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Evaluation of Potentially Inappropriate Drug Use in Older Adult Outpatients Using the Turkish Inappropriate Medication Use in the Elderly Criteria in Kütahya Province, Turkey

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ABSTRACT

Introduction: The population aged 65 years and older has the highest rates of drug use and is more sensitive to drug effects. Appropriate medication use among older adults is associated with poor clinical outcomes. The objective of this study was to use national criteria to evaluate inappropriate drug use among individuals aged 65 years and older who were admitted to the internal medicine outpatient clinic.

Methods: Our study was conducted using 385 randomized patients aged 65 years and older who were treated at the Evliya Çelebi Training and Research Hospital, Internal Medicine Outpatient Clinic of Kütahya University. The study was designed as a cross-sectional descriptive survey. It evaluated potentially inappropriate drugs and possible prescribing neglect according to the Turkish Inappropriate Medication Use in the Elderly (TIME) criteria.

Results: Potentially inappropriate drug use was detected in 127 patients (33%) using the TIME-to-STOP criteria. The first three potentially inappropriate medications determined by the TIME-to-STOP criteria were proton pump inhibitor deficient use, tight blood pressure control, and tight blood sugar control. Using the TIME-to-START criteria, potential prescribing omissions (PPO) were detected in 379 (98.4%) patients. The first three PPO in the TIME-to-START criteria were about vaccines deficient in patients.

Conclusion: Country-specific criteria are more effective for inappropriate medication use.

Keywords: Aged, disease, potentially inappropriate medications, inappropriate prescribing, Turkey

Introduction

Multimorbidity and polypharmacy are the main challenges faced by aging populations globally. With an aging world population, the fight against inappropriate medication use (IMU), polypharmacy, adverse drug events (ADEs), adverse drug reactions (ADRs) and medication costs has gained importance. Polypharmacy and the prescription of potentially inappropriate medications (PIMs) are the major elements of IMU in older adults. Attempts have been made to combat these issues using various explicit criterion lists (1). Potentially inappropriate prescriptions (PIP) comprise the prescription of PIMs and potential prescribing omissions (PPOs).

For older adults, this is a practical and cost-effective solution for adverse medications. In recent years, tools based on explicit PIM criteria have been developed to assist drug management in older adults for practical use in clinics.

These criteria are of great importance to prevent morbidity and mortality from ADRs and ADEs. Polypharmacy and PIMs are very common in older adults. Therefore, new strategies are needed to improve prescription quality and increase prescription safety. A review of the studies over the last 30 years indicates that criteria-based strategies have been established to prevent polypharmacy, including 42 prescription evaluation tools (2).

The criteria used for detection of PIMs and PPOs are divided into two groups, implicitly or explicitly. Although they are useful research tools, implicit criteria are not preferred in practical applications due to their complex structure and time consumption.

However, explicit criteria are useful research tools that are used in routine clinical practice. The American Geriatrics Society (AGS) Beers Criteria and the screening tool of older people's prescriptions (STOPP) and screening tool to alert to right treatment (START) criteria have been the most popular. In the 1990s, studies on PIPs using the Beers Criteria increased daily.

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The biggest reason for the diversity in these criteria is the differences in national prescribing habits. The STOPP/START criteria developed in Europe are widely used in drug reviews of older adults. It was first published in 2008 and then updated in 2015. It contains examples of PIM (STOPP) and PPO (START) separated by physiological systems. In the coming years, seniors' drug reviews will be mostly electronics. These electronic STOPP/START criteria will be administered by specialist pharmacists and will apply to lists of concurrent multimorbidity and associated polypharmacy in older adults (3).

The Beers Criteria are commonly used to evaluate PIPs in older adults. It was first published in 1991 and has been updated 5 times thus far. The last update was published in 2019. AGS has been updating the Beers Criteria since 2011. By reducing IMUs and ADEs, intended by the Beers criteria, improving the quality of care, reducing drug costs, and improving the care of older adults, it aims to reduce IMUs and ADEs by educating doctors and patients on appropriate pharmacotherapy (4).

