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RESEARCH

# FREQUENCY OF POLYPHARMACY AND USE OF POTENTIALLY INAPPROPRIATE MEDICATIONS IN THE ELDERLY

## Abstract

***Introduction:*** Increased rates of increase in the elderly population, chronic illnesses and drugs usage are inevitable, making polypharmacy more frequent in older adults. Our study aimed to investigate the frequency of polypharmacy in the elderly and to examine their medication use.

***Materials and Method:*** Three hundred elderly individuals (aged >65 years) who visited our family medicine polyclinic were included in the study. In addition to collecting socio-demographic information, a questionnaire about current drug use was administered. Currently used drugs were listed by doctors and screened using screening tools. Data were analysed using the chi-square and Student's t-tests; $p < 0.05$ was considered significant.

***Results:*** A total of 1,650 drugs were used by study participants. The mean number of drugs per patient was 5.50±2.84 (range, 1–14). Polypharmacy (≥5 drugs) was present in 187 (62.3%) participants; 5–9 drugs were used by 158 (52.7%). Hyperpolypharmacy (≥10 drugs) was present in 29 (9.7%) participants. In total, 317 (19.2%) drugs were on the list of the European Union Potentially Inappropriate Medications, and 195 (65%) patients were using at least one potentially inappropriate medication. A total of 124 (7.5%) medications were stopped due to unnecessary usage. Patients were referred to branch doctors because of 108 (6.5%) drugs.

***Conclusion:*** Polypharmacy and potentially inappropriate medication usage were both very frequent in this elderly population sample. Polypharmacy was positively related only to chronic diseases, negatively related to closely controlled therapy. For this reason, evaluation of drug use in the elderly is an important step.

***Key Words:*** Aging; Inappropriate prescriptions; Polypharmacy; Drug therapy; Drug prescription; Chronic disease

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ARAŞTIRMA

# YAŞLILARDA POLİFARMASİNİN SIKLIĞI VE POTANSİYEL UYGUNSUZ İLAÇ KULLANIMI

## Öz

***Giriş:*** Yaşlanma, kronik hastalıklar ve ilaç kullanımını artırması polifarmasi görülme sıklığını artırmaktadır. Çalışmamızda, yaşlı bireylerde polifarmasi sıklığını, neden olan risk faktörlerinin ve ilaç kullanımının incelenmesi amaçlanmıştır.

***Gereç ve Yöntem:*** Aile hekimliği polikliniğine başvuran 300 (65 yaş üzeri) birey alındı. Sosyodemografik verilerin yanı sıra, mevcut ilaç kullanımı ile ilgili sorulardan oluşan bir anket uygulanmıştır. Halen kullanılan ilaçlar doktorlar tarafından listelenmiştir. Avrupa Birliği Potansiyel Uygun Olmayan İlaçlar listesine göre taranmıştır. Veriler ki-kare ve Student-t testleri kullanılarak analiz edildi; $p <0.05$ anlamlı kabul edildi.

***Bulgular:*** Çalışmada katılımcıların toplam 1.650 ilaç kullandıkları tespit edildi. Hasta başına düşen ortalama ilaç sayısı 5.50±2.84 (aralık 1-14) idi. Polifarmasi (≥5 ilaç) 187 (% 62.3) katılımcıda varken; Hiper polifarmasi (≥10 ilaç) ise 29 (%9.7) katılımcıda mevcuttu. Avrupa Birliği Potansiyel Uygun Olmayan İlaçlar listesinde olan 317 (% 19.2) ilaç vardı. 195 (% 65) hasta en az bir potansiyel olarak uygun olmayan ilaç kullanıyordu. Gereksiz kullanım nedeniyle toplam 124 (% 7.5) ilaç durduruldu. Hastalar için 108 (% 6.5) kullandığı ilaçlar nedeniyle dal doktorlar sevk edildi.

***Sonuç:*** Polifarmasi ve uygun olmayan ilaç kullanımı yaşlı bireylerde sık görülmektedir. Polifarmasi kronik hastalıklarla artarken; yakın doktor kontrolü ile azalmaktadır. Bu nedenle yaşlıda ilaç kullanımını değerlendirme önemli bir basamaktır.

