

# Potentially Inappropriate Prescribing in a Falls Clinic Using the STOPP & START Criteria

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## Research Article

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# Abstract

## Background

Potentially inappropriate prescribing which may lead to adverse drug events and linked to polypharmacy is becoming increasingly common in older patients.

## Objective

This study applied the STOPP/START criteria to a clinical registry to determine the burden and profile of potentially inappropriate prescribing among patients attending a falls clinic.

## Setting

University of Malaya Medical Centre Falls Clinic

## Method

Data of individuals aged  $\geq 65$  years referred to the falls and syncope clinic were extracted from the falls registry. Potentially inappropriate prescribing was determined with the STOPP/START version 2 criteria. The relationship between potentially inappropriate prescribing with polypharmacy ( $\geq 5$  medications), comorbidities and clinical variables were determined using Pearson's chi-square and potential confounders adjusted for with multivariate regression.

## Main outcome measure

Potentially inappropriate medicines and/or omitted medicines using STOPP/START criteria

## Results

Data from 421 individuals, aged  $77.8 \pm 6.7$  years and 53.4% women, were included. Potentially inappropriate prescribing was present in 311 (74%). Potentially inappropriate medicines use accounted for 84.6% of the 325 prescriptions. 361/659 instances (54.8%) were falls-risk-increasing drugs, with vasodilators (49.3%) being the main potentially inappropriate medicine identified. Of the 177/421 with polypharmacy, 169/177 (95.5%) were exposed to  $\geq 1$  potentially inappropriate medicine. 129 instances of potentially omitted medicines were observed in 109 prescriptions (25.9%).

## Conclusion

STOPP/START criteria are useful to identify potentially inappropriate prescribing at the falls and syncope clinic. This finding has important implications for medication review strategies at falls clinic. Future research should determine whether identifying potentially inappropriate prescribing may reduce adverse falls outcomes among patients in this setting.

## Impact Of Findings On Practice

- The burden of potentially inappropriate prescribing is high (73.9%) amongst older patients in the falls and syncope clinic.
- STOPP/START criteria are useful tool to identify potentially inappropriate prescribing of fall-risk-increasing drugs in falls and syncope clinic.
- This study established evidence for possible association between potentially inappropriate medications to polypharmacy and comorbidities.
- Vasodilators are the main fall-risk-increasing drugs observed in the falls and syncope registry.

## Introduction

Global population ageing is associated with increased comorbidities, with increased deaths from ischaemic heart disease, stroke and chronic pulmonary disease. This leads to the use of multiple medications with the proportion of people aged  $\geq 65$  years consuming five or more medications in UK increasing from 12 to 49% over the past two decades [1][2]. Older age is also associated with increased adverse events with a systematic review reporting odds ratio (OR) for adverse drug events of 1.02 to 4.03 for individuals aged  $\geq 75$  years [3]. With increased use of prescribed medications, the risk of inappropriate prescribing also increases. Inappropriate prescribing may imply the prescription of medications with no clinical indication or when the risk of medication related harm outweighs the benefit of treatment, particularly when safer alternatives exist. The risk of adverse drug events is, therefore, further exacerbated with inappropriate prescribing [4].

Falls occur in one in four individuals aged  $\geq 65$  years [5]. With rapid population ageing, falls represent increasingly important public health concern. Falls are more likely to occur as a result of age-related muscle weakness which affects the balance, gait, and mobility; and/or modifiable risk factors such as medication use, poor lighting, and unsafe environment [6]. In many instances, it is the synergistic effect of polypharmacy and use of falls-risks-increasing drugs (FRIDs) that contributes to increased falls risk [7] [8]. The relationship between inappropriate medication prescribing and falls in older adults has not been well studied [9].

## AIM OF STUDY

The STOPP/START represents a set of criteria intended for clinical use to identify potentially inappropriate prescribing (PIP). Since its first iteration in 2008, it has been evaluated in hospital and

community settings in general population [10], [11]. Its use in falls assessment remains relatively unestablished. This cross-sectional study seeks to evaluate the utilization of the STOPP/START criteria in determining the burden of potential inappropriate prescribing (PIP) in older patients attending a falls and syncope clinic and to determine factors associated with potentially inappropriate medications (PIMs). If found suitable, the STOPP/START criteria could be used clinically to help identify PIP in the falls clinic settings.

