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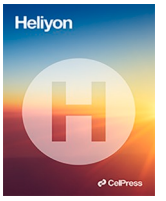

Research article

Examining potentially inappropriate medication use among elderly individuals in palliative care: A comprehensive study

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ABSTRACT

This study aimed to evaluate the prevalence of polypharmacy, the presence of potentially inappropriate medications and related factors in older adults receiving palliative care. This cross-sectional descriptive study was performed in 213 patients who were served from palliative care services. Mini Nutritional Assessment-Short Form, Katz Activities of Daily Living Scale and Charlson Comorbidity Index were applied. Polypharmacy was defined as the use of 5 or more medicines while the use of 10 or more medicines was considered as hyper-polypharmacy. PIM was assessed according to the TIME-to START and TIME-to STOP criteria. A total of 213 patients were included, mean age was 78.00 ± 9.08 years. Polypharmacy was present in 59.2 % of the patients and hyper-polypharmacy was present in 10.8 %. There was a statistically significant correlation between polypharmacy and marital status, history of falls, mid-upper arm, and calf circumference ($p = 0.017$, $p = 0.022$, $p = 0.010$, $p = 0.003$, respectively). The rate of inappropriate medication use of the cardiovascular system, gastrointestinal system, analgesics, musculoskeletal system, and nervous system drugs was high. There was at least one inappropriate medication use in 56.3 % of older adults. PIMs use was 18.3 % according to TIME-to-START criteria and was 48.4 % according to TIME-to-STOP criteria. There was a higher rate of PIMs use according to TIME criteria in the group with polypharmacy than non-polypharmacy ($p < 0.001$). The prevalence of polypharmacy and the presence of PIMs is high in older adults receiving palliative care. Polypharmacy could increase the PIMs use. The use of TIME criteria to evaluate palliative care patients may be helpful in reducing inappropriate medication use.

1. Introduction

Aging is a dynamic process that starts with birth and continues throughout the circle of life. Owing to advances in medicine and increased quality of life, the number of older adults is progressively increasing worldwide. In Turkey, older adults accounted for 9.9 % of whole population in 2022; however, it is estimated that it will reach 12.9 % in 2030, 16.3 % in 2060 and 25.6 % in 2080 [1]. The increase in older adults has led a rise in disorders requiring palliative care including neurological disorders such as Alzheimer's disease or Parkinson's disease, prolonged organ failures and cancers and, thus, increased number of patients in need for palliative care [2,3]. In addition, the number and diversity of the medicines used are also widened [4]. Polypharmacy is defined as "the use of 5 or more drugs

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per day" while hyper-polypharmacy is defined as "taking 10 or more medications concurrently" [5–9]. The prevalence of polypharmacy varies in different populations and increases with age. In a large study involving 1,742,336 older adults the prevalence of polypharmacy was 44 % [10]. The prevalence of polypharmacy among older adults was 63.3 % in Turkey [11]. Polypharmacy reduced quality of life and increases the risk of mortality by almost 1.8 times [12].

Potentially inappropriate medications (PIMs) are defined as medications that should be avoided due to their risk which outweighs their benefit and when there are equally or more effective but lower risk alternatives are available and are neglected when clinically indicated despite lack of contraindication [13,14]. Many criteria have been developed to assess inappropriate drug use by several countries, including Beers criteria, STOPP/START criteria and Medication Appropriateness Index [8]. However, the STOPP-Frail criteria have recently emerged with the aim of providing a clear and widely used resource that can be used in a broader and vulnerable population with chronic conditions. They are specifically designed for patients with end-stage irreversible pathology, limited life expectancy, severe functional or cognitive impairment and prioritizing symptom control over disease prevention [15].

Due to differences in prescribing practice and medicinal product market in Turkey, it was intended to specific medication criteria in elderly by updating guidelines. Thus, Turkish Inappropriate Medication Use in Elderly (TIME) criteria have been developed under the leadership of the Rational Drug Use Working Group of Turkish Academics Geriatrics Society. Overall, 112 TIME-to-STOP criteria for drugs that are usually or occasionally in appropriate for use in elderly but often inappropriately over-prescribed and 41 TIME-to-START criteria that are clinically indicated but frequently under-prescribed in elderly were developed [16]. In a study in palliative care setting, PIM rate was found to be 11.7 % according to TIME-to-STOP criteria [17].

