff of the Division of Pharmaceutical Care at the Faculty of Pharmacy, Thammasat University, and Thammasat University Hospital for providing the necessary resources and creating an academic environment conducive to my research.

My heartfelt appreciation goes to my family and friends for their unconditional love, patience, and encouragement. Their constant support has been a source of strength throughout my studies.

Thank you all for your invaluable contributions to this work.

Watcharasak Sombut

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LIST OF ABBREVIATIONS

Symbols/Abbreviations	Terms
ACBS	Anticholinergic Cognitive Burden Scale
ACCI	Age-Adjusted Charlson comorbidity Index
ACEi	Angiotensin-converting enzyme inhibitor
ADE	Adverse drug event
ADR	Adverse drug reaction
AGS	American Geriatrics Society
aHR	Adjusted hazard ratio
AIC	Akaike Information Criterion
aOR	Adjusted odds ratio
APACHE II score	Acute Physiology and Chronic Health Evaluation II
ARB	Angiotensin II receptor blockers
ARNI	Angiotensin receptor neprilysin inhibitor
AUC	Area Under the Curve
BIC	Bayesian Information Criterion
BMI	Body mass index
CCI	Charlson comorbidity Index
cHR	Crude hazard ratio
CI	Confidence interval
CKD	Chronic kidney disease
CNS	Central nervous system
COX-2	Cyclooxygenase-2
CRF	Case record form
CVD	Cardio vascular disease
D/C	Discharge
DAG	Directed acyclic graph

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Symbols/Abbreviations	Terms
DDI	Drug-drug interaction
DOACs	Direct oral anticoagulants
DOLA	Drug-Oriented Listing Approach
ED	Emergency department
EPV	Events per predictor Variable
GDMT	Guideline-directed medical therapy
HR	Hazard ratios
ICD	International Classification of Diseases
IQR	Interquartile range
LOS	Length of stay
LRDTE	List of Risk Drugs for Thai Elderly
MRA	Mineralocorticoid receptor antagonists
NSAIDs	Non-steroidal anti-Inflammatory drugs
NSTEMI	Non-ST elevation myocardial infarction
NVAF	Non-valvular atrial fibrillation
OPD	Outpatient department
OR	Odds ratio
OTC	Over-the-counter
PDx	Principal diagnosis
PH	Proportional hazards
PILA	Patient-in-Focus Listing Approach
PIMs	Potentially inappropriate medications
PIP	Potentially inappropriate prescribing
PPIs	Proton pump inhibitors
PPOs	Potential prescribing omissions
RCT	Randomized controlled trial
ROC	Receiver Operating Characteristic curve
SD	Standard deviation
SES	Socioeconomic status

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Symbols/Abbreviations	Terms
SGLT2	Sodium–glucose cotransporter 2
START	Screening Tool to Alert to Right Treatment
STOPP	Screening Tool of Older Persons' Prescriptions
VIF	Variance inflation factor
VTE	Venous thromboembolism

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CHAPTER 1
INTRODUCTION

The proportion of older adult populations is increasing in many countries worldwide. According to data from the WHO (World Health Organization), the number of individuals aged 60 and above, classified as older adults, is expected to rise to 1.4 billion by 2030 and exceed 2.1 billion by 2050, accounting for two-thirds of the global population.[1] This growth is particularly pronounced in countries with lower-middle-income economies, such as Thailand, which is already considered an aging society. According to 2022 census data, 19.21% of Thailand's population, or approximately 12.69 million people, were older adults.[2] It is projected that Thailand will transition into a "Super Aged Society" by 2035, with over 30% of its population being older adults.[3] The increasing number of older adults will undoubtedly have significant implications for Thailand's healthcare system in the future.

Older adults frequently encounter challenges related to medication use. Evidence indicates that hospitalizations among this population resulting from medication-related problems arise from multiple causes, including adverse drug events, poor adherence to prescribed regimens, and medication errors.[4] Adverse drug events in older individuals are often linked to the prescription of inappropriate medications, commonly referred to as Potentially Inappropriate Medications (PIMs). Beyond chronological age, geriatric syndromes such as frailty and multimorbidity exacerbate vulnerability to PIM-related adverse outcomes. Incorporating these dimensions would provide a more holistic understanding of medication-related risks in older adults. For example, first-generation antihistamines and antidepressants with strong anticholinergic activity elevate the likelihood of anticholinergic adverse effects, thereby increasing the risk of falls, delirium, and dementia. Likewise, benzodiazepine use is associated with heightened risks of cognitive decline, delirium, falls, and fractures, whereas non-COX-2-selective NSAIDs raise the risk of gastrointestinal ulceration or bleeding in older adults.[5] Systematic reviews and meta-analyses have demonstrated that PIM use in older patients increases the likelihood of adverse drug events by 1.34 to 1.44 times,[6-7] emergency department visits by 1.63 to 1.72 times,[6-8] and hospital admissions by 1.25 to 1.52 times,[6-8] compared with those who are not prescribed PIMs.

A review of the literature indicates that research on health outcomes associated with PIM use during transitional care remains scarce and inconsistent. Some investigations have demonstrated that PIMs prescribed at discharge are linked to a heightened risk of unplanned readmissions[9-12] or outpatient visits.[9] In contrast, other studies have reported no significant relationship[13-16], while a few have even suggested a decreased likelihood of adverse outcomes.[17-18] Such inconsistencies may be attributable to factors unique to each study, including sample size, inclusion and exclusion criteria, assessment approaches, follow-up periods, data analytic strategies, and outcome measures. Notably, the present review highlights that no comparable studies have been undertaken in Thailand. Most studies conducted in Thailand have primarily examined the use of PIMs during hospitalization, whereas prescribing PIMs at discharge has not been investigated.

This study aims to examine the prevalence of PIMs at discharge, identify predictive factors, and investigate the relationship between receiving PIMs at discharge and all readmissions, unplanned readmissions, and emergency-department visits within 90 days among older patients at a hospital. The evaluation will use the 2023 updated AGS Beers Criteria®[5], marking it as the first study in Thailand to investigate PIMs during transitional care. We hypothesize that the presence of PIMs at discharge is associated with an increased risk of all readmissions, unplanned readmissions, and emergency department visits within 90 days. The findings from this research will contribute to the improvement of medication prescribing practices. Specifically, the hospitalization provides an opportunity for healthcare providers to review and adjust the patient’s medication regimen appropriately, with support from pharmacists to ensure more suitable medication use.

CHAPTER 2
REVIEW OF LITERATURE

2.1 Potentially inappropriate medications: PIMs

2.1.1 The meaning of PIMs

Inappropriate prescribing or Potentially Inappropriate Prescribing (PIP) occurs when medications are prescribed that may cause more harm than benefit, or when necessary medications are omitted, which could result in harm or danger to older patients. PIP encompasses both PIMs and Potential Prescribing Omissions (PPOs). PIMs refer to medications that carry a higher risk of adverse effects than potential benefits for the patient, while PPOs involve medications that could be beneficial to the patient but are not prescribed due to oversight, potentially leading to adverse events.

2.1.2 Tools for assessing PIMs

Currently, the tools used to assess PIMs are categorized into three types based on the assessment approach: 1) Explicit tools, 2) Implicit tools, and 3) Tools combining explicit criteria with evaluator judgment. Explicit tools can be further divided into two categories: the Patient-in-Focus Listing Approach (PILA), which requires access to patient data to determine whether a medication qualifies as a PIM, and the Drug-Oriented Listing Approach (DOLA), which does not require patient data but instead evaluates the medication based solely on drug-related information. Meanwhile, DOLA+ refers to tools that require specific patient data, particularly the indication for the medication related to the patient's disease, to classify a medication as a PIM. A systematic literature review revealed 76 tools used for PIMs assessment, with only 9 categorized as PILA, 26 as DOLA, and 38 as DOLA+.[19] Notable tools widely used globally include the STOPP/START criteria, Amsterdam tool, Beers criteria, EU(7)-PIM list, and PRISCUS, among others.[20] The review found that Beers criteria and STOPP/START criteria are the most commonly used assessment tools.[21-22] However, these tools were developed for use in Western countries. Chang et al.[23] conducted a systematic review and concluded that explicit tools suitable for Asian countries should include those that address drug groups such as antipsychotics, antidepressants, and antihistamines.

2.1.3 STOPP/START criteria

The STOPP and START criteria were established by a European consortium of experts in geriatric pharmacotherapy. As explicit tools, they provide well-defined indicators for evaluation, encompassing STOPP criteria for potentially PIMs and START criteria for PPOs. Initially introduced in 2008 with 65 STOPP and 22 START items, the criteria have since been expanded. The latest edition, Version 3[24] (2023), comprises 133 STOPP and 57 START criteria, reflecting an increase of more than 67% compared with the 2015 version, which contained 80 STOPP and 35 START items, as presented in Table 2.1.

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Table 2.1 The differences in the number of criteria in the STOPP/START tool across different versions.[24]

Version/ Year of publication	No. of STOPP criteria	No. of START criteria	Increasing
Version 1, 2008	65	22	-
Version 2, 2015	80	34	31%
Version 3, 2023	133	57	67%

Abbreviations: No.= Number

The most recent version of the STOPP/START criteria was published in 2023, following updates based on the previous version. These updates were derived from a systematic literature review of academic publications from April 2014 to March 2022, conducted by a panel of experts in geriatric pharmacotherapy from eight European countries. The final version includes a total of 190 assessment criteria. The STOPP criteria comprise Sections A-M, consisting of 133 items categorized according to their effects on various body systems. The START criteria consist of Sections A-L, containing 57 items that address issues such as drug-drug interactions, disease-drug interactions, polypharmacy, and medications that may lead to significant adverse effects in older adults, such as those associated with an increased risk of falls.

2.1.4 Beers Criteria®

The Beers Criteria® was originally formulated in 1991 by Mark Beers at the University of California, Los Angeles, with the purpose of evaluating potentially inappropriate medication use among nursing home residents. It was later revised for use with the general older population in 1997 and further developed internationally in 2003. Since 2010, the American Geriatrics Society has overseen its updates, with revisions made every 3-4 years, including in 2012, 2015, 2019, and the most recent version in 2023. The Beers Criteria® is an explicit tool that provides clear assessment criteria to identify and classify potential risks of adverse drug reactions in older adults. This tool encourages healthcare professionals to make more appropriate medication choices or adjustments. The current version reflects the input of international experts in the relevant fields. The criteria are designed to assess inappropriate medication use in individuals aged 65 and older across various healthcare settings, including outpatient, emergency, and inpatient care, with the exception of end-of-life patients. Although the criteria are internationally recognized, they were initially developed and refined for use in the United States. It is recommended that when applying these criteria in other countries, clinical expert judgment must always be involved, as the criteria are not rigid requirements. Healthcare professionals should combine their medical knowledge and expertise to ensure the criteria are appropriately applied to each patient.

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The AGS 2023 updated Beers Criteria®[5] is based on a systematic literature review of academic publications published from June 1, 2017, to May 31, 2022. The list of potentially inappropriate medications consists of five key tables, which have been in use since the 2019 version, including table 2-6.

The key, commonly used table in the clinical practice of inappropriate medications in older patients is Table 2, which categorizes inappropriate medications by drug class or disease group. For instance, all drugs in the Antihistamines group in the first edition are classified as highly anticholinergic. As individuals advance in age, the efficiency of drug elimination declines, thereby elevating the likelihood of adverse effects such as sedation, cognitive impairment, xerostomia, constipation, and other anticholinergic manifestations. These adverse effects have been associated with an increased incidence of falls, delirium, and dementia—even among relatively younger members of the older adult population. Furthermore, the use of all non-COX-2-selective NSAIDs has been shown to heighten the risk of gastrointestinal bleeding and peptic ulcer disease, particularly in those aged 75 years and above.

The differences between the 2019 and 2023 editions are presented in Tables 8, 9, and 10 of the AGS 2023 updated Beers Criteria®[5]. For example, certain medications were added or removed from the evaluation criteria due to new scientific evidence. Some medications were removed because they were used infrequently in the United States, while others were moved from Table 4 to Table 2 based on supporting evidence. Additionally, some criteria or descriptions for specific medications were modified. Overall, the number of medications classified as potentially inappropriate has increased compared to the 2019 criteria. However, following the literature review conducted by the researcher, no studies have yet used the new criteria to date.

2.1.5 The differences between the Beers and STOPP Criteria

A systematic review of the literature indicated that the Beers Criteria and the STOPP/START criteria are the most frequently utilized instruments for evaluating PIMs.[21–22] Several investigations have compared these tools in terms of their assessment approaches and study outcomes. Findings from some studies[25–29] demonstrated that, when applied to the same cohort, the Beers Criteria® identified a higher prevalence of PIMs than the STOPP Criteria. In addition, Blanco-Reina et al.[28] reported that the Beers Criteria® exhibited greater sensitivity and broader applicability in clinical settings. Overall, the Beers Criteria® showed a stronger alignment with study outcomes, as evidenced by its higher detection rate of PIMs relative to the STOPP Criteria. Comparison of PIMs: AGS Beers criteria 2023[5] VS STOPP criteria V3 2023[24] is presented in Table 2.2. A summary of the differences among PIM assessment tools and the corresponding prevalence of patients with at least one identified PIM is presented in Table 2.3.

Table 2.2 Comparison of PIMs: AGS Beers Criteria 2023[5] VS STOPP Criteria V3 2023[24]

System / Drug Category	PIMs appearing in both Beers and STOPP	Unique to Beers 2023	Unique to STOPP V3 2023
1. Anticholinergic, Antihistamine	Diphenhydramine, Chlorpheniramine, Hydroxyzine, Promethazine	Cyproheptadine, Doxylamine, Meclizine, Triprolidine	Hyoscine, Tolterodine, Oxybutynin, Trihexyphenidyl, Procyclidine
2. Benzodiazepines, Z-drugs	All benzodiazepines (e.g., diazepam, lorazepam, temazepam); Z-drugs (zolpidem, zaleplon, zopiclone)	Explicitly includes 'avoid in delirium' and 'risk of abuse/addiction'	Specifies duration ≥4 weeks for BZDs and ≥2 weeks for Z-drugs; Adds context of falls, withdrawal, dementia-related agitation
3. Antipsychotics	Haloperidol, Olanzapine, Risperidone, Quetiapine	Aripiprazole	Chlorpromazine, Clozapine, Thioridazine, Fluphenazine; Duration limits (>3 months in dementia); Not to use in Parkinson’s disease or dementia with Lewy bodies
4. Antidepressants (TCAs, SSRIs)	Amitriptyline, Doxepin (>6 mg/day), Paroxetine	Imipramine, Nortriptyline	TCAs contraindicated in dementia, glaucoma, constipation, urinary retention; SSRIs with hyponatremia or bleeding history
5. Cardiovascular agents	Amiodarone (not first-line), Digoxin (avoid >0.125 mg/day), Non-selective alpha-blockers (e.g., doxazosin), Central alpha-agonists (clonidine)	Rivaroxaban (long-term AF/VTE), Dipyridamole short-acting, Warfarin vs DOAC preference	ACEI/ARB in hyperkalemia; Statin ≥85 years with frailty; Loop diuretic for ankle edema; Beta-blocker + Verapamil/Diltiazem; Thiazide with hyponatremia/hypokalemia

Table 2.2 Comparison of PIMs: AGS Beers Criteria 2023[5] VS STOPP Criteria V3 2023[24] (Continue)

System / Drug Category	PIMs appearing in both Beers and STOPP	Unique to Beers 2023	Unique to STOPP V3 2023
6. Anticoagulant, Antiplatelet	Aspirin for primary prevention, Ticlopidine, Combination Aspirin + Clopidogrel (long-term)	Explicitly differentiates VTE/AF indications	DOAC + Verapamil/Diltiazem; SSRIs + anticoagulant (bleeding risk); NSAIDs + anticoagulant
7. NSAIDs, Analgesics	Avoid chronic NSAIDs use; Avoid with heart failure or CKD	Adds long-term systemic use increases thrombotic risk	COX-2 exception; NSAIDs + Corticosteroid; NSAIDs with hypertension (>170/100 mmHg); NSAIDs >3 months for OA
8. Endocrine, Metabolic	Sulfonylureas (Glyburide/Glibenclamide)	Sliding-scale Insulin monotherapy	Glibenclamide, Glimepiride, Chlorpropamide (hypoglycemia); Thiazolidinediones in HF
9. Renal function-based avoidance	Nitrofurantoin if CrCl <30 mL/min	—	Nitrofurantoin if eGFR <45; DOAC if eGFR <15–30; Digoxin >125 µg/day if eGFR <30; Metformin if eGFR <30
10. CNS, Cognitive function	Anticholinergic burden (Antihistamines, TCAs, Antipsychotics); Benzodiazepines (falls, delirium, cognitive impairment)	Explicit cumulative anticholinergic exposure	Adds rule-based limits: delirium/dementia with potent Antimuscarinics; Nootropics (Ginkgo biloba, piracetam) no proven efficacy
11. Others, Miscellaneous	—	Meprobamate, Barbiturates (dependence risk); Hormonal agents (androgen/estrogen in VTE history)	Prochlorperazine/metoclopramide in Parkinsonism; Long-term corticosteroids in RA/OA; Megestrol for appetite stimulation

Table 2.3 The differences among the tools used to assess PIMs and the study outcomes regarding the prevalence of having at least one PIM(s) in the same sample group

First author, year of publication	Setting, Participants	Beers criteria		STOPP criteria	
		Version	Prevalence	Version	Prevalence
Bai et al., (2022)[25]	China, n = 369	2019	53.9%	V.2 (2015)	20.6%
Sharma et al., (2021)[26]	North India, n = 456	2019	91%	V.2 (2015)	73%
Perpétuo et al., (2021)[27]	Portugal, n = 616	2019	92.0%	V.2 (2015)	76.5%
Blanco-Reina et al., (2019)[28]	Spain, n = 582	2012 2015	47.9% 54%	V.1 (2008) V.2 (2015)	35.4% 66.8%
Ma et al., (2018)[29]	China, n = 863	2015	58.1%	V.2 (2015)	44.0%

Abbreviations: n = sample, V. = version

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2.2 The prevalence of receiving PIMs at both admission and discharge

Studies on the prevalence of PIMs among the older population have been conducted in various contexts, including studies outside of hospitals, in nursing homes, in primary care settings, outpatient departments (OPD visits), hospitals during admission, hospitalization, discharge, emergency departments, and specialized wards, among others. The researcher has a specific interest in examining the prevalence of PIMs among older adults at the point of hospital discharge. Multiple studies conducted in Asia have systematically compared the prevalence of PIMs at hospital admission and at discharge, consistently demonstrating similar patterns. Notably, the prevalence of PIMs identified at admission has been reported to range from 47% to 55%, which exceeds the prevalence observed at discharge, reported at 25% to 46%. This difference may be attributed to the fact that patients receive more closely monitored care while hospitalized, reducing the likelihood of receiving PIMs. However, it was observed that the prevalence of PIMs at discharge remains high, even during transitional care overseen by the attending physician. This may be because while patients are under hospital care, it presents a good opportunity for healthcare providers to review and optimize the patient's medication use.

However, based on the researcher’s literature review, although studies from various Asian countries have been identified, no similar studies have been conducted in Thailand. Table 2.4 illustrates the prevalence of patients who received at least one PIM at both admission and discharge, as reported in each study conducted in Asia.