## **ETHICS APPROVAL**

This study was approved by the Medical Research Ethics Committee, University Malaya Medical Centre (MREC ID No: 201943-7285).

## **Results**

### **Sample Characteristics**

Of the 531 patients' data extracted, 110 (20.7%) patients were younger than 65 years and excluded from the study. Data from 421 patients' ages ranged from 65 to 95 years, with a mean age of  $77.8 \pm 6.7$  years were analysed. 207 (49.2%) were aged 75 to 84 years old and 53.4% were women. Injuries from falls were reported by 15.7%; 9.5% experienced fractures, 5.9% required hospitalization and an additional 5.2% visited the doctor or Emergency department for treatment of injuries. The three most prevalent co-existing diseases observed were hypertension (57.2%), diabetes (34.0%), and dyslipidaemia (23.0%) (Table 1). Of the sample population, 311 (73.9%) had either PIMs, or POMs or both PIMs and POMs. PIMs and POMs are reported separately below.

Table 1  
Demographics by Presence of Potentially Inappropriate Medications

	<b>All</b>	<b>No PIM</b>	<b>≥ 1 PIM</b>	<b>p-value</b>
	<b>n, %</b>	<b>n, %</b>	<b>n, %</b>	
<b>Age Groups (years)</b>				
65–74	133 (31.6)	51 (38.3)	82 (61.7)	0.258
75–84	207 (49.2)	62 (30.1)	144 (69.9)	
≥ 85	77 (18.3)	28 (36.4)	49 (63.6)	
<b>Female Gender</b>	196 (46.6)	88 (39.1)	137 (60.9)	<b>0.034</b>
<b>Symptoms</b>				
Vertigo	21 (5.0)	4 (19.0)	17 (81.0)	0.160
Dizziness	154 (36.8)	33 (21.4)	121 (78.6)	<b>&lt; 0.001</b>
Pre-syncope	27 (6.5)	8 (29.6)	19 (70.4)	0.580
Syncope	187 (44.4)	54 (29.0)	132 (71.0)	<b>0.035</b>
Falls, Indoor	235 (55.8)	65 (27.8)	169 (72.2)	<b>0.001</b>
Falls, Outdoor	88 (20.9)	21 (23.9)	67 (76.1)	<b>0.018</b>
Injuries	66 (15.7)	16 (24.2)	50 (75.8)	0.056
Fractures	40 (9.5)	14 (35.0)	26 (65.0)	0.947
Medical Attention	22 (5.2)	5 (22.7)	17 (77.3)	0.232
Hospitalization	25 (5.9)	3 (12.0)	22 (88.0)	<b>0.015</b>
<b>Medical History</b>				
Diabetes	143 (34.0)	30 (21.0)	113 (79.0)	<b>&lt; 0.001</b>
Heart Disease	97 (23.0)	9 (9.3)	88 (90.7)	<b>&lt; 0.001</b>
Atrial Fibrillation	29 (6.9)	5 (17.9)	23 (82.1)	0.055
Hypertension	241 (57.2)	40 (16.7)	200 (83.3)	<b>&lt; 0.001</b>
Stroke	60 (14.3)	11 (18.6)	48 (81.4)	<b>0.006</b>
Dyslipidemia	121 (28.7)	26 (21.7)	94 (78.3)	<b>&lt; 0.001</b>
Asthma	22 (5.2)	5 (22.7)	17 (77.3)	0.232
*data missing in 5 individuals				
PIP = potentially inappropriate prescribing				

	All	No PIM	≥ 1 PIM	p-value
	n, %	n, %	n, %	
Liver Disease	3 (0.7)	2 (66.7)	1 (33.3)	0.240
Peptic Ulcer	6 (1.4)	1 (16.7)	5 (83.3)	0.354
Parkinson's	22 (5.2)	5 (22.7)	17 (77.3)	0.232
Depression	27 (6.4)	3 (11.1)	24 (88.9)	<b>0.008</b>
Hyperthyroid	10 (2.4)	1 (10.0)	9 (90.0)	0.099
Hypothyroid	15 (3.6)	4 (26.7)	11 (73.3)	0.515
Dementia	22 (5.2)	4 (18.2)	18 (81.8)	0.098
Osteoarthritis	43 (10.2)	9 (20.9)	34 (79.1)	0.048
Osteoporosis	44 (10.5)	10 (22.7)	34 (77.3)	0.082
Hearing Problems	31 (7.4)	2 (6.5)	29 (93.5)	<b>0.001</b>
Epilepsy	5 (1.2)	1 (20.0)	4 (80.0)	0.492
Visual Problems	55 (13.1)	5 (9.3)	49 (90.7)	<b>&lt; 0.001</b>
*data missing in 5 individuals				
PIP = potentially inappropriate prescribing				

