

Inappropriate Prescribing and Related Hospital Admissions in Frail Older Persons According to the STOPP and START Criteria

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Abstract

Background Over the last few years, the Screening Tool of Older Person's Prescriptions (STOPP) and Screening Tool to Alert doctors to Right Treatment (START) criteria have been increasingly used to evaluate the prevalence of inappropriate prescribing. However, very few studies have evaluated the link between these criteria and clinical outcomes.

Objectives The objectives of this study were to evaluate the prevalence of inappropriate prescribing according to STOPP and START in a population of frail elderly persons admitted acutely to hospital; to evaluate whether these inappropriate prescribing events contributed to hospital

admissions; and to identify determinants of hospital admissions potentially related to inappropriate prescribing. **Methods** This was a cross-sectional study including all frail older patients admitted to a 975-bed teaching hospital over a 12-month period. A pharmacist and a geriatrician independently detected events of prescribing of potentially inappropriate medication (PIM) and potential prescribing omission (PPO), using the STOPP and START criteria, respectively, in all patients included in the study. They determined whether the inappropriate prescribing event was the main cause or a contributory cause of hospital admission. Demographic, clinical and geriatric clinical syndromes (i.e. cognitive impairment, falls) were evaluated as potential determinants of hospital admissions related to inappropriate prescribing, using multivariate methods (i.e. logistic regression and a classification tree).

Results 302 frail older persons (median age 84 years) were included in the study. PIMs (prevalence 48 %) mainly involved overuse and/or misuse of benzodiazepines, aspirin and opiates. PPOs (prevalence 63 %) were mainly related to underuse of calcium and vitamin D supplementation, aspirin and statins. Overall, inappropriate prescribing according to STOPP (54 PIMs) and/or START (38 PPOs) led or contributed to hospital admission in 82 persons (27 %). The multivariate analyses indicated a relation between PIM-related admissions and a history of previous falls ($p < 0.001$), while the PPO-related admissions were associated with a history of osteoporotic fracture ($p < 0.001$) and atrial fibrillation ($p = 0.004$).

Conclusions Using the STOPP and START criteria, it was found that inappropriate prescribing events (both PIMs and PPOs) were frequent and were associated with a substantial number of acute hospital admissions in frail older persons. Fall-induced osteoporotic fracture was the most important cause of hospital admission related to

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inappropriate prescribing and should be a priority for pharmacological optimization approaches.

1 Introduction

Inappropriate prescribing is a major concern in frail older patients, as these patients are particularly sensitive to adverse drug events (ADEs) and related outcomes such as hospital admission [1]. Several tools are available to evaluate prescribing in older patients, including implicit (e.g. the Medication Appropriateness Index [MAI]) [2] and explicit (e.g. the Beers list) [3–5] criteria [6].

The Screening Tool of Older Person's Prescriptions (STOPP) and the Screening Tool to Alert doctors to Right Treatment (START) are explicit tools to assess medication appropriateness in patients aged 65 years and above. These tools were validated through a Delphi consensus process with 18 experts in geriatric pharmacotherapy [7].

The STOPP criteria include 65 situations of potential clinical risk where a medication (or a medication class, $n = 27$) should be stopped, while the START criteria include 22 situations where a medication (or a medication class, $n = 20$) should be started.

The STOPP criteria—and to a lesser extent the START criteria—have been used to evaluate the prevalence of inappropriate prescribing in different settings and various countries [8–11]. Furthermore, in a recent randomized controlled trial, Gallagher et al. [12] reported that the use of STOPP/START criteria to screen hospitalized older patients' medications, coupled with feedback provided to the attending hospital team, led to significant and sustained improvements in the appropriateness of prescribing. These tools have several advantages over other existing ones: they link clinical situations with evidence-based use of medications; the medications listed are available and used in Europe; the criteria encompass events of overuse, underuse and misuse of medications; and they are relatively easy to apply. According to the creators of the tools, application of the criteria takes only a few minutes to detect inappropriate prescribing events in a patient, providing that comprehensive data on the patient's medications and co-morbidities are available.

