

# ***Inappropriate medications in the geriatric population – the global and the national perspectives***

## **Niepoprawna farmakoterapia w populacji geriatrycznej – perspektywa globalna i krajowa**

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### **Abstract**

*The study aims to present current knowledge about inappropriate medications in the geriatric population. Inappropriate treatment is related to multimorbidity and polypharmacy; thus, it refers mainly to older patients. A medication review and tools for assessing the appropriateness of pharmacotherapy prevent inappropriate treatment. A medication review – structured critical analyses of medications list – gains popularity in multiple countries, and researchers confirmed its effectiveness in reducing drug-related problems. Currently, a pilotage program of medication review in Poland has been announced. Beers and STOPP/START criteria are the two most widespread tools for detecting the inappropriateness of pharmacotherapy. Globally both criteria turned out to be effective in potentially inappropriate medications findings. So far, researchers in Poland have performed a pilot study comprising 50 patients using those tools. Recently in Western Europe countries, interventional studies revealed that tools reduce the number of prescribed drugs and improve certain clinical outcomes. (Gerontol Pol 2023; 31; 87-93) doi: 10.53139/GP.20233110*

**Keywords:** *inappropriate medications, geriatric patients, medication review, Beers criteria, STOPP/START*

### **Streszczenie**

*Celem niniejszej pracy jest przedstawienie aktualnej wiedzy na temat niepoprawnej farmakoterapii w populacji geriatrycznej. Niepoprawna farmakoterapia jest ściśle związana ze zjawiskami wielochorobowości oraz polipragmazji, dlatego dotyczy głównie pacjentów starszych. Przegląd lekowy i narzędzia pozwalające uniknąć stosowania niepoprawnych leków zapobiegają niepoprawnej farmakoterapii. Przegląd lekowy – ustrukturyzowana krytyczna analiza listy leków – zyskuje popularność w wielu krajach, a naukowcy potwierdzili, że przegląd redukuje ilość problemów lekowych. Obecnie ogłoszony został program pilotażowy przeglądu lekowego w Polsce. Kryteria Beers'a oraz STOPP/START to dwa najczęściej używane narzędzia pozwalające uniknąć stosowania niepoprawnych leków. Badania w różnych krajach na świecie udowodniły, że oba kryteria skutecznie wykrywają potencjalnie nieprawidłowe leczenie. Dotychczas naukowcy w Polsce przeprowadzili badanie pilotażowe obejmujące 50 pacjentów z wykorzystaniem wyżej wymienionych kryteriów. Niedawno przeprowadzone w krajach Europy Zachodniej badania interwencyjne wykazały, że narzędzia zmniejszają liczbę przepisywanych leków i pozytywnie wpływają na niektóre aspekty kliniczne. (Gerontol Pol 2023; 31; 87-93) doi: 10.53139/GP.20233110*

**Słowa kluczowe:** *niepoprawna farmakoterapia, pacjenci geriatryczni, przegląd lekowy, kryteria Beers'a, STOPP/START*

### **Introduction – multimorbidity, polypharmacy, and inappropriate medication**

Old age is associated with specific medical problems – multimorbidity, polypharmacy, and inappropriate medication. World Health Organization (WHO) defines multimorbidity as the existence of two chronic conditions in a patient [1]. To state multimorbidity, different methods

can be applied – simply counting chronic conditions or creating a weighted index by estimating the weight of each disease [2]. Multimorbidity and advanced age are the two most important factors influencing a number of prescribed drugs [3]. Although the term “polypharmacy” is not strictly defined, the most commonly considered as the daily intake of five or more medications. That definition is typically associated with the distinction of two

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categories: polypharmacy (5 or more medications daily) and excessive polypharmacy (10 or more medications daily) [4]. The third feature mentioned above, potentially inappropriate medications (PIMs), encloses various drug-related problems: adverse drug events (ADEs), adverse drug reactions (ADRs), and drug-drug and drug-disease interactions. These are followed by clinical consequences, i.e., dizziness, falls, frail syndrome, more frequent hospitalizations, and higher mortality [3]. PIMs are closely related to multimorbidity and polypharmacy. Multiple studies showed that with each subsequent medication prescribed, the risk of drug-related problems highly increases [5]. Thus studies conducted on large cohort groups proved that polypharmacy itself is associated with a higher risk of hospitalization and all-cause mortality [6].

Two trends in polypharmacy are worth noting. Firstly, a number of prescribed drugs correlate with the patient's age. Hence polypharmacy as a medical problem refers mainly to geriatric patients. According to data from 17 European countries, the prevalence in people above 65 years ranges from 27% to 59%, depending on the country. The prevalence of polypharmacy varies within the geriatric population, peaking in patients above 85 years [7]. Secondly, polypharmacy is a relatively new phenomenon. Data from Ireland well illustrate the global situation. Studies on nearly a half-million study group revealed that between 1997 and 2012 prevalence of polypharmacy in older patients increased 4-fold and excessive polypharmacy 10-fold [5].