The Turkish Inappropriate Medication Use in the Elderly (TIME) criteria were originally derived from the STOPP/START version2 and CRIME (Criteria for assessing appropriate Medication use among older adults complex patients) criteria. As a result, 55 criteria were taken from the first criteria, 17 were removed and 60 were changed. Thus, 112 TIME-to-STOP and 41 TIME-to-START criteria were established, making 153 TIME criteria (5).

The current study evaluated the PIM and PPO distributions of TIME criteria specific to Turkey.

Methods

Setting, Design, and Study Population

This descriptive prospective cross-sectional study was conducted on patients aged over 65 years. It included 385 patients who were evaluated between February 25, 2020 and December 31, 2020 in the Internal Medicine Outpatient Clinic of Kütahya Health Sciences University, Evliya Çelebi Training and Research Hospital.

The sample size was calculated as 385 individuals with 50% prevalence and 0.05 (95% confidence) significance level in an infinite population. The participants included in the study were selected using a simple random sampling method. Individuals aged over 65 years and willing to participate were included in the study. The selection was carried out separately for the morning and afternoon groups (6). Because separate appointment groups were examined in the outpatient clinics both in the morning and afternoon, patients from the two groups were included. Patients younger than 65 years of age and those who did not cooperate with the doctor during the examination were not included in the study. According to the data obtained from the IT Information Technology Department of the hospital, 2,752 patients were admitted within the specified period. A total of 385 of the 2,752 patients who visited our clinic were then randomized (Figure 1). Only the first visit examinations were evaluated between the study dates of the participants, but the follow-up examinations were not evaluated. Data were obtained through face-to-face interviews with the participants.

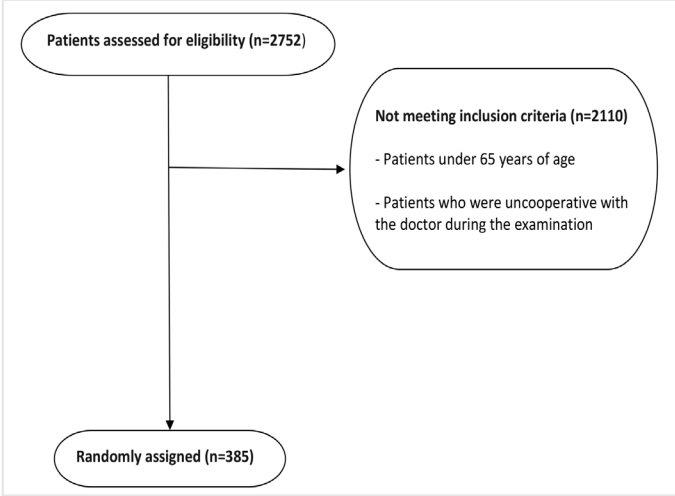

Figure 1. Flowchart of participant selection

Ethics Committee Approval

Ethics committee approval of our study was given by the Kütahya Health Sciences University (Turkey) Non-Invasive Clinical Research Ethics Committee (approval number: 2020/04-15, date: 25.02.2020). All volunteers were given oral information and provided informed consent. We carried out all stages of the study in accordance with the Declaration of Helsinki. We followed the guidelines in the "Helsinki Statement", "Guidelines for Good Medical Practices" and "Guidelines for Good Laboratory Practices".

Statistical Analysis

Data analysis was performed using IBM SPSS Statistics version 22 (IBM SPSS, Turkey). Baseline characteristics and agreement with TIME recommendations were analyzed using descriptive statistics. The suitability of the study data to a normal distribution was evaluated using the Kolmogorov-Smirnov test. The results showed that the study data did not show normal distribution. We compared quantitative data and descriptive statistical methods using the Mann-Whitney U test and Wilcoxon sign test. Furthermore, we evaluated PIMs and PPOs using TIME criteria. We calculated the number of patients with PIMs and PPOs (%) and the total number of PIM and PPO cases in the total study population.

Results

A total of 385 patients aged over 65 years were enrolled in this study. Among them, 124 (32.2%) were male and 261 (67.8%) were female. Of the 385 older adults included, 73.2% were between the ages of 65 and 74 years and 26.8% were aged over 75 years. Data on the demographic distribution are presented in Table 1.