***Anahtar Sözcükler:*** Yaşlanma; Uygunsuz reçeteleme; İlaç reçeteleme; Polifarmasi; İlaç tedavisi, Kronik hastalık

## INTRODUCTION

According to the Turkish Statistical Institute, there were 6,651,503 elderly individuals in Turkey in 2016, representing 8.3% of the national population (1). Due to advancements in the health sector, human life expectancy is increasing worldwide. The increases in the number of elderly individuals, chronic illnesses and number of drug used by patients are inevitable. As such, polypharmacy is becoming more frequenct in older adults. The word 'poly' is derived from a Greek word meaning 'more than one', and 'pharmacy' refers to the Greek word for drug 'pharmacon' (2). There is no consensus about the definition of polypharmacy, but it is most commonly defined in healthcare literature as taking five or more medications. Hyperpolypharmacy has been described as taking 10 or more medications (3).

Polypharmacy can be problematic. It can increase the risk of the use of potentially inappropriate medications (PIMs), medication non-adherence, drug duplication, drug–drug interactions, higher health care costs and adverse drug reactions (4). Treatment for medication errors and adverse drug events in the older adult population is estimated to cost more than $880 million United States of America per year (5).

Several screening tools have been developed to identify sub-optimal prescribing practices in the elderly (6). In 2008, the Screening Tool of Older Persons' Potentially Inappropriate Prescriptions (STOPP) and Screening Tool to Alert Doctors to the Right Treatment (START) criteria were introduced (7). The European Union PIM [EU(7)-PIM] list made by experts from seven European countries was introduced in 2015 (8). Our study aimed to investigate the frequency of polypharmacy in the elderly and to examine their medicine use based on these screening tools.

## MATERIALS AND METHOD

A prospective cross-sectional study was performed involving 300 elderly participants.

### Study population

A total of 4,725 patients aged over 65 years visited our clinic according to records from the previous year. Approximately 1,181 patients visited our clinic every 3 months. Sample size for this study was calculated from 1,181 patients with a 5% confidence interval (CI) using a sample size calculator, which revealed that a sample of at least 291 patients was required. Therefore, 300 participants were recruited for our study from the Sisli Hamidiye Etfal Training and Research Hospital Family Medicine Polyclinic using random sampling between July and September 2017.The CI was 4.88%. Inclusion criteria included age more than 65 years, having no communication barriers and wishing to participate in the study.

### Procedures

The study was approved by the ethics committee of the Sisli Hamidiye Etfal Training and Research Hospital on 13 June 2017 (no. 1583). Verbal permission was obtained from all participants.

### Measures

We composed and administered a questionnaire with 10 items (age, gender, economical status, marital status, education status, taking drugs according to the doctor's prescription, time of the last control and from which branch, missed medicine dose) collecting data on socio-demographic factors and drug use patterns and asked the participants to collect and check all the medicines they use. All drug types were listed according to systems and diseases for each patient. Drugs were classified as polypharmacy (≥5 drugs) or hyperpolypharmacy (≥10 drugs). Data were collected by conducting face-to-face interviews with participants. All listed medications were verified using the EU(7)-PIM list as a screening tool. Patients using incorrect drugs or who unnecessarily recorded some drugs were referred to branch doctors (internal medicine expert, endocrinologist or cardiologist).

**The EU(7)-PIM list**

The EU(7)-PIM list is an expert-consensus list of PIMs for older people which takes into consideration the medications appearing in six country-specific PIM lists, as well as medications used in seven European countries (Estonia, Finland, France, Germany, the Netherlands, Spain and Sweden).The development of the EU(7)-PIM list took several international PIM lists [i.e. the German PRISCUS, American Beers, Canadian and French lists] into consideration, as well as further drugs suggested by experts on geriatrics prescribed from seven European countries who specialised in various professions. In this list, there are 282 PIMs, 29 'questionable PIMs' and 3 'non-PIMs' (8).

**Statistical analysis**

Statistical analyses were performed using SPSS software version 20 (IBM SPSS, Chicago, IL, USA). Variables were investigated using visual (histograms, probability plots) and analytical (Kolmogorov–Smirnov) methods to determine data normality; data were abnormally distributed. Frequencies were calculated for variables related to demographic and clinical patient characteristics. Data were analysed using the chi-square and Student's t-tests, and values of $p<0.05$ were considered statistically significant.