However, only a few studies have evaluated the link between these events and clinical outcomes [13, 14]. Hamilton et al. [14] compared the Beers and STOPP criteria as risk factors for preventable serious ADEs. They concluded that the STOPP criteria are more sensitive to inappropriate prescribing resulting in ADEs than the Beers criteria. Furthermore, there is a lack of data on factors that place patients at risk of adverse consequences related to inappropriate prescribing. Identification of such factors

could help clinicians to identify patients at risk. Geriatric syndromes and frailty should be taken into account.

The objectives of this study were (a) to determine the prevalence of potentially inappropriate prescribing according to the STOPP and START criteria in a population of frail elderly people acutely admitted to hospital; (b) to evaluate to what extent these inappropriate prescribing events contributed to hospital admissions; and (c) to identify determinants of hospital admissions potentially related to inappropriate prescribing. Among the determinants, geriatric syndromes were analysed.

2 Methods

2.1 Study Population

This study was cross-sectional and included all frail older patients consecutively admitted to a 975-bed teaching hospital in Brussels (Belgium) over a 12-month period (December 2007–November 2008) and assessed by the interdisciplinary geriatric liaison team upon admission to the ward [15, 16]. The following inclusion criteria to receive a comprehensive geriatric assessment by the geriatric liaison team were used for the present study: age 75 years or older; admission for acute illness (as opposed to elective admission); a positive frailty profile (as defined by the presence of two or more of the six Identification of Seniors At Risk (ISAR) items: need for help in activities of daily living; an increase in this need related to the current illness; memory problems; significantly altered vision; hospitalization in the previous 6 months; and daily use of ≥ 3 medications at home) [17]. The geriatric liaison team (a nurse, dietitian, occupational therapist, physiotherapist, speech therapist, psychologist and geriatrician) aims to improve the care of older patients hospitalized in non-geriatric units by the means of recommendations following comprehensive geriatric assessment. Such geriatric liaison teams are widespread in Belgium, since they benefit from federal funding.

The study protocol was approved by the local clinical research ethics committee.

2.2 Data Collection

Demographic, clinical and medication data were collected upon hospital admission by the multidisciplinary geriatric liaison team, using the electronic patient record. The medication data included prescriptions as well as over-the-counter medicines that the patient was taking daily just before admission to hospital.

Because the medication data were routinely collected by the geriatric liaison team, the researchers could record

whether the patient was taking each of the 27 and 20 drugs (or drug classes) listed in the STOPP and START criteria, respectively (see Online Resource 1). The presence or absence of each comorbidity listed in the STOPP criteria ($n = 31$) and the START criteria ($n = 18$) was also registered (see Online Resource 1).

Information regarding the patient's frailty scores (ISAR and Katz [18]) and the presence or absence of six geriatric syndromes 2 weeks before hospital admission were obtained during interviews with the patient (or relatives in cases of cognitive impairment). These geriatric syndromes are those routinely evaluated by the geriatric liaison team: multiple falls (≥ 2 falls in the last 6 months), polypharmacy (≥ 5 daily medications), cognitive disorder (known dementia and/or an impaired Mini Mental State Examination [MMSE] score of $< 24/30$) [19], malnutrition (a body mass index of $< 21 \text{ kg/m}^2$ and/or a mid-arm circumference $< 23 \text{ cm}$), living alone, and functional dependency in activities of daily living (a Katz score of $\geq 9/24$).

2.3 Analysis

We evaluated the prevalence of inappropriate prescribing of medications used at home, as well as determinants of this inappropriate prescribing. To detect events of potentially inappropriate prescribing according to the 65 STOPP and 22 START criteria, a clinical pharmacist (O.D.) with experience in evaluation of prescribing for older patients and a geriatrician (B.B.) independently analysed all of the patient's medications and co-morbidities. The presence of contraindications to specific medications was taken into account, on the basis of information available in the electronic patient record. Discrepancies in the identification of potentially inappropriate prescribing events were discussed until a consensus was reached between both researchers. In addition, both researchers evaluated whether the inappropriate prescribing event was the main cause or contributed to the main reason for admission. Positive predictive values (PPVs) were calculated for inappropriate prescribing potentially linked to hospital admission ($\text{PPV} = \frac{\text{number of patients having an admission potentially related to the use of an inappropriately prescribed drug}}{\text{number of patients having this drug inappropriately prescribed}}$).