The participants in our study who met at least one relevant criterion were considered to have PIMs or PPOs. PIM was detected in 127 (33%) patients according to the TIME-to-STOP criteria. The first three PIMs determined by the TIME-to-STOP criteria were proton pump inhibitor (PPI) deficient use (9.6%), tight blood pressure control (3.1%), and tight blood sugar control (2.3%) in high-risk patients (Table 2). PPOs were detected in 379 (98.4%) patients according to the TIME-to-START criteria. The first three PPOs in the TIME-to-START criteria (herpes zoster,

Table 1. Data of demographic distribution		n (%)
Age group	65-74 years	282 (73.2)
	≥75 years	103 (26.8)
Sex	Female	261 (67.8)
	Male	124 (32.2)
Marital status	Married	244 (63.4)
	Single	1 (0.3)
	Widowed	137 (35.6)
	Divorced	3 (0.8)
Education	Illiterate	108 (28.1)
	Less than 8 years of education	242 (62.9)
	More than 8 years of education	25 (6.5)
	College	10 (2.5)
Profession	Retired	175 (43.5)
	Housewife	205 (53.2)
	Worker	3 (0.8)
	Officer	0 (80)
	Business owner	1 (0.3)
	Other	1 (0.3)

pneumococcal, and tetanus) were deficient in 98.4%, 96%, and 94.5% of the patients, respectively (Table 3).

There were no significant differences in PIMs and PPOs between the sexes ($p>0.05$). There were no significant differences in PIMs and PPOs between patients aged 65-74 years and those aged over 75 years ($p>0.05$).

When evaluated according to educational status, there was no statistically significant difference in terms of inappropriate drug use according to the TIME-to-STOP and TIME-to-START criteria in the participants who were illiterate, those with less than eight years of education, those with more than eight years of education, and those who had graduated from college.

Concerning the chronic disease distribution of the volunteers participating in the study, the following results were obtained: 1.6% (never), 16.6% (one), 35.8% (two), 29.9% (three), 11.4% (four), 3%.9 (five), 0.5% (six), 0.3% (seven). The most common chronic diseases in our study were hypertension, diabetes mellitus, and dyslipidemia. There was no significant difference in the number of diseases between patients with and without PPO who were evaluated for PPOs according to the TIME-to-START criteria. However, according to the TIME-to-STOP criteria, the number of diseases in patients with PIMs was found to be significantly higher than that in patients without PIMs ($p<0.05$).

Table 2. Potentially Inappropriate Medication according to TIME to-STOP criteria	
	(%) (n=385)
A2. The use of digoxin in doses higher than 0.125 mg/day is not appropriate (risk of toxicity).	1% (4)
A3. The use of digoxin is not appropriate in the indication of heart failure with preserved (normal) ejection fraction.	0.5% (2)
A6. Loop diuretic use is not appropriate for ankle edema without signs of heart failure, liver failure, nephrotic syndrome, or renal failure.	1.8% (7)
A8. In patients with urinary incontinence, the use of diuretics as the first step is not appropriate for the treatment of essential hypertension (it may impair quality of life by increasing incontinence and feeling of urgency, may increase falls).	1% (4)
A9. The use of alpha-1 blockers or centrally acting antihypertensives (e.g. methyldopa, rilmenidine, reserpine) is not appropriate in the treatment of hypertension, except when other classes of antihypertensives are not tolerated or are ineffective (increased heart failure and cardiovascular events, orthostatic hypotension, decrease with alpha-1 blocker antihypertensives), syncope, worsening of urinary incontinence in women; central nervous system side effects of centrally acting antihypertensives, sedation-depression-parkinsonism and orthostatic hypotension, bradycardia side effects).	1.3% (5)
A10. Because of the increased risk of orthostatic hypotension, vasodilator antihypertensive agents and nitrates are not suitable for use in patients with orthostatic hypotension.	0.8% (3)
A11. Tight blood pressure control (<140/90 mmHg) is not appropriate in patients with orthostatic hypotension/cognitive impairment (e.g. dementia)/functional limitation/low life expectancy (<2 years)/high risk of falling.	3.1% (12)
A16. Potassium-sparing drugs (aldosterone antagonists, triamterene, amiloride, ACEI, ARB) are not suitable for use in patients with GFR <30 mL/minute/1.73 m^2 and whose serum potassium level cannot be closely monitored (risk of hyperkalemia).	1.8% (7)
A18. NSAID use is not appropriate in patients with cardiovascular disease (severe hypertension, heart failure or previous myocardial infarction, stroke) (increased cardiovascular event: risk of myocardial infarction, stroke, heart failure and death).	1.3% (5)
A19. Beta-blocker use is not appropriate in diabetes mellitus patients with frequent hypoglycemic episodes.	1.3% (5)
A21. Long-term use of aspirin at doses higher than 75-150 mg/day is not appropriate for cardiovascular protection (both primary and secondary) (no proven additional benefit and increases bleeding risk).	0.3% (1)
A23. Concomitant use of aspirin and clopidogrel for secondary stroke prophylaxis is not appropriate unless there is a specific indication for concomitant use.	0.3% (1)
A30. The use of drugs with a narrow therapeutic index, such as warfarin and digoxin, is not appropriate for patients who have difficulty in using and managing their medication (e.g. patients with cognitive impairment) and who are not available to assist (e.g. caregivers) (risk of life-threatening toxicity).	0.3% (1)
B1. Tricyclic antidepressant use is inappropriate (high anticholinergic effect, cognitive deterioration, cardiac conduction disorder, orthostatic hypotension, urinary retention, worsening of prostatism, worsening of narrow-angle glaucoma).	0.3% (1)
B6. In case of GFR <60 mL/minute/1.73 m^2, the use of pregabalin and gabapentin without dose reduction is not appropriate.	1.6% (6)

