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RESEARCH

AN INTERDISCIPLINARY OVERVIEW OF START/STOPP CRITERIA IN ELDERLY PATIENTS' DRUG USAGE: A SPECIALIST'S PERSPECTIVE

ABSTRACT

Introduction: Elderly people have a high prevalence of chronic illness and multiple prescriptions. This study aimed to screen the inappropriate prescribing according to START/STOPP criteria, evaluate the related specialist's opinion, and discuss the difference between the screening tool and expert opinions in the elderly population.

Materials and Method: Data were collected via personal interview with the patient by a physiatrist. Screening tool START/STOPP criteria were used to identify inappropriate prescriptions at Physical Medicine and Rehabilitation outpatient clinic. The specialists examined the referred patients in their areas of expertise.

Results: We enrolled 374 patients aged over 65. According to STOPP criteria, 96 (25.6%) patients were accepted as potentially inappropriate medication recipients. Among those, 54 (4.2%) were found to be inappropriate according to both STOPP criteria and expert opinion. The most frequently observed inappropriate medications in the screening tool were 30 proton pump inhibitors and 14 sulfonylurea medications; however, only 4 proton pump inhibitors and 4 sulphonylurea usage were considered inappropriate after specialist consultation.

Conclusion: All specialists who treat the geriatric population should be aware of inappropriate drugs and refer the patients to the relevant departments. The alerts of STOPP/START criteria may help in finding individualized solutions for each patient.

Kew Words: Aged; Disease; Potentially Inappropriate Medication List.

ARAŞTIRMA

YAŞLI HASTALARIN İLAÇ KULLANIMINDA START/STOPP KRİTERLERİNİN İNTERDİSİPLİNER DEĞERLENDİRİLMESİ: UZMAN HEKİM PERSPEKTİFİ

ÖZ

Giriş: Yaşlılar yüksek kronik hastalık ve çoklu ilaç kullanım oranına sahiptirler. Bu çalışmanın amacı yaşlı populasyonda START/STOPP kriterlerine göre uygunsuz ilaçları taramak, ilgili uzman görüşü ile değerlendirmek ve uzman görüşü ile tarama aracı arasındaki farkları tartışmaktır.

Gereç ve Yöntem: Veriler bir fiziyatrist tarafından gerçekleştirilen yüz yüze görüşme ile toplandı. Fiziksel Tıp ve Rehabilitasyon polikliniğindeki uygunsuz reçetelemeleri belirlemek için START/STOPP kriterleri kullanıldı. Her hasta kendi alanında değerlendirilmek üzere uzman hekimlere danışıldı.

Bulgular: Çalışmaya 65 yaş üzerinde 374 hasta alındı. STOPP kriterlerine göre, 96 (25.6%) hasta uygunsuz ilaç kullanıcısı olarak değerlendirildi. Bu uygunsuz ilaç kullanıcıları arasında, 54 (%4.2)'ünde Hem STOPP kriterlerine göre hem de uzman görüşüne göre uygunsuzluk tespit edildi. Tarama aracına göre en çok uygunsuz kullanılan ilaçlar, 30 adet ile proton pompa inhibitörü (PPI) ve 14 adet ile sulfonilure olarak gözlemlendi. Ancak, sadece 4 proton pompa inhibitörü ve 4 sulfonüre kullanımı uzman görüşü sonrasında uygunsuz ilaç olarak değerlendirildi.

Sonuç: Geriatrik populasyonu tedavi eden tüm uzmanlar uygunsuz ilaç kullanımının farkında olmalı ve ilgili bölümlere hastaları danışmalıdır. STOPP/START kriterlerinin uyarısı her hasta için kişiye özgü çözümler bulmaya yardımcı olabilir.

Anahtar Sözcükler: Yaşlı; Hastalık; Potansiyel Sakıncalı İlaç Listesi.

Introduction

Elderly people have a high prevalence of chronic illnesses and multimorbidity. They have a significant potential for developing side effects due to the chronic use of drugs that may elicit strong systemic interactions. These patients commonly use multiple medications, which leads to inappropriate prescribing. Inappropriate prescribing is described as the use of medicines that introduce significant risk of an adverse drug-related event while there is evidence for an equally or more effective, lower risk alternative therapy available for treating the same condition (1). It includes drug–drug or drug–disease interactions, prolonged duration, and use of drugs at a higher frequency. It is an important public health, social, and economic problem in the community (2).