In the elderly, it is aimed to minimize burden, cost and side effects of medication [18]. Palliative care aims to optimize symptom control and maximize comfort in individuals with terminal conditions [19]. Older adults receiving palliative care services with polypharmacy are susceptible to medication related problems [17]. In palliative care service, attempts to control symptoms may lead inappropriate medication use occasionally. There is limited number of studies on inappropriate drug use in palliative care in Turkey. Best of our knowledge, there is no comprehensive study using recent TIME criteria. In our study, it was aimed to assess polypharmacy using TIME criteria in elder individuals managed in palliative care.

2. Materials and methods

2.1. Study design and participants

Before initiating the trial, Ethics Committee approval was obtained from Samsun University Faculty of Medicine Clinical Research Ethics Committee (2022/4/5, date: March 23, 2022). This cross-sectional study was conducted at eight palliative care wards in Samsun province between April 1, 2022, and October 15, 2022. The study universe included patients treated in all palliative care units in Samsun province. During study period, 443 patients were receiving palliative care in the units where data were collected. When polypharmacy frequency was considered as 50 %, sample size was estimated as 206 subjects at alpha error level of 0.05 with 80 % power and 95 % confidence interval.

The inclusion criteria were receiving treatment in a palliative care unit in Samsun province, age $\geq$65 years and taking at least one drug. The patients with physical or mental problem that is severe enough to hinder communication with patient or caregiver, those aged $<$65 years, those not taking any drug and those declining to give informed consent were excluded. Of 443 patients receiving palliative care, 118 were aged $<$65 years and 141 were not taking any drug. After exclusion of patients not fulfilling inclusion criteria, final study population included 213 patients. Data were collected from patients and caregivers via face-to-face interview.

2.2. Data collection tools

2.2.1. Demographic questionnaire

A demographic data sheet was used to collect data regarding demographic characteristics such as age, gender, marital status, education status, chronic disease, and caregiver information.

2.2.2. Mini Nutritional Assessment-Short Form

Mini Nutritional Assessment-Short Form (MNA-SF) is one of the most commonly used tools to assess nutrition in elder individuals in medical practice and clinical trials [20]. It consists of nine questions comprising anthropometric measurements (mid-arm and calf circumferences) combined with questions regarding clinical status, dietary assessment and self-perception of health status and nutrition. The total score ranges from 0 to 14 points: MNA-SF score $\leq$7 points, malnourished; 8–11 points, at risk of malnutrition, and 12–14 points, normal nutritional status [21].

Body Mass Index (BMI) was calculated as weight (kg)/height $(m)^2$. Weight and height and the MNA-SF were assessed by authors after admission to the palliative care service. The Turkish validity and reliability study was performed by Sarikaya et al. [22].

2.2.3. Katz Activities of Daily Living Scale

Katz is an instrument to assess functional status as a measurement of the person's ability to perform activities of daily living independently. The index ranks adequacy of performance in the six functions: bathing, dressing, toileting, transferring, continence, and feeding. Katz Activities of Daily Living (ADL) scale assesses six primary functions including bathing, dressing, going to toilet, transferring, continence and feeding. Turkish validity and reliability study was performed by Arik et al., in 2015 [23]. One point means the person is independent while zero point means the person requires assistance. Total score ranges from 0 to 6 points: 6 points, patient

independent; 0 points, patient completely dependent.

2.3. Charlson Comorbidity Index

Charlson Comorbidity Index (CCI) involves 19 diseases including myocardial infarction, angina pectoris or other cardiovascular diseases, dementia, hemiplegia, chronic obstructive pulmonary disease, connective tissue disorders, gastrointestinal diseases, hepatic disorders, diabetes mellitus, cerebrovascular disease, tumor, metastatic tumor, leukemia, lymphoma, and AIDS. Each condition is assigned a score from 0 to 6 points and total score indicates comorbidity severity index. The total score is used to predict 10-years survival [24].