In recent years several decisive studies about polypharmacy in the Polish geriatric population were conducted. PolSenior – the nationwide, comprehensive project, lasting from 2008 to 2011, encloses a representative group of 4,979 people above 65 years [8]. Among 4,793 participants with an evaluation of medication, polypharmacy was found in 55.3% and excessive polypharmacy in 11.3%. The average number of medications taken by the older person was  $5.1 \pm 3.6$ . Polypharmacy was associated with multiple chronic conditions, and excessive polypharmacy was related to the hospitalization in the last five years [9]. In a similar survey conducted ten years later (named PolSenior2), 5,987 people above 60 years were examined [10]. In the PolSenior2 study, the prevalence of polypharmacy and excessive polypharmacy was 51% and 12.4%, respectively [11]. Although the prevalence of polypharmacy was slightly lower compared to prior PolSenior, a younger population (60-64 years) was also included. Another interesting survey is based on a retrospective analysis of data from the Polish national payer organization for the years 2018–2019. The problem of polypharmacy concerned 11.7% of 38

million Polish citizens in 2018, achieving 43.1% among those aged 65 and more [12]. Summarizing the growing and significant phenomenon of polypharmacy in the elderly is well documented both from global and Polish perspectives. An urgent question: How does it effectively find and prevent potentially inappropriate medications associated with polypharmacy?

## How to prevent potentially inappropriate medications?

One of the most popular methods, medication review (MR), is based on a structured, critical analysis of a patient's list of medications considering clinical conditions simultaneously. In 2016 Pharmaceutical Care Network Europe (PCNE) defined MR as: "A structured evaluation of a patient's medicines with the aim of optimizing medicines use and improving health outcomes. This entails detecting drug-related problems and recommending interventions." PCNE proposed the classification of MR, distinguishing three levels (simple, intermediate, advanced) and four types of MR (1, 2a, 2b, 3). Simple level (type 1) – prescription review – relies only on the review of the medications list. Besides a list of medicine, the second intermediate includes a patient's interview (type 2a) or clinical data (type 2b). The most effective third type complies with a list of patients' medications, patient interview, and clinical conditions. A clinical pharmacist or medical doctor provides MR [13].

Multiple tools for assessing the appropriateness of pharmacotherapy in older patients have been created. Depending on the tool, drugs-to-avoid (potentially inappropriate medications - PIMs) and/or drugs-to-remember (potential prescription omissions - PPOs) are included. So far, the classification has distinguished between implicit tools (requiring intricate patient data) and explicit (based on criteria). Due to difficulty in making a clear distinction, a new classification has been proposed recently: PILA (patient in focus, requires intricate data), DOLA (drug-oriented listing approach), and DOLA+ (additionally including indications for drugs). In a systematic review, Pazan et al. identified 76 different tools to improve pharmacotherapy in patients above 65 years. However, only five positively impacted patients in at least one clinical trial. Beers and STOPP/START criteria are the two most widespread. Due to clinical validation and increasing popularity, FORTA also needs to be noted [14].

Beers Criteria, realising by the American Geriatrics Society (classified as DOLA+), contains a list of medications potentially inappropriate for older patients. The tool divides drugs into various groups: those which ge-

nerally are inappropriate for the elderly, medications harmful with certain medical conditions or diseases, and those which can be used with caution. The latest version of the Beers Criteria, published in 2019, includes 30 medications (or medication classes) generally inappropriate for the elderly and more than 40 that should be avoided in certain diseases or should be used with caution [15]. STOPP/START criteria (Screening Tool to Alert Doctors to the Right Treatment/Screening Tool of Older Persons' Prescriptions) were created by European experts. STOPP/START criteria facilitate the detection of PIMs (STOPP) and PPOs (START) [16]. Generally, both are implemented simultaneously. Thus STOPP/START was classified as PILA (although STOPP alone as Beers belongs to DOLA+ category) [14]. The most recent version two contains 114 criteria– 80 STOPP and 34 START [16]. The third tool mentioned above, FORTA List (Fit-fOR-The-Aged, classified as PILA), ranges medications from A (A-bsolutely) to B (B-eneficial), C (C-areful), and D (D-on't). Medications or medication classes receive positive or negative labels considering their therapeutic effect, safety, and age appropriateness. The most recent FORTA List 2021 includes 299 entries in 30 indications [17]. A new great challenge is designing software capable of automatically applying these tools. The clinical decision software system would support doctors and pharmacists, helping to provide appropriate pharmacotherapy to the elderly. The first attempts were made in the case of STOPP/START criteria [18,19].