## Potentially Inappropriate Medications

With the application of the STOPP criteria, ninety-five (22.6%) patients were on no medications. 325 (77.4%) had prescriptions ranging from one to sixteen medications, with a median of four medicines per patient (IQR, 1–6). The total number of medicines prescribed in this sample group was 1699. PIMs was seen in 275 (65.5%) of the study population and accounted for 84.6% of the 325 patient prescriptions. 659 occurrences (38.8%) of PIMs were identified (659/1699). The highest occurrences of PIM were related to 'drugs that predictably increase the risk of falls in older adults' (within STOPP K criteria) which accounted for 361 instances (54.8%) of the total 659 PIMs. Of these, 325 PIM (49.3%) were vasodilators and antihypertensive drugs (STOPP K3) (Fig. 1).

## Factors Associated with Potentially Inappropriate Medications

Table 1 summarises the comparisons between age, gender, symptoms and comorbidities with the presence of PIM. Significant associations were observed between the presence of one or more PIMs with male gender, dizziness, syncope, falls (indoor and outdoor), hospital admissions, diabetes, heart disease, hypertension, stroke, dyslipidaemia, depression, hearing problems, and visual problems as shown in Fig. 2.

# Polypharmacy

Polypharmacy was observed in 177 (42.1%) of the sample population. 169 (95.5%) were exposed to at least one PIM (OR = 27.3; 95% CI = 12.9 to 58.0) (Table 2). The presence of polypharmacy detected the presence of PIM with a sensitivity of 62% and specificity of 94%. The presence of polypharmacy was independently associated with the presence of any PIM following adjustment for age, sex, dizziness, falls indoors, falls outdoors, hospital admission, diabetes, heart disease, stroke, depression and visual problems (odds ratio = 18.64; 95% confidence interval = 8.46 to 41.08) (Model 2).

Table 2  
Association of potentially inappropriate medications and polypharmacy

	PIMs = 0 n (%)	PIMs ≥ 1 n (%)	p-value
Polypharmacy			
0–4 medications	137 (56.4)	106 (43.6)	< 0.001
≥ 5 medications	8 (4.5)	169 (95.5)	
Polypharmacy (≥ 5 medications)			
	Odds Ratio	95% Confidence Interval	
		Lower	Upper
Unadjusted	27.30	12.86	57.98
Model 1 <sup>a</sup>	25.95	12.20	55.20
Model 2 <sup>b</sup>	18.64	8.46	41.08
Comorbidities			
0–1 medical conditions	97 (61.4)	61 (38.6)	< 0.001
≥ 2 medical conditions	48 (18.3)	214 (81.7)	
≥ 2 Comorbidities			
	Odds Ratio	95% Confidence Interval	
		Lower	Upper
unadjusted	7.1	4.5	11.1
Model 3 <sup>a</sup>	6.9	4.4	10.8
Model 4 <sup>c</sup>	5.7	3.5	9.2
Model 5 <sup>d</sup>	3.2	1.8	5.5
<sup>a</sup> adjusted for age and sex			
<sup>b</sup> adjusted for age, sex, dizziness, falls indoors, falls outdoors, hospital admission, diabetes, heart disease, stroke, depression and visual problems			
<sup>c</sup> adjusted for age, sex, dizziness, falls indoors, falls outdoors and hospital admission			
<sup>d</sup> adjusted for age, sex, dizziness, falls indoors, falls outdoors, hospital admission and polypharmacy			

## Comorbidities

Eighty-two patients (20.0%) did not have any record of past medical history whilst 262 (62.1%) had two or more co-existing diseases of whom 214 (81.7%) were exposed to one or more PIM (OR = 7.1; 95% CI = 4.53 to 11.10). The presence of comorbidities provided a sensitivity of 79% and specificity of 67% for detection of PIM. The presence of two or more comorbidities was independently associated with PIM after adjustment for age, sex, gender, dizziness, indoor falls, outdoor falls and hospitalization (OR = 5.7; 95%CI = 3.5 to 9.2) (Model 4) and additional adjustment for polypharmacy (OR = 3.2; 95%CI = 1.8 to 5.5) (Model 5).