TIME-to-START and TIME-to-STOP.

Data collected were analyzed using TIME-to-START and TIME-to-STOP criteria developed by Turkish Academics Geriatrics Society [16]. The patients were classified as patients with or without polypharmacy. Again, they were classified as patient with or without PIM. Polypharmacy and PIM were assessed by comparing demographic characteristics, clinical features, Katz ADL, CCI and MNA-SF scores.

2.4. Statistical analysis

Data were analyzed using SPSS (Statistical Package for Social Sciences) version 25.0. The normality of data distribution was assessed using Shapiro-Wilk test. Sociodemographic data are presented as mean ± standard deviation or count (%). Student's *t*-test was used to assess binary variables. Pearson's correlation analysis was used to assess relations between continuous variables. Pearson's Chi-square test was used to compare categorical variables. A p value < 0.05 was considered as statistically significant.

Table 1
The associations between socio-demographic and clinical characteristics with polypharmacy and potentially inappropriate medication (PIM).

	Total (n = 213)	Polypharmacy		p	PIM		p
		Present (n = 126)	Absent (n = 87)		Present (n = 120)	Absent (n = 93)	
Gender							
Female	115 (54.0)	72 (57.1)	43 (49.4)	0.267	69 (57.5)	46 (49.5)	0.243
Male	98 (46.0)	54 (42.9)	44 (50.6)		51 (42.5)	47 (50.5)	
Marital status							
Single/Divorced	11 (5.2)	2 (1.6)	9 (10.3)	**0.017**	6 (5)	5 (5.4)	0.551
Widow	96 (45.1)	60 (47.6)	36 (41.4)		58 (48.3)	38 (40.9)	
Married	106 (49.8)	64 (50.8)	42 (48.3)		56 (46.7)	50 (53.8)	
Education status							
Illiterate	112 (52.6)	66 (52.4)	46 (52.9)	0.992	63 (52.5)	49 (52.7)	0.683
Primary School	73 (34.3)	43 (34.1)	30 (34.5)		39 (32.5)	34 (36.6)	
High School	17 (8.0)	10 (7.9)	7 (8.0)		10 (8.3)	7 (7.5)	
University	11 (5.2)	7 (5.6)	4 (4.6)		8 (6.7)	3 (3.2)	
Caregivers							
Absent	14 (6.6)	11 (8.7)	3 (3.4)	0.126	8 (6.7)	6 (6.5)	0.950
Present	199 (93.4)	115 (91.3)	84 (96.6)		112 (93.3)	87 (93.5)	
Mobility							
Independent	10 (4.7)	7 (5.6)	3 (3.4)	0.771	4 (3.3)	6 (6.5)	0.565
Semi-dependent	26 (12.2)	15 (11.9)	11 (12.6)		15 (12.5)	11 (11.8)	
Fully dependent	177 (83.1)	104 (82.5)	73 (83.9)		101 (84.2)	76 (81.7)	
History of falls	70 (32.9)	38 (30.2)	32 (36.8)	0.312	44 (36.7)	26 (28)	0.180
Reason for falling							
Mechanical cause	25 (35.7)	9 (23.7)	16 (50.0)	**0.022**	15 (34.1)	10 (38.5)	0.712
Dizziness	45 (64.3)	29 (76.3)	16 (50.0)		29 (65.9)	16 (61.5)	
Feeding method							
Nasogastric tube	23 (10.8)	15 (11.9)	8 (9.2)	0.600	11 (9.2)	12 (12.9)	0.692
Oral	97 (45.5)	60 (47.6)	37 (42.5)		56 (46.7)	41 (44.1)	
Percutaneous endoscopic gastrostomy	70 (33.0)	39 (31)	31 (35.6)		39 (32.5)	31 (33.4)	
Total parenteral nutrition	23 (10.8)	12 (9.5)	11 (12.6)		14 (11.7)	9 (9.7)	
Nutrition support	182 (85.4)	102 (81.0)	80 (92.0)	0.525	98 (81.7)	84 (90.3)	0.076
MNA classification							
Normal	16 (7.5)	67 (53.2)	42 (48.3)	0.780	66 (55)	43 (46.2)	0.086
Risk of malnourished	109 (51.2)	50 (39.7)	38 (43.7)		49 (40.8)	39 (41.9)	
Malnourished	88 (41.3)	9 (7.1)	7 (8.0)		5 (4.2)	11 (11.8)	
Pressure sore	119 (55.9)	67 (53.2)	53 (60.9)	0.263	74 (61.7)	46 (49.5)	0.075
Severity of pressure sore							
Stage-1	25 (44.1)	14 (20.9)	14 (20.9)	0.957	18 (24.7)	7 (15.2)	0.467
Stage-2	43 (36.1)	25 (37.3)	25 (37.3)		26 (35.6)	17 (37)	
Stage-3	24 (20.2)	14 (20.9)	14 (20.9)		12 (16.4)	12 (26.1)	
Stage-4	27 (22.7)	14 (20.9)	14 (20.9)		17 (23.3)	10 (21.7)	