### **Medication review – an effective instrument in the hands of pharmacists**

The effectiveness of MR, structured critical analyses of medications list, have been assessed in various cross-sectional, retrospective, and prospective studies. Gudi et al. performed a systematic search to find publications describing the impact of MR made by pharmacists. Among ten studies that met the inclusion criteria, pharmacists, through medication review found a significant amount of drug-related problems [20]. In another systematic review, authors analyzed the impact of community pharmacist-led interventions on clinical outcomes. Pharmacist-led interventions improved blood pressure and cholesterol level management. Moreover, MR contributed to better control of chronic obstructive pulmonary disease and asthma [21]. Interestingly in meta-analyses distinguishing three types of MR, different clinical outcomes depending on type were observed. Assessing the number of unplanned hospitalizations, only MR type III (comprehensive clinical evaluation) led to a reduc-

tion, whereas type I and II increased their number. Data suggest that MR type III most effectively influences patients' clinical outcomes [22]. Apart from medical conditions, economic aspects were also studied. With decreasing PIMs and the deprescribing process, patient and government funding cost savings follow [23].

In Australia, a unique government-funded system of performing MR was established. Residential Medication Management Review (RMMR) assesses elderly living in long-term facilities and Home Medicines Review (HMR) those living at home. A pharmacist, in collaboration with a general practitioner, provides medication review. Indicators such as Medication Appropriateness Index (MAI) and Drug Burden Index (DBI) proved to have a positive impact on clinical outcomes [24]. Several studies showed a significant reduction in a number of prescribed medications, hospitalizations, and PIP due to CMR [25]. Moreover, after RMMR, a reduction in weekly trends in some medications (e.g., statin and PPI) were observed in large-scale retrospective analyses [26]. Similar services were established in the USA named Medication Therapy Review and in the UK found as workstreams of the Pharmacy Integration Programme. In both, a pharmacist plays a key role [27, 28]. Data from 34 European countries proved that MR as an implemented service or project was provided in more than half of them. Depending on the country, different types of MR were used. The most popular were types 1 and 2a, and the most comprehensive type 3 was present only in four countries [29].

MR become popular in Poland over the past few years. The largest study conducted so far named OF-Senior, enabled 291 older patients with excessive polypharmacy. During three separate meetings, pharmacists performed MR, changed medications, and verified the effect of corrected pharmacotherapy. On average, patients included in this study used  $12.3 \pm 2.9$  medications daily and suffered from  $3.1 \pm 1.4$  drug-related problems. MR performed by pharmacists decreased the number of medications taken and improved clinical outcomes in 80.6% of patients [30]. Another study evaluated the willingness to conduct MR among Polish pharmacists. Out of 493 pharmacists, 63.9% were ready to perform MR, and 23.1% reported experiences in that service. The study revealed a high level of readiness in conducting MR [31]. In 2021 pilotage program of MR in Poland was announced. From 750 to 1000 patients will be enabled by pharmaceutical care during three meetings. Results will be presented in 2023 [32].

## How effectively can tools identify the inappropriateness of pharmacotherapy?

Following the development of tools detecting PIMs/PPOs, assessments of the prevalence of inappropriate pharmacotherapy were conducted. PIMs prevalence was assessed in multiple countries worldwide. Only some will be cited in this article, selected due to a large study group, a multicentre placing, and a recent survey time. The systematic review involving 63 studies of hospitalized older patients showed that PIMs prevalence ranged from 47% to 56% depending on tools, whereas PPOs prevalence based on START criteria was 55%. Most of the analyzed studies used Beers or STOPP/START criteria. Benzodiazepines, anticholinergics, and antipsychotics were the most common PIMs. Among PPOs lack of antiplatelet drugs was the most frequent. Presence of PIMs correlated with medication-related hospitalization, ADRs, and health care costs. Two research showed an association between PIMs and falls frequency. However, a link between PIMs and mortality and hospital readmissions was not observed [33]. Similarly to hospitalized patients, researchers assessed the appropriateness of pharmacotherapy among elderly living in long-term care facilities. A systematic review concerning residents of long-term care facilities revealed a high prevalence of inappropriate medication. Studies relying on Beers 2012 showed a frequency of PIMs from 63% to 82.6%. Those using STOPP/START criteria revealed medians 61.1% of PIMs and 48.6 PPOs. Due to the heterogeneity of included studies and used tools, drug classes associated with PIMs varied, although overuse of benzodiazepines was frequent [34].