## Potentially Inappropriate Omissions

Using START criteria, 129 instances of possible POMs were observed in 109 cases (25.9%) of the study population. Of these, 14 with possible omitted medicines were not on any medications, whilst 56 had polypharmacy. 57 instances (44.2%) were related to START\*A – Cardiovascular System Criteria, 32 (24.8%) were related to START\*C – Central Nervous System & Eyes and 31 (24.0%) related to START\*E – Musculoskeletal System.

Fifty-six (31.6%) individuals with polypharmacy had at least one POM (OR = 1.66; 95% CI = 1.07 to 2.58). 36.6% of those with comorbidities experienced potential prescribing omissions (OR = 6.45; 95% CI = 3.47 to 11.99). POMs within the cardiovascular system accounted for 41.0% of the total POMs with omissions of antiplatelet therapy (30 instances); statin therapy (3 instances); omission of beta-blocker with ischaemic heart disease (17 instances); and omission of anticoagulants in patients with atrial fibrillation (7 instances). Omission of Vitamin D and calcium supplement in patients with known osteoporosis and/or previous fragility fracture was observed in 26 instances (Fig. 3).

## Discussion

Application of the STOPP/START checklist to the falls and syncope data registry found that PIP was present in 74% individuals aged 65 years and over attending the falls and syncope service at a teaching hospital in Malaysia, compared to 42.1% with polypharmacy. PIMs were present in 65.5% of the overall study population accounting for 84.5% of all patient prescriptions, while POMs were observed in 26% of all older individuals attending the clinic. Both polypharmacy and multiple comorbidities were independently associated with PIMs, and the presence of polypharmacy was 94% specific for presence of PIMs.

The STOPP/START checklist was found unwieldy with the presence of 114 criteria [15]. However, once the researcher is familiarised with the criteria, it was possible to evaluate each patient's medication list within four to eight minutes. The use of the STOPP/START adds to rigor and provides standardization to the assessment of medication lists. However, five out of six of all prescriptions were then flagged as PIM in our clinic setting and three out of four of all patients had PIP from either PIM or POM or both PIM and POM. This was actually comparatively lower than the 98% reported by a recent study conducted in a falls and syncope clinic in the Netherlands [16]. While this could imply that the pattern of use of medications in our setting is far from desirable, the STOPP/START tool may conversely be interpreted as overly

sensitive in identifying PIP. However, the high number of falls-risk increasing drugs detected and the case that these individuals are being seen for falls or symptoms that may predispose to falls, suggests that inappropriate prescribing is a common issue in the falls and syncope clinic setting.

A previous survey in a local hospital indicated that 60.0% of physicians and pharmacists have no knowledge of the availability of such medication review tools that could be used to improve prescribing to older patients [17]. Malaysia, like nearly all other South-East Asian nations, is experiencing population ageing. While the country is rapidly expanding its healthcare workforce and is now experiencing a glut in production of both doctors and pharmacists through the numerous private and public universities that have emerged in the last two decades, the curricula of these institutions have yet to respond to the urgent need of population ageing [18]. The lack of training of healthcare personnel in geriatric medicine may therefore explain the high level of PIP detected in this study. The use of PIP checklists such as the STOPP/START tool may therefore aid safe prescribing among doctors and also enhance the role of pharmacist in this context.

Inappropriate prescribing includes underuse or non-use of medications that are indicated and justified [19]. The phrase "*potentially inappropriate*" connotes that these medications or its omission has the possibility to result in more adverse risks than benefits of achieving therapeutic goals for our patients. The prescriptions, may however, still be unavoidable due to other competing clinical priorities requiring careful weighing up potential harms and benefits [20]. This issue was not explored in the current study. It also remains to be explored whether PIP could be reduced with inclusion of undergraduate geriatric curricula, upskilling of existing healthcare work force, or application of prescribing checklists for older persons.