Several screening tools have been developed to assess inappropriate medications in elderly populations, such as inappropriate prescribing in elderly tool (IPET), the Beers Criteria, the Medication Appropriateness Index (MAI), Screening Tool of Older Persons' Potentially Inappropriate Prescriptions (STOPP), and the Screening Tool to Alert Doctors to the Right Treatment (START) (3). Although Beer's criteria have been widely used for a long time, it has several deficiencies, including the lack of drug–drug interactions and drug class prescription duplication. Developed in 2003, STOPP/START is considered to be more comprehensive (3). It comprises 65 criteria for potentially inappropriate prescribing incidences according to systems including drug–drug and drug–disease, falls and therapeutic duplications. A new version of START/STOPP focusing on commonly prescribed medicines in older people has been recently validated and published in 2015, it is not only valid and reliable, but also has comprehensive screening tools applicable to routine clinical practice (4).

The objectives of this study were to screen potentially inappropriate prescribing according to new version START/STOPP criteria, to evaluate related specialists' opinion, and to discuss the difference between the screening tool and experts' opinion in the elderly population.

Materials and Method

Patients

A prospective cross-sectional study was performed on a group of older patients. 374 elderly patients who were evaluated in the outpatient clinic at the Dışkapı Yıldırım Beyazıt Training and Research Hospital, Department of Physical Medicine and Rehabilitation during a four month period between May and August 2015 were recruited for the study. Those who were aged over 65 and were able to converse and complete the questionnaires in Turkish were selected to participate in the study.

All patients provided informed consent for participation. This study complies with the Declaration of Helsinki and was approved by the Local Ethics Committee.

Study Design

All data were collected by physiatrist via face to face interviews with the participants and/or caregivers. Medical histories, current diagnoses, current regular medications, number of medication and basic demographic data including age, gender, and educational level were elicited. Pharmacy records were asked if necessary.

START/STOPP criteria were used to identify inappropriate prescriptions (4). All patients were asked whether they had symptoms such as constipation, orthostatic hypotension or falling, incontinence, other medical conditions such as glaucoma, gout disease, or coronary stent insertions in the previous 12 months, deep venous thrombosis in the previous 6 months and pulmonary embolus in the previous 12 months. The patients' medications were classified as cardiovascular, gastrointestinal, endocrine, neurological, musculoskeletal, respiratory medicine, and psychiatric drugs. Potentially inappropriate drug–drug and drug–disease combinations were identified by START/STOPP criteria. The physiatrists referred the patients who were potentially inappropriate to related departments such as cardiology, gastroenterology, endocrinology, respiratory medicine, psychiatry, and urology.

The consulted specialists were trained to investigate inappropriate prescribing according to STOPP/START criteria. They examined the patients with detailed medical history and previous laboratory tests in their areas of expertise according to START/STOPP criteria. The patients were informed about inappropriate drugs and were recommended to use appropriate medication.

Descriptive statistical analysis was performed for all variables using the percentage, mean value, and standard deviation. SPSS 11.5 for Windows was used for all analyses (Chicago, IL, USA).

Results

374 patients aged over 65 were enrolled for the study. Among the patients, 116 (31%) were male and 258 (69%) female.

Table 1— Demographic Characteristics of the Patients.

	n=374
Age (years)*	72.9±6.2
Gender	
Female	258 (69%)
Male	116 (31%)
Education Level	
Illiterate	139 (37.2%)
Literate	69 (18.4%)
Primary School	138 (36.9%)
High School	18 (4.8%)
University	10 (2.7%)
Number of medication*	**3.3±2.2**
0	35 (9.4%)
1-2	106 (28.3%)
3-4	134 (35.8%)
≥5	99 (26.5%)
Most Common Comorbidities	
Cardiovascular system	
HT	254 (67.9%)
Ischemic hearth disease	62 (16.5%)
Hyperlipidemia	23 (6.1%)
Arrhythmia	21 (5.6%)
Congestive heart failure	5 (1.3%)
Gastrointestinal disorders	
Peptic Ulcer	35 (9.3%)
Gastroesophageal reflux	11 (2.9%)
Neurological diseases	
Cerebrovascular disease	8 (2.1%)
Dementia	6 (1.6%)
Parkinson	7 (1.8%)
Endocrinological disease	
Diabetes mellitus	102 (27.2%)
Hypothyroidism	31 (8.2%)
Hyperthyroidism	3 (0.8%)
Musculoskeletal disorders	
Degenerative disease	159 (42.5%)
Osteoporosis	62 (16.5%)
Polyneuropathy	25 (6.6%)
Rheumatoid arthritis	20 (5.3%)
Intervertebral disc disease	17 (4.5%)
Urological disease	
Benign prostate hyperplasia	40 (10.6%)

*Mean ± standard deviation.