## RESULTS

In total, 1,650 drugs (114 types) were used by study participants. The mean number of drugs per patient was 5.50±2.84 (range, 1–14). Polypharmacy (≥5 drugs) was present in 187 (62.3%) patients; 5–9 drugs were used by 158 (52.7%). Hyperpolypharmacy (≥10 drugs) was found in 29 (9.7%) patients.

A total of 300 patients [mean age, 76.27±8.6 (range 65–99)] were included in our study; 48.3% (145) of patients were aged 65–74 years. As shown in Table 1, 170 (56.7%) patients were females, 171 (57%) were married, 107 (35.7%) had an education level below high school, 131 (43.7%) had no income and 181 (60.3%) were retired. There were no statistical associations between polypharmacy and gender, marital status, education, economic status or retirement status (P=0.636, 0.106, 0.309, 0.156 or 0.769, respectively).

As shown in Figure 1, the most frequent bodily system treated by medication was the cardiovascular system. The three most frequent drugs were beta blocking agents, angiotensin receptor blockers (ARBs) and thrombolytics. The three most common chronic diseases treated were hypertension (HT), diabetes mellitus (DM) and cancer. As shown in Table 2, DM and HT were significantly related to polypharmacy according to the chi-square test (p=0.01 and 0.001, respectively), whereas cancers were not (p=0.327). A total of 118 participants used 212 oral anti-diabetic drugs (11 types). Most participants (61; 61.6%) used two or more drugs for DM. In addition, 143 participants used a total of 475 HT drugs (24 types). Approximately three drugs were used for HT per patient. Beta blocking agents (108, 36%) and ARBs (96, 32%) were mainly used for HT. Seventy-two participants had both DM and HT; these participants used an average of 6.85±2.81 drugs.

Our results indicated that 267 (89%) participants took drugs according to their doctors' prescriptions, whereas 33 (11%) occasionally changed their drugs on their own. Polypharmacy and changing drugs on one's own were not significantly related (p=0.828). A total of 102 participants (34%) had their medicines controlled ≤1 month ago, and 100 (33%) had them controlled by an internal medicine doctor. Polypharmacy was related with the monitoring times by doctors (P=0.00), but not with the type of doctor (P=0.532). Close monitoring decreased polypharmacy. In terms of missing medicine doses, 58 (19.3%) participants occasionally forgot to take their medications. Polypharmacy and missing medicine doses were related; patients forgot to take their medications with increasing number of drugs used (p=0.018).

**Table 1.** Distribution of socio-demographic factors and drug use patterns in elderly study participants.

| Factor | n | % |
|---|---|---|
| **Age (years)** | | |
| 64–74 | 145 | 49 |
| 75–84 | 94 | 31 |
| ≥85 | 61 | 20 |
| **Gender** | | |
| Women | 170 | 56.7 |
| Men | 130 | 43.3 |
| **Marital Status** | | |
| Married | 171 | 57 |
| Single | 129 | 43 |
| **Education Status** | | |
| Uneducated | 2 | 0.7 |
| Literate | 91 | 30.3 |
| Under high school | 107 | 35.7 |
| High school and above | 79 | 26.3 |
| **Economic Status** | | |
| No income | 131 | 43.7 |
| Minimum wage (≤1300 TL)* | 50 | 16.7 |
| Middle income (1300–3000)* | 109 | 36.3 |
| High income (≥3000)* | 10 | 3.3 |
| **Retired** | | |
| Yes | 181 | 60.3 |
| No | 119 | 39.7 |
| **Taking drugs according to doctors' prescription** | | |
| Yes | 267 | 89.0 |
| No | 33 | 11.0 |
| **Prescription given by** | | |
| Family physicians | 75 | 25.0 |
| Internal medicine | 100 | 33.0 |
| Cardiologist | 39 | 13.0 |
| Neurologist | 32 | 10.7 |
| Other | 54 | 18.0 |

*1300 TL (350 USD); 3000 TL(815 USD)