The presence of comorbidity in 62% and polypharmacy in 42% of our study population is comparable to two other studies conducted on older patients in nursing homes in Malaysia which identified the presence of polypharmacy in 44–48% [21][22]. The increase in the number of PIMs associated with the number of prescribed medications had been reported previously in many other studies [23]–[25]. Notably, a recent study concluded that it is the combination of PIMs and polypharmacy that increases the risk of falls in the older patients [7]. In resource limited setting, the STOPP/START may be applied selectively to those with polypharmacy with 94% specificity for detection of PIM, though sensitivity was limited at only 62%. However, with the potential harm that may emerge from PIP, resource allocation towards better detection of PIP should be considered. Emphasis towards further research on the measuring of adverse events as a result of PIP may subsequently enable effective strategies to reduce PIP among older persons.

Fall-risk-increasing drugs accounted for 53% of all PIMs in previous study [26] which was consistent with our study (54.8%), and further established that 49% of all PIM in our fall clinic setting were vasodilators. The high usage of vasodilators and cardiovascular drugs would be attributable to cardiovascular morbidity within this population. The rising burden on non-communicable disorders within developing nations, suggests that potentially inappropriate use of such drugs is likely to increase unless action is taken to both reduce non-communicable disease burden as well as to improve the quality of

prescriptions. A previous study has, however, challenged assumptions that antihypertensives was associated with increased risk of falls. While use of two or more antihypertensives was associated with increased falls risk, this was then attenuated by age and comorbidities [27]. The relatively fewer patients on psychotropic or neuroleptic drugs could be attributed to tight control of such drugs by regulatory agencies as well as possible dire shortage of psychiatry services. The extent by which deprescribing should occur or blood pressure lowering and secondary preventive treatment be withheld remains unclear and has been a hotbed for debate since conclusive evidence remains elusive [28].

Potentially omitted medications were identified in one in four individuals, though we had discounted the omission of vaccinations, which was not recorded in 100% of our sample. A national adult vaccination programme does not currently exist, and few healthcare professional and adult patients recognise the needs or benefits of immunization in older adults. Our findings were consistent with a previous prescribing omission study that demonstrated 22.7% prescribing omissions in the primary care setting [29]. Omissions of secondary prevention medications featured prominently. Under-treatment of cardiovascular diseases may result in cardiac rhythm disorders and increased risks of orthostatic hypotension, leading to gait and balance impairment and falls [16]. Omission of necessary medicines and under-treatment in older adults to reduce long term morbidity and disease progression can be just as detrimental as over-prescribing [30]. However, within the STOPP/START criteria, medications may be highlighted as PIM such as vasodilators in individuals with falls; but the omission of the same drug will then be considered a POM as in the case of omitting beta-blockers in ischemic heart disease. It was not possible to detect whether the POMs identified in this study were omitted because of other competing risks, further highlighted the issue that PIP were not always avoidable. The identification of PIP using checklists therefore still requires clinical judgement as to whether deprescribing or prescribing should occur. Clear documentation and communication should be advocated as multiple clinical teams often provide care for the same patient with multiple comorbidities. Lack of adequate communication often lead to inconsistencies in management of older patients resulting in polypharmacy and potential harm. [31].

This study is limited by the retrospective analysis of a patient registry. The lack of accompanying clinical assessments precluded the inclusion of five STOPP/START criteria. The medication list was consolidated by the electronic prescribing which ensured that all prescribed medications arising from the study institution were recorded, although some prescriptions obtained from outside the hospital setting, such as private general practitioners' clinics may be missed out. The hospital, however, had its own primary care centre with integrated medical records, where many of the patients also attended. While application of the STOPP/START checklist among older adults attending falls and syncope clinic no doubt highlighted PIP as almost ubiquitous, the underlying structural issues as well as potential solutions have yet to be established. Future research studies should include implementation research as well as randomised controlled studies on establishing the use of STOPP/START to identify PIP as well as to identify effective strategies to reduce PIP and changes in clinical outcomes associated with reduction in PIP.