Table 2. continued

	(%) (n=385)
B14. Benzodiazepines are not suitable for use for more than 4 weeks (prolonged sedation, confusion, balance disorder, falling, risk of traffic accidents).	0.3% (1)
B18. Continuous and long-term use of drugs such as betahistine, trimetazidine, dimenhydrinate is not appropriate in the treatment of vertigo (lack of evidence-based beneficial effects).	0.5% (2)
B20. Piracetam is not suitable for use except in the treatment of myoclonic convulsions.	0.8% (3)
B21. First-line use of carbamazepine, phenytoin, phenobarbital, or valproate is not appropriate in the chronic treatment of epilepsy (due to adverse effects on vitamin D, enzyme induction, risk of falling; there are also safer alternatives).	0.5% (2)
B22. Tramadol, neuroleptics/antipsychotics (clozapine, olanzapine, chlorpromazine, thioridazine), bupropion and maprotiline are not suitable for epilepsy patients.	0.3% (1)
B24. The use of citalopram at doses above 20 mg/day and escitalopram over 10 mg/day in the older adultsis not appropriate (due to the risk of QTc prolongation).	0.5% (2)
C1. Concomitant use of non-steroidal anti-inflammatory drugs with oral anticoagulants (vitamin K antagonists, direct thrombin inhibitors, factor Xa inhibitors) is not appropriate (risk of gastrointestinal bleeding).	1% (4)
C2. Aspirin, clopidogrel, non-steroidal anti-inflammatory drugs or steroids; It is not suitable for use without proton pump inhibitor in patients with a history of ulcer, in patients receiving additional antiplatelet therapy, in patients receiving concomitant anticoagulants, in patients using steroids, and in patients with dyspepsia-GER symptoms.	9.6% (37)
C3. Aspirin or non-steroidal anti-inflammatory drugs; Patients with a history of peptic ulcer (complicated or uncomplicated, gastric, or duodenal) are not suitable for chronic use without testing for *Helicobacter pylori*.	0.3% (1)
C4. For the treatment of erosive peptic esophagitis or uncomplicated peptic ulcer, the use of proton pump inhibitors at a therapeutic dose for longer than 8-12 weeks is not appropriate. (dose reduction or shorter interruption is indicated).	0.8% (3)
C5. Proton pump inhibitor use is not appropriate due to multiple drug use (no benefit, potential harm).	2.1% (8)
C6. The use of anticholinergic gastrointestinal antispasmodics (e.g. hyoscyamine) is not appropriate. Increased anticholinergic side effects (dizziness, decreased cognitive abilities, blurred vision, arrhythmia, bloating-constipation) and limited utility in theolder adults.	1% (4)
C7. In patients with chronic constipation, if there are alternatives that do not have this side effect, the use of drugs with a high probability of causing constipation (drugs with high anticholinergic effects, oral iron, opioids, verapamil, aluminum antacids) is not appropriate (risk of increased constipation).	1.3% (5)