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Table 2.4 The prevalence of at least one PIM during admission and discharge

First author, year of publication	Setting, Participants	Tools	Prevalence of PIMs	
			at admission	at discharge
Bai et al., (2022)[25]	China, n = 369	Beers 2019	53.9%	46.9%
Aida et al., (2021)[30]	Japan, n = 264	STOPP V.2	55%	28%
Wang et al., (2020)[31]	China, n = 604	Beers 2019	55%	33.4%
Komagamine J, (2019)[15]	Japan, n = 739	Beers 2019	47.2%	32.3%
Komagamine J, (2018)[32]	Japan, n = 689	Beers 2015	47.9%	25.1%

Abbreviations: n = sample, V. = version

2.3 Predictive factors for receiving PIMs at discharge

Aida et al. (2021) conducted research on 264 patients discharged from the emergency department of a university hospital in Tokyo, Japan, between September 2018 and August 2019. The study utilized the STOPP version 2 (2015) criteria to assess prescriptions for PIMs at discharge and applied multivariate logistic regression to identify predictors of PIM use. The results demonstrated that patient age, the number of medications prescribed at admission, the number of PIMs at admission, and the number of medications at discharge were significantly associated with PIM use upon discharge. The regression model also included gender, LOS, APACHE II score, and CCI as additional covariates.[30]

Similarly, Mori et al. (2017) investigated 230 elderly patients admitted to a Brazilian university hospital who had been receiving at least one medication before admission and had a documented history of cardiovascular disease (CVD). The prevalence of PIMs at discharge was evaluated using the STOPP version 1 (2008) criteria, and potential predictive factors were analyzed through multivariable binary regression. The study found that 13.9% of patients were discharged with at least one PIM; however, no significant predictors of PIM use at discharge were identified. Variables included in the analysis comprised gender, age, diabetes, and dyslipidemia.[33]

However, through the literature review conducted by the researcher, it was found that studies related to identifying predictive factors for receiving PIMs at discharge remain limited. Only two studies were identified, and each had a relatively small sample size, as shown in Table 2.5.

Table 2.5 Studies on the predictive factors for receiving PIMs at discharge.

First author, year of publication	**Setting, Participants**	**Tools, Analysis**	**Predictors associated with PIMs at D/C**	**Other variables entered into the model**
Aida et al., (2021)[30]	Japan, n = 264	- STOPP V.2 2015 - Logistic regression	- Age - No. of med. at admission - No. of PIMs at admission - No. of med. at D/C	- Gender - LOS - APACHE II score - CCI Score
Mori et al., (2017)[33]	Brazil, n = 230	- STOPP V.1 2008 - Logistic regression	- No predictors for PIMs were found	- Gender - Age group - Diabetes - Dyslipidemia

Abbreviations: D/C = Discharge, n = sample, V. = version, No. = number, med. = medication

2.4 The prevalence and factors associated with receiving PIMs in Thailand.

A literature review on the prevalence and factors associated with receiving PIMs in Thailand reveals that studies have been conducted in various settings, including community health promotion hospitals, primary care units, outpatient departments, community studies, and nursing homes. The prevalence of receiving PIMs in Thailand over the past 10 years ranges from 24.5% to 79%, with differences depending on the research methodology, sample population, and assessment tools used. Factors associated with receiving PIMs in older patients in Thailand include age, polypharmacy, and the presence of multiple comorbidities, which have been identified as predictors of receiving PIMs in several studies. However, the literature review indicates a gap in studies related to the prevalence and factors associated with receiving PIMs in inpatient settings, particularly with regard to PIMs at discharge. The studies on the prevalence and associated factors of receiving PIMs in Thailand are summarized in Table 2.6.

Moreover, evidence indicates that studies investigating PIMs in Thailand predominantly utilize assessment tools derived from the Beers Criteria and the List of Risk Drugs for Thai Elderly (LRDTE)[34]. The LRDTE, established in 2012, was formulated through expert consensus discussions on medication use among older adults in Thailand. This list was adapted from the 2012 Beers Criteria and the first version of the STOPP criteria published in 2008. It comprises 76 medications available within the Thai healthcare system, each accompanied by detailed prescribing recommendations, which are further stratified by age groups: 60–74 years and those older than 74 years. The same medication may have identical or different usage recommendations across these age groups. This tool is considered appropriate for Thailand’s healthcare context. However, as of now, it has not been updated to align with international assessment criteria.

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Table 2.6 Prevalence and factors associated with the use of PIMs in Thailand

First author, year of publication	Setting, Participants	Tools, Statistical Analysis	Prevalence of PIMs	PIM-related factors (aOR, 95% CI)
Jenghua et al., (2023)[35]	- 1 Secondary-care hospital in Phayao (Outpatients) - aged ≥60 years - n = 22,099	- Beers 2019 - Logistic regression	68.90%, (Category I)	- Female sex (1.08, 1.01–1.16) - Age ≥75 years (1.10, 1.01–1.21) - Polypharmacy (10.21, 9.31–11.21) - ≥3 diagnostic categories (2.31, 2.14–2.50) - ≥3 chronic morbidities (1.46, 1.26–1.68) - Comorbidity score of ≥1 (0.78, 0.71–0.86)
Vatcharavongvan et al., (2021)[36]	- 8 PCU from 4 regions - aged ≥ 60 years - n = 4,848	- LRDTE 2012 - Logistic regression	65.9%	- Polypharmacy (3.51, 2.81-4.32) - Having ≥3 chronic diseases (1.44, 1.04-2.01) - Age ≥75 years (1.18, 1.01-1.38)
Vatcharavongvan et al., (2021)[37]	- 8 PCU from 4 regions - aged ≥ 60 years - n = 20,671	- LRDTE 2012 - Logistic regression	45.7%	- Aged 75 years and older (1.3, 1.2-1.4) - Polypharmacy (1.7, 1.6-1.9) - DM (1.5, 1.4-1.7) - HT (1.2, 1.2-1.4) - DLP (1.7, 1.6-1.9) - URI (2.6, 2.2-2.9) - Dizziness (2.2, 1.8-2.6) - Muscle strain (2.5, 2.1-3.0)
Kaewsutthi et al., (2021)[38]	- 1 PCU and Internal Medicine Clinic in Chiang Rai (Outpatients) - aged ≥60 years - n = 200	- Beers 2019 - Logistic regression	24.5%	- Polypharmacy (4.00, 1.74-9.21)
Vatcharavongvan et al., (2019)[39]	- 1 PCU in Pathum Thani - aged ≥65 years - n = 264	- Beers 2015 - Logistic regression	59.0%	- Polypharmacy (3.93, 2.17-71.2) - Presence of ≥4 diseases (2.78, 1.39-5.56)

Abbreviations: aOR = adjusted odds ratio, CI= confidence interval, n = sample, PCU = primary care unit, DM = Diabetes Mellitus, HT = hypertension, DLP = Dyslipidemia, URI = Urinary Tract Infections, No. = Number, med. = medication

Table 2.6 Prevalence and Factors Associated with the Use of PIMs in Thailand (Continue)

First author, year of publication	Setting, Participants	Tools, Statistical Analysis	Prevalence of PIMs	PIM-related factors (aOR, 95% CI)
Jenghua et al., (2019)[40]	- 7 urban communities in Phayao - aged ≥60 years - n = 400	- LRDTE 2012 - Logistic regression	72.5%	- Having income ≥ 1,000 baht per month (1.83, 1.07-3.13) - Using dietary supplement/herbal medicine (3.12, 1.16-8.39) - Minor polypharmacy 5-9 items (2.45, 1.40-4.29) - Major polypharmacy (≥ 10 items) (6.18, 1.68-22.74)
Prasert et al., (2018)[41]	- 4 Community hospitals in Chonburi (Outpatients) - aged ≥60 years - n = 13,274	- LRDTE 2012 - Logistic regression	79%	- Hospital D (1.24, 1.07-1.43) - General practitioner prescribers (2.80, 2.44-3.21)
Pannoi et al, (2014)[42]	- a district hospital in the southern region (Outpatients) - aged ≥65 years - n = 2,128	- Beers 2012 - Logistic regression	28.1%	- Age of participant (1.018, 1.001-1.035) - Age of prescriber (1.105, 1.002-1.218) - No. of outpatient visits (0.58, 0.41-0.83) - No. of med. (2.50, 1.92-3.23)

Abbreviations: aOR = adjusted odds ratio, CI= confidence interval, n = sample, PCU = primary care unit, DM = Diabetes Mellitus, HT = hypertension, DLP = Dyslipidemia, URI = Urinary Tract Infections, No. = Number, med. = medication

2.5 The relationship between receiving PIMs and various health outcomes

A review of existing literature indicates that numerous studies have investigated patients prescribed PIMs across diverse healthcare settings, along with the associated risks for a range of health outcomes. These outcomes encompass adverse drug reactions, higher frequencies of outpatient consultations, emergency department utilization, hospital admissions, readmissions, and even mortality. Moreover, certain studies have specifically examined the association between PIM use and mortality rates.

Weir et al. (2020) conducted a prospective cohort study in a Canadian tertiary hospital involving 2,402 patients aged ≥65 years to assess the link between PIMs at discharge and adverse outcomes within 30 days. Using the 2015 Beers Criteria and STOPP v2, they found 66% received at least one PIM; 49% continued pre-admission PIMs, and 31% received new ones. Within 30 days, 9% experienced adverse drug events, and 36% had ED visits, were rehospitalized, or died. Newly prescribed PIMs raised ADE risk by 21% (OR 1.21), and continued PIMs by 10% (OR 1.10). Cox models showed increased risks of ED visits, rehospitalization, or death by 13% (HR 1.13) and 5% (HR 1.05) for new and continued PIMs, respectively.[43]

Varavithya et al. (2022) investigated the association between PIM use and hospital admissions among patients attending the outpatient department of Thammasat Hospital in 2015. The 2019 Beers Criteria were applied to identify PIMs. Among the 32,261 patients included, 63.98% had received at least one PIM prescription. Analysis using log-binomial regression demonstrated that PIM exposure was linked to a 1.31-fold increased risk of hospitalization (adjusted risk ratio [aRR] = 1.31, 95% confidence interval [CI]: 1.21–1.41, $p < 0.001$). Additional factors significantly associated with hospitalization included older age, male sex, polypharmacy, and a higher number of outpatient department visits.[44]

Xing et al. (2019) conducted a systematic review and meta-analysis of 33 studies published up to February 1, 2018, to examine the relationship between PIM use and adverse clinical outcomes. The analysis revealed that PIM exposure was significantly associated with an increased risk of adverse drug reactions (OR = 1.44) and hospital admissions (OR = 1.27), while no significant correlation was identified with mortality (OR = 1.04). In addition, patients prescribed two or more PIMs were more likely to experience adverse outcomes than those prescribed a single PIM.[7]

Liew et al. (2019) performed a meta-analysis of eight observational studies with low risk of bias (n = 77,624) to examine the impact of PIP in primary care. Although no significant association with mortality was observed, PIP was associated with higher rates of emergency department visits, adverse drug events, functional deterioration, hospital admissions, and reduced health-related quality of life.[6]

Weeda et al. (2020) performed a meta-analysis to investigate the influence of PIMs on hospital-related outcomes. The review encompassed studies published globally between 1991 and 2019, concentrating on hospital admissions and ED visits. A total of 21 studies were analyzed, representing more than 3,137,188 patients. Results indicated that in 18 of these studies, over 20% of patients had been prescribed PIMs, with a median follow-up duration of 12 months. The analysis demonstrated a significant relationship between PIM use and both hospital admissions (OR = 1.52; 95% CI = 1.40–1.65) and ED visits (OR = 1.72; 95% CI = 1.33–2.24).[8]

Malakou et al. (2021) conducted a systematic review to compare healthcare expenditures among elderly patients exposed to PIMs and those not exposed. Data were retrieved from PubMed, Scopus, and the Institute for Scientific Information databases, covering publications up to 2020. The review demonstrated that the use of PIMs substantially increases the economic burden in older populations. On average, elderly patients receiving PIMs incurred healthcare costs of USD $2,000, exceeding those of patients without PIM exposure. Moreover, in Canada alone, the healthcare costs attributable to PIM use among elderly individuals were estimated at USD $419 million in 2013.[45]

A review of the literature conducted by the researcher revealed that both systematic reviews and meta-analyses indicated that the use of PIMs did not increase the risk of mortality from all causes. Additionally, some studies did not clearly specify the context or setting in which PIMs were administered. Many studies referred to PIMs that patients had received prior to hospitalization. However, this study specifically focuses on examining the outcomes associated with PIM use at discharge. Examples of studies examining the relationship between PIM use and various health outcomes are presented in Table 2.7.

Table 2.7 The relationship between PIMs and various health outcomes

First author, year of publication	Study design	Health outcomes measured	Effect sizes (95% CI)
Weir et al., (2020)[43]	Prospective cohort	- ADE (New PIMs) - ADE (Continued PIMs) - ED visits, rehospitalization, death (New PIMs) - ED visits, rehospitalization, death (Continued PIMs)	aOR = 1.21, (1.01-1.45) aOR = 1.10, (1.01-1.21) aHR = 1.13, (1.03-1.26) aHR = 1.05, (1.00-1.10)
Varavithya et al., (2022)[44]	Retrospective cohort	- Hospitalization	aRR = 1.31 (1.21-1.41)
Xing et al., (2019)[7]	A Systematic Review and Meta-analysis	- ADRs - Hospitalizations - Mortality	OR = 1.44, (1.33-1.56) OR = 1.27, (1.20-1.35) OR = 1.04, (0.75-1.45)
Weeda et al., (2020)[8]	A Systematic Review and Meta-analysis	- Hospital admissions - ED visits	OR = 1.52, (1.40-1.65) OR = 1.72, (1.33-2.24)
Liew et al, (2019)[6]	A Systematic Review and Meta-analysis	- Mortality - Emergency visits - Adverse drug events - Functional decline - Hospitalizations - Health-related quality of life	RR = 0.98, (0.93-1.05) RR = 1.63, (1.32-2.00) RR = 1.34, (1.09-1.66) RR = 1.53, (1.08-2.18) RR = 1.25, (1.09-1.44) SMD = -0.26, (-0.36 to -0.16)
Malakouti et al, (2021)[45]	A Systematic Review	- Costs among elderly persons	The mean cost for older adults with PIMs use was almost USD$2000 more than the mean cost for older adults without PIMs

Abbreviations: ED = emergency department, RR = risk ratio, SMD = standardized mean difference, ADRs = adverse drug reactions, USD = United States dollar

2.6 The relationship between receiving PIMs at discharge and the risk of readmission or ED visits

A review of the literature by the researcher revealed several studies examining the relationship between PIMs at discharge and readmission or outpatient visits. Each study varied in terms of the study setting, population characteristics, assessment tools, follow-up duration, data analysis methods, and outcome measures. The researcher classified the studies based on their outcomes into three groups, as follows:

2.6.1 Four studies have found no association between PIMs at discharge and clinical outcomes

Akkawi et al. (2023) conducted a retrospective cohort study at a Malaysian medical center, involving a sample of 600 participants, and collected data from January to September 2022. The Beers Criteria 2019 (Tables 2–6) were applied to assess PIMs at discharge. The findings indicated a 3-month hospital readmission rate of 25.3%. Logistic regression analysis, which included factors such as polypharmacy, age, ethnicity, number of discharge medications, length of hospital stay, and the age-adjusted Charlson Comorbidity Index (ACCI), revealed no significant association between exposure to at least one PIM and hospital readmission within three months. However, male sex was found to be significantly correlated with the likelihood of readmission.[13]

De Vincentis et al. (2020) conducted a prospective cohort study in Italy including 2,631 individuals aged 65 years and older. PIMs at discharge were assessed using the 2019 Beers Criteria and the 2015 STOPP criteria. No significant relationships were found between PIMs, anticholinergic burden (ACB) scores, or drug-drug interactions (DDIs) and outcomes such as mortality, rehospitalization, or decline in physical function at three months. However, both a higher number of discharge medications and polypharmacy (defined as the use of more than five drugs) were significantly associated with increased risks of mortality (adjusted hazard ratios [aHR] 1.05 and 1.70, respectively) and rehospitalization (aHR 1.05 and 1.31, respectively)[14].

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Komagamine et al. (2019) conducted a prospective cohort study in Japan involving 739 patients admitted to an internal medicine ward between May 1, 2017, and May 31, 2018. The 2015 Beers Criteria (Tables 2 and 3) were applied to identify PIMs at discharge, and participants were monitored for 90 days. Within 30 days, unplanned readmissions occurred in 5.0% of patients discharged with PIMs and in 5.4% of those without. The prescription of PIMs at discharge was not significantly associated with unplanned readmissions at either 30 days (OR = 0.93; 95% CI = 0.46–1.87) or 90 days (OR = 0.78; 95% CI = 0.48–1.24), even after adjustment for confounding factors. In contrast, sex and CCI score were identified as significant predictors.[15]

Fabbietti et al. (2018) performed a multicenter prospective cohort study in Italy involving 647 patients aged 65 years and older. Applying the 2015 Beers and STOPP criteria, the investigators observed no significant association between PIMs prescribed at discharge and readmission within three months. However, polypharmacy, defined as the use of more than eight medications, was strongly linked to an increased likelihood of readmission (OR = 2.72; 95% CI = 1.48–4.99). Furthermore, prolonged hospitalization, a history of in-hospital adverse drug reactions (ADRs), and the presence of chronic kidney disease (CKD) were identified as significant predictors of readmission. [16]

The literature review reveals that although all studies yielded consistent results, namely, no association between the receipt of PIMs at discharge and unplanned readmission or outpatient visits, the differences between studies could influence the findings. These differences include the criteria and tools used to assess patients receiving PIMs, the timing of PIMs assessment, sample size, the number of participants, the study setting, data analysis methods, and the variables adjusted for in the models. However, common elements across all studies included a follow-up period of 3 months and relatively small sample sizes. All studies that reported no association between the receipt of PIMs at discharge and unplanned readmission or outpatient visits are summarized in Table 2.8.

Table 2.8 The studies that found no association between PIMs at discharge and clinical outcomes

First author, year of publication	Study design & setting	Study population	Data collection	Outcome measures	Results
Akkawi et al., (2023)[13]	- A retrospective cohort study, Malaysia - Beers criteria 2019 (Table 2-6)	- ≥60 years old - January-September 2022 - discharged with at least 1 medication - 600 patients	Data were extracted from patients' electronic medical records, including demographic characteristics, medical history, dates of hospital admission and discharge, medications used prior to hospitalization, serum creatinine measurements, newly identified diagnoses, and medications prescribed at discharge. Topical agents, such as ophthalmic drops and ointments, were not included in the analysis.	The primary outcome assessed was hospital readmission within three months. To evaluate potential associations, logistic regression analysis was conducted with polypharmacy, patient age, gender, race, total number of medications at discharge, length of hospitalization, and ACCI included as covariates in the model.	Of 600 patients, 152 (25.3%) were readmitted within three months. Gender was the only significant predictor, while other variables in the regression model showed no significant association with readmission.

Abbreviations: ACCI = age-adjusted Charlson comorbidity index, CIRS = Cumulative Illness Rating Scale, BI = The Barthel Index, DDIs = drug–drug interactions, aHR = adjusted hazard ratio, CI = confidence interval, CCI = Charlson comorbidity index, OR = odds ratio, BADL = basic activity of daily living, MMSE = Mini-mental state exam, GDS = Geriatric Depression Scale, CKD = Chronic Kidney Disease

Table 2.8 The studies that found no association between PIMs at discharge and clinical outcomes (Continue)

First author, year of publication	Study design & setting	Study population	Data collection	Outcome measures	Results
De Vincentis et al., (2020)[14]	A prospective cohort study, Italy - Beers criteria 2019 and STOPP 2015	- Patients aged ≥ 65 years - Multicenter study across 107 Italian medical wards - Enrollment conducted one week per quarter (totaling four weeks per year) from 2010 to 2016 - Total sample size: 2,631 patients	Comorbidity burden was evaluated using the CIRS. Functional disability was defined by a Barthel Index (BI) score of ≤ 90, cognitive impairment by a Short Blessed Test score of ≥ 10, and depressive symptoms by a Geriatric Depression Scale score of ≥ 2.	Examined the relationships between PIMs, ACB score, and the number of DDIs with 3-month outcomes, including mortality, rehospitalization, and decline in physical function. - Applied Cox proportional hazards models to assess mortality and rehospitalization risks, and employed mixed linear models to analyze changes in functional status over time. - All models were controlled for potential confounding variables, including age, sex, the CIRS comorbidity index, duration of hospitalization, and the total number of medications prescribed at discharge.	- None of the evaluated indicators demonstrated a significant association with either mortality or rehospitalization. - Decline in physical function was observed to be associated exclusively with the ACB score. - Among the therapy-related variables, the total number of discharge medications—particularly in cases of polypharmacy (defined as more than five drugs per day)—was the only factor independently associated with elevated risks of mortality (aHR 1.05; 95% CI 1.01–1.10, and 1.70; 95% CI 1.12–2.58, respectively) and rehospitalization (aHR 1.05; 95% CI 1.01–1.08, and 1.31; 95% CI 1.01–1.71, respectively).