**Table 2.** The relationship between study parameters and polypharmacy in elderly study participants.

| Parameter | Total | | Polypharmacy | | | | |
|---|---|---|---|---|---|---|---|
| | | | Positive | | Negative | | |
| | n | % | n | % | n | % | p |
| **Gender** | | | | | | | |
| Women | 170 | 56.7 | 104 | 55.6 | 66 | 58.4 | |
| Men | 130 | 48.3 | 83 | 44.4 | 47 | 41.6 | 0.636 |
| **Age (years)** | | | | | | | |
| 64–74 | 145 | 49 | 89 | 48 | 56 | 50 | |
| 75–84 | 94 | 31 | 61 | 32 | 33 | 29 | |
| ≥85 | 61 | 20 | 37 | 20 | 24 | 21 | 0.822 |
| **DM** | | | | | | | |
| Positive | 118 | 39 | 91 | 49 | 27 | 24 | |
| Negative | 182 | 61 | 96 | 51 | 86 | 76 | 0.00 |
| **HT** | | | | | | | |
| Positive | 157 | 52 | 103 | 55 | 40 | 35 | |
| Negative | 143 | 48 | 84 | 45 | 73 | 65 | 0.001 |
| **Cancer** | | | | | | | |
| Positive | 96 | 32 | 56 | 30 | 40 | 35 | |
| Negative | 204 | 68 | 131 | 70 | 73 | 65 | 0.327 |
| **Time of verification** | | | | | | | |
| ≤1 month | 102 | 34.0 | 54 | 32 | 48 | 43 | |
| 1–6 months | 61 | 20.3 | 29 | 17 | 32 | 28 | |
| 6–12 months | 39 | 13.0 | 31 | 19 | 8 | 7 | |
| 1–5 years | 42 | 14.0 | 12 | 7 | 10 | 9 | |
| ≥5 years | 56 | 18.7 | 41 | 25 | 15 | 13 | 0.000 |
| **Missed drugs** | | | | | | | |
| Yes | 58 | 19 | 44 | 23.5 | 14 | 12 | |
| No | 242 | 81 | 143 | 76.5 | 99 | 88 | 0.018 |

DM, diabetes mellitus; HT, hypertension

PIMs used by study participants according to EU(7)-PIM are shown in Table 3. A total of 317 (19.2%) drugs were listed in EU(7)-PIM, and 195 (65%) patients took a minimum of one PIM. According to EU(7)-PIM, some oral anti-diabetics such as glimepiride, sitagliptin and glibenclamide were PIMs. All (51) were referred to their branch doctors by our team. Twenty-three (7.7%) participants used warfarin. The mean number of drugs in patients who used warfarin was 5.08±2.77 (range, 1–10). We referred these patients to a cardiologist and encouraged them to maintain close control of their medication within the international normalised ratio.

**Table 3.** List of PIMs among drugs taken by patients according to EU(7)-PIM list.

| Drug | n | % |
|---|---|---|
| **Oral anti-diabetics** | | |
| Glimepiride | 6 | 2 |
| Insulin | 41 | 13 |
| Sitagliptin | 4 | 1 |
| **Cardiovascular drugs** | | |
| Trimetazidine | 15 | 5 |
| Spironolactone | 9 | 3 |
| Nifedipine | 11 | 3 |
| Verapamil | 4 | 1 |
| Diltiazem | 18 | 6 |
| Digoxin | 5 | 2 |
| **PPI** | 84 | 26 |
| **Iron** | 17 | 5 |
| **Trimetazidine** | 15 | 5 |
| **Doxazosin (both for BPH and CVD)** | 16 | 5 |
| **NSAID** | 43 | 14 |
| **Tramadol** | 2 | 0.5 |
| **Ginkgobiloba** | 9 | 3 |
| **Clozapine** | 4 | 1 |
| **Risperidone** | 4 | 1 |
| **Diazepam** | 2 | 0.5 |
| **Theophylline** | 8 | 3 |
| **Total** | **317** | **100** |

BPH, benign prostatic hyperplasia; CVD, cardiovascular disease; EU(7)-PIM list, European Union Potentially Inappropriate Medication list; NSAID, non-steroid anti-inflammatory drug; PIM, potentially inappropriate medication; PPI, proton pump inhibitor

A total of 84 (38%) participants used proton pump inhibitors. Lansoprazole was the most commonly used PPI (34 participants, 40.5%). A long-term (>8 weeks), high-dose PPI therapy is associated with an increased risk of *C. difficile* infection and hip fracture according to EU(7)-PIM. Therefore, we controlled for indication of use, and drugs were referred or stopped if unnecessary; 59.5% (50) were stopped and others were referred.