Pearson Chi-square test. $p < 0.05$.

3. Results

Of the 213 patients receiving palliative care, 54.0 % (n = 115) were female. The mean age was 78.0 ± 9.1 years (min-max: 65–102 years). From a demographic perspective, 49.8 % (n = 106) were married. The most common reason for hospitalization was malignancy at 30.0 % (n = 83). The most common comorbid disease was hypertension (52.6 %; n = 112). Overall, 177 patients (83.1 %) were fully dependent. Of the patients, 32.0 % (n = 70) had history of falling within prior year. The history of falling was significantly higher in the polypharmacy group (p = 0.022). Of the patients, 45.5 % (n = 97) were fed orally while 32.4 % (n = 69) percutaneous endoscopic gastrostomy (PEG) method. Of the older adults, 51.2 % (n = 109) were at risk for malnutrition while 41.3 % (n = 88) were malnourished. Pressure sores were present in 55.0 % (n = 119) of patients and the majority of them were stage-2 sores in 36.3 % (n = 43). The prevalence of polypharmacy was found to be higher among single adults (p = 0.017) (Table 1).

The average BMI was 22.94 ± 4.40 kg/m^2 while the mean mid-arm circumference was 26.10 ± 5.35 cm and the mean calf circumference was 36.71 ± 7.78 cm. It was found that mid-upper arm and the mean calf circumference were significantly higher in polypharmacy group when compared to non-polypharmacy group (p = 0.010 and p = 0.003, respectively). It was found that the mean Katz ADL score was 0.54 ± 1.40, while the mean CCI score was 6.29 ± 2.46 (Table 2).

The median total number of medications per patient was 5.28 ± 2.72. It was found that 48.4 % of subjects (n = 103) were using 5 to 10 medicines. Polypharmacy was detected in 59.2 % (n = 126) while hyper-polypharmacy in 10.8 % (n = 23) of the subjects. Based on TIME criteria, at least one PIM was detected in 56.3 % (n = 120) of the patients. There was PIM in 39 patients (18.3 %) according to TIME-to-START criteria and in 103 patients (48.4 %) according to TIME-to-STOP criteria (Table 3).

In our study, it was seen that the cardiovascular system, musculoskeletal system, and nervous system drugs were inappropriate medications used according to TIME-to-STOP. It was seen that vaccines, digestive system drugs and supplements were inappopriate medications used according to TIME-to-START (Table 4).

4. Discussion

Among the geriatric population with multiple chronic diseases, polypharmacy is a common phenomenon. The treatment of side effects of the medicine used further deepens polypharmacy. This results in chaos regarding indications, predisposing PIM.

