ORIGINAL ARTICLE

EVALUATING POTENTIALLY INAPPROPRIATE MEDICATIONS IN THE ELDERLY WITH SEVEN DIFFERENT SCREENING TOOLS

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Abstract

Introduction: We aimed to determine the rates of potentially inappropriate medications using various screening tools and also the affecting factors in elderly patients.

Materials and Method: In this prospective cross-sectional study, we recorded in detail the concomitant chronic diseases, geriatric syndromes, and drugs used in elderly patients admitted to a university hospital and then assessed potentially inappropriate medications using seven different screening tools.

Results: The study included 315 patients (190 female; 125 male). We evaluated potentially inappropriate medication use with the PRISCUS, EU(7), Beers 2019, STOPP v2, and TIME-to-STOP criteria and evaluated potential prescription omissions with the START v2 and TIME-to-START criteria; the resulting identified rates of PIMs were 15.9%, 45.1%, 48.9%, 44.8%, 48.3%, 73.9%, and 97.5%, respectively. The lowest value was found with PRISCUS, as it uses fewer criteria than the others. The EU(7), Beers 2019, STOPP v2, and TIME-to-STOP results were similar to one another. START v2 and TIME-to-START yielded higher outcomes than the others due to the omission of vaccines in patients. The highest outcome was found with TIME-to-START due to the omission of the herpes zoster vaccine (97.5%), which appears only in that screening tool. Potentially inappropriate medication rates increased with the number of drugs used and with the number of concomitant chronic diseases.

Conclusion: This study detected potentially inappropriate medication use in approximately half of the patients with the EU(7), Beers 2019, STOPP v2, and TIME-to-STOP screening tools. There was a positive correlation between potentially inappropriate medications and polypharmacy and increased disease burden.

Keywords: Potentially Inappropriate Medication List; Polypharmacy; Aged.

INTRODUCTION

The number of drugs used and rates of polypharmacy have increased in the elderly due to an increase in concomitant chronic diseases and geriatric syndromes (1). Although diverse definitions are used, *polypharmacy* is most commonly accepted as the use of five or more drugs per day (2).

In the elderly, rates of medication use errors and potentially inappropriate medications (PIMs) as well as the risk of potential drug-drug interactions and adverse drug reactions increase with polypharmacy (3).

A PIM is a drug that should not be given because the risk of adverse effects outweighs the clinical benefit when there is evidence of safer, more effective alternative treatments for the same indication in the elderly (4–8). In addition, the omission of drugs or vaccines when there is a relevant indication, termed a potential prescribing omission (PPO), is accepted as inappropriateness (6,9).

Numerous screening tools have been developed for PIMs. The most commonly used include Beers criteria, the Screening Tool of Older Persons' potentially inappropriate Prescriptions/Screening Tool to Alert to Right Treatment (STOPP/START) criteria, the PRISCUS list, and the European Union (7)– Potentially Inappropriate Medications (EU[7]-PIM) list (5-8). Beers criteria were developed by Beers et al. in 1991 to evaluate drugs used by the elderly living in nursing homes; they were last updated by the American Geriatrics Society in 2019 (5). The STOPP/START criteria were developed by Gallagher et al. in 2008 as an alternative to Beers criteria that accounts for drugs used in Europe in evaluating medications used by the elderly. It was updated in 2015 as STOPP/START version 2 (v2) (6). The PRISCUS list was developed in Germany in 2010 and identified 83 drugs deemed potentially inappropriate for use in the elderly (7). The EU(7)-PIM was developed in 2015 by geriatricians from seven European countries (Germany, Estonia, France, Netherlands, Spain, Finland, and Sweden) and includes 282 drugs that are seen as PIMs in the elderly (8). In Turkey, the Academic Geriatrics Society developed the Turkish Inappropriate Medication use in the Elderly (TIME) criteria (TIME-to-STOP and TIME-to-START) in 2020 based on the STOPP/START criteria and the drugs used in our country (9).

This study employed seven different screening tools to evaluate the drugs used in elderly patients admitted to the hospital. We used five tools (Beers 2019, STOPP v2, PRISCUS, EU(7), and TIME-to-STOP) to identify PIM use and two (START v2 and TIME-to-START) for PPOs. We aimed to contribute to the literature by comparing different screening tools to determine PIM rates in the elderly and also by identifying factors affecting PIM use.