Abbreviations: ACCI = age-adjusted Charlson comorbidity index, CIRS = Cumulative Illness Rating Scale, BI = The Barthel Index, DDIs = drug–drug interactions, aHR = adjusted hazard ratio, CI = confidence interval, CCI = Charlson comorbidity index, OR = odds ratio, BADL = basic activity of daily living, MMSE = Mini-mental state exam, GDS = Geriatric Depression Scale, CKD = Chronic Kidney Disease

Table 2.8 The studies that found no association between PIMs at discharge and clinical outcomes (Continue)

First author, year of publication	Study design & setting	Study population	Data collection	Outcome measures	Results
Komagamine et al., (2019)[15]	- A prospective cohort study, Japan - Beers Criteria 2015 (Table 2&3)	- aged ≥ 65 years - Internal medicine ward - from 1 May 2017 to 31 May 2018 - 739 patients	Data were obtained from electronic medical records and included patients' age, sex, CCI, primary admission diagnosis, as well as relevant social and medical histories. Topical agents, including eye drops and intranasal preparations, were excluded from the analysis.	The primary outcome was defined as unplanned hospital readmission within 30 or 90 days. The secondary outcome focused on the prevalence of PIM use at the time of admission and at discharge. Logistic regression analysis was employed to examine associations, adjusting for age, sex, CCI, polypharmacy at discharge, and length of hospital stay.	- The prevalence PIM use was 47.3% at admission and declined to 32.2% at discharge. - The 30-day unplanned readmission rates were comparable between patients discharged with PIMs (5.0%) and those without PIMs (5.4%). - Discharge with PIMs was not significantly associated with an increased risk of unplanned readmission within 30 days (OR 0.93; 95% CI 0.46–1.87) or within 90 days (OR 0.78; 95% CI 0.48–1.24). - These associations remained non-significant after controlling for age, sex, length of hospitalization, polypharmacy, and comorbidity burden. - Sex and CCI scores were also assessed as potential predictors.

Abbreviations: ACCI = age-adjusted Charlson comorbidity index, CIRS = Cumulative Illness Rating Scale, BI = The Barthel Index, DDIs = drug–drug interactions, aHR = adjusted hazard ratio, CI = confidence interval, CCI = Charlson comorbidity index, OR = odds ratio, BADL = basic activity of daily living, MMSE = Mini-mental state exam, GDS = Geriatric Depression Scale, CKD = Chronic Kidney Disease

Table 2.8 The studies that found no association between PIMs at discharge and clinical outcomes (Continue)

First author, year of publication	Study design & setting	Study population	Data collection	Outcome measures	Results
Fabbietti et al., (2018)[16]	A multicenter prospective cohort study, Italy - Beers criteria 2015 and STOPP 2015	- aged ≥ 65 years - 3 acute care wards of geriatric medicine - between January and December 2013 - 647 patients	Number of discharge medications, polypharmacy (>8 drugs), age, sex, emergency admission, living alone, baseline BADL, cognitive impairment (MMSE < 24), depression (GDS > 5), in-hospital ADRs, prior hospitalization within 12 months, number of diagnoses, and selected diagnoses potentially influencing readmission risk	- The primary outcome was hospital readmission within three months following discharge. - Logistic regression analysis was performed to assess this outcome. - The model was adjusted for potential confounders, including age, sex, type of admission (emergency vs. elective), cognitive impairment, depression, dependence in at least one BADL at discharge, and the total number of diagnoses.	- Polypharmacy exhibited a significant association with the outcome (OR = 2.72, 95% CI 1.48–4.99). - In contrast, the Beers criteria (OR = 0.85, 95% CI 0.46–1.56), STOPP criteria (OR = 1.60, 95% CI 0.85–3.01), and their combined application (OR = 0.99, 95% CI 0.57–1.74) were not significantly associated. - Additional factors significantly associated with the outcome included length of hospital stay, prior history of ADRs during hospitalization, and the presence of CKD. - The relationship between polypharmacy and 3-month readmission remained significant in logistic regression models adjusted for Beers criteria (OR = 2.88, 95% CI 1.55–5.34), STOPP criteria (OR = 2.64, 95% CI 1.43–4.87), or both combined (OR = 2.80, 95% CI 1.51–5.21).

Abbreviations: ACCI = age-adjusted Charlson comorbidity index, CIRS = Cumulative Illness Rating Scale, BI = The Barthel Index, DDIs = drug–drug interactions, aHR = adjusted hazard ratio, CI = confidence interval, CCI = Charlson comorbidity index, OR = odds ratio, BADL = basic activity of daily living, MMSE = Mini-mental state exam, GDS = Geriatric Depression Scale, CKD = Chronic Kidney Disease

2.6.2 Four studies have found that PIMs at discharge increase the risk of adverse clinical outcomes

Liang et al. (2022) conducted a retrospective cohort study in Taiwan, involving 3,061 participants aged 65 and older. Data were collected between April and December 2017, and the Beers Criteria 2015 was used as the tool to assess PIMs. Additionally, the ACBS score was also applied. The study found that all three drug-use indicators (i.e., no dementia, age over 80 years, and frailty) were associated with readmissions and emergency room revisits within 1, 3, and 6 months after discharge, except for PIMs, which showed no significant association with readmission within 6 months.[9]

Thomas et al. (2020) conducted a retrospective cohort study in Canada involving 82,935 participants aged 65 years and older. The presence of PIMs at discharge was evaluated using the Beers Criteria 2019 and STOPP 2015. Data collection spanned from March 2013 to February 2018. Their findings demonstrated that PIM exposure, as defined by the Beers Criteria, was significantly associated with hospital readmission, with an aOR of 1.14 (95% confidence interval [CI]: 1.13–1.14). Furthermore, the total number of discharge medications was also linked to readmission risk (aOR: 1.09; 95% CI: 1.09–1.09).[10]

Wang et al. (2019) conducted a prospective cohort study of 508 patients aged 65 years or older who were admitted to a hospital in China between June 2015 and December 2017. PIMs at discharge were assessed using the Beers Criteria 2015 and the Chinese Criteria 2017. Participants were monitored for 12 to 36 months with evaluations conducted quarterly. The findings indicated that 69.3% of patients were prescribed at least one PIM based on the Beers Criteria, which was significantly associated with an increased risk of all-cause rehospitalization (aHR: 1.31; 95% CI: 1.03–1.66). However, no significant relationship was identified with all-cause mortality.[11]

Lau et al. (2017) performed a retrospective cohort study at a hospital in Hong Kong, including 182 patients aged 75 years and older who were discharged on a regimen of at least five medications. Data were collected in May 2016, and PIMs at discharge were assessed using the STOPP 2015 criteria, focusing particularly on drug-disease interactions. Their analysis revealed that receiving PIMs at discharge was significantly correlated with an increased risk of unplanned hospital readmission within 28 days, after adjustment for confounders identified in univariable analyses (aOR: 6.56; 95% CI: 2.89–14.97).[12]

A review of the literature reveals that although all studies show a similar trend—indicating that receiving PIMs at discharge increases the risk of readmission or emergency room revisits—several differences exist between the studies. These differences include the criteria used to identify PIMs, the duration of follow-up, the definition of outcomes (e.g., unplanned or all-cause readmissions), participant age, the number of participants, and the methods of data analysis. These factors can influence the results, as shown in Table 2.9.

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Table 2.9 Studies that found PIMs at discharge to be associated with an increased risk of unplanned readmissions or ED visits

First author, year of publication	Study design & setting	Study population	Data collection	Outcome measures	Results
Liang et al., (2022)[9]	A retrospective cohort study, Taiwan - Beers criteria 2015 and ACBS	- aged ≥ 65 years - between April and December 2017 - 3,061 patients	- Data sourced from electronic health records - Minor polypharmacy: use of 5–9 drugs; major polypharmacy: ≥10 drugs - Three medication use indicators were assessed within specific subgroups: patients without dementia, those aged over 80 years, and individuals exhibiting frailty.	- Emergency room revisits and readmissions at 1, 3, and 6 months post-discharge - Analyzed using logistic regression	All three indicators of medication use demonstrated significant associations with hospital readmission and emergency department revisits, with the exception of PIMs, which did not exhibit a statistically significant relationship with readmission within six months.

Abbreviations: ACBS = anticholinergic cognitive burden scale, PPOs = potential prescribing omissions, OR = odds ratio, AGS = American Geriatrics Society, BMI = Body Mass Index, CCI = Charlson comorbidity index, ADL = activities of daily living, CMMSE = Chinese version of the Mini-Mental State Examination, CFS = Clinical Frailty Scale, MNA-SF = short-form mini nutritional assessment

Table 2.9 Studies that found PIMs at discharge to be associated with an increased risk of unplanned readmissions or ED visits (Continue)

First author, year of publication	Study design & setting	Study population	Data collection	Outcome measures	Results
Thomas et al., (2020)[10]	A retrospective cohort study, Canada - Beers criteria 2019 and STOPP 2015	- aged ≥ 65 years - March 2013 through February 2018 - 4 acute-care hospitals - 82,935 patients	- Alberta Health Services (AHS) registration database - age, sex, admission and discharge diagnoses, comorbidities, numbers of medications on admission and discharge, numbers of PIMs and PPOs	- all-cause rehospitalization and all-cause death within 6 months of discharge. - Logistic regression - adjusting for age, sex, comorbidities, numbers of medications, PIMs and PPOs.	- The odds ratios (ORs) for hospital readmission were reported as follows: number of medications, 1.09 (95% confidence interval [CI], 1.09–1.09); AGS PIMs, 1.14 (1.13–1.14); STOPP PIMs, 1.15 (1.14–1.15); START PPOs, 1.04 (1.02–1.06); and correctly prescribed START PPOs, 1.16 (1.14–1.17). - Regarding 6-month post-discharge mortality, the adjusted ORs were: number of medications 1.02 (1.01–1.02), STOPP PIMs 1.07 (1.06–1.08), AGS PIMs 1.11 (1.10–1.12), START PPOs 1.31 (1.27–1.34), and correctly prescribed START PPOs 0.97 (0.94–0.99).

Abbreviations: ACBS = anticholinergic cognitive burden scale, PPOs = potential prescribing omissions, OR = odds ratio, AGS = American Geriatrics Society, BMI = Body Mass Index, CCI = Charlson comorbidity index, ADL = activities of daily living, CMMSE = Chinese version of the Mini-Mental State Examination, CFS = Clinical Frailty Scale, MNA-SF = short-form mini nutritional assessment

Table 2.9 Studies that found PIMs at discharge to be associated with an increased risk of unplanned readmissions or ED visits (Continue)

First author, year of publication	Study design & setting	Study population	Data collection	Outcome measures	Results
Wang et al., (2019)[11]	A prospective cohort study, Beijing, China - Beers criteria 2015, Chinese criteria 2017	- aged ≥ 65 years - June 2015 to December 2017 - exclusion criteria: patients taking no medication, having severe and terminal illnesses, bedridden patients - 508 patients	Patients were classified into PIM and non-PIM groups according to their use of PIMs. The variables analyzed included age, sex, BMI, comorbid conditions, prescribed medications, length of hospital stay, CCI, Katz ADL, CMMSE, CFS, and MNA-SF.	Follow-up assessments were performed over a period of 12 to 36 months, with evaluations conducted every three months via telephone interviews or home visits. The primary outcomes included all-cause hospital readmission and mortality. Cox proportional hazards regression models were utilized, adjusting for potential confounders such as age, sex, CCI, BMI, duration of follow-up, number of medications, living alone status, independence in ADL, and cognitive impairment.	- The detection rates of PIMs were 66.7% (339/508) by the 2017 Chinese criteria and 69.3% (352/508) by the 2015 Beers criteria. - According to the Beers criteria, PIM use was associated with a 1.31-fold increased risk of rehospitalization after adjustment, but not with all-cause mortality. - PIM use defined by the Chinese criteria showed no association with all-cause mortality or hospital readmission.

Abbreviations: ACBS = anticholinergic cognitive burden scale, PPOs = potential prescribing omissions, OR = odds ratio, AGS = American Geriatrics Society, BMI = Body Mass Index, CCI = Charlson comorbidity index, ADL = activities of daily living, CMMSE = Chinese version of the Mini-Mental State Examination, CFS = Clinical Frailty Scale, MNA-SF = short-form mini nutritional assessment

Table 2.9 Studies that found PIMs at discharge to be associated with an increased risk of unplanned readmissions or ED visits (Continue)

First author, year of publication	Study design & setting	Study population	Data collection	Outcome measures	Results
Lau et al., (2017)[12]	A retrospective cohort study, Hong Kong - STOPP 2015 (drug-disease)	- Patients aged ≥ 75 years - Discharged with ≥ 5 medications, including ≥ 1 drug implicated in drug-disease interactions per STOPP v2 criteria - Study period: 1–31 May 2016 - Sample size: 182 patients	Data were obtained from electronic patient records, including variables such as age, gender, number of chronic medications, identified PIMs, types and number of comorbidities, as well as records of emergency readmissions.	- The objective was to examine the relationship between exposure to PIMs, as determined by selected STOPP version 2 criteria concerning drug–disease interactions, and the occurrence of unplanned early hospitalizations within 28 days. - A logistic regression analysis was performed, adjusting for gastrointestinal disorders and gout, which were significant ($P < 0.05$) in univariable analyses.	- The utilization of PIMs (57.1% vs. 17.1%, $p < 0.001$), along with the presence of gout (31% vs. 11.5%, $p = 0.003$) and gastrointestinal disease (11.9% vs. 2.5%, $p = 0.026$), was significantly associated with a higher likelihood of readmission within 28 days. - No other factors assessed showed significant correlation with readmission.

Abbreviations: ACBS = anticholinergic cognitive burden scale, PPOs = potential prescribing omissions, OR = odds ratio, AGS = American Geriatrics Society, BMI = Body Mass Index, CCI = Charlson comorbidity index, ADL = activities of daily living, CMMSE = Chinese version of the Mini-Mental State Examination, CFS = Clinical Frailty Scale, MNA-SF = short-form mini nutritional assessment

2.6.3 Two studies have found that PIMs at discharge reduce the risk of adverse clinical outcomes

Allore et al. (2022) conducted a prospective cohort study in the United States that enrolled 117,570 veterans aged 65 years or older with at least one musculoskeletal diagnosis and self-reported pain intensity of 4 or higher. PIMs were assessed using the 2015 Beers Criteria (Table 2). The use of both central nervous system (CNS) and non-CNS PIMs following hospital discharge was associated with a reduced risk of 30-day all-cause readmission, with aHR of 0.93 (95% CI 0.89–0.96) and 0.85 (95% CI 0.82–0.88), respectively. In contrast, CNS PIMs were linked to an elevated risk of 30-day all-cause mortality (aHR 1.37, 95% CI 1.25–1.51), whereas non-CNS PIMs were associated with decreased mortality risk (aHR 0.75, 95% CI 0.69–0.82). For 30-day ED visits, exposure to one CNS PIM (aOR 0.94, 95% CI 0.91–0.97) and one non-CNS PIM (aOR 0.88, 95% CI 0.85–0.91) was associated with a lower risk.[17]

Hammouda et al. (2021) conducted a retrospective cohort study in New York that included 7,591 patients aged 65 years and older who visited the ED between January 2012 and November 2015. The 2015 Beers Criteria were applied to evaluate PIMs (Table 2). Patients who were prescribed PIMs had lower 30-day ED revisit rates compared to those without PIM exposure (12% vs. 16%; OR 0.79, 95% CI 0.65–0.95), along with fewer hospital admissions (4% vs. 7%; OR 0.75, 95% CI 0.56–1.00). Furthermore, several additional variables emerged as significant risk factors for these outcomes.[18]

From the literature review, it is evident that although the two studies mentioned above yielded similar results—namely, that receiving PIMs at discharge reduces the risk of readmission or emergency room revisits—both studies were conducted in the United States with relatively large sample sizes. However, the study designs were quite specific. For example, one study focused solely on CNS PIMs, while another investigated patients discharged from the emergency department, looking at readmission to the emergency department. Therefore, when applying the findings of these studies, the study characteristics should be taken into consideration. Studies demonstrating that receiving PIMs at discharge is associated with a reduction in unplanned readmissions or outpatient visits are summarized in Table 2.10.

Regarding studies in Thailand, the researcher's literature review did not identify any studies exploring the relationship between receiving PIMs at discharge and the occurrence of unplanned readmissions or outpatient visits.

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Table 2.10 Studies that found receiving PIMs at discharge reduce the risk of unplanned readmission or ED visits

First author, year of publication	Study design & setting	Study population	Data collection	Outcome measures	Results
Allore et al., (2022)[17]	- a prospective cohort study, US - Beers Criteria 2015 (Table 2)	- aged ≥65 years - had one or more musculoskeletal diagnoses and at least 1 pain intensity rating of 4 or higher during outpatient visits between October 2012 to 30 September 2013 - 117,570 patients	- grouped PIMs into CNS PIMs and non-CNS PIMs. - PIM exposure was categorized as 0 (reference) versus 1 or ≥2 - age, sex, race/ethnicity, marital status, CCI	- readmission to hospital for any reasons and all-cause mortality within 30 days of discharge (Cox proportional hazard model) - outpatient ER visits and PCC visits within 30 days of discharge (logistic regression) - adjusting for age, sex, marital status, and race/ethnicity groups, number of non-PIMs, and CCI	- Both CNS-related and non-CNS PIMs were linked to a reduced likelihood of hospital readmission within 30 days, with adjusted hazard ratios (aHR) of 0.93 (95% CI: 0.89–0.96) and 0.85 (95% CI: 0.82–0.88), respectively. - CNS PIMs exhibited a dose-dependent increase in 30-day mortality risk: one prescription was associated with an aHR of 1.15 (95% CI: 1.07–1.23), while two or more prescriptions had an aHR of 1.37 (95% CI: 1.25–1.51). - Conversely, non-CNS PIMs were linked to a reduced 30-day mortality risk, with an aHR of 0.83 (95% CI: 0.77–0.89) for one prescription and 0.75 (95% CI: 0.69–0.82) for two or more prescriptions. - A single CNS PIM was associated with decreased odds of emergency room visits (adjusted odds ratio [aOR] 0.94; 95% CI: 0.91–0.97), whereas two or more CNS PIMs increased the odds of ER visits (aOR 1.06; 95% CI: 1.01–1.10). - Both one and two or more non-CNS PIM prescriptions were correlated with reduced odds of ER visits, with aORs of 0.88 (95% CI: 0.85–0.91) and 0.91 (95% CI: 0.88–0.95), respectively. - Regarding primary care clinic (PCC) utilization of three or more visits within 30 days post-discharge, only two or more non-CNS PIM prescriptions were significantly associated with increased odds (aOR 1.07; 95% CI: 1.02–1.12).

Abbreviations: US = United States, PIMs = Potentially Inappropriate Medications, CNS = Central Nervous System, CCI = Charlson comorbidity index, ER = Emergency Room, PCC = Primary Care Center, aHR = adjusted hazard ratio, CI = confidence interval, aOR = adjusted odds ratio, NY = New York, ED = emergency department, ESI = Emergency Severity Index, OR = odds ratio

Table 2.10 Studies that found receiving PIMs at discharge reduce the risk of unplanned readmission or ED visits (Continue)

First author, year of publication	Study design & setting	Study population	Data collection	Outcome measures	Results
Hammouda et al., (2021)[18]	A retrospective cohort study, NY, US - Beers criteria 2015 (Table 2)	- aged ≥ 65 years - January 2012 - November 2015 - at least one drug prescribed in the emergency department (ED) - 7,591 patients	- Data were extracted from electronic medical records. - Variables collected comprised age, sex, race/ethnicity (categorized as White, Black, Asian, Hispanic, and Other), emergency department arrival and discharge dates, triage acuity as measured by the ESI score, and comorbidity assessed using the CCI. - Duplicate visits were excluded from the analysis.	- Primary outcomes, derived from a Medicare database linked to hospital ED patients, included ED revisits within 3 and 30 days following the index ED discharge. Secondary outcomes comprised hospital admissions occurring within the same 3- and 30-day periods. Logistic regression analyses were performed, adjusting for covariates including age, gender, race, number of discharge medications, CCI, ESI, chief complaint, Medicaid status, and the number of ED visits in the preceding 90 days.	- The rate of thirty-day ED revisits was lower in the PIMs cohort compared to the non-PIMs group (12% vs. 16%; odds ratio [OR] 0.79, 95% confidence interval [CI] 0.65–0.95; $p < 0.005$). - Similarly, thirty-day hospital admissions were reduced in the PIMs cohort (4% vs. 7%; OR 0.75, 95% CI 0.56–1.00; $p < 0.005$). - Covariates significantly associated with thirty-day ED revisits included comorbidity burden, history of prior ED visits, presenting complaint, and Medicaid enrollment. Risk factors for hospitalization encompassed these variables in addition to age and emergency severity index, whereas race and ethnicity were not significantly linked.