Potassium-sparing agents (e.g. spironolactone) were listed as PIMs in EU(7)-PIM when used in excess of the recommended dose (>25 mg/dL). However, all nine study participants who used these drugs took 25 mg for heart failure.

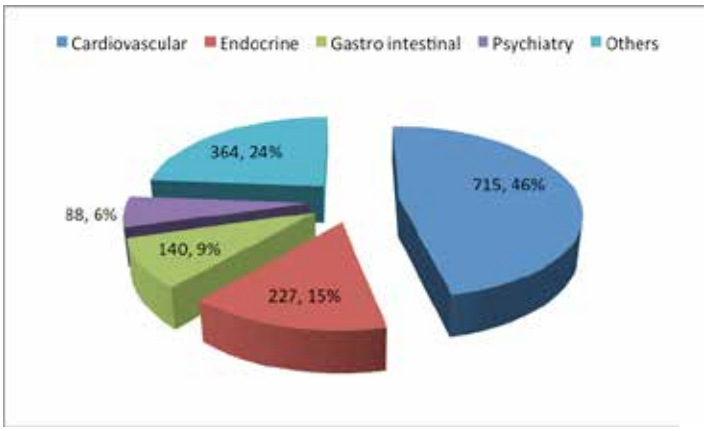


**Figure 1.** Drug types used by elderly study participants (listed as number of patients, percentage).

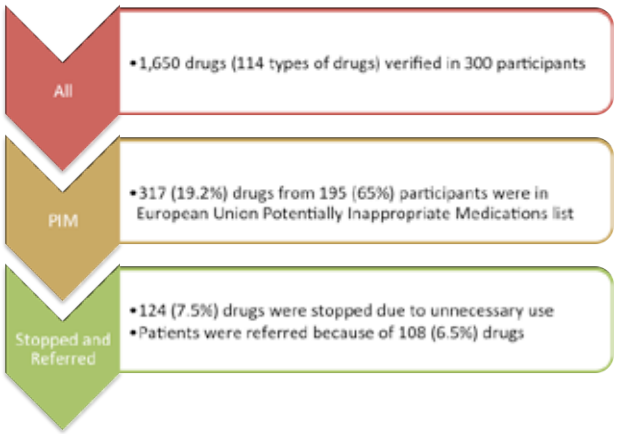


**Figure 2.** Overall study results regarding drug use in elderly study participants.

Fifteen participants used trimetazidine at a normal dose and indication for ischemic heart diseases.

In total, 43 (14.3%) participants used non-steroid anti-inflammatory drugs (NSAIDs); all these were stopped because of unnecessary use. Twenty-two (7.3%) participants used muscle relaxants; all these were self-medications, and were thus stopped due to unnecessary use.

Vitamins and mineral use was also verified; 43 (14.3%) participants used vitamin B12, 17 (5.6%) used iron and 11 (3.6%) used calcium with vitamin D. We also verified participants' early laboratory data and diagnoses and found no unnecessary use.

Lastly, 19 (6.3%) participants used steroid creams (e.g. desoximetasone) for itching without their doctors' prescription. We therefore stopped these medications and referred the patients to a dermatologist.

In total, 124 (7.5%) drugs were stopped due to unnecessary use (Figure 2). The most commonly used self-medication drugs were NSAIDs (43; 14.3%). Patients were referred because of 108 (6.5%) drugs.

## DISCUSSION

During the 20th century, significant changes were observed worldwide in terms of demographic, morbidity and mortality rates, although at different magnitudes. According to the World Health Organization, the average global life expectancy at birth is 71.4 years (males, 69.1 years; females, 73.7 years) (9). According to Turkish national statistics, the number of elderly individuals was 6,651,503 in 2016 and accounted for 8.3% of the Turkish population (males, 43.9%; females, 56.1%), and the life expectancy at birth was 66.2 years (10). Accordingly, 56.7% of our sample population was female, which is likely the result of the longer life expectancy of females.

Due to the growing elderly population, certain issues such as polypharmacy are becoming more frequent due to the increased prevalence of chronic diseases in the elderly. In a study conducted in the USA, it was observed that 57% of females over 65 years of age used five or more drugs and 12% used 10 or more drugs (11). According to another study (12), the frequency of polypharmacy in the elderly was 36%. In our sample population including males and females aged more than 65 years, the frequency of polypharmacy (5 or more drugs) was 62.3% and that of hyperpolypharmacy (10 or more drugs) was 9.7%. These results revealed that polypharmacy affected approximately half of the elderly population under study.