Mean age was 72.9±6.2 years. Patients were using a total of 1259 medications and the mean number of medications was 3.3±2.2 medications per patient. Patients' demographics are presented in Table 1.

96 (25.6%) patients were found to be under potentially inappropriate medication according to STOPP criteria. Those patients were assessed by related departments. Among 96 patients (120 medications), 73 patients were consulted by one department, 21 patients with two departments, and 2 patients with three departments. 28 patients (30 medications) refused to be consulted by related departments. 68 patients (90 medications) were consulted by related departments. From 120 potentially inappropriate medications, which comprised 9.5% of the total medications, 54 (4.2%) were found to be inappropriate medication according to both STOPP criteria and expert opinion. Details of these patients are demonstrated in the flowchart (Figure 1).

Among potentially inappropriate medications according to STOPP criteria, proton pump inhibitors (PPI) were the most frequent (in 30 patients) and sulphonylureas were the second most frequent (in 14 patients) medication. After consultation with the specialists, nonsteroid anti-inflammatory drugs (NSAID) and nonselective alpha blockers were found to be the most frequent inappropriate medications. Table 2 presents potentially inappropriate medications and inappropriate medications after specialists' opinion.

Thirty patients were referred to gastroenterology outpatient clinic. All of the patients were consulted for potentially inappropriate -PPI usage. PPIs were considered appropriate in 10 patients who had gastric erosion or esophagitis in their upper gastrointestinal endoscopy which was recently done, and in five patients who had clinical gastroesophageal reflux disease (GERD) symptoms (heartburn, acid regurgitation). Control upper gastrointestinal endoscopy was advised in the latter group. Additionally, PPIs were decided to be appropriate in 11 patients. Of these patients, six patients were using aspirin for coronary artery disease, two patients had a history of previous peptic ulcer disease, two patients were using warfarin therapy for heart valve replacement, and one patient was using steroid and immunosuppressive drugs. Only in the four patients, PPIs were considered inappropriate, and the patients were informed.

Fourteen patients were referred to an endocrinology outpatient clinic. All patients had type-2 diabetes and all were using oral antidiabetic medications. Mean duration of diabetes was 14.1±7.9 years and mean age was 73.9±6.7. According to the blood tests, mean hemoglobin A1c level was 7.1 %, serum BUN, creatinine, AST, and ALT values were within normal ranges. None of the patients had experienced severe hypoglycemic symptoms and three patients noted probable symptomatic hypoglycemia less than twice a year. 11 patients were using sulfonylureas combined with other anti-