Abbreviations: US = United States, PIMs = Potentially Inappropriate Medications, CNS = Central Nervous System, CCI = Charlson comorbidity index, ER = Emergency Room, PCC = Primary Care Center, aHR = adjusted hazard ratio, CI = confidence interval, aOR = adjusted odds ratio, NY = New York, ED = emergency department, ESI = Emergency Severity Index, OR = odds ratio

2.6.4 Methodological and population characteristics potentially explaining discrepancies across studies

When synthesizing the key methodological and population characteristics that may explain the discrepancies in findings among studies investigating the association between PIMs at discharge and readmission or outpatient visits, three main patterns emerge. Studies reporting no association often suffer from small sample sizes, short follow-up durations, and limited covariate adjustment, which reduce the statistical power to detect true associations. In contrast, studies demonstrating an increased risk typically involve larger and frailer populations with more extended observation periods, thereby enhancing the likelihood of identifying significant effects. Meanwhile, studies showing a decreased risk may reflect specific subpopulations—such as U.S. veterans or patients discharged from emergency departments—where PIMs may act as markers of appropriate symptom management or indicate well-coordinated post-discharge care. A summary of these interpretations is presented in Table 2.11.

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Table 2.11 Methodological and population characteristics potentially explaining discrepancies across studies

Study Outcome Group	Key Methodological Characteristics	Population Characteristics	Possible Explanations for Discrepancies
No Association (Akkawi 2023[13]; De Vincentis 2020[14]; Komagamine 2019[15]; Fabbietti 2018[16])	- Small sample sizes (600–2,600) - Prospective/retrospective cohorts in Asia or Europe - 3-month follow-up - Beers 2015/2019, STOPP 2015 used - Limited covariate adjustment (age, sex, CCI, polypharmacy)	- Older adults (≥65 years) - Moderate frailty - Internal medicine or geriatric wards - Moderate polypharmacy (5–8 meds) - Short hospital stay	- Underpowered to detect effects - Short follow-up - Variability in PIM definitions - Low event rates dilute associations
Increased Risk (Thomas 2020[10]; Wang 2019[11]; Lau 2017[12]; Liang 2022[9])	- Large to very large samples (500–82,000) - Retrospective or multicenter cohorts (Canada, China, Taiwan, Hong Kong) - Beers 2015/2019, STOPP 2015, or local criteria - 3–12 month follow-up - Comprehensive covariate adjustment	- Older adults (≥75 years) - High polypharmacy (≥10 meds) - Frailty and cognitive impairment common - High baseline readmission risk	- Higher power - Inclusion of frail, multimorbid patients - Longer observation increases detection - Rigorous adjustment isolates PIM effect
Decreased Risk (Allore 2022[17]; Hammouda 2021[18])	- Large cohorts (7,000–117,000) in U.S. Veterans or ED patients - Beers 2015 (CNS vs non-CNS PIMs) - Stratified analysis; 30-day readmission/ED revisit - Extensive adjustment (CCI, ESI, prior ED visits)	- U.S. Veterans or ED discharges - Younger-old (65–75 years) - Integrated care systems - Better post-discharge follow-up and medication monitoring	- Selection bias (healthier survivors, integrated care) - CNS vs non-CNS distinction reflects clinical appropriateness - Short-term effects only.

Abbreviations: US = United States, PIMs = Potentially Inappropriate Medications, ESI = Emergency Severity Index, ED = Emergency Department, CNS = central nervous system

2.7 The relationship between receiving PIMs and the risk of readmission or ED visits in Thailand

From a review of the literature conducted exclusively within the Thai healthcare setting, no study has yet examined the association between PIM use at discharge and unplanned hospital readmissions or ED visits. However, two studies have explored the relationship between PIM use during other stages of care specifically, PIMs prescribed during the index hospitalization and PIMs prescribed to OPD and subsequent hospital readmission outcomes.

Varavithya et al. (2022) conducted a retrospective cohort study at Thammasat University Hospital to investigate the association between PIM use based on prescriptions issued to OPD patients and hospital readmission among Thai older adults aged ≥60 years. Among 32,261 participants, 63.98% were prescribed at least one PIM according to the 2019 Beers Criteria. During a two-year follow-up period, hospital readmission occurred in 14.6% of PIM users compared with 7.98% of non-PIM users. After adjusting for potential confounders, PIM use remained significantly associated with an increased risk of hospitalization (aRR = 1.31, 95% CI: 1.21–1.41, $p < 0.001$). Additional predictors included advanced age, male sex, polypharmacy, and frequent outpatient visits.[44]

Jenghua et al. (2025) conducted a retrospective cohort study involving 20,629 hospitalized older adults aged ≥60 years to examine the association between PIM use during the index hospitalization, defined according to the 2023 Beers Criteria, and one-year rehospitalisation outcomes. Although the prevalence of PIM use was remarkably high (91.3%), overall PIM exposure was not significantly associated with an increased risk of rehospitalisation (aHR = 1.02, 95% CI 0.87–1.19), prolonged hospital stay (adjusted mean difference (aMD) = 0.35 days, 95% CI −1.31 to 2.01), or higher readmission costs (aMD = 2,039 THB, 95% CI −9,824 to 13,901). However, PIM Group 3 (drugs to be used with caution) demonstrated a significant association with an elevated risk of rehospitalisation (aHR = 1.16, 95% CI 1.09–1.23).[46]

A summary of two studies is presented in Table 2.12.

Table 2.12 Comparison of Thai studies examining the association between PIM use and hospital readmission

First author, year of publication	Study design & setting	Study population	Data collection	Outcome measures	Results
Varavithya et al. (2022)[44]	Retrospective cohort study conducted at Thammasat University Hospital, Thailand	32,261 older adults aged ≥ 60 years discharged from hospital between 2015–2019	Electronic medical records and pharmacy dispensing data	All-cause rehospitalisation within 2 year	PIMs at discharge (2019 Beers Criteria) were significantly associated with increased hospital readmission (adjusted RR = 1.31; 95% CI 1.21–1.41; $p < 0.001$).
Jenghua et al. (2025)[46]	Retrospective cohort study at a tertiary care hospital in Phitsanulok Province, Thailand	20,629 hospitalized older adults aged ≥ 60 years admitted during 2021–2023	Hospital electronic medical record (EMR) database	All-cause rehospitalisation within 1 year	Overall PIM use (2023 Beers Criteria) was not significantly associated with rehospitalisation (adjusted HR = 1.02; 95% CI 0.87–1.19). Only PIM Group 3 (drugs requiring caution) was linked with higher rehospitalisation risk (aHR = 1.16; 95% CI 1.09–1.23).

Abbreviations: PIMs = Potentially Inappropriate Medications, RR = Relative Risk, CI = Confidence Interval, aHR = Adjusted Hazard Ratio

CHAPTER 3
RESEARCH METHODOLOGY

3.1 Research Design

This study has three main objectives. First, a descriptive cross-sectional study was conducted to determine the prevalence of PIMs at discharge. Second, the study identified predictors associated with PIMs at discharge using binary logistic regression analysis. Third, an analytical investigation of the association between PIMs and clinical outcomes (all-cause readmissions, unplanned readmissions, and ED visits) within 90 days post-discharge was conducted as a retrospective cohort study.

3.2 Population and sample

3.2.1 Population

The study population consists of older patients who were hospitalized for at least 24 hours at Thammasat University Hospital and then discharged from the medical wards to home.

3.2.2 Sample

Participants were identified through electronic health records (EHRs) of patients hospitalized for at least 24 hours and later discharged home from medical services. The recruitment period extended from September 2021 to September 2023. Eligible patients were those aged 60 years or older at the time of discharge. For individuals with multiple hospital admissions during the recruitment period, only the first admission was considered as their index hospitalization.

3.2.3 Inclusion criteria

The study included patients aged 60 years and above at the time of their index admission who were discharged from medical wards during the study period.

3.2.4 Exclusion criteria

There was no exclusion criteria for participants in the present study

3.3 Sample size estimation

3.3.1 Sample size estimation for identifying predictors of PIM use at hospital discharge. The sample size was calculated based on the principle recommended by Peduzzi et al. (1996)[47], which suggests that for logistic regression analyses, an adequate statistical power requires approximately 10 to 20 outcome events per predictor variable (EPV). From a review of previous studies, three variables were consistently associated with PIM use at hospital discharge, namely age, the number of medications at discharge, and PIM use at admission[30]. In addition, the investigator was interested in exploring other variables, including sex, length of hospital stay, and comorbidities, as these factors were hypothesized to influence the outcome. Therefore, a total of seven predictor variables were considered, requiring at least 140 outcome events (assuming 20 EPV). Based on the study by Komagamine et al. (2019)[19], which reported a prevalence of PIM use at discharge of 32.2%, a minimum sample size of 435 participants was required to ensure sufficient statistical power for logistic regression analysis.

3.3.2 For the analysis using proportional hazards models in survival analysis to examine the association between PIM use at discharge and unplanned readmission or emergency department (ED) visits within 90 days, the outcome incidence was estimated to be 15.0%. This estimation was based on the previous study by Komagamine et al. (2019)[19], which reported a 30-day unplanned readmission rate of 5%. Given that the present study extended the follow-up period to 90 days, the incidence of unplanned readmission was expected to increase to approximately 15%. The investigator planned to include five potential confounders age, sex, comorbidities, length of hospital stay, and the number of medications at discharge together with PIM use at discharge, yielding a total of six predictor variables. According to the rule of thumb proposed by Peduzzi et al. (1996)[47], ensuring adequate statistical power for regression analysis requires approximately 10 to 20 events per predictor variable (EPV). Therefore, at least 120 outcome events were needed for six predictors. Based on an expected event rate of 15%, a minimum total sample size of approximately 800 participants was required to achieve sufficient power for the proportional hazards regression analysis.

3.4 Definition of Terms

3.4.1 **Older patients**: Defined as individuals aged 60 years or older at the time of hospital admission (index admission).

3.4.2 **Index admission**: Refers to the first hospitalization in the internal medicine ward lasting at least 24 hours during the study period, from September 2021 to September 2023.

3.4.3 **Potentially inappropriate medications (PIMs)**: Refer to drugs considered inappropriate according to the 2023 updated AGS Beers Criteria®, as listed in Tables 2 and 3.

3.4.4 **PIMs at admission**: refer to PIMs recorded in the medication reconciliation form within the electronic database at the time of the index admission.

3.4.5 **Discharge**: refers to the record in the electronic database indicating that the patient was released from the hospital to home.

3.4.6 **PIMs at discharge**: refer to PIMs recorded in the home medication list within the electronic database at the time of discharge.

3.4.7 **Unplanned readmission**: refers to a patient who was recorded in the electronic database as having been discharged from the hospital and subsequently rehospitalized for at least 24 hours without a prior scheduled appointment by the attending physician. Such cases were identified based on the department code indicating that the patient was admitted through the emergency department.

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3.4.8 **Emergency department visits**: refer to unscheduled visits to the emergency department that were not arranged in advance by the attending physician. These visits were identified based on the department code indicating that the patient presented to the emergency department after hospital discharge.

3.4.9 **Polypharmacy**: refers to the concurrent use of five or more prescription medications.

3.5 Data collection

Patient information was retrieved from the hospital's electronic database for individuals who met the study's inclusion criteria. Specifically, this comprised patients aged 60 years and above at the time of their index admission, who had been discharged from the internal medicine ward between September 2021 and September 2023. The dataset was provided by the Information Technology Department of the study hospital on July 17, 2024, and was made available for use exclusively in the present research project. The authors did not have access to information that could identify individual participants during or after data collection.

Sample data was extracted from the hospital's electronic database as follows:

3.5.1 Information at index admission included the date, gender, age, body mass index (BMI) (if the patient did not have a recorded BMI at the time of index admission, weight and height were collected at admission for BMI calculation), marital status, and initial diagnosis. Data on the number and list of medications were obtained from the medication reconciliation record in the electronic database, comparing medications prescribed before hospital admission with those at admission (excluding external-use medications and cases where the same medication was prescribed in different doses, which were counted as a single entry).

3.5.2 Information at discharge included comorbidities, length of hospital stay (LOS), discharge date, principal diagnosis (PDx), and ICD diagnosis codes. Data on the number and list of medications were recorded in the Home Medication record in the electronic database at discharge (excluding external-use medications and cases where the same medication was prescribed in different doses, which were counted as one entry).

PIMs among participants were identified based on the 2023 American Geriatrics Society (AGS) Beers Criteria[5]. The identification process followed two main steps. First, medications classified as "drugs to avoid in most older patients" with a strong recommendation (listed in Table 2 of the 2023 criteria) were considered PIMs. The presence of any of these medications in the study population was categorized as a PIM. Second, medications classified as "drugs to avoid in older adults with specific diseases or syndromes" due to drug–disease or drug–syndrome interactions that may exacerbate the condition (listed in Table 3 of the 2023 criteria) were assessed. For each patient prescribed any of these medications, drug–disease or drug–syndrome interactions were evaluated based on their principal diagnosis and comorbidities recorded in the EHRs. We did not include medications listed in Table 4 of the 2023 criteria, which require clinical judgment for appropriate use, as the criteria emphasize caution rather than absolute avoidance in determining PIM status.

The Charlson Comorbidity Index (CCI) was used to quantify patients' comorbidity burden. It was derived from ICD-10 diagnosis codes recorded at hospital discharge in the EHRs. This study used the Charlson command in Stata, which follows the algorithm developed by Quan and colleagues for mapping diagnoses to 17 comorbid conditions[48]. Each condition carries a specific weight based on its mortality risk, and the total score was calculated as the sum of these weights. The CCI score was then entered as a numeric variable and modeled as continuous in regression analyses.

3.5.3 Clinical outcomes data were collected for readmission and emergency department visits occurring within 90 days following discharge. In cases where patients had multiple readmissions or emergency department visits during the follow-up period, only the first occurrence of each event was documented. Time-to-event data were collected for all-cause readmissions, unplanned readmissions and ED visits. Those patients who did not meet event criteria were censored at 90 days post-discharge.

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3.6 Data analysis

Missing data were addressed using complete case analysis, whereby only records with no missing values for the variables included in the models were analyzed. This approach was appropriate because the proportion of missing data was small and assumed to be missing completely at random (MCAR).

3.6.1 Participant baseline characteristics

Descriptive statistics were employed to summarize the baseline characteristics of the study population. Categorical variables—such as gender, marital status, receipt of PIMs at admission, polypharmacy at admission, and polypharmacy at discharge were presented as frequencies and percentages. Quantitative variables, including age, CCI score, LOS, number of medications at admission, number of PIMs at admission, number of medications at discharge, number of PIMs at discharge, BMI, were examined for their data distribution. Normally distributed variables were reported using means and standard deviations (SD), whereas non-normally distributed variables were expressed as medians and interquartile ranges (IQR).

Inferential statistical analyses were conducted to compare baseline characteristics between patients who were discharged with and without PIMs. Categorical variables were assessed using the Chi-square test or Fisher's exact test as appropriate. Continuous variables were assessed using independent t-tests for normally distributed data or Mann-Whitney U tests for variables with non-normal distributions.

3.6.2 Prevalence and predictors of PIMs at discharge

The prevalence of PIM use at discharge was determined by calculating the proportion of patients who received at least one PIM relative to the total study population, with the findings expressed as a percentage. The prevalence of PIMs was also reported by the number of PIMs found at discharge. Predictors of PIM use at discharge were examined through multiple logistic regression analysis, incorporating sex, PIM use at admission (were entered into the regression model as a binary variable), age, CCI score, length of hospital stay and number of medications prescribed at discharge (were entered into the regression model as a continuous numeric variable) as covariates. Results were presented as adjusted ORs with corresponding 95% CIs, with statistical significance set at $p < 0.05$.

The predictive performance of the multivariable model was assessed using the area under the receiver operating characteristic (ROC) curve.

3.6.3 Association of PIMs with readmission and ED visits

The incidence of all readmissions, unplanned readmissions, and emergency department visits was analyzed and reported as the number of events per the follow-up period of the sample.

The relationship between receiving PIMs (a binary variable: received/did not receive) and all readmissions, unplanned readmissions, and emergency department visits was analyzed using Cox regression analysis. The associations were presented as adjusted HR with corresponding 95% confidence intervals, with statistical significance defined at $p < 0.05$. The model incorporated the following covariates: sex (was entered into the regression model as a binary variable), age, CCI score, LOS, number of discharge medications (were entered into the regression model as a continuous numeric variable), and discharge status regarding PIMs (received versus not received), utilizing a full adjustment approach including all variables.

The association between the number of PIMs prescribed at discharge (treated as a continuous variable) and outcomes including all-cause readmissions, unplanned readmissions, and emergency department visits was also examined using Cox proportional hazards regression analysis.

To explore the robustness of the association between receiving PIMs and outcomes including all-cause readmissions, unplanned readmissions, and emergency department visits, parametric survival analyses were conducted using Weibull, exponential, lognormal, and log-logistic distributions. Associations were reported as model coefficients and the model fit was assessed with the Akaike Information Criterion (AIC) and Bayesian Information Criterion (BIC).

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The proportional hazards assumption was examined using Schoenfeld's residuals method, analyzing the relationship between the residuals of the hazard and time. A p-value greater than 0.05 will indicate the assumption is met.

Multicollinearity among variables will be evaluated by calculating variance inflation factors (VIFs), with a VIF value exceeding 5 indicating significant multicollinearity.

All analyses were performed using Stata 18 (StataCorp, College Station, TX). Statistical significance was set at $p < 0.05$, and all hypothesis tests were two-sided.

3.7 The conceptual framework of the research.

A review of the literature reveals several variables associated with the outcomes of interest, namely unplanned readmissions and emergency-department visits, as presented in Table 10. These variables can be represented in a directed acyclic graph (DAG), as shown in Figure 3.1.

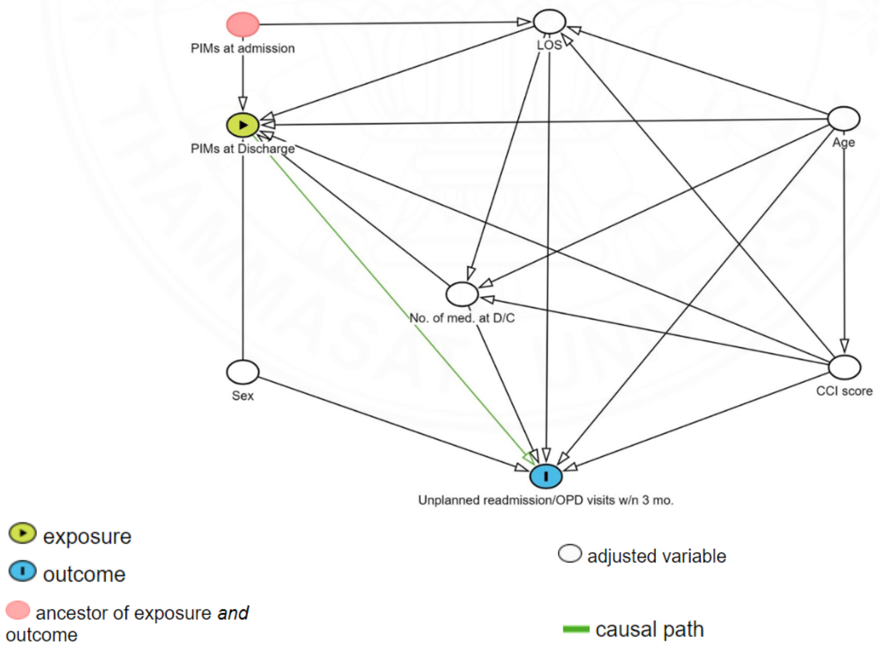

Figure 3.1 DAGs of significant predictors in the fully adjusted models.