There are many factors driving polypharmacy. Some studies have shown a relationship between polypharmacy and both female sex and age over 80 years (13,14). In our study, there was no relationship between socio-demographic factors and polypharmacy. We believe this was due to characteristics of the study group.

In our study, chronic diseases were related to polypharmacy. According to previous studies (15, 16), the most frequent chronic disease in the elderly was hypertension, and the most commonly used drugs were cardiovascular drugs (17), as observed in our study. Also, consistent with our findings, HT (18) and DM (19) were both related to polypharmacy in previous studies. This finding indicates that polypharmacy may be partly due to the increasing number of elderly individuals with chronic diseases and complications.

In a previous study, the frequency of polypharmacy specifically in the cancer outpatient setting was 41% (20). According to a review, chemotherapy treatment itself presents an increased risk for polypharmacy, with 96% of patients taking prescription drugs and 69% taking vitamins, herbs, or supplements within 3 days of chemotherapy administration (21). In our study, there was no relationship between cancer and polypharmacy because not all cancer patients were undergoing chemotherapy, and after treatment, cancer patients were afraid to use drugs and asked doctors before use because they learned about the drug side effects and reactions.

In our study, polypharmacy decreased with close control by a doctor; therefore, to prevent polypharmacy, healthcare professionals should be aware of the risks and fully evaluate all medications at each patient visit (22). Taking too many drugs leads not only to pharmacological outcomes (e.g. inappropriate drug, adverse drug events, adherence) but also certain clinical outcomes (e.g. morbidity, functionality). In our study, polypharmacy also led to some patients missing their medications and thus uncontrolled therapy.

Use of PIMs has been analysed by several authors and ranges from 20% to 79% depending on the population studied, setting or country and specific tools used (23). In our study, the EU(7)-PIM list was used as a screening tool. The frequency of PIMs in previous studies were 57.2% (28) and 66.7% (24) according to the EU(7)-PIM list. Similar to our study, the frequency of PIMs was 65%, and the most commonly used self-medication drugs were NSAIDs (43; 14.3%), as observed in a study from Brazil (13). Our study highlights the importance of ensuring that drugs are controlled by doctors, and that more

than half of elderly individuals have a high risk (e.g. medication non-adherence, drug duplication, drug–drug interactions and adverse drug reactions) because of PIMs. PIM was not only problematic for the elderly but also affected the overall population, as PIMs increased hospitalisation and incurred heavy costs in the health sector.

It is known that drug–drug interactions in warfarin-treated patients on multiple medications are common and are associated with increased bleeding risks (25), similar to the findings of our study. Twelve (52.2%) warfarin-treated patients in our study had polypharmacy. Therefore, we must pay attention to warfarin-treated patients about using other drugs because of their increased risk of drug–drug interactions.

As shown in Figure 2, 1,650 drugs (114 types) were verified in 300 patients. Frequency of polypharmacy (5 or more drugs) was 187 (62.3%); 158 (52.7%) participants used 5–9 drugs, and 29 (9.7%) had hyperpolypharmacy (10 or more drugs). In total, 317 (19.2%) drugs were on the European Union PIM list, and 195 (65%) patients used a minimum of one PIM. A total of 124 (7.5%) medications were stopped due to unnecessary use. Patients were referred because of 108 (6.5%) drugs.

In conclusion, polypharmacy and PIM use were both very frequent in the elderly population in our study. According to our study, polypharmacy was positively related only to chronic diseases, negatively related to closely controlled therapy and led to missing of medication dose in some participants. Given these findings, we suggest that doctors verify all medications taken by elderly patients. Branch physicians do not always have time to examine all medications used by patients due to their heavy workload. Family physicians are well positioned to encourage appropriate use of medications in older adults. Introducing a program related to PIMs into clinical practice would be useful. However, just as we require evidence-based, age-specific, pharmacological information for efficient clinical decision making, we also require solid evidence for strategies that consistently improve the quality of pharmacological treatments at the health system to shape 'age-attuned' health and drug policies. There is a great need for interventions to improve pharmacotherapy in elderly populations. Therefore, we suggest planned educational programmes at post-secondary education level and medical schools to promote increased knowledge and prevent the use of polypharmacy and PIMs.

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