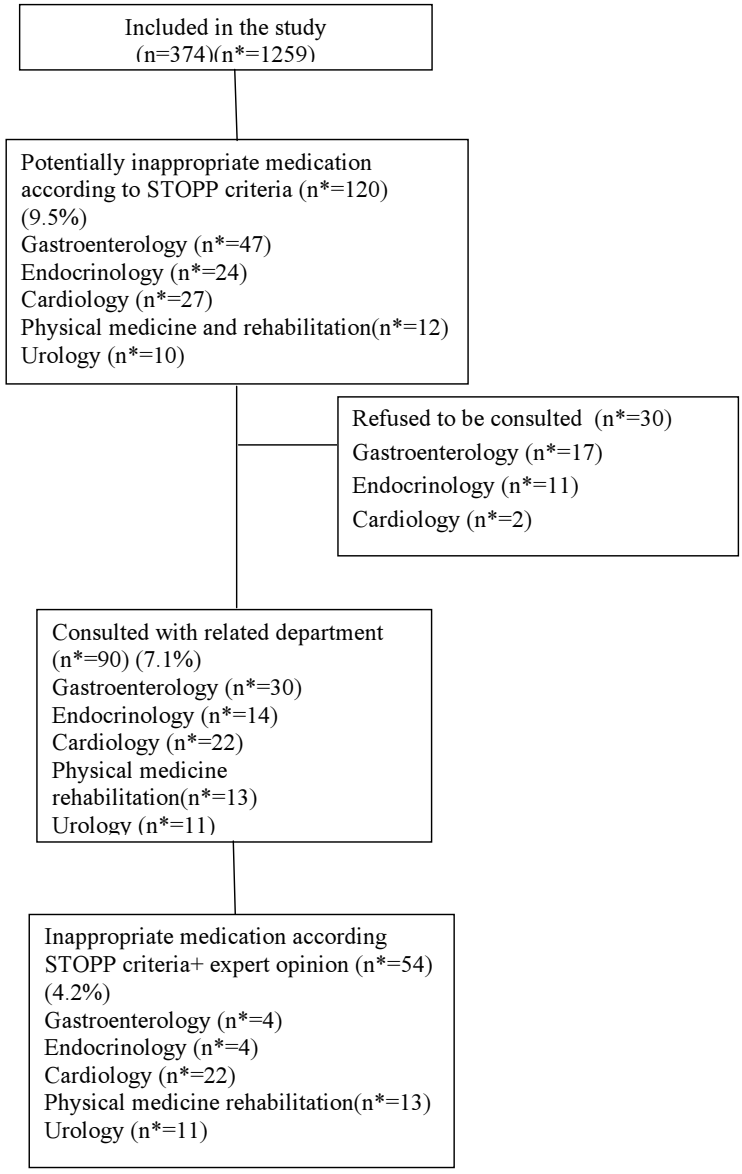

Figure 1— Flowchart of the study.
n = number of patients
n* = number of medications

diabetics and three patients were using only sulfonylureas. 12 patients were using modified release gliclazide and two patients were using glimepride. None of the patients were using glibenclamide or chlorpropamide which are sulphonylureas with a long duration of action. Sulphonylureas were not considered inappropriate for 10 patients, however, they were considered inappropriate for four patients due to symptomatic or probable symptomatic hypoglycemia and very low hemoglobin A1c levels. The patients were informed about the inappropriateness. In one patient insulin, and in two patients' sitagliptin and repaglinid, were recommended because of insufficient glycemic control.

Table 2— Potentially Inappropriate Medication According to STOPP Criteria.

	Consultant Department	Potentially inappropriate medication according to STOPP criteria n=90(%)	Inappropriate medication according STOPP criteria + expert opinion n=54(%)
PPI for uncomplicated peptic ulcer or erosive osephagitis full dosage ≥8 weeks	Gastroenterology	30 (33.3)	4(7.4)
Sulphonylureas with long duration of action with DM	Endocrinology	14(15.5)	4(7.4)
Long term use of NSAID (≥3 months)	PMR	10(11.1)	10(18.5)
Nonselective alpha blockers in those with orthostatic hypotension	Urology	10(11.1)	10(18.5)
Aspirin ≥160 mgr./day	Cardiology	9(10)	9(16.6)
μ blockers in DM with frequent hypoglycemic episodes	Cardiology	1(1.1)	1(1.8)
Duplication drug class		10(11.1)	10(18.5)
Antiaggregan	Cardiology	5	
Diuretic	Cardiology	2	
Ca canal blocker	Cardiology	1	
NSAID	PMR	1	
Alfa-blocker	Urology	1	
Vasodilator drug with persistent postural hypotension	Cardiology	1(1.1)	1(1.8)
Thiazide using with gout disease	Cardiology	2(2.2)	2(3.6)
Digoxin for heart failure with normal systolic function	Cardiology	1(1.1)	1(1.8)
Long term use of colchicine (≥3 months)	PMR	2(2.2)	2(3.6)

PPI: proton pump inhibitors, NSAID: nonsteroidal anti-inflammatory drugs, DM: diabetes mellitus PMR: physical medicine and rehabilitation.

Twenty-one patients were referred to the cardiology outpatient clinic. Nine patients were using high dose aspirin, five patients were using dual anti-platelet therapy without any clinical indications, one patient with diabetes mellitus was using a beta-blocker, one patient was using only an alpha-blocker for hypertension, two patients without heart failure were using dual diuretic therapy for hypertension, one patient was using digoxin without atrial fibrillation or heart failure, one patient was using angiotensin converting enzyme inhibitor and had symptomatic orthostatic hypotension, and finally two patients with gout disease were using thiazide diuretics. These medications were considered inappropriate and the patients were informed about it.