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Table 3.1 The variables associated with unplanned readmissions and ED visits, as identified through the literature review

Variables	References
Age	Hammouda et al., (2021)[18]
Sex	Komagamine et al., (2019)[15] Akkawi et al., (2023)[13]
CCI score	Komagamine et al., (2019)[15] Hammouda et al, (2021)[18]
Length of hospital stay	Fabbietti et al., (2018)[16]
Number of medications at hospital discharge	Thomas et al., (2020)[10] De Vincentis et al., (2020)[14] Fabbietti et al., (2018)[16]

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CHAPTER 4
RESULTS AND DISCUSSION

4.1 Results

4.1.1 Characteristics of the study population

The study evaluated a cohort of 4,012 patients discharged from the inpatient unit within the study timeframe. The participant flowchart of the total cohort is presented in Figure 4.1. Among them, 2,299 patients were prescribed at least one PIM at discharge. The median age of patients receiving PIMs was 74 years (IQR: 67–82), with a mean age of 74.98 years, both significantly higher than the median age of 72 years (IQR: 66–81) and mean age of 73.75 years observed in patients not prescribed PIMs. Furthermore, the PIM group exhibited significantly elevated CCI scores, a higher number of medications prescribed at discharge, increased prevalence of polypharmacy (defined as concurrent use of five or more medications), and longer hospitalization durations relative to the non-PIM group. Notably, the incidence of polypharmacy was substantially greater in the PIM group compared to their counterparts (86.56% vs. 52.89%), as presented in Table 4.1.

Within the cohort of 4,012 individuals, data on medication use before admission were available for 1,397 participants (Table 4.2). This subgroup included 854 patients who were prescribed at least one PIM at discharge and 543 patients who were not. Significant differences between the groups were identified in terms of the number of medications before admission, the prevalence of polypharmacy, the presence of at least one PIM before admission, and the total count of PIMs before admission. A detailed summary of the study population characteristics with data on medication before admission is presented in Table 4.2.

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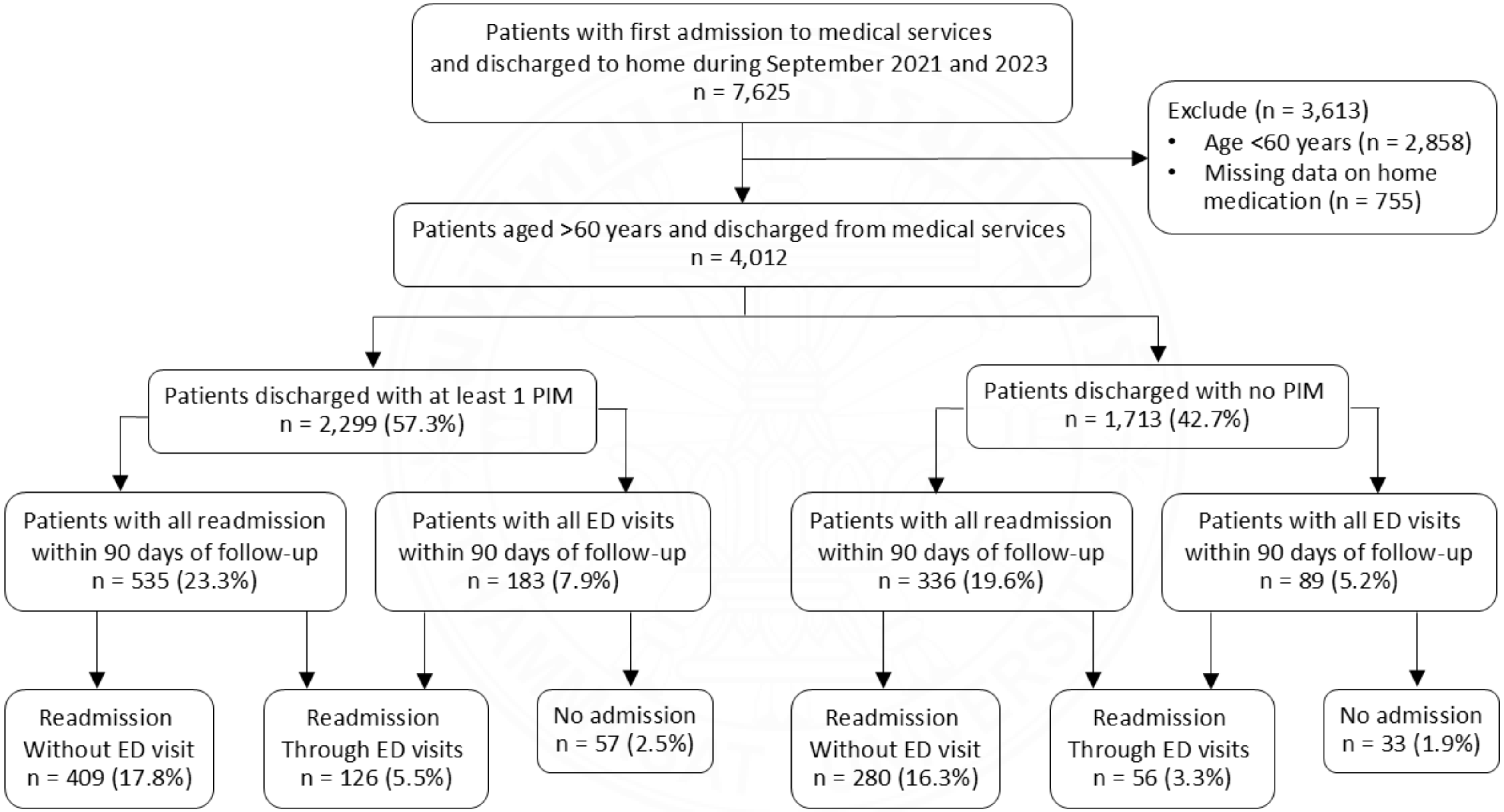

Figure 4.1 Participant flowchart

Table 4.1 Demographic and clinical characteristics of study patients divided according to the occurrence of at least 1 PIMs at discharge (n = 4,012 at discharge)

Characteristics	Overall (n=4,012)	PIMs at discharge (n = 2,299)	No PIMs at discharge (n = 1,713)	*P-value**
Age, median (IQR)/ mean (SD)	74 (67-82)/ 74.46 (9.17)	74 (67-82)/ 74.98 (9.24)	72 (66-81)/ 73.75 (9.04)	< 0.001
Male gender, n (%)	1,919 (47.83)	1,076 (46.80)	843 (49.21)	0.131
Marital status, n (%)				
Single	1,351 (33.67)	777 (33.80)	574 (33.51)	0.848
Married	2,661 (66.33)	1,522 (66.20)	1,139 (66.49)	
CCI score, median (IQR)/ mean (SD)	0 (0-1)/ 0.78 (1.15)	1 (0-1)/ 0.84 (1.18)	0 (0-1)/ 0.69 (1.11)	< 0.001
1. CCI score = 0, n (%)	2,170 (54.09)	1,146 (49.85)	1,024 (59.79)	< 0.001
2. CCI score = 1, n (%)	989 (24.65)	634 (27.58)	355 (20.72)	
3. CCI score = 2, n (%)	664 (16.55)	401 (17.44)	263 (15.35)	
4. CCI score = 3, n (%)	124 (3.09)	75 (3.26)	49 (2.86)	
5. CCI score ≥ 4, n (%)	65 (1.62)	43 (1.87)	22 (1.28)	
No. of medication at discharge, median (IQR)/ mean (SD)	7 (4-10)/ 7.51 (4.23)	9 (6-12)/ 9.01 (4.03)	5 (3-8)/ 5.49 (3.61)	< 0.001
Polypharmacy at discharge, n (%)	2,896 (72.18)	1,990 (86.56)	906 (52.89)	< 0.001
Length of hospital stay (day), median (IQR)/ mean (SD)	5 (3-10)/ 8.79 (11.89)	6 (3-13)/ 10.41 (13.74)	4 (2-8)/ 6.62 (8.33)	< 0.001

*The two groups were compared using an independent t-test for means, a Wilcoxon rank-sum test for medians, and a Chi-square test for proportions.

Abbreviations: IQR = Interquartile Range, SD = standard deviation, n = sample, BMI = Body Mass Index, CCI = Charlson comorbidity index, No. = number

Table 4.2 Demographics and clinical characteristics of study patients stratified by the occurrence of at least 1 PIM at discharge (n = 1,397 with data on medications before admission)

Characteristics	Overall (n=1,397)	PIMs at discharge (Total=854)	No PIMs at discharge (Total=543)	*P-value**
Age, median (IQR)/ mean (SD)	74 (67-83)/ 74.88 (9.12)	75 (68-83)/ 75.23 (9.11)	74 (67-82)/ 74.32 (9.13)	0.071
Male gender, n (%)	681 (48.75)	398 (46.60)	283 (52.12)	0.044
Marital status, n (%)				
Single	462 (33.07)	281 (32.90)	181 (33.33)	0.868
Married	935 (66.93)	573 (67.10)	362 (66.67)	
CCI score, median (IQR)/ mean (SD)	0 (0-1)/ 0.84 (1.21)	1 (0-2)/ 0.92 (1.27)	0 (0-1)/ 0.70 (1.10)	< 0.001
1. CCI score = 0, n (%)	730 (52.25)	407 (47.66)	323 (59.48)	0.252
2. CCI score = 1, n (%)	336 (24.05)	232 (27.17)	104 (19.15)	
3. CCI score = 2, n (%)	256 (18.32)	161 (18.85)	95 (17.50)	
4. CCI score = 3, n (%)	48 (3.44)	33 (3.86)	15 (2.76)	
5. CCI score ≥ 4, n (%)	27 (1.93)	21 (2.46)	6 (1.10)	
Length of hospital stay (day), median (IQR)/ mean (SD)	6 (3-12)/ 9.86 (12.13)	7 (3-15)/ 11.69 (13.96)	4 (2-9)/ 6.99 (7.67)	< 0.001
No. of medication before admission, median (IQR)/ mean (SD)	8 (5-11)/ 8.32 (4.98)	8 (5-12)/ 8.71 (5.01)	7 (4-11)/ 7.70 (4.87)	< 0.001
Polypharmacy before admission, n (%)	1,061 (75.95)	674 (78.92)	387 (71.27)	< 0.001
At least 1 PIMs before admission, n (%)	787 (56.34)	564 (66.04)	223 (41.07)	< 0.001
No. of PIMs before admission, median (IQR)/ mean (SD)	1 (0-1)/ 0.87 (0.96)	1 (0-2)/ 1.05 (1.00)	0 (0-1)/ 0.58 (0.80)	< 0.001

*The two groups were compared using an independent t-test for means, a Wilcoxon rank-sum test for medians, and a Chi-square test for proportions. Abbreviations: IQR = Interquartile Range, SD = standard deviation, n = sample, BMI = Body Mass Index, CCI = Charlson comorbidity index, No. = number

4.1.2 Prevalence of PIMs at discharge

Of the 4,012 patients included in the study, 2,299 (57.3%) were prescribed at least one PIM at discharge. Among these patients, the proportions receiving 1, 2, 3, and more than 3 PIMs at discharge were 36.58%, 15.48%, 4.54%, and 0.7%, respectively. The three most frequently prescribed PIMs were proton pump inhibitors (25.42%), aspirin (13.14%), and lorazepam (11.04%). The prevalence of PIMs at discharge, along with the ten most commonly prescribed PIMs, is presented in Table 4.3.

Table 4.3 Prevalence of PIMs at discharge (n = 4,012)

No. of PIMs at discharge per patient	**Prevalence, n (%)**
1 PIM	1,468 (36.58)
2 PIMs	621 (15.48)
3 PIMs	182 (4.54)
> 3 PIMs	28 (0.70)
At least 1 PIMs	2,299 (57.30)
The most prevalent PIMs at discharge	**n (%)**
1. PPIs	1,020 (25.42)
2. Aspirin	672 (16.75)
3. Lorazepam	443 (11.04)
4. Warfarin	202 (5.03)
5. Quetiapine	191 (4.76)
6. Doxazosin	180 (4.49)
7. Glipizide	135 (3.36)
8. Clonazepam	69 (1.72)
9. Metoclopramide	50 (1.25)
10. Alprazolam	42 (1.05)
10. Orphenadrine	42 (1.05)

Abbreviations: PIMs = Potentially Inappropriate Medications, n = sample, PPIs = Proton pump inhibitors

4.1.3 Factors associated with PIMs at discharge

A predictive analysis was conducted to identify factors associated with the receipt of PIMs at discharge. Univariable analysis revealed that age ([cOR] 1.01, 95% [CI] 1.01–1.02, $p < 0.001$), CCI score ([cOR] 1.13, 95% [CI] 1.07–1.20, $p < 0.001$), LOS ([cOR] 1.04, 95% [CI] 1.03–1.05, $p < 0.001$), and the number of medications at discharge ([cOR] 1.27, 95% [CI] 1.25–1.30, $p < 0.001$) were significant predictors. However, in the multivariable model, only CCI score ([aOR] 1.08, 95% [CI] 1.01–1.15, $p = 0.016$), LOS ([aOR] 1.01, 95% [CI] 1.00–1.02, $p = 0.01$), and the number of medications at discharge ([aOR] 1.26, 95% [CI] 1.24–1.29, $p < 0.001$) remained significantly associated with PIMs prescription at discharge among the cohort of 4,012 patients. Detailed findings are presented in Table 4.4.

When medication data prior to admission were included in the model, the sample size was reduced to 1,397 patients. Despite this reduction, the results remained consistent with the previous analysis. Specifically, CCI score ([aOR] 1.17, 95% [CI] 1.05–1.30, $p < 0.001$), LOS ([aOR] 1.02, 95% [CI] 1.01–1.04, $p < 0.001$), number of medications at discharge ([aOR] 1.22, 95% [CI] 1.18–1.26, $p < 0.001$), and presence of PIMs prior to admission ([aOR] 2.32, 95% [CI] 1.82–2.96, $p < 0.001$) were identified as significant predictors of receiving PIMs at discharge, after adjusting for other covariates. These results are detailed in Table 4.5.

Table 4.4 Univariable and multivariable analyses for factors associated with PIMs at discharge (n = 4,012)

Variables	Unadjusted OR (95% CI)	*P-value*	Adjusted OR (95% CI)	*P-value*
Age	1.01 (1.01-1.02)	< 0.001	1.00 (0.99-1.01)	0.959
Male gender	0.91 (0.80-1.03)	0.131	0.93 (0.81-1.06)	0.272
CCI score	1.13 (1.07-1.20)	< 0.001	1.08 (1.01-1.15)	0.016
Length of stay	1.04 (1.03-1.05)	< 0.001	1.01 (1.00-1.02)	0.010
Number of medications at discharge	1.27 (1.25-1.30)	< 0.001	1.26 (1.24-1.29)	< 0.001

Abbreviations: PIMs = Potentially Inappropriate Medications, OR = Odds ratio, CI = confidence interval, CCI = Charlson comorbidity index. Age, CCI score, length of stay, and number of medications at discharge were entered into the analysis as numeric variables, while gender was entered as a categorical variable.

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Table 4.5 Univariable and multivariable analyses for factors associated with PIMs at discharge (n = 1,397 with data on medications before admission)

Variable	**Unadjusted OR (95% CI)**	***P-value***	**Adjusted OR (95% CI)**	***P-value***
Age	1.01 (1.00-1.02)	0.071	0.99 (0.98-1.01)	0.536
Male gender	0.80 (0.65-0.99)	0.045	0.88 (0.69-1.12)	0.301
CCI score	1.18 (1.07-1.30)	< 0.001	1.17 (1.05-1.30)	< 0.001
Length of stay	1.05 (1.04-1.07)	< 0.001	1.02 (1.01-1.04)	< 0.001
PIMs before admission	2.79 (2.24-3.48)	< 0.001	2.32 (1.82-2.96)	< 0.001
Number of medications at discharge	1.26 (1.22-1.30)	< 0.001	1.22 (1.18-1.26)	< 0.001

Abbreviations: PIMs = Potentially Inappropriate Medications, OR = Odds ratio, CI = confidence interval, CCI = Charlson comorbidity index. Age, CCI score, length of stay, and number of medications at discharge were entered into the analysis as numeric variables, while gender was entered as a categorical variable.

The multivariable model exhibited strong discriminative ability, achieving an area under the curve (AUC) of 0.7508 in the full cohort (n = 4,012) and 0.7671 in the reduced cohort (n = 1,397), as illustrated in Figures 4.2 and 4.3, respectively.

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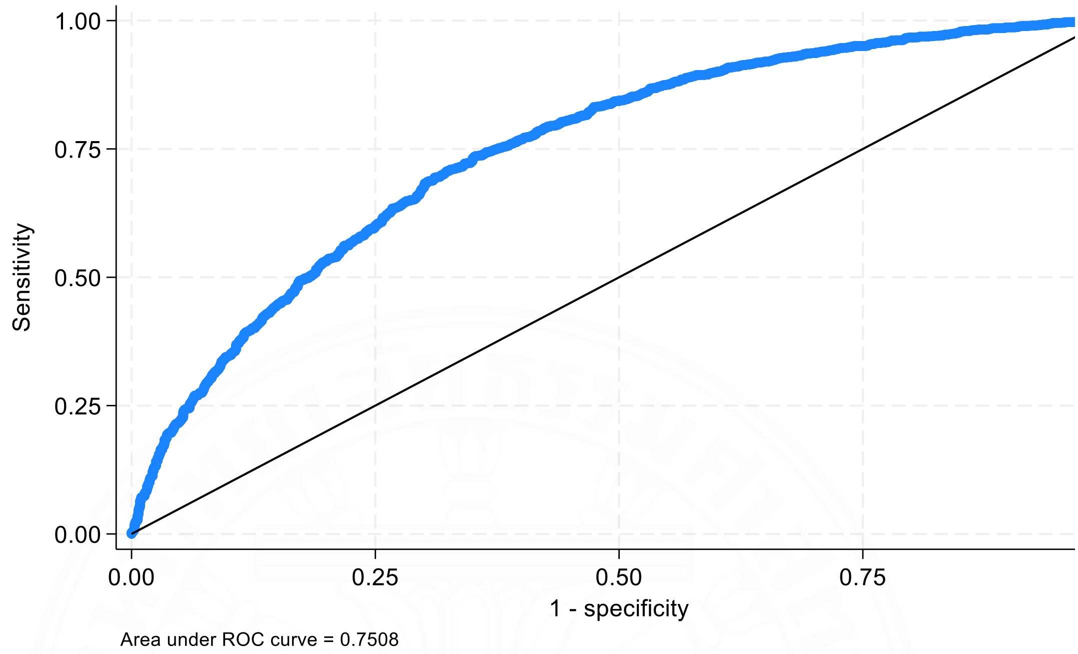

Figure 4.2 Discriminatory performance of the multivariable model (n=4,012).