Comorbidities (renal failure [i.e. a glomerular filtration rate of $< 50 \text{ mL/min}$]; atrial fibrillation; presence or history of cardiovascular disease, hypertension, heart failure, angina, diabetes, chronic obstructive pulmonary disease [COPD], chronic type 1 respiratory failure, Parkinson's disease, depression, gastroesophageal acid reflux disease, diverticular disease, rheumatoid disease or osteoporosis), demographic characteristics (age, gender, place of

residence, number of medications before admission, ISAR score) and the six previously mentioned geriatric syndromes were evaluated as potential determinants of inappropriate prescribing as well as related hospital admissions.

2.4 Statistical Analysis

Continuous variables were analysed using medians (with 25th–75th percentiles [P_{25} – P_{75}]) because they were not normally distributed. For categorical variables, numbers and percentages are presented. A univariate analysis (see Online Resource 1) and a multivariate logistic regression analysis were used to identify determinants of potentially inappropriate prescribing and related hospital admissions.

Variables with a p value of < 0.20 in the univariate analysis were submitted for multivariate regression analysis. A stepwise elimination procedure using Akaike's information criterion was used to identify independent multivariate predictors. A p value of < 0.05 was considered statistically significant. A classification tree analysis was conducted to analyse determinants of hospital admissions related to potentially inappropriate prescribing [20, 21]. The one-standard-error rule was used to select the best tree [22]. Statistical analyses were performed using R software version 2.12.0 (Free Software Foundation, Inc., Boston, MA, USA) and CART version 6.6 (Salford Systems, San Diego, CA, USA).

3 Results

The inclusion criteria were met by 302 frail older patients (median [P_{25} – P_{75}] age 84 [81–88] years; proportion of females 62.6 % ($n = 189$); median [P_{25} – P_{75}] ISAR score 3 [3–4]). Upon hospital admission, the median [P_{25} – P_{75}] number of geriatric syndromes per patient was 2 [2–3] (out of 6). The three most frequent geriatric syndromes were polypharmacy [≥ 5 daily medications] (74.5 %), multiple falls in the last 6 months (58.3 %) and dependency in activities of daily living (43.7 %). The three most prevalent co-morbidities were hypertension (55.0 %), ischaemic disease (40.7 %) and renal failure (37.4 %) (Table 1). Overall, the 302 patients used 2,028 medications daily (median [P_{25} – P_{75}] 6 [4–9]). The medications and/or medication classes listed in the STOPP and START criteria that were most frequently used at home were for cardiovascular and neurological conditions (Table 1). Patients were mainly admitted to the hospital because of falls (34.0 %, $n = 104$) or cardio-respiratory problems (37.4 %, $n = 113$). Other reasons for admission were gastro-intestinal symptoms ($n = 38$), infectious diseases ($n = 31$) or miscellaneous ($n = 16$).

Table 1 Characteristics of the study population ($n = 302$)

Variable	Value
Sociodemographic variables	
Age (years; median [P ₂₅ –P ₇₅])	84 [81–88]
Sex (n [%])	
Female	189 [62.6]
Male	113 [37.4]
Place of residence (n [%])	
Home	252 [83.4]
Nursing home	50 [16.6]
No. of medications per patient (median [P ₂₅ –P ₇₅])	6 [4–9]
ISAR score (median [P ₂₅ –P ₇₅])	3 [3–4]
Geriatric syndromes (n [%])	
Polypharmacy (≥ 5 medications/day)	225 [74.5]
≥ 2 falls in the last 6 months	176 [58.3]
Dependency in activities of daily living (Katz score $\geq 9/24$)	132 [43.7]
Living alone	131 [43.4]
Malnutrition ^a	90 [29.8]
Cognitive disorder	75 [24.8]
Most frequent comorbidities (n [%])	
Hypertension	166 [55.0]
Ischaemic disease (heart/cerebral)	123 [40.7]
Renal failure (glomerular filtration rate < 50 mL/min)	113 [37.4]
Osteoporosis with fracture	78 [25.8]
Persistent atrial fibrillation	77 [25.5]
Depression	76 [25.2]
Diabetes	69 [22.8]
Medication classes most frequently used at home (prevalence > 20 %; n [%])	
Antithrombotic agents (including aspirin and vitamin K antagonist)	181 [59.9]
Psycholeptics (benzodiazepines and antipsychotics)	156 [51.7]
Agents acting on the renin-angiotensin system	142 [47.0]
β -blockers	115 [38.1]
Diuretics	102 [33.8]
Psychoanaleptics (antidepressants)	82 [27.2]
Analgesics	80 [26.5]
Lipid-modifying agents (statins)	66 [21.9]
Calcium channel blockers	65 [21.5]