MATERIALS AND METHOD

We obtained ethics committee approval for this prospective cross-sectional study. Patients were included who were aged 65 and over, had at least one chronic disease, used at least one drug per day for it, were admitted to general internal medicine outpatient clinics of Bursa Uludag University Hospital, Turkey, and agreed to participate in the study. Written consent was obtained from all patients. Patients who did not provide voluntary consent or could not answer the questionnaire were not included in the study.

Sociodemographic characteristics (such as age, gender, marital status, cohabitation, education level, concomitant chronic diseases, geriatric syndromes, and drugs used) were recorded by interviewing the patients in person using a pre-prepared questionnaire form. As part of the comprehensive geriatric assessment, we conducted some tests; the Mini Nutritional Assessment (MNA) for malnutrition, Yesavage Geriatric Depression Scale (GDS) for depression, Standardized Mini Mental Test (SMMT) for dementia, and 'Fatigue, Resistance, Ambulation,

Illnesses, Loss of weight' (FRAIL) scale for frailty. But we could not detect sarcopenia, which is a geriatric syndrome, because of no hand grip device in our unit at the time of study period.

The Charlson Comorbidity Index (CCI) was used to measure chronic disease burden (10). In this study, daily use of ≥ 5 drugs was accepted as polypharmacy, and the use of ≥ 10 drugs was accepted as hyperpolypharmacy (2). The rates of polypharmacy, urinary incontinence, chronic pain (pain lasting longer than three months), frailty, history of falling, insomnia, and malnutrition were investigated as geriatric syndromes.

The drugs used by the patients at the time of admission were evaluated in terms of PIMs and PPOs using the PRISCUS, EU(7), Beers 2019, STOPP/START v2, TIME-to-STOP and TIME-to-START screening tools. We investigated the relationship between PIMs and gender, age group (65-74 years and ≥ 75 years), presence of polypharmacy, and CCI score.

Statistical Analysis

Statistical analyses of the study were performed with JASP 0.16.3 software. The categorical variables were presented as frequencies and percentages, and the quantitative variables were presented as the mean, standard deviation, and minimum and maximum values. The Shapiro-Wilk test was used to determine whether the quantitative variables fit the normal distribution. The Mann-Whitney U test was used for two-group comparisons of non-normally distributed quantitative variables.

The Fisher chi-square, Yates chi-square, and Pearson chi-square tests were used to compare groups of qualitative variables. For all tests, a p-value of $< .05$ was considered statistically significant.

RESULTS

A total of 315 patients were included in the study during the one-year period between February 15, 2021 and February 15, 2022, of whom 190 were female and 125 male (female/male ratio: 1.52). The mean age was 70.6 ± 5.5 years. Table 1 shows their sociodemographic characteristics, and the most common concomitant chronic diseases and geriatric syndromes are shown in Table 2.

Table 1. Sociodemographic characteristics of the patients.

	Number (%)
Gender	
Female	190 (60.3%)*
Male	125 (39.7%)
Age groups	
65-74	261 (82.8%)*
≥ 75	54 (17.1%)
Marital status	
Single	2 (0.6%)
Married	235 (74.6%)*
Divorced	12 (3.8%)
Widoved	66 (21%)*
Household status	
Alone	42 (11.3%)*
With spouse	235 (74.6%)*
With children	35 (11.1%)
Others	3 (0.95%)
Education status	
Illiterate	22 (7%)*
Just literate	38 (12%)
Primary school	124 (39.4%)
Secondary school	49 (15.6%)
High school	46 (14.6%)**
University	36 (11.4%)**

*; p<0.01, **; p<0.001.

Table 2. Distribution of the most common concomitant chronic diseases and geriatric syndromes by gender.