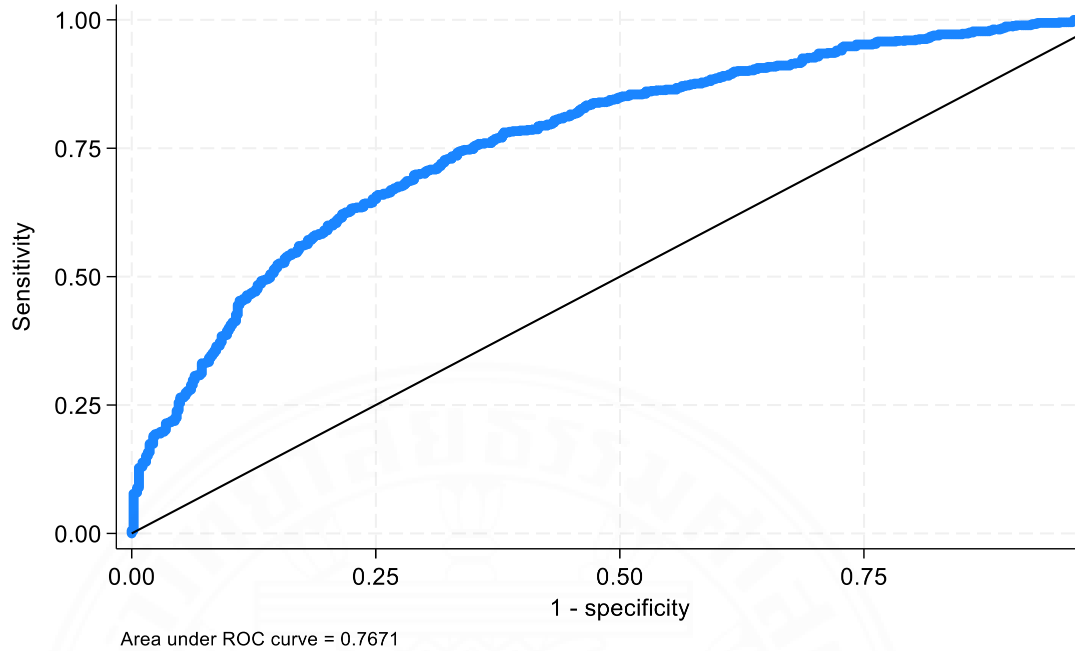

Figure 4.3 Discriminatory performance of the multivariable model (n=1,397).

4.1.4 Incidence of readmission and ED visits

Over a 90-day follow-up period, a total of 871 all-cause readmissions were observed. Of these, 535 cases (61.42%) occurred in the group that received PIMs at discharge, while 336 cases (38.58%) were identified in the group that did not receive PIMs at discharge. The mean time to all-cause readmission was 29.82 days in the PIM group and 32.43 days in the non-PIM group. When analyzing unplanned readmissions specifically, the total number decreased to 182 cases, representing 20.90% of all readmissions. Among 182 cases with unplanned readmission, 126 (69.23%) were prescribed PIMs at the index discharge, while 56 (30.77%) were not. Additionally, the mean time to unplanned readmission was shorter than that for all-cause readmission, as detailed in Table 4.6.

The analysis of unplanned readmission and emergency department visits, defined as emergency department visits occurring within 90 days post-discharge, identified a total of 272 patients. Among these, 183 patients (67.28%) were from the group that received PIMs at discharge, while 89 patients (32.72%) were from the group that did not receive PIMs. The median duration until unplanned readmission or emergency department visit was 21 days for the PIM group and 25 days for the non-PIM group. However, the mean time to these events was similar between the groups, measuring 28 days and 28.85 days, respectively. These results are detailed in Table 4.6.

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Table 4.6 Time-to-event and number of events for each outcome

Outcome	Follow-up (Days) median (IQR)/ mean (SD)	Events	Cumulative incidence
All readmission (n = 871)			
With PIMs at discharge	22 (12-46)/ 29.82 (22.56)	535	61.42
Without PIMs at discharge	26 (12-50)/ 32.43 (23.50)	336	38.58
Unplanned Readmission (n = 182)			
With PIMs at discharge	21 (11-35)/ 25.25 (19.50)	126	69.23
Without PIMs at discharge	28.5 (10-38)/ 28.48 (20.88)	56	30.77
Unplanned readmission and ED visits (n = 272)			
With PIMs at discharge	21 (8-42)/ 28.00 (23.40)	183	67.28
Without PIMs at discharge	25 (8-44)/ 28.85 (24.18)	89	32.72

Abbreviations: IQR = Interquartile Range, SD = standard deviation, n = sample

4.1.5 Principal diagnosis of all readmissions and unplanned readmissions

Among the 871 patients who experienced all-cause readmission, the five most frequent principal diagnoses were atherosclerotic heart disease of the native coronary artery (64 cases, 7.34%), congestive heart failure (39 cases, 4.47%), urinary tract infection (35 cases, 4.01%), malignant neoplasm of an unspecified part of the bronchus or lung (33 cases, 3.78%), and non-ST elevation myocardial infarction (NSTEMI) (32 cases, 3.67%). Additional principal diagnoses associated with all-cause readmissions are summarized in Table 4.7.

Among the 182 patients who experienced unplanned readmission, the five most frequent principal diagnoses were urinary tract infection (14 cases, 7.69%), congestive heart failure (13 cases, 7.14%), pneumonitis due to inhalation of food and vomit (9 cases, 4.95%), chronic obstructive pulmonary disease with acute exacerbation (8 cases, 4.40%), and other viral pneumonia (7 cases, 3.85%). Further details on principal diagnoses associated with unplanned readmissions are provided in Table 4.8.

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Table 4.7 Top principal diagnosis of all readmissions (n = 871)

ICD-10	Principal diagnosis	n	(%)
I251	Atherosclerotic heart disease of native coronary artery	64	7.34
I500	Congestive heart failure	39	4.47
N390	Urinary tract infection	35	4.01
C349	Malignant neoplasm of unspecified part of bronchus or lung	33	3.78
I214	Non-ST elevation (NSTEMI) myocardial infarction	32	3.67
C220	Liver cell carcinoma	20	2.29
J128	Other viral pneumonia	19	2.18
J189	Pneumonia, unspecified organism	16	1.83
J441	Chronic obstructive pulmonary disease with (acute) exacerbation	16	1.83
J690	Pneumonitis due to inhalation of food and vomit	16	1.83
N185	Chronic kidney disease, stage 5	13	1.49
E871	Hypo-osmolality and hyponatremia	13	1.49
K830	Cholangitis	13	1.49
C20	Malignant neoplasm of rectum	12	1.38
I509	Heart failure, unspecified	12	1.38
J440	Chronic obstructive pulmonary disease with (acute) lower respiratory infection	12	1.38
C833	Diffuse large B-cell lymphoma	10	1.15
J209	Acute bronchitis, unspecified	10	1.15
N179	Acute kidney failure, unspecified	10	1.15
A099	Diarrhoea and gastroenteritis of presumed infectious origin	9	1.03
C187	Malignant neoplasm of sigmoid colon	9	1.03

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Table 4.7 Top principal diagnosis of all readmission (n = 871) (Continue)

ICD-10	Principal diagnosis	n	(%)
I260	Pulmonary embolism with acute cor pulmonale	8	0.92
I635	Cerebral infarction due to unspecified occlusion or stenosis of cerebral arteries	8	0.92
J00	Acute nasopharyngitis [common cold]	8	0.92
N10	Acute pyelonephritis	8	0.92
R91	Abnormal findings on diagnostic imaging of lung	8	0.92

Ref. code: 25686518030066AYF

Table 4.8 Top principal diagnosis of unplanned readmission (n = 182)

ICD-10	Principal diagnosis	n	(%)
N390	Urinary tract infection	14	7.69
I500	Congestive heart failure	13	7.14
J690	Pneumonitis due to inhalation of food and vomit	9	4.95
J441	Chronic obstructive pulmonary disease with (acute) exacerbation	8	4.40
J128	Other viral pneumonia	7	3.85
C349	Malignant neoplasm of unspecified part of bronchus or lung	5	2.75
J189	Pneumonia, unspecified organism	5	2.75
N185	Chronic kidney disease, stage 5	5	2.75
E110	Type 2 diabetes mellitus with ketoacidosis without coma	4	2.20
I214	Non-ST elevation (NSTEMI) myocardial infarction	4	2.20
J440	Chronic obstructive pulmonary disease with (acute) lower respiratory infection	4	2.20

Ref. code: 25686518030066AYF

4.1.6. Univariable and multivariable Cox proportional hazards models analyses of the association of PIMs use with outcome

4.1.6.1 All readmission

Univariable Cox proportional hazards analysis identified age, male sex, CCI score, LOS, number of medications at discharge, and PIM use at discharge as factors associated with all-cause readmissions. Following multivariable adjustment, four factors remained significantly associated with readmission risk: male sex ([aHR] 1.23, 95% [CI] 1.08–1.41, $p < 0.01$); each one-point increase in CCI score (aHR 1.12, 95% CI 1.06–1.17, $p < 0.01$); each additional day of LOS (aHR 1.01, 95% CI 1.00–1.01, $p < 0.01$); and each additional discharge medication (aHR 1.03, 95% CI 1.01–1.04, $p < 0.01$).

Although patients receiving PIMs at discharge exhibited a 5% higher risk of all-cause readmission compared to those not receiving PIMs (aHR = 1.05, 95% CI: 0.91–1.22, $p = 0.49$), this association was not statistically significant, as shown in Model 1 (Table 4.9). The proportional hazards assumption was examined using Schoenfeld's residuals, and the results are presented in Table 4.10. Figure 4.4 shows the Kaplan–Meier survival curve for Model 1.

When the variable "PIMs at discharge" was replaced by the "number of PIMs at discharge" in Model 2, the findings remained unchanged. Specifically, each additional PIM prescribed at discharge corresponded to a 1% increase in the risk of all-cause readmission ([aHR] = 1.01, 95% confidence interval [CI]: 0.93–1.10, $p = 0.78$). Nevertheless, this association did not reach statistical significance, as presented in Model 2 (Table 4.11). The proportional hazards assumption was presented in Table 4.12.

Table 4.9 Model 1: Multivariable Cox proportional hazards models to determine the association of PIMs use with all readmissions (n = 4,012).

Variables	Univariable		Multivariable	
	cHR (95% CI)	*P-value*	aHR (95% CI)	*P-value*
Age*	1.01 (1.00-1.01)	0.040	1.01 (1.00-1.01)	0.088
Male	1.24 (1.09-1.42)	0.001	1.23 (1.08-1.41)	0.002
CCI score*	1.13 (1.08-1.18)	< 0.001	1.12 (1.06-1.17)	< 0.001
LOS*	1.01 (1.01-1.01)	< 0.001	1.01 (1.00-1.01)	0.001
No. of med. at D/C*	1.04 (1.02-1.06)	< 0.001	1.03 (1.01-1.04)	0.004
PIMs at D/C	1.22 (1.06-1.40)	0.004	1.05 (0.91-1.22)	0.487

Abbreviations: PIMs = Potentially Inappropriate Medications, CCI = Charlson comorbidity index, LOS = Length of stay, No. = number, med. = medications, D/C = discharge, cHR = crude hazard ratios, aHR = adjusted hazard ratios, CI = confidence interval, *Continuous variables were used.

Table 4.10 Test for proportional-hazards assumption of model 1

Variables	rho	chi^2	df	Prob>chi^2
Age	-0.033	0.98	1	0.322
Male	0.027	0.64	1	0.424
CCI score	-0.070	3.07	1	0.079
LOS	-0.045	1.48	1	0.224
No. of med. at D/C	0.004	0.01	1	0.905
PIMs at D/C	-0.033	1.00	1	0.316
Global test		7.94	6	0.242

Abbreviations: CCI = Charlson comorbidity index, LOS = Length of stay, No. = number, med. = medications, D/C = discharge, df = degrees of freedom

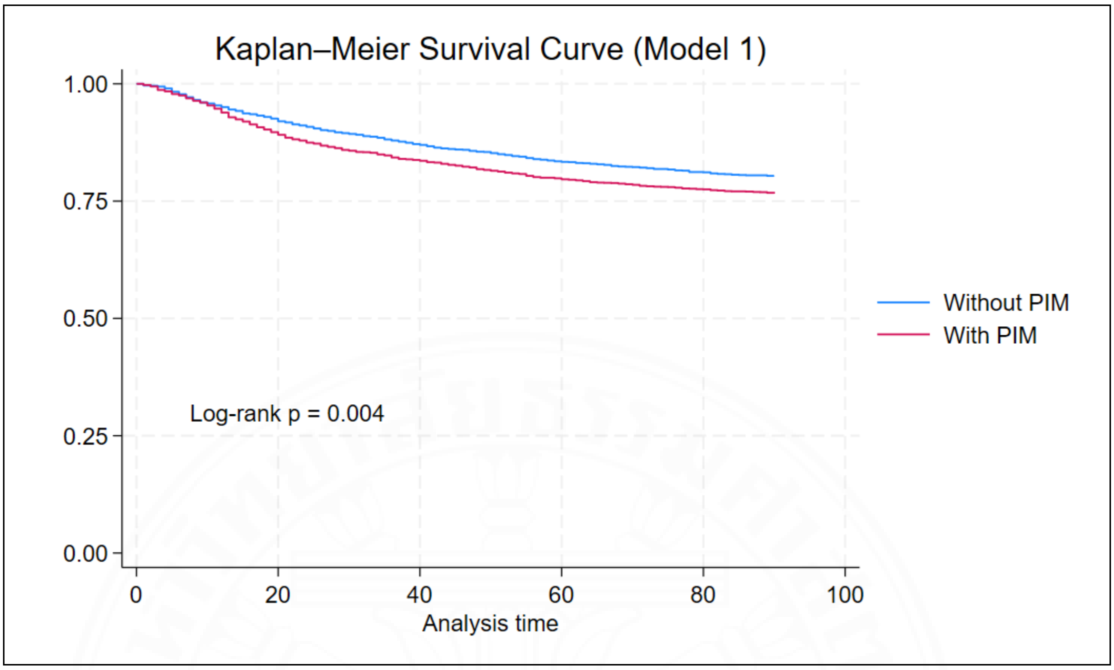

Figure 4.4 Kaplan–Meier survival curve for Model 1

Table 4.11 Model 2: Multivariable Cox proportional hazards models to determine the association of PIMs use with all readmissions (n = 4,012).

Variables	Univariable		Multivariable	
	cHR (95% CI)	*P-value*	aHR (95% CI)	*P-value*
Age*	1.01 (1.00-1.01)	0.040	1.01 (1.00-1.01)	0.086
Male	1.24 (1.09-1.42)	0.001	1.23 (1.08-1.41)	0.002
CCI score*	1.13 (1.08-1.18)	< 0.001	1.12 (1.06-1.17)	< 0.001
LOS*	1.01 (1.01-1.01)	< 0.001	1.01 (1.00-1.01)	0.001
No. of med. at D/C*	1.04 (1.02-1.06)	< 0.001	1.03 (1.01-1.05)	0.004
No. of PIMs at D/C*	1.11 (1.03-1.19)	0.004	1.01 (0.93-1.10)	0.778

Abbreviations: CCI = Charlson comorbidity index, LOS = Length of stay, No. = number, med. = medications, D/C = discharge, cHR = crude hazard ratios, aHR = adjusted hazard ratios, CI = confidence interval, *Continuous variables were used.

Table 4.12 Test for proportional-hazards assumption of model 2

Variables	rho	chi^2	df	Prob>chi^2
Age	-0.034	1.03	1	0.310
Male	0.026	0.63	1	0.427
CCI score	-0.070	3.03	1	0.081
LOS	-0.045	1.46	1	0.227
No. of med. at D/C	0.004	0.02	1	0.888
No. of PIMs at D/C	-0.028	0.74	1	0.391
Global test		7.64	6	0.266

Abbreviations: CCI = Charlson comorbidity index, LOS = Length of stay, No. = number, med. = medications, D/C = discharge, df = degrees of freedom

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4.1.6.2 Unplanned readmission

A univariable Cox proportional hazards analysis conducted among patients discharged and subsequently experiencing unplanned readmissions identified age, LOS, number of medications at discharge, and PIMs at discharge as significant predictors of unplanned readmission. Notably, receipt of PIMs at discharge was associated with a 72% increased risk of unplanned readmission (aHR = 1.72, 95% CI: 1.26–2.36, $p < 0.01$).

After adjustment for age, male gender, CCI score, LOS, number of medications at discharge, and PIMs at discharge, only three variables remained significantly associated with unplanned readmission: (1) age, where each additional year conferred a 3% increase in risk (aHR = 1.03, 95% CI: 1.01–1.05, $p < 0.01$); (2) LOS, where each additional hospital day increased risk by 1% (aHR = 1.01, 95% CI: 1.00–1.02, $p < 0.01$); and (3) number of medications at discharge, where each additional medication increased risk by 6% (aHR = 1.06, 95% CI: 1.02–1.10, $p < 0.01$).

Although receipt of PIMs at discharge was associated with a 27% higher risk of unplanned readmission (aHR = 1.27, 95% CI: 0.91–1.76, $p = 0.16$), this association did not reach statistical significance, as shown in Model 3 (Table 4.13). The proportional hazards assumption was presented in Table 4.14. Figure 4.5 shows the Kaplan–Meier survival curve for Model 3.

When the variable “PIMs at discharge” was replaced with “number of PIMs at discharge” in Model 4, the results remained largely unchanged. Specifically, each additional PIM prescribed at discharge was associated with an 8% increase in risk of unplanned readmission (aHR = 1.08, 95% CI: 0.91–1.27, $p = 0.40$); however, this association was also not statistically significant (Table 4.15). The proportional hazards assumption was presented in Table 4.16.

Table 4.13 Model 3: Multivariable Cox Proportional-Hazards models to determine the association of PIMs use with unplanned readmission (n = 4,012).

Variables	Univariable		Multivariable	
	cHR (95% CI)	*P-value*	aHR (95% CI)	*P-value*
Age*	1.03 (1.02-1.05)	< 0.001	1.03 (1.01-1.05)	< 0.001
Male	1.14 (0.85-1.52)	0.388	1.18 (0.88-1.58)	0.259
CCI score*	1.07 (0.96-1.20)	0.238	1.05 (0.94-1.18)	0.378
LOS*	1.01 (1.01-1.02)	< 0.001	1.01 (1.00-1.02)	0.018
No. of med. at D/C*	1.09 (1.06-1.13)	< 0.001	1.06 (1.02-1.10)	0.001
PIMs at D/C	1.72 (1.26-2.36)	0.001	1.27 (0.91-1.76)	0.162

Abbreviations: No. = number, med. = medications, D/C = discharge, cHR = crude hazard ratios, aHR = adjusted hazard ratios, CI = confidence interval, *Continuous variables were used.

Table 4.14 Test for proportional-hazards assumption of model 3

Variables	rho	chi^2	df	Prob>chi^2
Age	0.023	0.10	1	0.753
Male	0.073	0.97	1	0.325
CCI score	0.001	0.00	1	0.990
LOS	-0.006	0.00	1	0.965
No. of med. at D/C	0.086	1.23	1	0.267
PIMs at D/C	-0.095	1.62	1	0.203
Global test		3.24	6	0.778

Abbreviations: No. = number, med. = medications, D/C = discharge, df = degrees of freedom

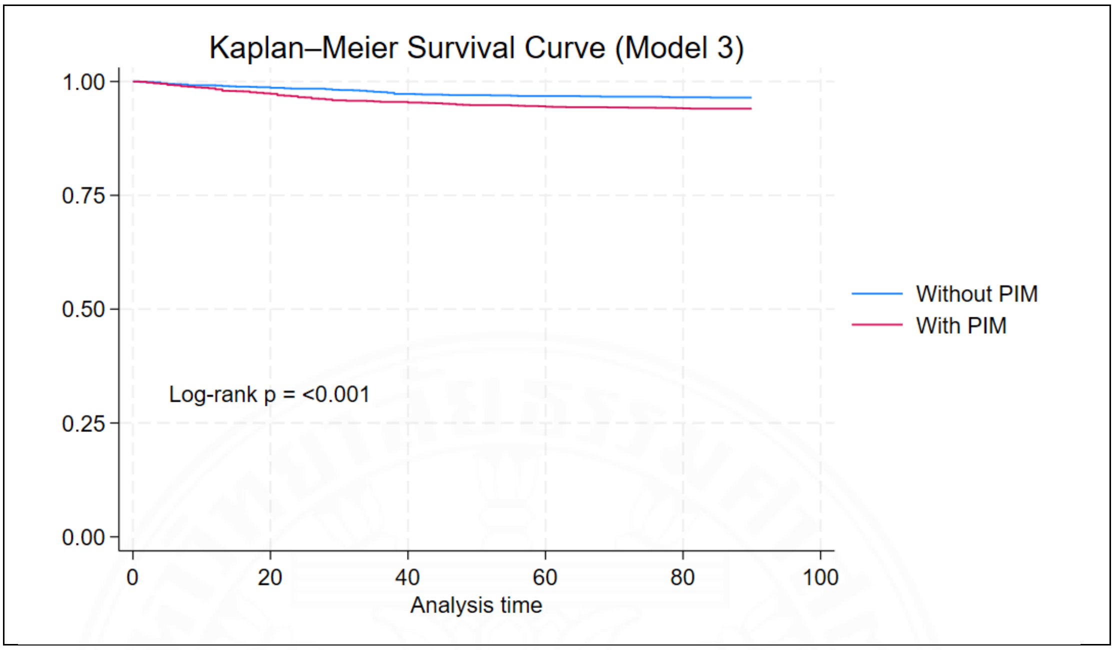

Figure 4.5 Kaplan–Meier survival curve for Model 3

Table 4.15 Model 4: Multivariable Cox Proportional-Hazards models to determine the association of PIMs use with unplanned readmission (n = 4,012).