ISAR Identification of Seniors at Risk

^a Malnutrition was defined as a body mass index of < 21 kg/m² or a mid-arm circumference of < 23 cm

3.1 Inappropriate Prescribing According to STOPP

According to the STOPP criteria, 210 events of prescribing of potentially inappropriate medication (PIM) were detected. Three drug classes accounted for 61 % of these PIMs, namely benzodiazepines (33 %, $n = 72$), aspirin (17 %, $n = 35$) and opiates (11 %, $n = 24$). Specifically, fall-risk-

increasing drugs (referred to in the STOPP criteria as “drugs that adversely affect fallers”), accounted for half of all PIMs (53 %, $n = 112$): benzodiazepines ($n = 70$), opiates ($n = 24$), neuroleptics ($n = 13$) and first-generation antihistamines ($n = 5$). PIMs were found in 144 of the 302 frail older persons, giving a prevalence of 47.7 %, with the following distribution: 1 PIM (29 %), 2 PIMs (16 %) and ≥ 3 PIMs (3 %). The five most frequent PIMs according to STOPP (benzodiazepines, aspirin, opiates, β -blockers and tricyclic antidepressants), their prevalence and their corresponding STOPP items are listed in Table 2. A multivariate logistic regression analysis identified two geriatric syndromes as strong determinants of PIM, namely a history of recent multiple falls (odds ratio (OR) [95 % confidence interval (CI)] 2.7 [1.6, 4.7]; $p < 0.001$) and polypharmacy (≥ 5 daily medications) (OR [95 % CI] 1.9 [1.1, 3.5]; $p = 0.026$). No significant association was observed with any other geriatric syndrome, demographic characteristic or co-morbidity in the multivariate analysis.

3.2 Inappropriate Prescribing According to START

362 events of potential prescribing omission (PPO) were detected according to the START criteria. Three medical conditions accounted for 52 % of all PPO events, namely diabetes (31 %), ischaemic disease (19 %) and osteoporotic fracture (14 %). The prevalence of PPOs was 62.9 % (190/302), with the following distribution: 1 (29 %), 2 (19 %), and ≥ 3 (15 %). Table 3 lists the prevalence of the five most frequent co-morbidities linked with PPOs, namely type 2 diabetes, osteoporosis, ischaemic disease/secondary cardiovascular prevention, persistent atrial fibrillation and COPD. The most frequent corresponding omitted medications were aspirin; statins; metformin; calcium, vitamin D and bisphosphonates; warfarin; and bronchodilators. In a multivariate analysis, PPOs were significantly associated with five co-morbidities, namely diabetes (OR [95 % CI] 13.1 [5.0, 34.2]; $p < 0.001$), atrial fibrillation (OR [95 % CI] 7.9 [3.5, 17.9]; $p < 0.001$), osteoporotic fracture (OR [95 % CI] 4.3 [2.0, 9.2]; $p < 0.001$), COPD (OR [95 % CI] 3.8 [1.3, 10.6]; $p = 0.012$) and ischaemic disease (OR [95 % CI] 2.1 [1.1, 4.2]; $p = 0.037$). No significant association was found with any other comorbidity, demographic data or geriatric syndrome.