4.1. Polypharmacy and associated factors

In this study, polypharmacy was detected in 59.2 % and hyper-polypharmacy in 10.8 % of the subjects in agreement with previous studies. In the literature, polypharmacy rate ranges in elderly based on settings (community, nursery home, hospital etc.) and country, resulting in a wide variation in polypharmacy prevalence. A meta-analysis including patients aged≥65 years (2005–2020), showed that polypharmacy frequency ranged from 4 % to 96.5 % based on healthcare setting and region [25]. In a study involving elderly population from 18 countries, polypharmacy incidence was reported as 26.3–39.9 % [26]. In a study on sarcopenia and polypharmacy in hospitalized elderly individuals, it was found that polypharmacy and hyper-polypharmacy rates were 70.2 % and 13 %, respectively [27]. In a systematic review on drug use in elderly individuals residing in nursing home setting, it was found that polypharmacy prevalence ranged from 38.1 % to 91.2 % and that hyper-polypharmacy prevalence was 65 % [28]. In a study including patients receiving palliative care, Sevilla-Sanchez et al. found hyper-polypharmacy in 46.8 % of the patients [29]. In two studies at palliative care services across Turkey, polypharmacy rate was reported to be 47 % and 79.6 % [18,19].

In our study, only marital status was found to be associated with polypharmacy with no correlation between polypharmacy and remaining sociodemographic characteristics. Polypharmacy rate was found to be higher among single individual (p = 0.017). This may be due to tendency of the partners to use more prescribed and non-prescribed drugs resulting concerns about relieving symptoms. In a study on polypharmacy in elderly, Eyigor et al. found significant correlations between polypharmacy and sociodemographic characteristics including age, gender and marital status and that polypharmacy group tended to be older and male. Authors found that polypharmacy rate was lower in married individuals when compared to divorced or widowed individuals [30].

In our study, upper mid-arm circumference (p = 0.010) and calf circumference (p = 0.003) were found to be higher in

Table 2
Comparison of clinical characteristics in terms of polypharmacy and potentially inappropriate medication (PIM).

	Total (mean ± sd)	Polypharmacy		p	PIM		p
		Present (n = 126)	Absent (n = 87)		Present (n = 120)	Absent (n = 93)	
Age	78.00 ± 9.08	77.68 ± 8.99	78.47 ± 9.23	0.534	78.49 ± 9.31	77.38 ± 8.79	0.372
Height (cm)	166.45 ± 7.88	166.44 ± 7.18	166.48 ± 8.84	0.968	165.84 ± 7.72	167.25 ± 8.05	0.197
Weight (kg)	63.52 ± 12.23	64.83 ± 11.83	61.63 ± 12.65	0.060	62.55 ± 11.61	64.78 ± 12.96	0.187
BMI (kg/m^2)	22.94 ± 4.40	23.42 ± 4.33	22.25 ± 4.43	0.056	22.75 ± 4.28	23.19 ± 4.57	0.468
Mid-upper arm circumference (cm)	26.10 ± 5.35	26.88 ± 5.07	24.98 ± 5.57	**0.010**	26.03 ± 4.7	26.19 ± 6.11	0.834
Calf circumference (cm)	36.71 ± 7.78	38.02 ± 7.52	34.83 ± 7.80	**0.003**	36.61 ± 7.3	36.85 ± 8.4	0.826
Katz ADL score	0.54 ± 1.40	0.59 ± 1.46	0.48 ± 1.31	0.566	0.44 ± 1.22	0.68 ± 1.60	0.204
Charlson comorbidity index score	6.29 ± 2.46	6.26 ± 2.27	6.33 ± 2.73	0.841	6.24 ± 2.39	6.35 ± 2.57	0.741

Independent t-Test.p < 0.05.

Table 3
Comparison of polypharmacy and potentially inappropriate medications (PIMs).