D1. The use of antimuscarinic bronchodilator drugs (ipratropium, tiotropium) is not appropriate in patients with narrow-angle glaucoma or urinary outflow obstruction (risk of worsening glaucoma and urinary retention).	0.5% (2)
D2. Theophylline is not suitable for the maintenance treatment of COPD or asthma bronchialene (due to the narrow therapeutic index and high risk of insomnia, arrhythmia in theolder adults).	2.1% (8)
E1. If there is an additional alternative treatment, it is not appropriate to use non-steroidal anti-inflammatory drugs for more than 3 months.	0.5% (2)
E2. Non-steroidal anti-inflammatory drugs are not suitable for use in patients with GFR <50 mL/minute/1.73 m^2 (risk of worsening renal function).	0.5% (2)
E11. The use of systemic muscle relaxant (skeletal muscle) agents (thiocolchicoside, tizanidine, chlorzoxazone, carisoprodol, chlorphenezine carbamate, cyclobenzaprine, metaxalone, methocarbamol and orphenadrine ... etc.) is not suitable for musculoskeletal pain (sedation, drowsiness, dizziness, dry mouth), constipation, due to cognitive side effects).	0.5% (2)
F3. Anticholinergic drug use for the bladder is not appropriate without post micturition residue determination (risk of urinary retention and postrenal kidney failure) in the older adults with prostate hyperplasia (obstruction risk) or diabetes mellitus complications (neurogenous bladder risk) or frail older adults (reduced contractility risk with detrusor hyperactivity).	0.5% (2)
F5. Non-uroselective alpha 1 blockers (e.g. doxazosin, terazosin) are not suitable for the treatment of lower urinary tract symptoms due to benign prostatic hyperplasia in patients with orthostatic hypotension (increased orthostatic hypotension, syncope, and falls).	0.3% (1)
G1. Tight blood glucose control (HbA1C <7%) is not appropriate in patients with a low life expectancy (<5 years) or a history of decline or cognitive impairment.	2.3% (9)
G2. The use of metformin is not appropriate in the frail or malnourished older adults (due to the gastrointestinal side effects and anorexia effect of metformin).	0.8% (3)
G5. The use of thiazolidinediones (rosiglitazone, pioglitazone) is not appropriate in patients with documented heart failure/fracture history/ increased fracture risk/bladder cancer history or on insulin therapy (worsening heart failure, increased fracture, and bladder cancer risk).	0.3% (1)
G8. It is not appropriate to use SGLT-2 inhibitors in cases with GFR <45 mL/minute/1.73 m^2.	0.5% (2)
H1. Use of drugs with high anticholinergic effects in conditions such as falls, dementia, constipation, narrow-angle glaucoma, delirium, urinary retention, concomitant use of drugs with high anticholinergic effects not suitable.	0.5% (2)

ACEI: Angiotensin converting enzyme inhibitor, ARB: Angiotensin receptor blocker, SGLT-2 inhibitors: Sodium glucose Co-transporter 2 inhibitor, COPD: Chronic obstructive pulmonary disease, GER: Gastroesophageal reflux, HbA1C: Hemoglobin A1C, GFR: Glomerular filtration rate, NSAID: Non-steroidal anti-inflammatory drugs