3.3 Hospital Admissions Related to Inappropriate Prescribing

Overall, inappropriate prescribing (PIMs and/or PPOs) according to the STOPP and/or START criteria led or contributed to hospital admissions in 82 of the 302 patients

Table 2 Prevalence of the most frequent prescribing of inappropriate medications according to the STOPP criteria ($n = 302$)

Table 2 Prevalence of the most frequent prescribing of inappropriate medications according to the STOPP criteria (<i>n</i> = 302)	Inappropriate medication	Related medical condition	(<i>n</i> [%]) ^a
	Benzodiazepines		72 [24]
		Fall in the last 3 months	61 [20]
		Long acting and long term (>1 month)	14 [5]
	Aspirin		35 [12]
		Dosage >150 mg/day	25 [8]
		Primary cardiovascular prevention	7 [2]
	Opiates		24 [8]
		Fall in the last 3 months	14 [5]
		Powerful opiate for mild to moderate pain	2 [1]
<i>COPD</i> chronic obstructive pulmonary disease, <i>STOPP</i> Screening Tool of Older Person's Prescriptions	β-blockers		19 [6]
		Diabetes and hypoglycaemic episodes	13 [4]
		Non-selective β-blockers and COPD	4 [1]
^a As patients could have several inappropriate prescribing events, the numbers may not add up to the stated totals	Tricyclic antidepressants		15 [5]
		Dementia	6 [2]
		Glaucoma	2 [1]

Table 3 Prevalence of the most frequent potential prescribing omissions according to the START criteria ($n = 302$)

	Medical condition	Omitted medication	(n [%])
<i>COPD</i> chronic obstructive pulmonary disease, <i>START</i> Screening Tool to Alert doctors to Right Treatment	Type 2 diabetes		112 [37] ^a
		Aspirin	33 [11]
		Statin	39 [13]
		Metformin	25 [8]
	Osteoporosis		80 [26]
		Calcium and vitamin D (used in cases of osteoporotic fracture)	51 [17]
		Bisphosphonates (used in cases receiving maintenance corticosteroids)	29 [10]
	Ischaemic disease/need for secondary cardiovascular prevention		64 [21]
		Aspirin	41 [14]
		Statin	23 [8]
^a Only the most frequent prescribing omissions are listed for this condition	Persistent atrial fibrillation		37 [12]
		Vitamin K antagonists	34 [11]
		Aspirin (used in cases of contraindications to vitamin K antagonists)	3 [1]
	COPD or asthma		22 [7]
		Inhaled β ₂ -agonist/anticholinergic agent (used in mild to moderate cases)	20 [6]
		Inhaled corticosteroid (used in moderate to severe cases)	2 [1]

(27.1 %). Table 4 summarizes the medical problems leading to these admissions and the medications involved.

Fifty-four of the 302 admissions (17.9 %) were related to PIMs, of which 46 involved a fall associated with a major fracture. The latter 46 patients were receiving 66 inappropriately prescribed drugs (35 benzodiazepines, 13 opiates, 12 neuroleptics and 2 antihistamines) at home. The proportion of PIM-related admissions for a fall with a fracture in patients inappropriately receiving fall-risk-increasing drugs was 67.6 % (PPV = 46/68 [0.68]).

A multivariate logistic regression analysis indicated that a history of recent falls was a strong independent determinant of admissions related to PIMs (OR [95 % CI] 5.2 [2.2, 12.3]; $p < 0.001$). No other geriatric syndrome nor any comorbidity was a significant determinant of PIM-related admissions. The classification tree (Fig. 1a) confirmed the role of a history of multiple falls as a determinant of PIM-related admissions, the prevalence of which was 26.1 % ($n = 46$) in the 176 patients with a history of multiple falls as compared with 6.3 % ($n = 8$) in the 126 other patients.