Variables*		Nonpolypharmacy, n (%)	Polypharmacy, n (%)	Multivariable analyses p value
PIMs	Absent	52 (59.8)	41 (32.5)	**<0.001**
	Present	35 (40.2)	85 (67.5)	
PIMs according to TIME to START	Absent	76 (87.4)	98 (77.8)	0.076
	Present	11 (12.6)	28 (22.2)	
PIMs according to TIME to STOP	Absent	59 (67.8)	51 (40.5)	**<0.001**
	Present	28 (32.2)	75 (59.5)	

Pearson Chi-square test.$p < 0.05$.

polypharmacy group when compared to non-polypharmacy group. In addition, it was found that BMI was markedly higher in polypharmacy group; however, the difference did not reach statistical significance ($p = 0.056$). This finding suggests that polypharmacy is associated with body weight. Such a correlation may be due to either weight gain resulting from adverse effects of drugs or need for more drug due to more severe metabolic disorders in overweight individuals. It may also be related to doctors' views that patients are healthy enough to benefit from medications for some non-communicable diseases (NCDs). When patients become weaker, doctors may decide to stop certain medications for lack of benefits rather than risks. As a result, body weight and polypharmacy can be associated with each other in a vicious cycle. It was seen that patients with polypharmacy had higher BMI in a study on polypharmacy as a risk factor for sarcopenia [31].

In our study, fall incidence was higher in the polypharmacy group ($p = 0.022$). The relationship between polypharmacy and fall has long been investigated and it has been generally reported that there is a positive correlation between polypharmacy and fall. In the UK, the fall incidence was found to be higher in elder individuals with polypharmacy by 21 % when compared to non-polypharmacy group [32]. In a study by Montero Odasso et al. it was reported risk for falls was increased by 12–16 % while the risk for incident falls was increased by 5–7% with each additional drug [33]. The correlation between falls and polypharmacy, in addition to being associated with multiple medication use, also appears to be attributable to PIMs, particularly in individuals taking anticholinergic medications [34].

4.2. Potentially inappropriate medication and associated factors

In our study, there was at least one PIM in 56.3 % of the subjects. There was PIM in 39 patients (18.3 %) according to TIME-to-START criteria and in 103 patients (48.4 %) according to TIME-to-STOP criteria. It was found that the "Vaccines" were the most neglected part of TIME-to-START criteria. When PIM was assessed, gastrointestinal system medicines (8.0 %) and supplements (3.3 %) were the most common drugs used inappropriate manner. It was seen that musculoskeletal criteria and analgesics (13.6 %), cardiovascular system drugs (13.1 %) and central nervous system drugs were the three most frequent PIMs among the TIME-to-STOP criteria. In the literature on PIMs, there are some differences in the results as different guidelines were used in these studies. In a study on subjects aged>65 years using STOPP-START criteria (2008), Fahrni et al. found that cardiovascular system medicines were the most used drug among subjects and that PIM prevalence was 58.5 % [35]. Authors found that the most common PIM was in the item "aspirin use in patients without coronary, cerebral or peripheral vascular symptom or history of arterial occlusive events" (18.6 %) based on STOPP criteria whereas in the item "anti-platelet therapy should be initiated in diabetes mellitus if there is one or more major cardiovascular risk factors" (30.8 %) based on START criteria [36]. In a systematic review including studies investigating PIM in elderly individuals using Beers criteria, it was found that PIM prevalence was 65.0 % and that gastrointestinal medicines (15.3 %) and proton-pump inhibitors (27.7 %) were two major drug classes prescribed inappropriately [37]. In a study on patients receiving palliative care, McNeill et al. found PIM prevalence as 19 % [37]. In a Turkish study on patients receiving home care services, it was found that PIM prevalence was 53 % according to Beers criteria and 40 % according to the TIME-to-STOP criteria [34]. In a study about elderly patients receiving palliative care, Sevilla-Sanchez et al. investigated PIM using STOPP-Frail criteria and found that there was at least one PIM in 67.2 % of the patients and that "inappropriate use of gastrointestinal system and metabolism medicines without clinic indication" was the most common PIM [29]. In a study at the palliative care unit, Celikci et al. found that PIM prevalence was 8.3 % according to Beers criteria and 11.7 % according to TIME-to-STOP criteria [19]. Again, in a study in a palliative care setting from Turkey, oral nutrition products (88.9 %), HMG-CoA (3-hydroxy-3-methyl Glutaryl CoA) reductase inhibitors (80 %) and drugs used in the treatment of dementia (84.6 %) were the most common treatments needed to be started according to the TIME-to-START criteria. According to the TIME-to-STOP criteria, the most common PIM was anti-psychotic medicines (90.9 %) in elderly; followed by beta-histine (90 %) and alpha blockers (75 %) [30].