Table 3. Potential prescribing omissions according to TIME to-START criteria

	(%) (n=385)
A1. It is appropriate to initiate antiplatelet therapy (aspirin or clopidogrel) for secondary prevention in patients with atherosclerotic coronary artery disease and a history of atherosclerotic cerebrovascular disease.	0.8% (3)
A2. Atherosclerotic coronary artery disease, cerebrovascular disease or statin for secondary prevention in patients with peripheral artery disease It is appropriate to start treatment.	2.1% (8)
C1. In cases with symptomatic constipation unresponsive to lifestyle changes (diet-exercise), it is appropriate to exclude fecal plug and start fiber support (psyllium, methylcellulose, polycarbophil, wheat dextrin) or polyethylene glycol.	45.5% (175)
E1. It is appropriate to initiate replacement therapy in patients with daily dietary vitamin D intake <800-1000 IU or elemental calcium intake <1000-1200 mg.	0.5% (2)
E2. It is appropriate to initiate an anti-resorptive (bisphosphonate, denosumab) or anabolic agent (parathormone analog) in patients with documented osteoporosis with fragility fracture and/or bone mineral densitometry T-score (femur total, femoral neck or lumbar <-2.5).	0.5% (2)
E8. It is appropriate to start a xanthine oxidase inhibitor (primarily allopurinol) in patients with recurrent gout attacks.	0.3% (1)
H1. Annual influenza vaccination is appropriate.	74.8% (288)
H2. Pneumococcal vaccine (one dose for each of the 13 valent conjugate and 23 valent polysaccharide vaccines) is appropriate.	96.9% (373)
H3. Herpes zoster vaccination is appropriate (reduces the risk of shingles infection and postherpetic neuralgia).	98.4% (379)
H4. It is appropriate to perform tetanus vaccine (tetanus-diphtheria toxoid) every 10 years.	94.5% (364)
I1. In the older adults with malnutrition or malnutrition risk, initiation of oral nutritional supplements is appropriate if nutritional counseling and nutritional supplementation are not sufficient to increase dietary intake and achieve nutritional goals.	3.4% (13)

Discussion

Country-specific criteria are more effective for PIMs and PPOs. As shown in the first publication of our study, country-specific criteria for detecting PIMs and PPOs were found to be significantly superior (6). Since our study is one of the first conducted studies with the TIME criteria, it can have an important place in terms of providing resources and comparison opportunities for studies to be conducted in Turkey for IMU. In particular, we shared the distribution of PIMs and PPOs in detail.

In addition, differences are detected when examining the distribution of PIMs and PPOs; in particular, country-specific prescribing habits affect this. Even when compared with comprehensive studies such as Optimizing Therapy to Prevent Avoidable Hospital Admissions in Multimorbid Older Adults, PIMs and PPOs are concentrated on different criteria (7). According to the results of a study conducted with 206 patients using STOPP v2, the distribution of PIMs was related to dietary supplements such as vitamins and minerals (22.1%), antihypertensive drugs (17.2%), and PPIs (10.7%) (8). In our study, only the inappropriate use of PPIs was similar in the first 3 PIMs. When the studies conducted using the STOPP/START v1 and v2 in China were examined, the most determined criteria still differed (9).

Considering the study conducted in Turkey comparing Beers 2012 and the STOPP version 2, the rates of PIM use in Turkey were found to be 33.3% and 39.1%, respectively. In our study, it was 33% according to TIME criteria. Although the rate in our study seems to be lower when comparing the rates of PIM use, this may be because the two studies were conducted in different years. This reflects that recent studies on IMUs have reached their goal. When the most common drugs related to PIMs were examined, PPIs came to the fore in our study, whereas Bahat et al. (10) found that aspirin and antipsychotics were prominent in their study. Our study could not objectively evaluate geriatric syndromes such as dementia, frailty, and malnutrition. Therefore, the main reason for the differences between the most commonly used inappropriate drugs may be the difference in the evaluation of patients rather than the change in prescribing habits. We think that other reasons may be due to the change in the habits of prescribing according to years or the studies examining patients from two different outpatient clinics, such as geriatrics and internal medicine.

In addition, in countries where the official language is not English and the rate of foreign language proficiency is low, the existence of country-specific criteria for combating PIMs and PPOs is crucial. Therefore, the success rate of the TIME criteria increases (11). To some extent, this complicates comparison studies with popular medication lists such as the Beers criteria and START/STOPP. International validity studies of TIME criteria based on the Delphi process were also conducted. According to the results of this study, the criteria set can be applied in both central and eastern Europe (12).