# Conclusion

Using the STOPP/START criteria, PIP was present in three out of four individuals aged  $\geq 65$  years attending a falls and syncope service at a tertiary hospital in Malaysia. PIP increases with polypharmacy and co-morbidities. Further evaluation is needed to identify structural issues leading to the high level of PIP as well as to guide implementation of PIP checklists and strategies to effectively and safely reduce PIP.

# Declarations

## Funding

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## Conflict/Competing Interests

None declared

## Availability of Data and Material

The data that support the findings of this study are available from the corresponding author upon reasonable request

## Code Availability

Available upon reasonable request, if applicable

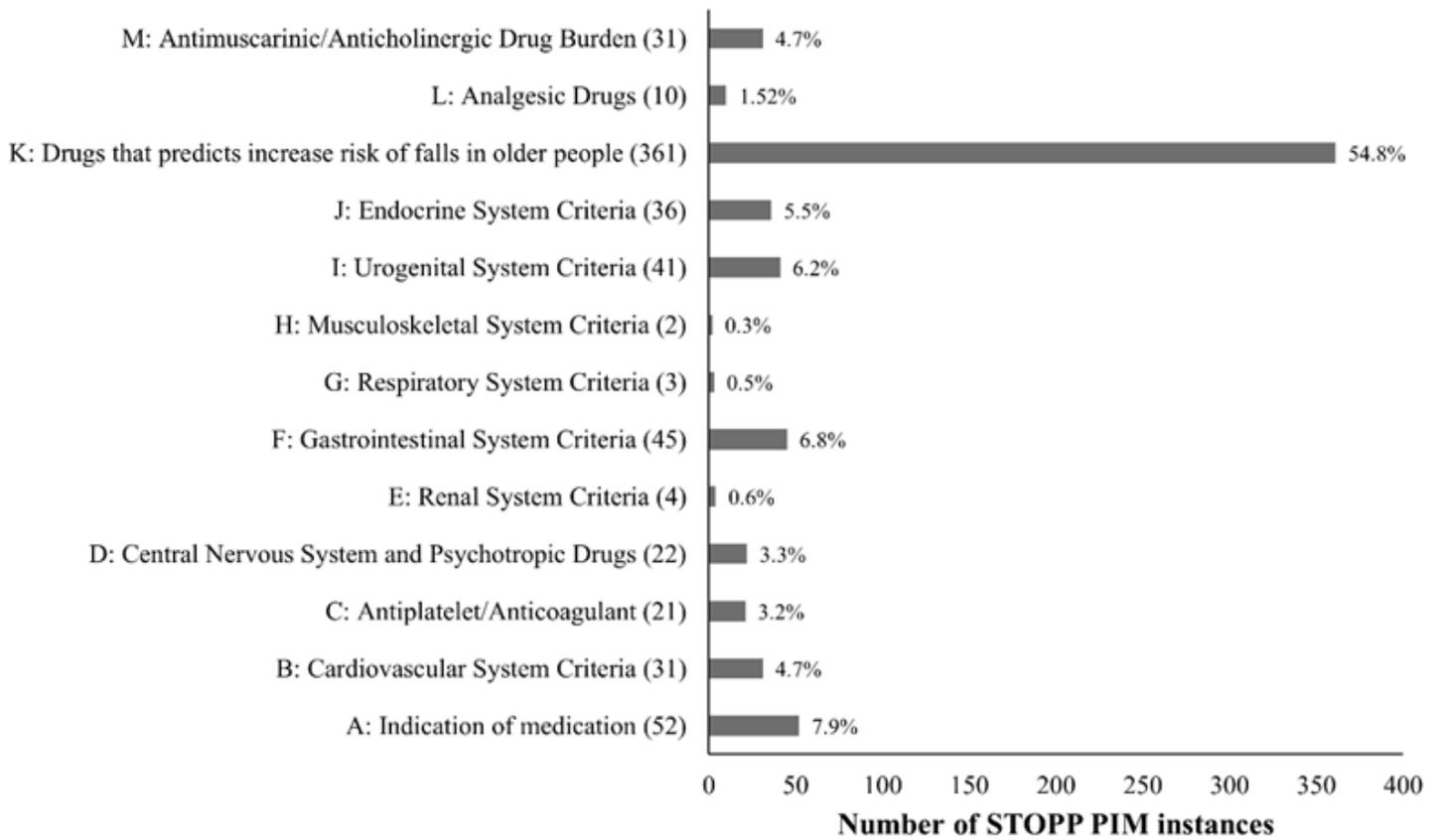
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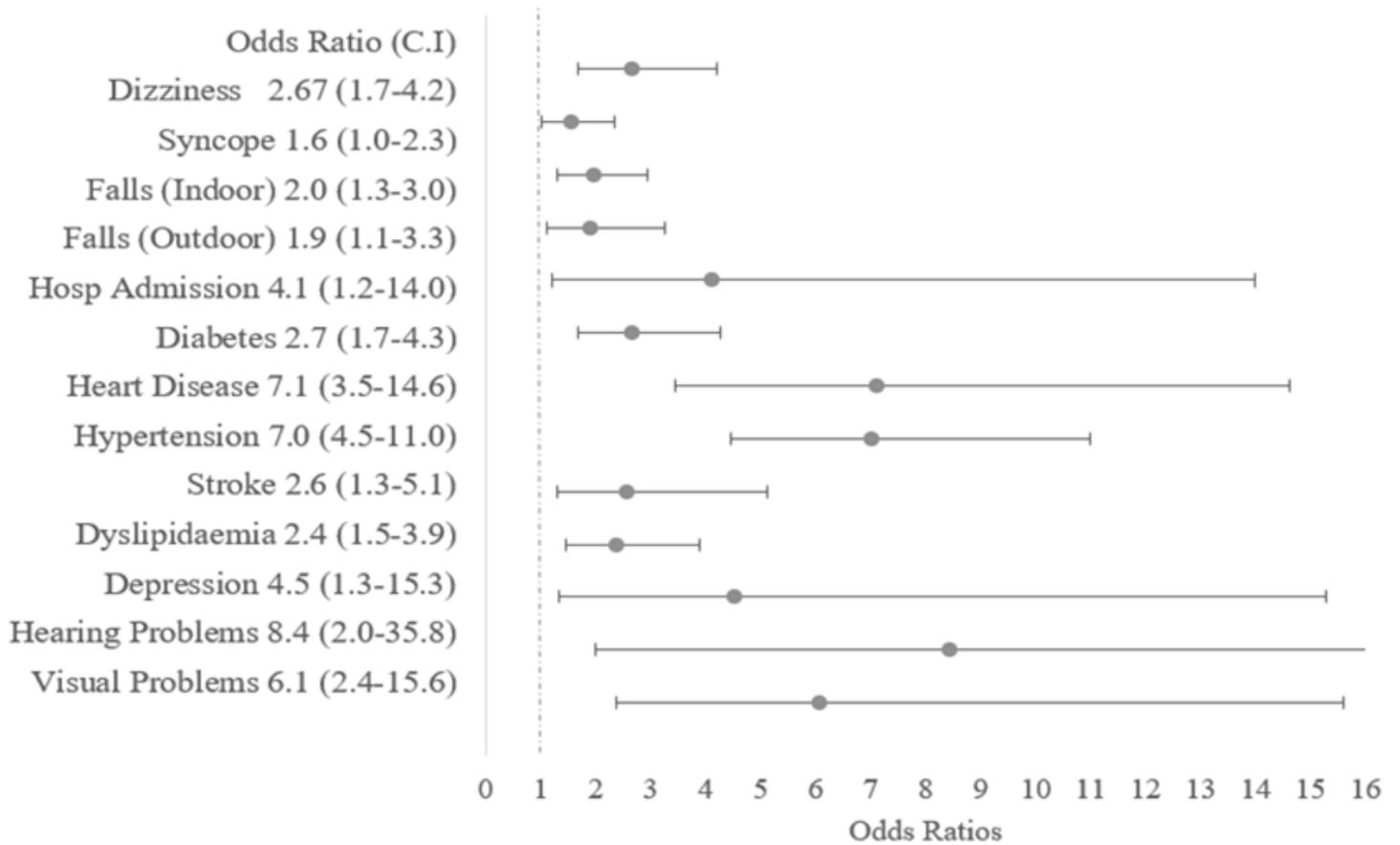
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## Figures