Variables	Univariable		Multivariable	
	cHR (95% CI)	*P-value*	aHR (95% CI)	*P-value*
Age*	1.03 (1.02-1.05)	< 0.001	1.03 (1.01-1.05)	< 0.001
Male	1.14 (0.85-1.52)	0.388	1.18 (0.88-1.58)	0.262
CCI score*	1.07 (0.96-1.20)	0.238	1.05 (0.94-1.18)	0.373
LOS*	1.01 (1.01-1.02)	< 0.001	1.01 (1.00-1.02)	0.017
No. of med. at D/C*	1.09 (1.06-1.13)	< 0.001	1.06 (1.02-1.10)	0.001
No. of PIMs at D/C*	1.28 (1.11-1.49)	0.001	1.08 (0.91-1.27)	0.392

Abbreviations: No. = number, med. = medications, D/C = discharge, cHR = crude hazard ratios, aHR = adjusted hazard ratios, CI = confidence interval, *Continuous variables were used.

Table 4.16 Test for proportional-hazards assumption of model 4

Variables	rho	chi^2	df	$Prob>chi^2$
Age	0.021	0.08	1	0.781
Male	0.072	0.95	1	0.329
CCI score	0.004	0.00	1	0.968
LOS	-0.005	0.00	1	0.971
No. of med. at D/C	0.093	1.48	1	0.223
No. of PIMs at D/C	-0.097	1.77	1	0.183
Global test		3.40	6	0.757

Abbreviations: No. = number, med. = medications, D/C = discharge, df = degrees of freedom

4.1.6.3 Unplanned readmission and ED visits

An analysis using univariable Cox proportional hazards models among patients discharged who subsequently visited the emergency department yielded results comparable to those for unplanned readmissions. Age, LOS, the number of medications at discharge, and PIMs prescribed at discharge were all significantly associated with unplanned readmissions and emergency department visits. Notably, receiving PIMs at discharge was linked to a 55% higher risk of these outcomes (aHR = 1.55, 95% CI: 1.21–2.00, $p < 0.01$).

However, after adjusting for age, male gender, CCI score, LOS, number of medications at discharge, and PIMs at discharge, only three variables remained significantly associated with unplanned readmissions and emergency department visits. Each additional year of age increased the risk by 3% (aHR = 1.03, 95% CI: 1.01–1.04, $p < 0.01$), each additional day of hospitalization increased the risk by 1% (aHR = 1.01, 95% CI: 1.00–1.01, $p < 0.01$), while each additional medication increased the risk by 7% (aHR = 1.07, 95% CI: 1.03–1.10, $p < 0.01$).

Although PIMs at discharge were associated with a 15% higher risk of unplanned readmission and emergency department visits (aHR = 1.15, 95% CI: 0.87–1.51, $p = 0.32$), this association did not reach statistical significance, as shown in Model 5 (Table 4.17). The proportional hazards assumption was presented in Table 4.18. Figure 4.6 shows the Kaplan–Meier survival curve for Model 5.

Furthermore, when the variable “PIMs at discharge” was replaced with “number of PIMs at discharge” in Model 6, the results remained similar. Specifically, the number of PIMs at discharge was not significantly associated with an increased risk of unplanned readmissions and emergency department visits (aHR = 1.00, 95% CI: 0.87–1.15, $p = 0.96$), as presented in Model 6 (Table 4.19). The proportional hazards assumption was presented in Table 4.20.

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Table 4.17 Model 5: Multivariable Cox proportional hazards models to determine the association of PIMs use with unplanned readmission and ED visits (n = 4,012).

Variables	**Univariable**		**Multivariable**	
	cHR (95% CI)	***P-value***	**aHR (95% CI)**	***P-value***
Age*	1.03 (1.02-1.05)	< 0.001	1.03 (1.01-1.04)	0.001
Male	1.12 (0.89-1.43)	0.335	1.17 (0.92-1.49)	0.187
CCI score*	1.06 (0.96-1.16)	0.246	1.04 (0.95-1.15)	0.396
LOS*	1.01 (1.01-1.02)	< 0.001	1.01 (1.00-1.01)	0.020
No. of med. at D/C*	1.09 (1.06-1.12)	< 0.001	1.07 (1.03-1.10)	< 0.001
PIMs at D/C	1.55 (1.21-2.00)	0.001	1.15 (0.87-1.51)	0.317

Abbreviations: No. = number, med. = medications, D/C = discharge, cHR = crude hazard ratios, aHR = adjusted hazard ratios, CI = confidence interval, *Continuous variables were used.

Table 4.18 Test for proportional-hazards assumption of model 5

Variables	rho	chi^2	df	Prob>chi^2
Age	-0.017	0.09	1	0.769
Male	0.064	1.12	1	0.290
CCI score	0.000	0.00	1	0.992
LOS	-0.005	0.00	1	0.961
No. of med. at D/C	0.029	0.23	1	0.634
PIMs at D/C	-0.020	0.11	1	0.737
Global test		1.51	6	0.959

Abbreviations: No. = number, med. = medications, D/C = discharge, df = degrees of freedom

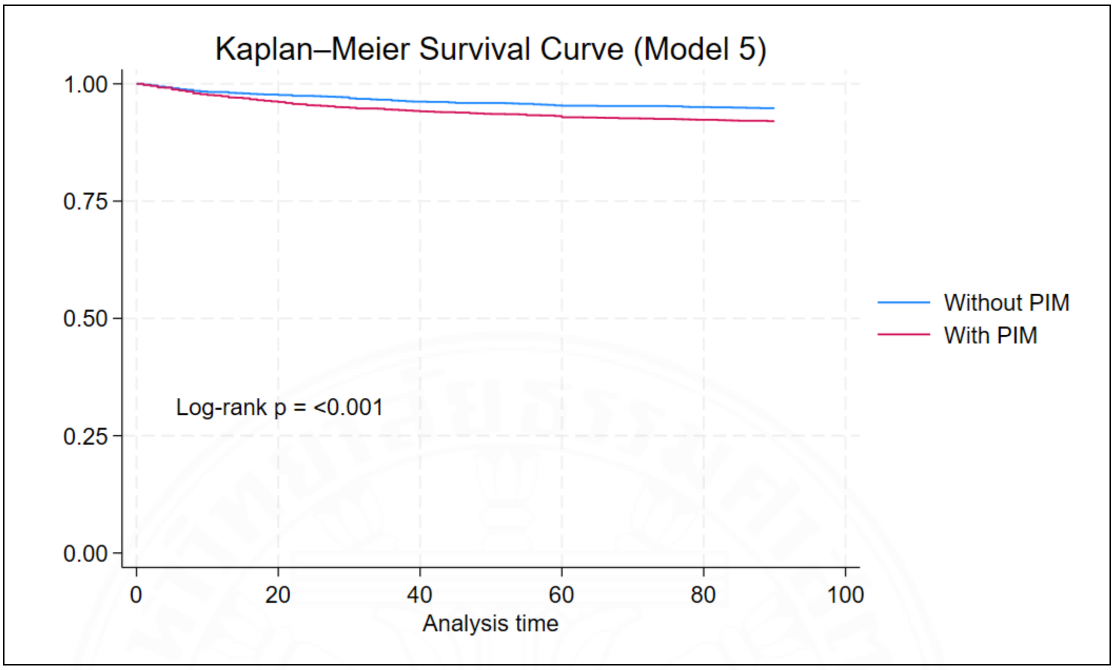

Figure 4.6 Kaplan–Meier survival curve for Model 5

Table 4.19 Model 6: Multivariable Cox proportional hazards models to determine the association of PIMs use with unplanned readmission and emergency-department visits (n = 4,012).

Variables	Univariable		Multivariable	
	cHR (95% CI)	*P-value*	aHR (95% CI)	*P-value*
Age*	1.03 (1.02-1.05)	< 0.001	1.03 (1.01-1.04)	< 0.001
Male	1.12 (0.89-1.43)	0.335	1.17 (0.92-1.49)	0.195
CCI score*	1.06 (0.96-1.16)	0.246	1.04 (0.95-1.15)	0.378
LOS*	1.01 (1.01-1.02)	< 0.001	1.01 (1.00-1.01)	0.018
No. of med. at D/C*	1.09 (1.06-1.12)	< 0.001	1.07 (1.04-1.10)	< 0.001
No. of PIMs at D/C*	1.21 (1.07-1.37)	0.002	1.00 (0.87-1.15)	0.958

Abbreviations: No. = number, med. = medications, D/C = discharge, cHR = crude hazard ratios, aHR = adjusted hazard ratios, CI = confidence interval, *Continuous variables were used.

Table 4.20 Test for proportional-hazards assumption of model 6

Variables	rho	chi^2	df	Prob>chi^2
Age	-0.018	0.09	1	0.764
Male	0.064	1.13	1	0.287
CCI score	0.000	0.00	1	0.997
LOS	-0.006	0.00	1	0.955
No. of med. at D/C	0.023	0.15	1	0.701
No. of PIMs at D/C	-0.005	0.01	1	0.928
Global test		1.40	6	0.965

Abbreviations: No. = number, med. = medications, D/C = discharge, df = degrees of freedom

Table 4.21 Multivariable Cox proportional hazards models to determine the association between PIMs and outcomes across all models. (n = 4,012)

Model*	**Univariable**		**Multivariable**	
	cHR (95% CI)	***P-value***	**aHR (95% CI)**	***P-value***
Model 1	1.22 (1.06-1.40)	0.004	1.05 (0.91-1.22)	0.487
Model 2	1.11 (1.03-1.19)	0.004	1.01 (0.93-1.10)	0.778
Model 3	1.72 (1.26-2.36)	0.001	1.27 (0.91-1.76)	0.162
Model 4	1.28 (1.11-1.49)	0.001	1.08 (0.91-1.27)	0.392
Model 5	1.55 (1.21-2.00)	0.001	1.15 (0.87-1.51)	0.317
Model 6	1.21 (1.07-1.37)	0.002	1.00 (0.87-1.15)	0.958

*In Models 1, 3, and 5, PIM exposure was entered into the model as a dichotomous variable, whereas in Models 2, 4, and 6, it was entered as a continuous variable. In Models 1 and 2, the outcome was all-cause readmission; in Models 3 and 4, the outcome was unplanned readmission; and in Models 5 and 6, the outcome was a composite of unplanned readmission and emergency department visits.

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Parametric survival tests were also conducted for those variables in the previous models of Cox proportional hazard regressions (Models 3, 4, 5, and 6). The statistically significant associations identified are consistent with the results obtained from multivariable Cox proportional hazards models, as detailed in Tables 4.22-4.25.

Table 4.22 Parametric survival analysis of unplanned readmission with PIMs as a covariate

Variables	Weibull	P-value	exponential	P-value	lognormal	P-value	loglogistic	P-value
Age	0.029	<0.001	0.029	<0.001	-0.046	<0.001	-0.044	<0.001
Male	0.174	0.24	0.179	0.23	-0.269	0.24	-0.264	0.23
CCI score	0.053	0.20	0.056	0.18	-0.101	0.18	-0.082	0.20
LOS	0.009	<0.001	0.010	<0.001	-0.022	<0.001	-0.015	<0.001
No. of med. at D/C	0.059	<0.001	0.060	<0.001	-0.085	<0.001	-0.088	<0.001
PIMs at D/C	0.242	0.16	0.243	0.16	-0.394	0.12	-0.364	0.15
AIC	1945.052		1977.400		1928.157		1943.025	
BIC	1995.428		2021.479		1978.534		1993.402	

Abbreviations: PIMs = Potentially Inappropriate Medications, No. = number, med. = medications, D/C = discharge, AIC= Akaike Information Criterion, BIC = Bayesian Information Criterion

Table 4.23 Parametric survival analysis of unplanned readmission with number of PIMs as a covariate

Variables	Weibull	P-value	exponential	P-value	lognormal	P-value	loglogistic	P-value
Age	0.030	<0.001	0.030	<0.001	-0.046	<0.001	-0.044	<0.001
Male	0.172	0.24	0.178	0.23	-0.262	0.25	-0.262	0.24
CCI score	0.054	0.19	0.057	0.17	-0.101	0.18	-0.083	0.20
LOS	0.009	<0.001	0.010	<0.001	-0.022	<0.001	-0.015	<0.001
No. of med. at D/C	0.061	<0.001	0.062	<0.001	-0.089	<0.001	-0.092	<0.001
No. of PIMs at D/C	0.073	0.39	0.074	0.39	-0.123	0.36	-0.108	0.39
AIC	1946.307		1978.656		1929.592		1944.349	
BIC	1996.683		2022.735		1979.968		1994.726	

Abbreviations: PIMs = Potentially Inappropriate Medications, No. = number, med. = medications, D/C = discharge, AIC= Akaike Information Criterion, BIC = Bayesian Information Criterion

Table 4.24 Parametric survival analysis of unplanned readmission and emergency-department visits with PIMs as a covariate

Variables	Weibull	P-value	exponential	P-value	lognormal	P-value	loglogistic	P-value
Age	0.027	<0.001	0.027	<0.001	-0.046	<0.001	-0.043	<0.001
Male	0.161	0.18	0.163	0.18	-0.254	0.22	-0.265	0.18
CCI score	0.041	0.28	0.042	0.28	-0.077	0.32	-0.068	0.30
LOS	0.007	<0.001	0.007	<0.001	-0.021	<0.001	-0.014	<0.001
No. of med. at D/C	0.064	<0.001	0.064	<0.001	-0.106	<0.001	-0.104	<0.001
PIMs at D/C	0.140	0.31	0.141	0.31	-0.205	0.37	-0.222	0.31
AIC	2747.898		2816.542		2725.419		2744.455	
BIC	2798.274		2860.622		2775.796		2794.832	

Abbreviations: PIMs = Potentially Inappropriate Medications, No. = number, med. = medications, D/C = discharge, AIC= Akaike Information Criterion, BIC = Bayesian Information Criterion

Table 4.25 Parametric survival analysis of unplanned readmission and emergency-department visits with number of PIMs as a covariate

Variables	Weibull	P-value	exponential	P-value	lognormal	P-value	loglogistic	P-value
Age	0.027	<0.001	0.027	<0.001	-0.046	<0.001	-0.044	<0.001
Male	0.159	0.19	0.160	0.19	-0.246	0.23	-0.260	0.19
CCI score	0.043	0.26	0.043	0.26	-0.082	0.30	-0.070	0.28
LOS	0.007	<0.001	0.007	<0.001	-0.021	<0.001	-0.014	<0.001
No. of med. at D/C	0.069	<0.001	0.069	<0.001	-0.116	<0.001	-0.112	<0.001
No. of PIMs at D/C	0.004	0.95	0.004	0.94	0.018	0.87	-0.003	0.97
AIC	2748.914		2817.576		2726.155		2745.438	
BIC	2799.291		2861.655		2776.531		2795.814	

Abbreviations: PIMs = Potentially Inappropriate Medications, No. = number, med. = medications, D/C = discharge, AIC= Akaike Information Criterion, BIC = Bayesian Information Criterion

4.2 Discussion

4.2.1 Main finding

The study identified a prevalence of 57.3% for receiving PIMs at discharge. Key predictors for receiving PIMs at discharge included the CCI score, LOS, PIMs at admission, and the number of medications at discharge. Statistically significant associations were observed between LOS and the number of medications at discharge with all examined outcomes, including all-cause readmissions, unplanned readmissions, and unplanned readmission and emergency department visits. However, the variables "PIMs at discharge" and "number of PIMs at discharge" did not demonstrate statistically significant associations with any of the outcomes in Cox proportional hazard and parametric survival analyses.

4.2.2 Prevalence of PIMs at discharge

The present study revealed a prevalence of 57.3% for receiving at least one PIM at discharge among older adults in internal medicine wards. Comparatively, a study by Komagamine et al. (2019), conducted in Japan between 2017 and 2018, reported a prevalence of 32.2% for PIMs at discharge[15]. Similarly, a study by Perpétuo et al. (2023), conducted in Portugal in 2019, identified a prevalence of 87.2%[49], while Wang et al. (2020) 's study in China during the same year reported a prevalence of 33.4%[31]. In Malaysia, Akkawi et al. 's 2022 study observed a prevalence of 86.7% for PIMs at discharge[13].

In Thailand, Sriboonruang et al. (2023)[50] and Jenghua et al. (2025)[46] reported PIM prevalences during hospitalization of 28% and 91.32%, respectively. These variations highlight the differing practices and prevalence rates of PIM use across countries and healthcare settings.

The prevalence of receiving PIMs at discharge varies between 28% and 91%, with these differences likely reflecting a range of factors, including the country of the study, the clinical department providing care, the research methodology employed, and the specific criteria used to assess PIMs.

The criteria used to assess PIMs in the present study were based on the updated AGS 2023 Beers Criteria®, the latest version. In contrast, most previous studies (Perpétuo et al. (2023)[49], Wang et al. (2020)[31], Akkawi et al. (2023)[13], Sriboonruang et al. (2023)[50]) used the Beers Criteria® 2019, and some studies (Komagamine et al. (2019)[15]) used the Beers Criteria® 2015. The study by Jenghua et al. (2025)[46] used the Beers Criteria® 2023.

The differences between the 2019 and 2023 editions are numerous. These include the modification of certain medications being added or removed from the assessment criteria in various tables due to the emergence of new scientific evidence. For example, Warfarin has been included for the treatment of nonvalvular atrial fibrillation (NVAF) or venous thromboembolism (VTE) due to its high risk of bleeding. Additionally, opioids and anticholinergics have been added for patients with memory impairment, depression, or confusion. The inclusion of skeletal muscle relaxants has also been updated. Some medications, such as Nitrofurantoin, have been removed from the market due to their limited use in the United States. Furthermore, certain drugs have been moved from Table 4 (drugs to be used with caution in older adults) to Table 2 (potentially inappropriate medication use in older adults), including aspirin for the primary prevention of cardiovascular disease, following supporting scientific evidence. Changes to the criteria or descriptions for some medications have also been implemented.

Overall, it was found that the number of PIMs increased when comparing the 2023 criteria to the 2019 criteria. The finding of a higher number of PIMs using the newer guidelines aligns with studies comparing PIMs across different assessment criteria, such as the one by Wang et al. (2020)[31] comparing the 2015 and 2019 guidelines. Therefore, the present study found a higher prevalence of PIMs at discharge compared to studies that used the 2019 assessment criteria.

Studies reporting a higher prevalence than the present study attribute these differences to the selection of various tables within the assessment criteria. For instance, Perpétuo et al. (2023)[49] utilized the 2019 criteria for Tables 2, 3, and 4, while Akkawi et al. (2023)[13] applied the 2019 criteria for Tables 2, 3, 4, 5, and 6.

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Jenghua et al. (2025)[46] employed the 2023 criteria for Tables 2, 3, 4, 5, 6, 7, and 8. In contrast, the present study focused solely on the primary tables essential for evaluating PIMs, namely Table 2 (PIMs use in older adults) and Table 3 (PIMs use in older adults due to drug–disease or drug–syndrome interactions).

The observed high prevalence of PIMs at discharge carries important clinical implications for older adults. As outlined in the 2023 updated Beers Criteria® by the AGS, inadequate management of PIMs may contribute to a range of adverse consequences, including medication-related adverse events, an elevated risk of falls and related injuries, accelerated cognitive decline and delirium, increased healthcare expenditures, and ultimately, a diminished quality of life.