	Female	Male	Total
Chronic diseases			
Hypertension	150 (77.3%)	94 (77.7%)	244 (77.4%)
Diabetes Mellitus	88 (45.4%)	60 (49.6%)	144 (46.9%)
Dyslipidemia	73 (37.6%)	51 (42.1%)	124 (39.3%)
Depression	66 (34%)*	26 (21.5%)	92 (29.2%)
Chronic kidney disease (GFR < 60 ml/min)	51 (26.3%)	39 (32.2%)	90 (28.6%)
Coronary artery disease	30 (15.5%)	43 (35.5%)**	73 (23.2%)
Osteoporosis	58 (29.9%)**	9 (7.4%)	67 (21.3%)
Hypothyroidism-Hyperthyroidism	55 (28.4%)**	10 (8.3%)	65 (20.6%)
Peptic ulcer-Gastritis-Gastroesophageal reflux	34 (17.9%)	16 (12.8%)	50 (15.9%)
Dementia	41 (21.1%)	8 (6.6%)	49 (15.6%)
Asthma-COPD	27 (14.2%)	18 (14.4%)	45 (14.3%)
Arthrosis- Arthritis	29 (15.3%)	15 (12.%)	44 (14%)
Neuropathy	28 (14.4%)	16 (13.2%)	44 (14%)
Benign prostatic hypertrophy		43 (34.4%)**	43 (13.7%)
Arrhythmia	16 (8.2%)	10 (8.3%)	26 (5.1%)
Geriatric syndromes			
Polypharmacy	114 (60%)	73 (58.4%)	187 (59.4%)
Urinary incontinence	45 (23.2%)	34 (28.1%)	79 (25.1%)
Chronic pain	52 (27.4%)*	16 (12.8%)	68 (21.6%)
Frailty	45 (23.2%)	19 (15.7%)	64 (20.3%)
Fall	40 (20.6%)	23 (19%)	63 (20%)
Insomnia	44 (22.7%)*	14 (11.6%)	58 (18.4%)
Malnutrition	11 (5.7%)	11 (9.1%)	22 (7%)

*; $p<0.05$, **; $p<0.001$.

Abbreviations: GFR; glomerular filtration rate, COPD; chronic obstructive pulmonary disease.

In this study, the number of female patients and patients aged 65-74 was significantly higher than the number of males and those ≥ 75 years, respectively. There was no difference between the age groups in terms of marital status, but the rate of being married was higher in men, and the rate of being widowed was higher in women. There was no difference between the age groups in terms of household status. The prevalence of living alone was higher in female patients, while living with a spouse was higher in male patients. The prevalence of being illiterate was higher in female patients, whereas high school and university graduation was more likely in male patients and in the 65-74 age group.

Table 3. Distribution of the number of drugs used daily by gender and age groups.

Number of drugs used daily	Gender		Total	Age groups	
	Female	Male		65-74	≥ 75
1-4 drugs	76 (40%)	52 (41.6%)	128 (40.6%)	107 (41%)	21 (38.9%)
5-9 drugs	90 (47.4%)	64 (51.2%)	154 (48.9%)	128 (49%)	26 (48.1%)
≥ 10 drugs	24 (12.6%)	9 (7.2%)	33 (10.5%)	26 (10%)	7 (13%)

Table 4. Most frequently used drugs by patients.

Drugs used	Number (%)
ACEIs/ARBs	179 (56.8%)
Diuretics	120 (38.1%)
Beta blockers	118 (37.5%)
Metformin	113 (35.9%)
ASA	109 (34.6%)
PPIs	102 (32.4%)
CCBs	97 (30.8%)
Statins	84 (26.7%)
DPP-4 inhibitors	57 (18.1%)
Levothyroxine	54 (17.1%)

Abbreviations: ACEIs; Angiotensin converting enzyme inhibitors, ARBs; Angiotensin receptor blockers, DPP-4; dipeptidyl peptidase-4, ASA; Acetylsalicylic acid, PPIs; Proton pump inhibitors, CCBs; Calcium channel blockers.