Table 4 Description of acute hospital admissions related to inappropriate prescribing ($n = 82$)

Main reason for admission	Medications prescribed/omitted inappropriately	<i>n</i>	PPV ^b
PIM-related admission		54 ^a	
Fall with fracture	Fall-risk-increasing drugs ^c	46	0.68
Bleeding	Aspirin/NSAID	3	0.07
Heart failure	NSAID	2	0.25
PPO-related admission		38 ^a	
Fall with fracture	Calcium, vitamin D and bisphosphonates	19	0.25
Ischaemic heart disease	Platelet aggregation inhibitors	5	0.07
	Statins	5	0.09
Stroke	Antithrombotic agents	2	0.06
Heart failure	ACE inhibitors	3	0.25
COPD exacerbation	Regular inhaled β_2 agonist or anticholinergic agent	2	0.10

ACE angiotensin-converting enzyme, COPD chronic obstructive pulmonary disease, NSAID nonsteroidal anti-inflammatory drug, PIM prescribing of potentially inappropriate medication, PPO potential prescribing omission, PPV positive predictive value

^a Only the most frequent inappropriate prescribing events are listed

^b PPV = the number of patients who had an admission potentially related to inappropriate prescribing of a drug divided by the number of patients who had that drug prescribed inappropriately

^c Fall-risk-increasing drugs: benzodiazepines ($n = 35$), opiates ($n = 10$), neuroleptics ($n = 12$) and antihistamines ($n = 2$)

In the group of fallers, the next splitter was a history of myocardial infarction. The prevalence of PIM-related admission was higher in the group of fallers who had no history of myocardial infarction. Prescribing of ≥ 3 daily medications used at home was a further determinant of PIM-related hospital admission in the last group of patients.

PPOs were related to 38 of the 302 admissions (12.6 %). The large majority of PPOs were for drugs used to treat musculoskeletal ($n = 19$) or cardiovascular ($n = 16$) conditions. Amongst patients not receiving musculoskeletal drugs (such as calcium, vitamin D and bisphosphonates), the proportion of patients with a PPO-related admission for a fall with a fracture was 25 % (PPV = 0.25). In the multivariate logistic regression analysis, osteoporotic fracture (OR [95 % CI] 5.0 [2.2, 11.4]; $p < 0.001$) and atrial fibrillation (OR [95 % CI] 3.4 [1.5, 8.0]; $p = 0.004$) were significantly associated with PPO-related admissions. The classification tree (Fig. 1b) confirmed that PPO-related admissions were more frequent when a history of osteoporotic fracture was present than when it was absent (26.9 % [21/78] vs. 7.6 % [17/224]; $\chi^2_{1df} = 19.66$; $p < 0.001$). In the 224 patients without osteoporotic fracture, severe functional dependency (a Katz score of $\geq 21/24$) was the next determinant of PPO-related admission.

4 Discussion

The present study showed that inappropriate prescribing of medications used at home was frequent, as 48 % of frail