Ten patients were referred to the urology clinic. These patients had orthostatic hypotension due to a-1 blockers used for prostate hypertrophy. The patients were informed about the inappropriateness and were recommended to use more selective a1 blockers. Only one patient had a history of nausea after silodosin treatment; therefore, tamsulosin was recommended for this specific patient.

The physiatrist evaluated 11 patients for inappropriateness. 10 patients were using long term NSAID (≥3 months) due to osteoarthritis related pain and two patients were using long term colchicine (≥3 months) due to gout disease, one patient was using combined NSAID and colchicine. The patients were informed about the inappropriateness.

None of the patients had potential inappropriateness in the respiratory and psychiatry departments.

Discussion

This study revealed 9.5% potentially inappropriate medication according to STOPP/START criteria and 4.2% inappropriate medication after specialists' opinion in a total of 1259 medications. 26.5% of patients were using > 5 medicines simultaneously. To our concern, this is the first study eva-

luating the difference between specialists' opinions and the suggestions in the screening tool STOPP/START criteria. From potentially inappropriate drugs, PPIs and long duration of action sulfonylureas were mostly considered appropriate by the specialists.

Older patients have multiple co-morbidities and are prescribed multiple medications. The decline in physiological functions can be a factor that alters drug disposition and can have important influences on pharmacokinetics in geriatric patients. Health care professionals should be aware of the risks and interventions aiming to reduce exposure and minimize the risk associated with potentially harmful drug combinations (5). In our study 26.5% used > 5 medications simultaneously and this ratio went up to 57% in a US study (6). With the increase in the number of prescribed medications, the risk of side effects and interactions dramatically increases. Polypharmacy, chronic drug use, self-medication, and non-compliance are common factors in the elderly population. There is no standard definition of polypharmacy but it is a concept associated with both quantity and appropriateness of medication (7). Inappropriate prescription results in major morbidity and mortality. Our study showed that 9.5% of the medications were potentially inappropriate according to START/STOPP criteria and 4.2% of medications were inappropriate according to specialists' opinion after the evaluation of individual patients. Kara et al and Yayla et al found that respectively 41.2% and 14.8% of the patients were inappropriate according to STOPP/START criteria (8,9). Because some of the patients had inappropriateness reported from various departments, we calculated the inappropriate medicines, not the patients in our study.

PPIs are extensively prescribed worldwide in particular for GERD and dyspeptic patients (10). Kara et al found that the most common potentially inappropriate medication were PPIs (9). Patients with dyspepsia after an average of 50 years of age or with the presence of alarm symptoms are advised endoscopy in the guidelines (11). Organic dyspepsia is common in elderly dyspeptic patients and the most common causes of organic dyspepsia are GERD and peptic ulcer disease (12). GERD is a common disorder among elderly patients and has a higher rate of complications such as erosive esophagitis (10). In our study it was considered appropriate to use full-dose PPI treatment as a maintenance treatment for people with severe esophagitis or gastric erosion, either approved by endoscopy or the presence of severe symptom history. Current guidelines recommend the use of PPI therapy for 8 weeks for GERD. Moreover, maintenance of PPI therapy should be administered for the patients who keep on having symptoms after the PPI is discontinued and for the patients with complications including erosive esophagitis (12). In addition, prophylactic PPI treatment is prescribed for people at high risk (older age, previous ulceration, concurrent anticoagulant and steroids use) (13). In the study by Hsu et al, patients with a high GI risk (history of bleeding peptic ulcer, prior peptic ulcer, age > 70 years) concomitant drug therapy with non-steroidal anti-inflammatory drugs, other antiplatelet agents (clopidogrel or anticoagulants), and steroids should be recommended with proton pump inhibitors (14). For these reasons, PPI treatment was considered appropriate in most of the patients. It is not possible for any physician or specialist excluding gastroenterologists to decide whether the patient had a complicated ulcer or not.