In Poland, a large-scale analysis among the elderly evaluating pharmacotherapy and PIMs has never been conducted. Recently a pilot study comprising 50 patients was performed. Researchers used multiple tools (inter alia STOPP/START and Beers criteria) to assess PIP. The STOPP/START criteria revealed the highest amount of PIP – 3.4 per patient on average. The most frequent problems concerned the lack of vaccination against pneumococci and excessive use of PPI. The authors emphasize the effectiveness of PIPA, especially STOPP/START [35].

Although a comprehensive assessment of drug-related problems on a larger scale has not been conducted so far, there are studies describing pharmacotherapy of specific medical problems among the elderly. Worth noting study concerned pain treatment. Researchers involved around 200 residents of community-dwelling elderly people aged at least 65 years. Firstly, residents were divided into cognitively intact subjects and those with cognitive

impairment. Next, the pain was evaluated and set together with analgesics. Among pain-experiencing cognitively intact residents, 42% had ineffective pain treatment, whereas 22% did not receive analgesics. Among pain-experiencing residents with cognitive impairment, results were even worse – more frequently pain remained untreated. Even when analgesics were prescribed, both the frequency of usage and the daily doses were inappropriate [36]. Abovementioned studies indicate common drug-related problems in older Polish patients. Thus there is an obvious need to perform a larger, comprehensive pharmacotherapy assessment.

## Next step – to assess the real impact of tools on older patient's clinical outcome

Researchers created tools to identify PIMs/PPOs and confirm their effectiveness in PIMs/PPOs findings. In recent years, studies assessing the real positive impact of deprescribing practice were conducted. In the last ten years, there have been several intervention studies and controlled trials, mainly in Western Europe countries. To validate the FORTA list, a controlled trial named VALFORTA was conducted. Within VALFORTA, 409 older patients with multimorbidity and polypharmacy were assessed. FORTA score (sum of inappropriate medications according to the FORTA list) was the primary endpoint, whereas clinical outcomes constitute secondary points. The intervention group achieved a lower FORTA score compared to the control group. Moreover, multiple clinical outcomes improved within the intervention group. Reduction in the number of ADRs and the increased score in activities of daily living (ADL) were observed [37].

Concerning STOPP/START criteria, a number of studies have been published recently. O'Connor et al. used STOPP/START among older patients with polypharmacy during hospitalization due to acute medical or surgical illness. Medication optimization was made within 48 of admission. Significant reductions in ADR incidence and medication costs were observed compared to the control group, although the median length of stay was similar [38]. Another intervention study was performed in a chronic geriatric facility in Israel. In that randomized study, using the STOPP/START tool reduced falls, the number of medications, and costs in the facility [39]. Other results derive from a clinical trial conducted in Spain. 503 community-dwelling elderly people above 70 years and receiving at least eight medications daily were assessed. Among the intervention group, STOPP/START criteria were implemented leading to reduce of potentially inappropriate medication and the number of

prescribed drugs. However, no difference in the number of emergency visits, hospitalizations, and deaths was noticed compared to the control group [40].

The SENATOR and the OPERAM - two multi-center trials involved a larger research group and used specially designed software to apply STOPP/START criteria. Both studies aimed to assess the value of software that automatically apply STOPP/START criteria together with standard pharmaceutical care, compared to standard pharmaceutical care alone. In the SENATOR trial, ADRs occurring within 14 days of randomization were assessed. This clinical intervention did not prove that the uptake of software-generated medication advice decreased ADRs [18]. The second trial evaluated OPERAM drug-related hospitalization within 12 months of randomization. Although the number of inappropriate medications prescribed decreased, the influence on the frequency of drug-related hospital admissions was not observed [19]. Authors of both trials conclude that more studies are needed to identify interventions leading to the effective reduction of inappropriate medication.

### Conclusion – current knowledge and future direction

Polypharmacy is a significant medical problem in the elderly, associated with inappropriate pharmacotherapy.

In multiple countries, there is an increasing effort to counteract the problem of polypharmacy and inappropriate treatment. Medication review, a structured critical analysis of the medications list, became one of the main methods to cope with inappropriate treatment. Simultaneously, tools detecting PIMs/PPOs were created; some of them (Beers, STOPP/START, FORTA list) were also validated. Numerous studies proved the effectiveness of these tools in finding PIMs/PPOs. Although several interventional studies and clinical trials were recently conducted, there is still a strong need to prove the association between PIMs/PPOs and clinical outcomes. Two other challenges are: spreading the above-mentioned tools among clinicians and designing software capable of automatically applying them.

The problem of inappropriate treatment among older patients gains popularity in Poland. In the last ten years, researchers assessed the prevalence of polypharmacy and revealed its widespread in the Polish population. Recently medication review pilotage program started, and a pilot study with Beers and STOPP/START criteria use was published. Future directions are large-scale analyses using tools detecting PIMs/PPOs and government-funded systems counteracting the problem of inappropriate treatment.

Conflict of interest  
None

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