Polypharmacy and associated PIM are generally questioned together in the medical history of patients. In our study, we found a significant correlation between polypharmacy and the presence of at least one PIM. In addition, we observed a higher PIM rate in the polypharmacy group based on TIME-to-STOP criteria. Likewise, Sevilla-Sanchez et al. reported a significant correlation between PIM and polypharmacy or hyper-polypharmacy in elderly individuals receiving palliative care [29]. In another study assessing drugs used in elderly patients admitted to a palliative care unit, a significant correlation was detected between PIM and hyper-polypharmacy [19]. These findings suggest that polypharmacy should be considered as an alarm for PIM in patients.

Our study has some limitations. First, a causal relationship cannot be established due to cross-sectional design of the study. Although this is a multi-center study, outcomes cannot be generalized to Turkey due to the sample size and study settings including

Table 4
Distribution of potentially inappropriate medication (PIM) by TIME to START and TIME to STOP Criteria.

		PIM	
		Absent n (%)	Present n (%)
TIME to START			
Central Nervous System Criteria	Time Start B1–B2	213 (100.0)	–
	Time Start B3	212 (99.5)	1 (0.5)
	Time Start B4	208 (97.7)	5 (2.3)
	Time Start B5–B8	213 (100.0)	–
Gastrointestinal System Criteria	Time Start C1	196 (92.0)	17 (8.0)
Respiratory System Criteria	Time Start D1	210 (98.6)	3 (1.4)
	Time Start D2-D3	213 (100.0)	–
Musculoskeletal Criteria and Analgesic Drugs	Time Start E1-E8	213 (100.0)	–
	Time Start E9	212 (99.5)	1 (0.5)
	Time Start E10	211 (99.1)	2 (0.9)
Vaccines	Time Start H1	50 (23.5)	163 (76.5)
	Time Start H2	19 (8.9)	194 (91.1)
	Time Start H3	2 (0.9)	211 (99.1)
	Time Start H4	1 (0.5)	212 (99.5)
	Time Start H5	1 (0.5)	212 (99.5)
Supplements	Time Start I1	212 (99.5)	1 (0.5)
	Time Start I2	206 (96.7)	7 (3.3)
	Time Start I3	212 (99.5)	1 (0.5)
	Time Start I4	206 (96.7)	7 (3.3)
TIME to STOP			
Cardiovascular System Criteria	Time Stop A1	213 (100.0)	–
	Time Stop A2	211 (99.1)	2 (0.9)
	Time Stop A3-A6	213 (100.0)	–
	Time Stop A7	185 (86.9)	28 (13.1)
	Time Stop A8	211 (99.1)	2 (0.9)
	Time Stop A9-A15	213 (100.0)	–
	Time Stop A16	208 (97.7)	5 (2.3)
	Time Stop A17	210 (98.6)	3 (1.4)
	Time Stop A18	212 (99.5)	1 (0.5)
	Time Stop A19-A22	213 (100.0)	–
	Time Stop A23	212 (99.5)	1 (0.5)
	Time Stop A24-A29	213 (100.0)	–
	Time Stop A30	212 (99.5)	1 (0.5)
	Time Stop A31-A33	213 (100.0)	–
	Time Stop A34	207 (97.2)	6 (2.8)
	Time Stop A35	213 (100.0)	–
Central Nervous System Criteria	Time Stop B1	213 (100.0)	–
	Time Stop B2	212 (99.5)	1 (0.5)
	Time Stop B3–B6	213 (100.0)	–
	Time Stop B7	211 (99.1)	2 (0.9)
	Time Stop B8–B9	213 (100.0)	–
	Time Stop B10	212 (99.5)	1 (0.5)
	Time Stop B11	188 (88.3)	25 (11.7)
	Time Stop B12	213 (100.0)	–
	Time Stop B13	212 (99.5)	1 (0.5)
	Time Stop B14	210 (98.6)	3 (1.4)
	Time Stop B15–B19	213 (100.0)	–
	Time Stop B20	210 (98.6)	3 (1.4)
	Time Stop B21	212 (99.5)	1 (0.5)
	Time Stop B22–B23	213 (100.0)	–
	Time Stop B24	211 (99.1)	2 (0.9)
Gastrointestinal System Criteria	Time Stop C1–C2	213 (100.0)	–
	Time Stop C3	212 (99.5)	1 (0.5)
	Time Stop C4	210 (98.6)	3 (1.4)
	Time Stop C5	205 (96.2)	8 (3.8)
	Time Stop C6–C7	213 (100.0)	–
	Time Stop C8	207 (97.2)	6 (2.8)
	Time Stop C9	213 (100.0)	–
	Time Stop D1-D2	213 (100.0)	–
	Time Stop D3	212 (99.5)	1 (0.5)
Respiratory System Criteria	Time Stop E1	206 (96.7)	7 (3.3)
	Time Stop E2	210 (98.6)	3 (1.4)
	Time Stop E3	213 (100.0)	–
	Time Stop E4	212 (99.5)	1 (0.5)
	Time Stop E5-E8	213 (100.0)	–