Hypertension, diabetes mellitus, dyslipidemia, depression, and chronic kidney disease were the most common concomitant diseases. The prevalence of hypothyroidism-hyperthyroidism (28.4% vs. 8.3%, p< .001), osteoporosis (29.9% vs. 7.4%, p< .001), depression (34% vs. 21.5%, p< .05), and dementia (21.1% vs. 6.6%, p<.001) was higher in female patients, while coronary artery disease (35.5% vs. 15.5%, p< .001) was higher in male patients. Moreover, approximately one-third of men (34.4% in men) had benign prostatic hypertrophy. The prevalence of chronic kidney disease (42.6% vs. 25.7%, p< .05), arrhythmias (18.5% vs. 6.1%, p< .01), and heart failure (14.8% vs 2.7%, p< .001) was higher in the ≥ 75 age group. There was no difference between the gender and age groups in terms of other concomitant chronic diseases. In addition to 59 patients diagnosed with depression and 8 patients with dementia at the time of admission, 33 patients were diagnosed with depression by the GDS, and 41 patients were diagnosed with dementia by the SMMT; appropriate recommendations and guidance were provided.

The most common geriatric syndromes were polypharmacy, urinary incontinence, and chronic pain. Chronic pain (27.4% vs. 12.8%, p< .05) and insomnia (22.7% vs. 11.6%, p< .05) were more common in women. Frailty (31.5% vs. 18%, p< .05) was higher in the ≥ 75 age group. There was no difference between the gender and age groups in terms of other geriatric syndromes.

Patients using at least one drug per day were included in the study, and the total number of drugs used by the patients at the time of admission was 1,873. Of these, 1,746 drugs that are used regularly every day (excluding 127 used for local effect, such as eye drops, nasal spray, and inhaler drugs) and used in weekly and monthly periods were evaluated. The mean number of drugs used daily by the patients was 5.5 ± 1.8. The rate of polypharmacy was 59.4%, and that of hyperpolypharmacy was 10.5% (Table 3). There was no difference between the gender and age groups in terms of polypharmacy and hyperpolypharmacy. The most frequently used drugs related to organs/systems were cardiovascular system (CVS) drugs in

Table 5. Distribution of potential inappropriate medications according to different screening tools by gender, age groups, number of drugs and disease burden.

	PRISCUS	EU-7	Beers 2019	STOPP v2	TIME-to-STOP	START v2	TIME-to-START
Total PIMs	50 (15.9%)	142 (45.1%)	154 (48.9%)	141 (44.8%)	152 (48.3%)	233 (73.9%)	307 (97.5%)
Gender							
Female (n:190)	25 (12.9%)	87 (44.8%)	103 (53.1%)	88 (45.4%)	97 (50%)	150 (77.3%)	185 (97.4%)
Male (n:125)	25 (20.7%)	55 (45.5%)	51 (42.1%)	53 (43.8%)	55 (45.5%)	83 (68.6%)	122 (97.6%)
Age groups							
65-74 (n:261)	40 (15.3%)	116 (44.4%)	122 (46.7%)	113 (43.3%)	121 (45.4%)	190 (72.8%)	254 (97.3%)
≥ 75 (n:54)	10 (18.5%)	26 (48.1%)	32 (59.3%)	28 (51.9%)	31 (57.4%)	43 (79.6%)	53 (98.1%)
Number of drugs used							
1-4 drugs (n:128)	5 (3.9%)	33 (25.8%)	36 (28.1%)	36 (28.1%)	37 (28.9%)	93 (72.7%)	124 (96.9%)
5-9 drugs (n:154)	33 (21.4%)*	82 (53.2%)*	89 (57.8%)*	82 (53.2%)*	87 (56.5%)*	116 (75.3%)	151 (98.1%)
≥ 10 drugs (n:33)	12 (36.4%)**	27 (81.8%)**	29 (87.9%)**	23 (69.7%)**	28 (84.8%)**	24 (72.7%)	32 (97%)
Disease burden (CCI score)							
0 point (n:52)	7 (13.5%)	17 (32.7%)	21 (40.4%)	21 (40.4%)	18 (34.6%)	37 (71.2%)	51 (98.1%)
1-2 points (n:175)	25 (14.3%)	71 (40.6%)	82 (46.9%)	69 (39.4%)	77 (44%)	127 (72.6%)	170 (97.1%)
3-4 points (n:69)	13 (18.8%)*	41 (59.4%)*	38 (55.1%)*	38 (55.1%)*	43 (62.3%)**	54 (78.3%)	67 (97.1%)
≥ 5 points (n:19)	5 (26.3%)**	13 (68.4%)**	13 (68.4%)**	13 (68.4%)**	14 (73.7%)**	15 (78.9%)	19 (100%)
Most frequently detected potentially inappropriate drugs/criteria	**Drugs** → -NSAIDs (3.2%) -Piracetam (%3.2)-Alpha-1 blockers (2.5%) -Digoxin (1.3%) -Solifenacin (1.3%)	**Drugs** → -PPIs (9.5%) -NSAIDs (8.3%)-Trimetazidin (5.7%) -Glimepiride/ Sitagliptin (5.4%) -Diltiazem (3.8%)	**Drugs** → -PPIs (9.5%) -ASA (9.2%) -Antidepressant (8.9%) -NSAIDs (5.4%) -Anticholinergic (4.1%)	**Criteria** → -Indication of medicationcriteria (19.3%) -CVS criteria (12.3%) -GIS criteria (11.7%) -Antiplatelet/ Anticoagulant drugs (7.9%) -Musculoskeletal system criteria (7.6%) **Drugs** → -PPIs (9.5%) -ASA (7.6%) -NSAIDs (6%)	**Criteria** → -CVS criteria (20%) -GIS criteria (15.2%) -Musculoskeletal system criteria (9.8%) - Nervous system criteria(9.2%) -Antimuscarinic/ Anticholinergic drug burden criteria (2.5%) **Drugs** → -PPIs (9.5%) -ASA (7.6%) -NSAIDs (6%)	**Criteria** → -Vaccines criteria (57.5%) -CVS criteria (36.1%) -GIS criteria (15.6%), -Musculoskeletal system criteria (14.6%) -Analgesics criteria(1.6%)	**Criteria** → -Vaccines criteria (97.5%) -CVS criteria (20.6%) -GIS criteria (11.7) -Nervous system criteria (14.3%) -Musculoskeletal system criteria (10.2%)