Diabetes mellitus is an important health problem for the geriatric population and carries the risk of micro- and macrovascular complications in younger age groups (15). Glycemic targets should be individualized according to the patients' life expectancy, coexisting chronic illnesses, as well as patients' cognitive and physical function (16). Risk of hypoglycemia should be considered while prescribing any antihyperglycemic medication. Patients with diabetes in the geriatric population are prone to hypoglycemia for reasons such as age-related declines in renal function, hepatic enzyme activity, insulin deficiency, polypharmacy, etc. Consequently, use of long acting sulfonylureas such as glibenclamide or chlorpropamide is not recommended according to the current guidelines (16,17). Currie CJ et al. showed that very low hemoglobin A1c levels were associated with increased mortality and cardiac events as high levels (18). Therefore, it is important to evaluate older diabetic patients both with laboratory tests and self-monitoring of blood glucose at routine intervals to achieve the safest glycemic targets in order to minimize the risk of hypoglycemia. In the present study, the patients were not using glibenclamide, or chlorpropamide. None of the consulted patients using modified-release gliclazide and glimepiride had experienced severe hypoglycemia; three patients noted probable symptomatic hypoglycemia less than twice a year. A potential reason of this situation may be that the patients enrolled in our study were relatively healthy, were not too old and had relatively short duration of diabetes.

When we evaluated the cardiac medications of patients, we observed that the most frequent mistake was the dosage of aspirin usage. Previously, doses of 500–1500 mg daily were found to be effective for cardiovascular disease in clinical trials. However, a meta-analysis has shown that daily doses of

75–150 mg are as effective as the previously used higher doses (19). In another study performed in our country, Yayla et al also found that aspirin at dose > 150 mg/d was the second cause of potential inappropriateness (8). The second potentially inappropriate drug consulted to cardiology was dual antiplatelet therapy. Current guidelines recommend the use of dual antiplatelet therapy for 1 year after acute coronary syndrome and/or stent implantation even though there is a debate about the treatment duration. Single antiplatelet therapy such as aspirin only should be continued indefinitely (20). Physicians should be aware of this issue and be alert to the potential harmful effects of antiplatelet therapy.

Currently available α1-blockers include: alfuzosin hydrochloride, doxazosin mesylate, silodosin, tamsulosin hydrochloride, terazosin hydrochloride. There are three alpha-1 adrenergic receptor subtypes: alpha-1A, -1B, and -1D. Silodosin and tamsulosin hydrochloride are more selective α1A-blockers. Although different formulations result in different pharmacokinetic and tolerability profiles, the overall clinical impact of the different formulations is similar and modest (21). The most frequent adverse events associated with α1-blockers are asthenia, dizziness, and (orthostatic) hypotension. Vasodilating effects are most common for doxazosin and terazosin, and are less common for alfuzosin and tamsulosin (22). Moreover, patients with cardiovascular comorbidity and/or vaso-active co-medication may be susceptible to α1-blocker-induced vasodilatation (23). In contrast, silodosin appears less likely to cause cardiovascular side effects because it has a low selectivity for α1B-adrenoceptors involving blood pressure control (24). The frequency of hypotension with the α1A- selective blocker silodosin is comparable with placebo. Therefore, silodosin was considered for the patients with orthostatic hypotension.

Nonsteroidal anti-inflammatory drugs (NSAIDs) are widely used for the treatment of musculoskeletal pain in the elderly population. Additionally, therapeutic duplication is frequent in NSAIDs. Yayla et al, showed that the most common inappropriate drugs used were NSAIDs (8). In elderly population, use of non-pharmacological treatments should be encouraged as an alternative to NSAIDs. In our study, we found frequent inappropriate use of NSAIDs, which was consistent with the previous study (8).

Gout is an inflammatory metabolic disease. It is increasingly seen in the elderly population. Colchicine therapy is advised as a prophylaxis for 6 months when used in combination with urate lowering drugs (25). As none of our patients were using urate lowering therapy, we informed the patients about the inappropriateness.

In this study, as a screening tool we considered 9.5% of the medicines potentially inappropriate, but after consulting the patients to the related departments it was 4.2%. START/STOPP criteria were never meant to replace clinical judgement based on high-level clinical knowledge and experience; rather they were intended as an aid to routine pharmacotherapy.

The difference of our study from the others was that we screened the patients by physiatrists and the patients were evaluated by the specialists for the final decision. It had some limitations. The patients participating in the study were admitted to the same outpatient clinic, but our hospital is one of the referral hospitals from the other cities.

To sum up, polypharmacy is a common problem in elderly patients. No screening tool can replace the clinical knowledge, experience and judgement of health care professionals in determining the most appropriate medications for their patients. All specialists who treat geriatric patients should be aware of inappropriate drugs and consult the patients to the related departments. It will be the patients' benefit when their treatment is organized in a multidisciplinary and individual fashion.

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