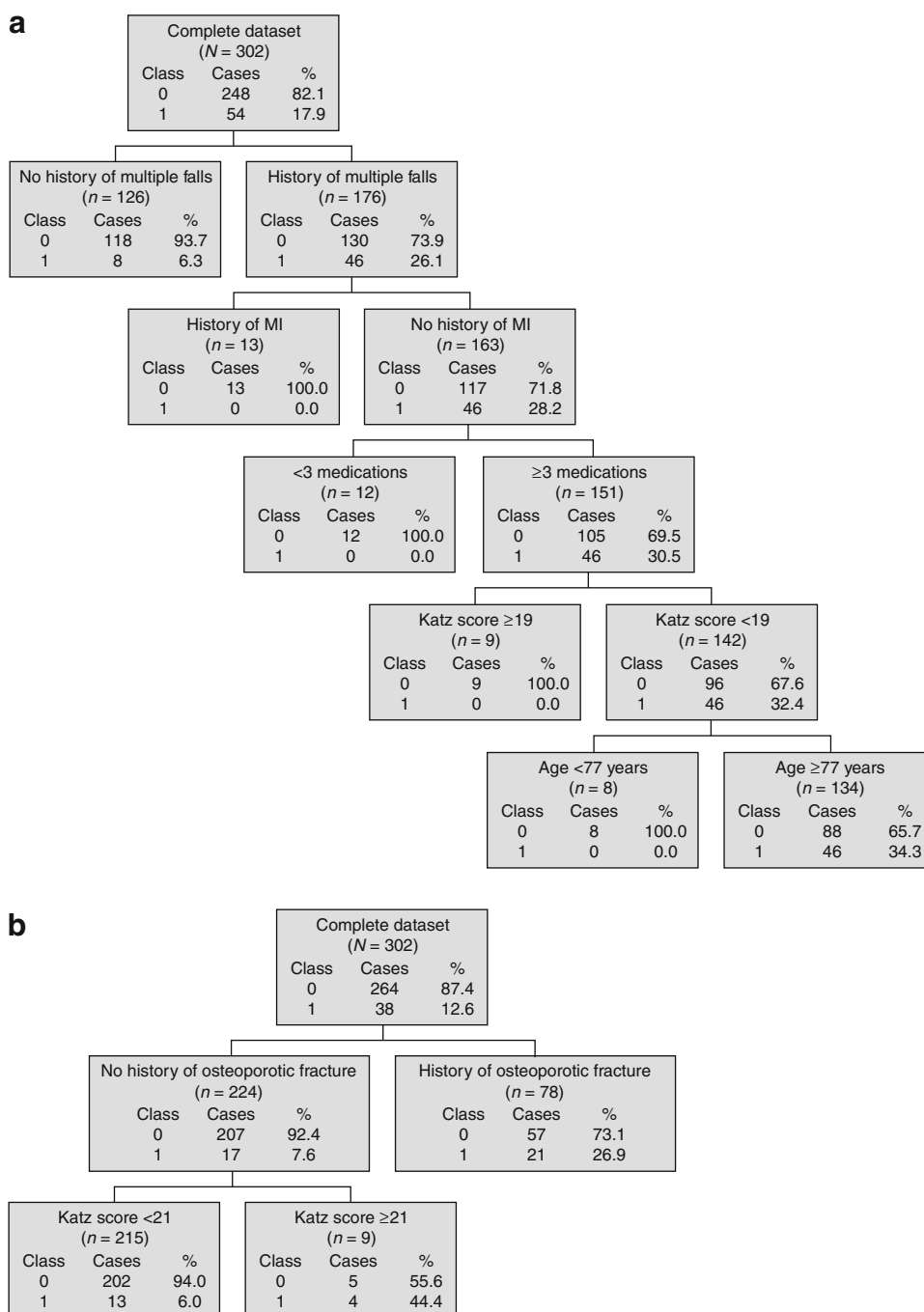
older patients received an inappropriately prescribed medication (PIM) according to STOPP and 63 % had a prescribing omission (PPO) according to START. Importantly, these events of inappropriate prescribing contributed or led to 27 % of hospital admissions. A history of previous falls and of osteoporotic fractures were the main determinants of PIM- and PPO-related admissions, respectively. To our knowledge, this is the first study investigating hospital admissions possibly related to events of inappropriate prescribing according to both STOPP and START in a population of older patients with frailty features. Our data are enriched by the evaluation of possible determinants, including geriatric syndromes.

Our prevalence results are consistent with those of previous studies of inappropriate prescribing according to STOPP and START. A recent international multicentre study of patients in acute geriatric units found prevalence rates of 51 % for PIMs and 59 % for PPOs on admission [23]. Other studies with older inpatients reported prevalence rates of 35–77 % for PIMs [13, 24] and 58–66 % for PPOs [24, 25]. In contrast, the prevalence of PIMs and PPOs was lower in studies of community-dwelling older people [8, 9].

Several risk factors for PIMs have been previously identified in the literature, namely polypharmacy [9, 23, 24], a history of recent falls [24], cognitive impairment [24], hospitalization in the preceding year [24], female gender [9] and advanced age [9, 23]. The first two, which are geriatric syndromes, were confirmed by our multivariate analysis.

The multivariate analysis showed that PPOs were associated with five co-morbidities (diabetes, atrial

Fig. 1 Classification trees showing the main determinants of hospital admissions following (a) prescribing of potentially inappropriate medications (PIMs; according to the STOPP criteria) and (b) potential prescribing omissions (PPOs; according to the START criteria). Class 1 represents the number of patients who had a hospital admission related to inappropriate prescribing, and class 0 represents the others. *START* Screening Tool to Alert doctors to Right Treatment, *STOPP* Screening Tool of Older Person's Prescriptions



fibrillation, osteoporotic fracture, COPD and ischaemic disease). This finding is consistent with published data on the number of co-morbidities [23, 24]. Living in an institutional setting was a predictor of both PIMs and PPOs in a study by Lang et al. [24] but was not significant in our study, probably because of the limited number of institutionalized patients. Polypharmacy was related to PIM events but not to PPO events, as was previously reported by Steinman et al. [26].