*; p<0.01, **; p<0.001.

Abbreviation: NSAIDs; Nonsteroidal anti-inflammatory drugs

260 (82.5%) patients, endocrine system drugs in 183 (58.1%) patients, and gastrointestinal system (GIS) drugs in 116 (36.8%) patients, respectively (Table 4). Table 5 shows the seven screening tools used to evaluate the patients' drugs for PIMs.

We separately evaluated the patients' drugs in terms of PIMs using five different screening tools (PRISCUS, EU[7], Beers 2019, STOPP v2, and TIME-to-STOP), finding no difference between the gender and age groups according to these tools. The rates of PIMs were significantly higher in patients with polypharmacy and in those with a greater chronic disease burden. When these screening tools were compared with one another, the rate of PIMs detected with PRISCUS was significantly lower than the others, while the rates of PIMs detected with EU(7), Beers 2019, STOPP v2, and TIME-to-STOP were similar. The most common drugs identified as PIMs were PPIs, ASA, and NSAIDs. PPOs, a type of PIM in which drugs/vaccines are omitted even though they are indicated, were evaluated with two screening tools (START v2 and TIME-to-START), and the rates of PIMs were higher than found by the other five screening tools. The most common reason for PPOs was omission of vaccines criteria. The vaccine omission rates were 45.7% for influenza vaccine, 45.1% for 13-valent pneumococcal vaccine, 76.8% for 23-valent pneumococcal vaccine, 84.8% for diphtheria-tetanus vaccine, and 97.5% for herpes zoster vaccine. The rate of PPO was higher with TIME-to-START, as it includes diphtheria-tetanus and herpes zoster vaccine criteria in addition to the influenza and pneumococcal vaccine criteria in START v2.

DISCUSSION

Drug use and polypharmacy are common in the elderly, and different rates of polypharmacy have been reported according to study setting, such as in the general community, nursing homes, primary care institutions, outpatient clinics, and inpatient clinics. In a population-based survey conducted in the USA, the rates of polypharmacy and hyperpolypharmacy in the elderly are reported as 57% and 12% in women and 44% and 12% in men, respectively (11). A study examining the data of 466 patients in primary care in Germany reports that patients used an average of 3.7 prescription drugs and 1.4 over the counter drugs per day for a total of 5.1 drugs per day, and the rate of chronic polypharmacy was 26.7% (12). In a study of 1,332 elderly patients hospitalized in 38 internal medicine wards in Italy, polypharmacy rates are reported as 51.9% at admission and 67.0% at discharge (13). In a previous study with 721 elderly patients admitted to the General Internal Medicine outpatient clinic of our hospital, the mean number of drugs used daily was 4.6 ± 2.8, and the rates of polypharmacy and hyperpolypharmacy were 49.4% and 6.0%, respectively (14).