(*continued on next page*)

Table 4 (*continued*)

		PIM	
		Absent n (%)	Present n (%)
	Time Stop E9	211 (99.1)	2 (0.9)
	Time Stop E10	184 (86.4)	29 (13.6)
	Time Stop E11	211 (99.1)	2 (0.9)
	Time Stop E12-E17	213 (100.0)	–
Urogenital System Criteria	Time Stop F1–F4	213 (100.0)	–
	Time Stop F5	207 (97.2)	6 (2.8)
	Time Stop F6–F7	213 (100.0)	–
Endocrine System Criteria	Time Stop G1	205 (96.2)	8 (3.8)
	Time Stop G2	208 (97.7)	5 (2.3)
	Time Stop G3-G13	213 (100.0)	–

only one province. However, this is the first study investigating PIM in palliative care using TIME criteria with multi-centric setting; thus, our results are valuable. We believe that the data from this study may be guiding for larger studies to create outcomes which may be generalized to Turkey.

5. Conclusion

In this study, we explored the prevalence of polypharmacy and PIM among patients receiving palliative care, shedding light on critical aspects of geriatric pharmacotherapy. Our findings observed correlations between polypharmacy, PIM, and clinical outcomes emphasizing the importance of comprehensive medication review processes and tailored interventions to optimize therapeutic regimens for elderly patients in palliative care. Additionally, larger-scale studies across diverse settings are needed to validate our findings and inform the development of targeted interventions aimed at improving medication safety and quality of care for elderly patients receiving palliative care in Turkey and beyond.

Ethics statement

Ethical permission (date: March 23rd, 2022, decision no: BAEK/2022/4/5) was obtained from a Samsun University Clinical Research Ethics Committee. The study was carried out in accordance with the Declaration of Helsinki. All participants provided written informed consent for the use of their data for scientific research purposes.

Disclosure of conflicts of interest

We, the authors listed, affirm our collective responsibility for this work, having contributed to its conception, design, writing, and revision. We confirm its originality, with no prior publication or ongoing consideration for publication elsewhere. Furthermore, we declare no conflicts of interest.

Data availability

Data associated with the study has not been deposited into a publicly available repository. Data are available from the corresponding author on reasonable request.

CRediT authorship contribution statement

Ozlem Kirci: Writing – original draft, Visualization, Supervision, Project administration, Methodology, Investigation, Data curation, Conceptualization. **Mahcube Cubukcu:** Writing – original draft, Supervision, Resources, Project administration, Methodology, Investigation, Formal analysis. **Remzi Bahsi:** Validation, Supervision, Project administration, Investigation. **Nur Simsek Yurt:** Writing – review & editing, Validation, Resources, Formal analysis, Data curation. **Kivanc Kirci:** Visualization, Formal analysis, Data curation.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: Mahcube Cubukcu reports non-financial support. If there are other authors, they declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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