Acute hospital admission was related to PIMs and PPOs in 18 % and 13 % of patients, respectively. A similar study

of acutely ill older patients, using the STOPP criteria, found that PIMs contributed to 12 % of all admissions [13]. Furthermore, the same research group found that PIMs were significantly associated with preventable ADEs causing or contributing to hospital admission [14]. These results suggest good predictive validity of the STOPP criteria.

In contrast, to our knowledge, no study has addressed the link between hospital admissions and PPOs according to the START criteria. The present work shows that a significant percentage of patients are possibly admitted to

hospital because of prescribing omissions. Further studies are needed to confirm these results.

The use of classification trees in this study allowed us to segment the population into subgroups, using cut-off values that may be used in future risk-assessment exercises. Particular attention should be given to a subgroup of patients with a history of falls and/or osteoporosis, which should be studied further. The Katz threshold might be the object of validation in similar future studies.

Inappropriate use of medication in patients who experience falls is of particular concern. Similarly to previous studies, a substantial number of patients with previous falls were receiving fall-risk-increasing drugs ($n = 50$), and/or were not receiving medications that decrease the risk of fractures ($n = 71$) [8, 13, 14, 23–25]. These criteria were also those with the highest PPVs for hospital admission. Importantly, we found that recent falls were a significant determinant of medication-related admission. Falls are a major concern in older people, as they increase morbidity (including hospital admission) and mortality [27, 28]. Withdrawal of fall-risk-increasing drugs has been proven to be effective and cost-effective in older persons for fall prevention [29–31]. Such withdrawals, particularly of benzodiazepines, remain a challenge in daily practice.

Other clinical situations deserve special attention. First, cardiovascular prevention and inappropriate use of aspirin accounted for a significant proportion of inappropriate prescribing events, mainly misuse (a daily dose of >150 mg) and underuse. Moreover, six and two admissions were related to underuse or overuse of aspirin, respectively [32, 33]. Second, as has been highlighted in many other studies, underuse of vitamin K antagonists in patients with chronic atrial fibrillation was frequent [34–37]. Our analysis identified atrial fibrillation as an independent determinant of PPO-related hospital admissions. Third, diabetes was a significant determinant of PPOs (mainly of aspirin, metformin and ACE inhibitors) but did not predict PPO-related hospital admissions. There is evidence that such medications can decrease morbidity or mortality in adults but not in older persons. Therefore, clinicians often face difficulties to find the right balance between recommendations and therapies that are acceptable for older patients [38–40]. If we had applied the criteria to the 69 diabetic patients in our study, their mean number of daily drugs would have risen from 8.0 to 9.6. Therefore, the START criteria related to diabetes might need some revision.

This study had limitations. First, it was observational and monocentric. Second, the evaluation of the link between inappropriate prescribing events and hospitalization was based on clinical judgment. Similarly to previous studies, two types of professionals (i.e. a geriatrician and a clinical pharmacist) were involved. No inter-rater reliability

(i.e. kappa coefficient) was calculated to measure the researchers' agreement, and no evaluation of preventability was performed.

The findings of this study underline the importance of regularly evaluating pharmacological treatment of frail older patients, knowing that inappropriate prescribing can be related to hospital admissions. Clinicians' attention should be drawn particularly to the treatment of patients with a history of falls, osteoporosis or cardiovascular disease such as atrial fibrillation. Use of the STOPP and START criteria should be encouraged, as these tools are useful and efficient in screening patients' medications and detecting inappropriate prescribing [12].

5 Conclusion

The use of the STOPP and START criteria revealed a high prevalence of inappropriate prescribing of medications used at home by a frail older population. Moreover, inappropriate prescribing in this population contributed to one in four acute hospital admissions. Optimizing prescribing of medications in patients with previous falls and osteoporotic fractures should be a priority for clinicians as well as evaluative researchers.

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