In the present study, the mean number of drugs used daily is 5.5 ± 1.8, and the rates of polypharmacy and hyperpolypharmacy are 59.4% and 10.5%, respectively. These values in the present study may be higher than in the previous study because, while all elderly patients were included in the previous study, the present study recruited only patients who had at least one chronic disease and used at least one drug per day.

The most common cause of polypharmacy is that chronic diseases and geriatric syndromes are common in the elderly. The most common chronic diseases in an Italian study were hypertension, diabetes mellitus, coronary heart diseases, atrial fibrillation, and chronic obstructive pulmonary disease (COPD) (13). In the previous study in our unit, hypertension, diabetes mellitus, dyslipidemia, and coronary artery disease were the most common chronic diseases (14). Similarly, the most common chronic diseases in the present study are hypertension, diabetes mellitus, dyslipidemia, depression, and chronic kidney disease.

An important consequence of polypharmacy is an increased risk of PIMs in patients. To identify PIMs, the present study employed the criteria of

PRISCUS, EU(7), Beers 2019, STOPP v2, and TIME-to-STOP to evaluate the drugs used by elderly patients; we used the START v2 and TIME-to-START criteria to identify PPOs .

In a study using PRISCUS to examine 335 different drugs in 2,363 prescriptions of 92 elderly patients in a geropsychiatry unit in Germany, 30.4% had at least one PIM, and the three most common PIMs were lorazepam, clonazepam, and olanzapine (15). In a study based on the health insurance database in Germany, the rate of PIMs with PRISCUS was 22%, and the three most common PIMs were antidepressants (6.5%), antihypertensives (3.8%), and antiarrhythmic drugs (3.5%) (16).

In a study using the EU(7)-PIM list in 428 elderly patients with cognitive impairment in Sweden, the rate of PIMs was 40.9%, and the three most common PIMs were zopiclone, digoxin, and sodium picosulfate (17). A study conducted with EU(7) in six European countries reports the rates of PIMs as 71.4% in Spain, 67.5% in Turkey, 67.1% in Portugal, 55.5% in Hungary, 50.2% in Czechia, and 42.8% in Serbia (18).

In a study using the Beers 2019 criteria to examine 8,477 drugs used by 1,874 patients in an outpatient clinic in China, the rate of PIMs was 35%, and the most common PIMs were alprazolam, estazolam, and pseudoephedrine compounds (19).

In a study conducted with the STOPP and START v2 criteria in a cohort of 102 patients in a geriatric psychiatry unit in Switzerland, the rates of PIMs are reported as 78% and 47%, respectively. According to the STOPP v2 criteria, the most common PIMs were benzodiazepines and neuroleptics in patients with a history of falls in the past three months. According to the START v2 criteria, the most prominent PPO was the omission of statin in independent patients with a history of coronary, cerebral, or peripheral vascular disease and more than five years of life expectancy (20).

Some studies have compared the scanning tools we used in the present study. In a study conducted with 3,189 patients in Germany, the rates of PIMs were 24.7% with PRISCUS and 70.1% with EU(7), and the most common PIMs identified by PRISCUS were amitriptyline, acetyldigoxin, nifedipine, and zopiclone, whereas the EU(7) most commonly identified omeprazole, diclofenac, ibuprofen, and ASA (21). In a study that evaluated the data of 400 patients in Brazil with different screening tools, the rates of PIMs were 46.2% with STOPP v2 and 59.5% with EU(7), and the most common PIMs were clonazepam, amiodarone, and glibenclamide with STOPP v2 and clonazepam, nifedipine, and amiodarone with EU(7) (22). In a study examining 4,386 prescriptions of 593 patients in Spain, the rates of PIMs were 57.4% with STOPP v2 and 68.8% with Beers 2019, and the most common PIM was prolonged use of benzodiazepines (36.6%) with STOPP v2 and prolonged use of PPIs (43.8%) with Beers 2019 (23).