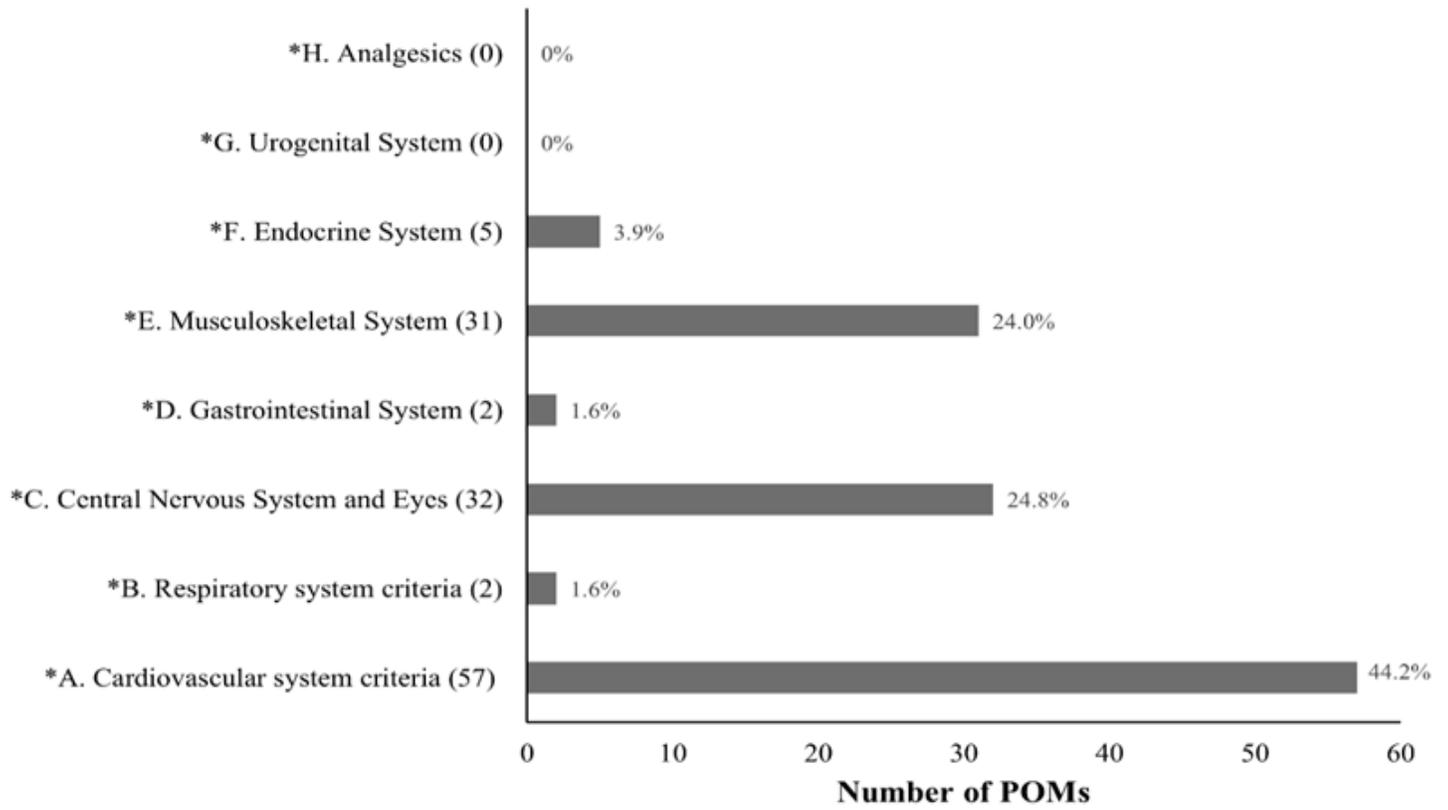
**Figure 1**

Potentially inappropriate medications according to STOPP category Bar chart indicating the frequency in percentage total prescriptions which fulfil the STOPP criteria by category within the registry



**Figure 2**

Risk factors for potentially inappropriate medications Forrest plot indicating the odds ratios (round circle) with 95% confidence intervals (errors bars) for individual factors which is associated with potential inappropriate medications



**Figure 3**

Potentially Omitted Medications according to START criteria Bar chart indicating the frequency in percentage total omissions according to the START criteria by category within the registry