An increase in the use of various mobile applications in the near future can be beneficial for IMUs. Simultaneously, clinicians trained on this subject and increasing cooperation with clinical pharmacology disciplines can decrease the rates of PIMs and PPOs (3).

As a result of the increase in the older adult population in Turkey, measures are taken and studies are carried out by the official authority on this issue. The rate of population increase of those aged 65 years and over in Turkey was 3.3% in 1950, 6.7% in 2000, and 9.5% in 2020, with a population that has reached 7,953,555. It is predicted that this rate will increase to 10.2%, 16.3%, and 25.6% in 2023, 2040, and 2080, respectively (13). According to the latest TUIK data, the population aged 65 and over was 8 million 451 thousand 669 people in 2022, and its ratio in the total population increased to 9.9% in 2022.

Expanding the use of the TIME criteria, which is a criterion specific to Turkey, and supporting it with mobile applications should be among the targets that need to be urgently addressed in this regard (14).

There are three different terms in the World Health Organization [(WHO); Adherence to long-term therapies: Evidence for action] report: "compliance, adherence, concordance". Compliance is defined as the patient's use of the drug at the given dose at the recommended intervals for the required time according to the treatment protocol. It is necessary to increase health literacy to improve this situation, which is very important for preventing IMU (15).

Health literacy is when a patient is given medical information, understands, and interprets this information, and acts accordingly. Although health literacy was first defined by Simond in 1974, its importance has only recently been understood in Turkey. As a result of the "Reliability and Validity Study of the Turkish Health Literacy Scales (TSOY-32)" conducted in 2016 under the editorship of Abacigil et al. (16) with the contribution of the Ministry of Health, the Turkish Adaptation of the European Health Literacy Scale and the TSOY-32 for Turkish society were added to the literature. In Hazer and Ateşoğlu (17) in the mainland province of Turkey, the health literacy of older adult individuals was insufficient and problematic. The success of healthy aging in older adults with high health literacy was also high (17). The importance of health literacy in maintaining and improving the level of health on both an individual and community basis has been emphasized by the WHO (18).

In a study using STOPP/START version 2, PIMs were 62.5% and PPOs were 36.6% (not including vaccine data). Including vaccine data, 225 (97%) patients had at least one PPO (19). The inclusion of vaccine data significantly increased the rate of PPOs, as also observed in our study. This demonstrates the importance of immunization for PPOs and how they fall behind. In another study conducted in Australia, when vaccination rates were included, PPOs (99%) were similarly high as in our study (20). In a study conducted in the Netherlands, PPOs was 84.8% (ranging from 77.4 to 90.6%) (21). In PPOs, vaccination deficiencies were the most common. Physicians should be more conscious of adult immunization needs when providing healthcare to the older adult population.

Consequently, both PIMs and PPOs are gaining importance in older individuals. This is one of the main factors in the prevention of IMU, polypharmacy, ADRs and ADEs. The TIME criteria better reveal PIMs and PPOs in Turkish society.

Study Limitations

There are some limitations to this study. The first is that it is a single-center study. It also has a modest sample size. Studies in the literature with IMUs are generally multicentered and performed with large patient groups. Another limitation of the study is that some TIME criteria related to malnutrition, frailty, and dementia cannot be evaluated objectively.

Conclusion

Our study is one of the first IMU studies conducted with TIME criteria and reveals important findings about the prescribing habits of Turkey. Turkey will be an important resource for the comparison of national and international criteria for the prevention of IMU. Extending the use of country-specific criteria in clinical practice should be one of our important goals.

Ethics Committee Approval: Ethics committee approval of our study was given by the Kütahya Health Sciences University (Turkey) Non-Invasive Clinical Research Ethics Committee (approval nubmer: 2020/04-15, date: 25.02.2020).

Informed consent: Informed consent forms were obtained from all patients.

Peer review: Externally peer-reviewed.

Authorship Contributions: Concept - E.B., T.P.K., F.Ö.; Design - E.B., T.P.K., F.Ö.; Data Collection or Processing - E.B., T.P.K.; Analysis or Interpretation - E.B., T.P.K.; Literature Search - E.B., T.P.K., F.Ö.; Writing - E.B., T.P.K.

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