In a study conducted with 90 patients in a nursing home in Portugal, the rates of PIMs were 64.4% with EU(7) and 85.5% with STOPP v2, and the most common PIMs were benzodiazepines with STOPP v2 and prolonged use of anxiolytics, sedatives, and hypnotics with EU(7) (24). A hospital study in Croatia evaluated the data of 276 patients and found rates of PIMs of 69% with STOPP v2 and 66.7% with EU(7); both screening tools identified the most common PIMs as benzodiazepines, PPIs, and tramadol (25).

The screening tools used in the present study yielded PIM rates of 15.9% with PRISCUS, 45.1% with EU(7), 48.9% with Beers 2019, 44.8% with STOPP v2, and 48.3% with TIME-to-STOP. The rate was significantly lower with PRISCUS than with the others because a total of 83 drugs were evaluated in the PRISCUS list, whereas > 250 drugs were evaluated in the EU(7), Beers 2019, STOPP v2, and TIME-to-STOP criteria. The PIM rates were similar among the latter screening tools. The most common PIMs were NSAIDs and piracetam with PRISCUS; PPIs and NSAIDs with EU(7); PPIs, ASA, and antidepressants with Beers 2019; PPIs, ASA, and

NSAIDs with STOPP v2; and PPIs, ASA, and NSAIDs with TIME-to-STOP. The most common cause of PIMs was the use of PPIs for longer than 8–12 weeks (except in special cases) and the use of PPIs due to polypharmacy. The PIM criteria for PPI were not included in the PRISCUS list; they are included in the EU(7) and TIME-to-STOP criteria, and they were added to the updated Beers 2015 and 2019 and the STOPP v2 criteria.

PPOs are accepted as a form of PIM, and the screening tools we used to examine PPO rates in our patients yielded rates of 73.9% (START v2) and 97.5% (TIME-to-START), which were higher than those found by the other screening tools. The most common PPO detected by both screening tools was omission of vaccines criteria. The rate of PPOs was higher with TIME-to-START than with START v2 because the latter includes only the omission of the pneumococcal vaccine and the annual influenza vaccine in the vaccine criteria, whereas TIME-to-START also includes the omission of the herpes zoster vaccine and the tetanus-diphtheria vaccine. The herpes zoster vaccine was not administered in 97.5% of the patients, probably because the vaccine was not available in the market for most of the study period.

The main limitation of our study is that it relied on single-center data, but we believe that our data reflect the patient profile in our country's tertiary university hospitals. Another limitation is that we identified the drugs used by our patients based on their own statements. To minimize this risk, however, the patients were asked to bring the drugs they used on their next visit, the use of drugs was questioned in detail, and the approval of the patient's relatives/caregivers was obtained.

In summary, the present study used five different screening tools to evaluate the drugs used by patients and found that the rates of PIMs were higher with the EU(7), Beers 2019, STOPP v2, and TIME-to-STOP than with PRISCUS. We also evaluated PPOs with two different screening tools and observed that the rates of PIMs found by START v2 and TIME-to-START were higher than found by PRISCUS, EU(7), Beers 2019, STOPP v2, and TIME-to-STOP. Moreover, we observed that PIM rates increase with the number of medications used and with the chronic disease burden score.

In conclusion, polypharmacy and its associated PIMs pose significant risks for the elderly. In our opinion, the PIM criteria is very important for rational drug use. These criteria can guide physicians in drug selection in the elderly. There may be differences in the drugs used in different countries. Therefore, it is important to identify and publish PIM criteria for drugs available in that country. However, it is also useful to know other country criteria and all these criteria should be updated periodically. As an example of the importance of updating, the PIM criterion related to PPIs was added to the updated criteria in 2015 and later. The most common drugs identified as PIMs were PPIs, ASA, and NSAIDs in this study. Determining and publishing PIM rates and the drugs that most commonly identified as PIM in different countries will increase physicians' awareness of the risks associated with the use of these drugs and contribute to rational drug use. Therefore, PIM lists are important educational tools and should be part of a comprehensive geriatric assessment. To reduce drug-related risks in the elderly, all patients should be evaluated with a comprehensive geriatric assessment, drugs with potential risks should be avoided, and indicated drugs and vaccines should not be omitted.

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