An umbrella review by Veronese et al. (2024) demonstrated that deprescribing significantly reduces both the total number of medications and PIMs in older adults, across care settings[51]. Similarly, Kimura et al. (2022) reported that pharmacist-led interventions, combining PIM detection criteria with deprescribing algorithms, effectively corrected PIM use and reduced medication burden[52]. These findings support promoting deprescribing, particularly through pharmacist involvement, to reduce PIM use.

The present study identified the top 10 PIMs, which were consistent with those found in the study by Jenghua et al. (2025)[46], conducted in a hospital in Thailand using the AGS 2023 updated Beers Criteria®[5]. Both studies identified six common medications, including PPIs, Lorazepam, Quetiapine, Glipizide, Metoclopramide, and Orphenadrine. However, the variation in PIMs observed across different hospitals may be influenced by factors such as physician prescribing practices, which can affect the medications identified as PIMs in each study.

The present study found that Warfarin, classified as a PIM, was used in 202 cases, accounting for 5.03% of the total. According to the AGS 2023 updated Beers Criteria®[5], Warfarin is considered a PIM due to its higher risk of major bleeding (particularly intracranial bleeding) compared to direct oral anticoagulants (DOACs), as well as its similar or lower effectiveness in treating nonvalvular atrial fibrillation and venous thromboembolism (VTE). However, within the context of Thailand, access to

DOACs remains limited, as these medications are not yet included in the Thailand National List of Essential Medicine (NLEM). This highlights the need for using Warfarin in a substantial number of older patients.

4.2.3 Factors associated with PIMs at discharge

The present study identified CCI score, LOS, PIMs prior to admission, and the number of medications at discharge as significant predictors of PIMs at discharge, whereas sex and age were not associated. These findings regarding the predictive roles of CCI score and the number of discharge medications align with the results of Perpétuo et al. (2023), who reported that polypharmacy and multiple comorbidities were associated with PIM prevalence at discharge[49]. Similarly, Wang et al. (2020) found that PIMs at discharge correlated with both the number of prescribed medications and the presence of comorbidities, including acute and chronic heart failure[31]. Notably, both studies employed the 2019 Beers Criteria to identify PIMs.

In contrast, Aida et al. (2021) observed no significant association between CCI score or LOS and PIM use at discharge[30]. This discrepancy may be attributable to their use of the STOPP version 2 criteria and the relatively small sample size (n = 264), which could have limited the statistical power to detect such associations.

In the present study, multivariable analysis demonstrated that the presence of PIMs prior to hospital admission significantly increased the likelihood of receiving PIMs at discharge, with an adjusted odds ratio (aOR) of 2.32 (95% CI: 1.82–2.96, $p < 0.01$). These results align with the findings reported by Aida et al. (2021)[30], who also observed that a greater number of PIMs at admission was independently associated with a higher risk of PIMs being prescribed at discharge (aOR = 1.71, 95% CI: 1.12–2.63, $p = 0.01$). This notable association highlights the crucial role pharmacists can play in identifying PIMs at the point of admission, particularly through interventions such as medication reviews and medication reconciliations. Implementing these strategies could help reduce the prevalence of PIMs during hospitalization and at discharge, ultimately lowering the risk of adverse drug events (ADEs) related to PIMs.

This is consistent with the findings of a randomized controlled trial (RCT) by Lee et al. (2023), which showed that pharmacist-led interventions incorporating comprehensive medication reconciliation and PIM criteria reduced the difference in ADEs between intervention and control groups within 30 days post-discharge in older patients[53].

The discriminatory performance of the multivariable logistic regression model in the present study was 0.75 for the cohort without PIMs before admission and 0.76 for the cohort with PIMs before admission. The cohort without information on PIMs included 4,012 individuals, while the cohort with data on PIMs before admission comprised 1,397 individuals. These results indicate that the variables selected for the model were appropriate, as they were chosen based on prior research. The analysis identified several variables that serve as strong predictors of PIMs. However, it should be noted that the reported AuROC was obtained from the development model using the same dataset employed for model estimation. This may lead to overfitting, resulting in an overestimation of the model's true discriminative performance. Overfitting occurs when a model captures random noise or sample-specific patterns rather than generalizable relationships, causing the predictive accuracy to appear higher than it actually is in external data. Therefore, future studies should consider internal validation techniques, such as bootstrapping or k-fold cross-validation, or conduct external validation using independent datasets to better assess the model's generalizability. Moreover, these findings could be used to develop an algorithm to predict the likelihood of receiving PIMs at discharge for individual patients upon admission. However, risk prediction models are typically designed to forecast future or unobserved clinical events with substantial outcomes. Given that PIMs at discharge can be readily identified from medication records, the necessity and clinical utility of predicting them are questionable.

Studies on factors associated with PIMs at discharge within the Thai context remain scarce. Nonetheless, a study by Jenghua et al. (2025) , which investigated predictors of PIMs in hospitalized patients using the 2023 Beers Criteria[46], reported findings consistent with those of the current study. Specifically, factors

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associated with PIM use included female sex, longer length of stay, a greater number of prescribed medications, and the presence of three or more chronic conditions.

However, the present study found that sex was not a factor associated with PIMs at discharge, which contrasts with previous findings. This discrepancy regarding sex as a predictor of PIMs may be attributed to differences in study populations, the timing of PIM assessment, and the analytical adjustments applied across studies. Jenghua et al. (2025)[46] examined PIMs prescribed during hospitalization and found that female sex was significantly associated with a higher likelihood of receiving PIMs. This association may reflect acute prescribing patterns, such as the use of sedatives or gastrointestinal medications that are more frequently administered to female patients during inpatient care. In contrast, the present study focused on PIMs at discharge after medication review and reconciliation where sex differences in prescribing may be less pronounced. Additionally, the present analysis included extensive covariate adjustments (e.g., age, comorbidities, length of stay, and number of discharge medications), which may have attenuated the crude association observed in prior inpatient-based studies. Therefore, the observed inconsistency likely stems from variations in clinical context, study design, and statistical modeling approaches.

However, the researchers believe that studying the predictors of PIMs at discharge is more important than focusing on PIMs among hospitalized patients. While patients are hospitalized, they remain under close medical supervision. However, once discharged, the follow-up for ADEs resulting from PIMs becomes more limited. Therefore, it is crucial to reduce the use of PIMs before patients are discharged to minimize potential risks after leaving the hospital.

4.2.4 Association of PIMs use with outcome

The present study found that the receipt of PIMs at discharge, or the number of PIMs at discharge, was not associated with any of the outcomes tested, including all-cause readmission, unplanned readmission, and emergency department visits within 90 days.

The outcome of all-cause readmission in the present study aligns with the findings of Akkawi et al. (2023)[13], De Vincentis et al. (2020)[14], and Fabbietti et al. (2018)[16], all of whom found that PIMs at discharge did not significantly impact any hospital readmissions during the 3-month follow-up. However, these results contradict those of some studies, including Thomas et al. (2020)[10] and Wang et al. (2019)[11], which found an association between all-cause rehospitalization and the receipt of PIMs at discharge. Notably, the study by Thomas et al. (2020) followed outcomes for 6 months after discharge and analyzed the data using multiple logistic regression[10]. The study by Wang et al. (2019) had a follow-up period of up to 36 months[11]. The longer follow-up duration in these studies may have introduced additional factors influencing outcomes related to PIMs. Therefore, the differing findings may be attributed to the shorter 90-day follow-up period in the present study, which focused exclusively on the early outcomes associated with PIMs at discharge. Furthermore, the present study corroborates previous findings, suggesting that the impact of PIMs may not be observed in the early period following discharge.

Previous studies measuring outcomes related to unplanned readmissions, such as the study by Komagamine et al. (2019), found results consistent with the present study. Specifically, PIMs at discharge were not significantly associated with an increased risk of 90-day unplanned readmissions[15]. Another study by Lau et al. (2017) found that PIMs increased the risk of 28-day unplanned early hospitalization[12]. However, this study focused on participants aged 75 and older, with a sample size of only 182 individuals, and adjusted for only two variables—gastrointestinal disorders and gout—using multiple logistic regression. The discrepancies in population characteristics, sample size, and adjustment for confounding factors may help explain the differing findings among studies.

Regarding the outcome of emergency department visits, the present study found that only age, LOS, and the number of medications at discharge were associated with this outcome, while PIMs at discharge were not. These results align with those for unplanned readmissions, as the present study assessed unplanned readmissions based on patients who visited the emergency department and were subsequently admitted within 24 hours. Therefore, the sample of patients who experienced unplanned readmissions is a subset of those who visited the emergency department. In a previous study by Liang et al. (2022), the number and use of PIMs were positively correlated with emergency room revisits within 1, 3, and 6 months. However, that study employed multivariable logistic regression for data analysis, and PIMs at discharge were determined based solely on the list of drugs to avoid in the 2015 Beers Criteria (Table 2: Medications Considered as Potentially Inappropriate), which includes medications identified as strong PIMs[9]. In contrast, the present study used the 2023 Beers Criteria, incorporating both Table 2 and Table 3, which may account for the differing results. However, a further review of the literature reveals that there are limited studies on the impact of receiving PIMs at discharge on emergency department visits. Therefore, additional research is needed in this area to confirm these effects further.

In Thailand, a review of the literature conducted by the researchers found no studies examining the relationship between receiving PIMs at discharge and the occurrence of unplanned readmissions or emergency department visits. Therefore, the present study is the first to investigate this association.

It is evident that the results of previous studies are mixed, with some finding an association between receiving PIMs at discharge and outcomes such as all-cause readmission, unplanned readmission, and emergency department visits, while others did not. This discrepancy can be attributed to several factors, including differences in study locations, the characteristics of the study populations, assessment tools used, data collection methods, follow-up durations, and data analysis techniques. However, the most appropriate study design to establish a causal relationship between PIMs and outcomes would likely be a RCT. However, randomization involving PIMs may be considered unethical, making it challenging to conduct such a study. Therefore, well-designed and appropriately analyzed observational studies, which account for confounding effects, are likely the best approach to addressing this question.

The outcomes (including all-cause readmission, unplanned readmission, and emergency department visits within 90 days) chosen in the present study could explain the null effect of PIMs in this study. These health outcomes may not adequately represent the impact of PIMs. When examining the principal diagnoses for all-cause and unplanned readmissions, many were unlikely to be directly associated with the PIMs in question. In contrast, other outcome measures previously used to assess the effects of PIMs, such as adverse drug events, falls, bleeding, functional decline, and health-related quality of life, may be more suitable to capture the impact of PIMs post-discharge. However, these outcomes were not available to the electronics database. Choosing appropriate health outcome measures could yield a more apparent association.

For the data analysis, separate models were constructed to evaluate the association between the presence of PIMs at discharge and the number of PIMs at discharge with each outcome. This approach aimed to determine whether a higher number of PIMs was linked to any of the outcomes, including all-cause readmission, unplanned readmission, and emergency department visits within 90 days. The fact that the results remained consistent when the variable "number of PIMs at discharge" replaced "PIMs at discharge" suggests that the relationship between PIMs and the outcomes is not influenced by whether PIMs are treated as a binary variable or a count of the number of PIMs. This indicates that both the presence and the quantity of PIMs may not play a role in determining patient outcomes, reinforcing the potential impact of PIMs on post-discharge healthcare events.

The lack of association between PIMs at discharge and 90-day outcomes observed in the present study may, in part, be explained by the typical onset time of ADEs related to specific PIMs. Many PIM-related ADEs, particularly those linked to long-term pharmacologic exposure, develop gradually over months or years rather than within a short post-discharge window. For example, low-dose aspirin is associated with an increased risk of major gastrointestinal bleeding, which typically manifests after several years of continuous use, while the cognitive decline or falls associated with chronic benzodiazepine or anticholinergic exposure also tend to appear over longer durations. Consequently, a 90-day follow-up may not be sufficient to capture the onset of such delayed ADEs.

The present study found that for each additional medication prescribed at discharge, the risk of all-cause readmission, unplanned readmission, and emergency department visits within 90 days increased by 3%, 6%, and 7%, respectively. This finding suggests that the increasing number of medications may pose a higher risk of readmission and emergency visits than the PIMs themselves. The support of this notion includes the finding that polypharmacy is an important factor associated with admission and emergency visits. Therefore, pharmacists have an essential role in evaluating medication appropriateness, detecting possible therapeutic duplications, reducing polypharmacy, and limiting the use of PIMs at the point of discharge. This aligns with evidence from systematic reviews and meta-analyses conducted by Dautzenberg et al. (2021)[54] and Mekonnen et al. (2016)[55], which highlighted the effectiveness of pharmacist-led medication reconciliation interventions in optimizing post-discharge healthcare utilization.

In the present study, an analysis was also conducted using parametric survival models. The consistency of the association between the independent and dependent variables across both the semiparametric Cox regression model and parametric survival models strengthens the reliability of the present study findings. The Cox model, which does not assume a specific baseline hazard, offers flexibility in handling the underlying distribution of the survival times. In contrast, parametric models make assumptions about the hazard function (e.g., exponential, Weibull, lognormal, loglogistic). The agreement between the results of these two approaches suggests that the conclusions of the present study are robust and not overly dependent on the assumptions of any particular model. This consistency

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enhances the validity of the present study results and suggests that the observed associations are likely to be generalizable across different statistical frameworks.

Although the present study demonstrated that an increasing number of discharge medications was associated with higher risks of all-cause and unplanned readmissions as well as ED visits within 90 days, it is important to acknowledge that not all forms of polypharmacy are inherently harmful. In some clinical contexts, the concurrent use of multiple medications represents evidence-based, guideline-directed therapy rather than inappropriate prescribing. For instance, guideline-directed medical therapy (GDMT) for heart failure consists of a “four-pillar” regimen renin–angiotensin system inhibitors (ARNI or ACEi/ARB), evidence-based beta-blockers, mineralocorticoid receptor antagonists (MRA), and sodium–glucose cotransporter 2 (SGLT2) inhibitors which has been shown to improve both survival and quality of life.[56]

Therefore, the observed association between the number of discharge medications and adverse outcomes in the present study may not solely reflect the adverse effects of “polypharmacy” per se, but rather the complex interplay between disease burden, treatment intensity, and patient vulnerability. Patients with multiple comorbidities often require more medications to achieve optimal disease control; thus, medication count may also act as a proxy for clinical complexity rather than inappropriate prescribing. This distinction underscores the importance of differentiating appropriate polypharmacy (therapeutic necessity) from potentially inappropriate polypharmacy (avoidable or harmful use) when interpreting these findings.

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CHAPTER 5
CONCLUSIONS AND RECOMMENDATIONS

5.1 Conclusion

The study reported that 57.3% of patients were prescribed PIMs at discharge. Significant predictors for receiving PIMs at discharge included the CCI score, LOS, presence of PIMs at admission, and the total number of medications prescribed at discharge. LOS and the number of discharge medications demonstrated statistically significant associations with all evaluated outcomes, namely all-cause readmissions, unplanned readmissions, and emergency department visits. In contrast, neither "PIMs at discharge" nor the "number of PIMs at discharge" was significantly associated with any of these outcomes in the studied models.

5.2 Limitations

1. Since the present study is an observational study rather than a randomized controlled design, some confounding factors may have introduced bias. However, the present study employed statistical methods to mitigate this, using multivariable Cox proportional hazards models, adjusting for several potential confounding variables. Additionally, the present study also tested multiple models to confirm the finding. The results obtained were consistent across these different models.

2. The present study was conducted at a single center and included older adults admitted to the internal medicine ward. Consequently, the findings may not be fully generalizable to other settings or patient populations. Nonetheless, certain findings are partly consistent with trends observed in previous studies conducted in different settings and countries, which provides some external support for the robustness of the present results. Further multicenter or population-based studies are warranted to confirm the generalizability of these findings.

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3. Since this is a retrospective observational study utilizing data from a database, certain outcome measurements may be subject to misclassification, such as unplanned readmissions. However, to ensure the accuracy of the data, the present study implemented several procedures to assess the outcomes. For example, readmissions occurring within 24 hours of a patient's visit to the emergency department were considered unplanned readmissions.

4. The present study do not have data on patient adherence to medications after discharge, including over-the-counter (OTC) drugs purchased by patients independently. This is particularly relevant in the context of Thailand, where pharmacies are legally authorized to dispense prescription medications to patients. Therefore, the observed outcomes may be influenced by medication use behaviors that are not solely based on prescriptions provided by physicians.

5. The present study did not evaluate several important factors, such as socioeconomic status (SES), due to limitations in data access. SES was not included as a covariate in the present analysis due to data unavailability. This may represent a potential confounder, as SES could influence both the likelihood of receiving PIMs and post-discharge outcomes. Patients with lower SES may have limited access to healthcare services, lower health literacy, or reduced opportunities for medication review, thereby increasing their risk of PIM exposure. Moreover, lower SES has been associated with poorer disease management, higher rates of readmission, and emergency department visits. The omission of this factor may therefore have introduced residual confounding, and future studies should incorporate socioeconomic indicators such as income, education, or insurance status to more accurately adjust for this potential bias.

6. Death represents a potential competing risk for readmission or ED visits, which was not accounted for in the present study. If a substantial number of patients died during the follow-up period, they would not have been able to experience the outcomes of interest and would have been classified as having no readmission or ED visit. This misclassification may have attenuated the observed associations, making it appear as though patients receiving PIMs had no subsequent hospital utilization.

Consequently, the absence of competing risk analysis (e.g., Fine–Gray model) could have led to an underestimation of the actual effect of PIM exposure on post-discharge outcomes.

5.3 Strengths of the study

Despite the aforementioned limitations, the present study has several notable strengths.

1. It utilized a large sample size of older adults, which increased the statistical power and precision of the estimates.

2. The study applied updated and comprehensive criteria the 2023 AGS Beers Criteria[5] to identify PIMs, ensuring clinical relevance and alignment with the most current geriatric pharmacotherapy standards.

3. The study employed a DAG framework to guide covariate selection, thereby minimizing bias from overadjustment and enhancing the causal interpretability of the regression models.

4. The use of multivariable Cox proportional hazards and parametric survival models strengthened the robustness of the findings through consistency across statistical approaches.

5. The study leveraged real-world hospital electronic medical record data, providing a pragmatic perspective that reflects actual prescribing and patient outcomes in clinical practice. Collectively, these methodological and analytical strengths contribute to the reliability, validity, and generalizability of the study’s conclusion.

5.4 Implications of the present study

The high prevalence of receiving PIMs at discharge suggests that healthcare providers may need to be more vigilant when evaluating the therapeutic plan at discharge for older patients. Increased awareness and attention to medication choices at discharge could help reduce the prevalence of PIMs.

Although the present study found no significant relationship between receiving PIMs at discharge and any of the outcomes examined (all-cause readmissions, unplanned readmissions, and ED visits), the present study identified that LOS and the number of medications at discharge were factors associated with these outcomes. Therefore, it is the responsibility of healthcare providers to help mitigate these risks, such as by reducing the use of unnecessary medications, reviewing medication regimens, and conducting medication reconciliation. Additionally, there should be an increased focus on educating the public about PIMs.

5.5 Recommendations for further research

A prospective study design should be used to ensure comprehensive, accurate, and precise data collection.

Further research should explore the relationship between other factors that have not yet been studied, such as socioeconomic status, the use of OTC medications, and medications obtained from pharmacies.

Further research should examine the relationship between the receipt of PIMs and other outcomes, such as medication-related adverse events, an increased risk of falls and injuries, a heightened risk of cognitive decline and delirium, as well as increased healthcare costs and reduced quality of life.

Extending the study duration could be suggested as a potential area for future work. Future studies should consider a longer follow-up period to capture delayed ADEs and long-term clinical consequences associated with PIMs. Many ADEs related to PIMs, such as gastrointestinal bleeding from chronic aspirin use or cognitive decline associated with long-term benzodiazepine or anticholinergic exposure, may occur months or years after discharge. Therefore, a follow-up beyond 90 days for example, 6 months, 1 year, or even multi-year longitudinal studies would provide a more comprehensive understanding of the temporal relationship between PIM exposure and adverse outcomes, as well as enhance the external validity and generalizability of the findings.

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