

Polypharmacy – a growing problem in the elderly community

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Abstract

Introduction and purpose. Polypharmacy refers to a simultaneous use of at least five drugs by an individual patient. As civilization has progressed, so has medicine, leading to a clear upward trend in life expectancy over the past decades. The population of those aged 65 and older, which stood at 90.5 million at the beginning of 2019, is projected to reach 129.8 million by 2050 across the 27 European Union countries. With increasing life expectancy, the incidence of chronic diseases—such as those associated with modern lifestyles—also rises. *Description of the state knowledge.* Polypharmacy is widely recognized as a significant public health concern, as it increases the risk of adverse effects, impacting both health outcomes and healthcare costs. Given the close relationship between polypharmacy and multimorbidity, it is not surprising that this practice raises major concerns among the patients. Seniors face unique challenges in pharmacological therapy due to age-related metabolic changes and the co-occurrence of multiple disorders, which require complex medication regimens. When polypharmacy combines with aging-related physiological changes, the likelihood of drug-drug interactions (DDIs) increases. Consequently, emergency departments are seeing a growing number of polypharmacy patients, making it more challenging to diagnose and prevent the worsening of chronic diseases during care. *Summary.* Older individuals with chronic conditions are typically treated with pharmacotherapy, which often necessitates prescribing combinations of medications. To address this complexity several clinical guidelines and algorithms have been developed, including the well-known STOPP/START and Beers criteria. *Geriatrics* 2024;18:103-111. doi: 10.53139/G.20241813

Keywords: polypharmacy, multimorbidity, drug to drug interactions, elderly, geriatrics

Introduction and purpose

According to the World Health Organization, polypharmacy occurs when a patient receives at least five drugs simultaneously. The concept of polypharmacy is closely associated with multimorbidity, which is defined as the occurrence of two or more long-term chronic conditions, such as mental or physical diseases, chronic

pain, sensory impairments or substance abuse. While this phenomenon may apply to all patient groups, it is particularly concerning for the elderly and those living in care homes. This patient group faces numerous health burdens due to multiple comorbidities [1]. Among the most important socioeconomic developments of the 20th century is the substantial increase in life expect-

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tancy. However, as people live longer and fertility rates decrease, the population is gradually aging [2]. At the start of 2019, 90.5 million people aged 65 years or older lived in the 27 European Union countries. By 2050, this group is projected to grow to 129.8 million. Additionally, the number of people aged 85 years or older is estimated to increase from 12.5 million in 2019 to 26.8 million by 2050. Furthermore, the number of centenarians (people aged 100 years or more) is expected to rise from 96,600 in 2019 to nearly half a million (484,000) by 2050 [3]. In Poland around 2/5 of the population is going to be aged over 60 by 2050, according to a report of the state agency of Central Statistical Office (GUS) [4]. With the increase in life expectancy, the number of chronic diseases increases, and thus the number of drug treatments. According to the Polish National Health Fund (NFZ), one-third of Poles over the age of 65 take at least five drugs daily. In 2018, according to the same report, there were 321 patients taking more than 20 drugs every day [5]. The risk of drug interactions and potentially incorrect medicine prescriptions increases when many medications are taken. Simultaneously, the term ‘drug-drug interaction’ describes a pharmacological or clinical reaction to a combination of drugs that wouldn’t have been anticipated, based on the individual side effects of each medicine, when administered separately. The majority of drug-drug interactions involve cardiovascular medications. The most frequent adverse effects associated with medication interactions are hypotension, abrupt renal failure, and neuropsychological (delirium) [6]. Polypharmacy is frequently referred to as a serious public health issue. It raises the possibility of negative consequences, which significantly impacts the health outcomes and healthcare costs. The biggest risks of polypharmacy are: adverse drug reactions (ADRs), fall hazards, drug-drug interactions, cognitive decline, non-adherence, and inadequate nutrition [1].

Description of the state knowledge

Polypharmacy is not a straight-forward problem – there are cases when polypharmacy is ‘appropriate’ and needed but there are also instances where it is ‘inappropriate’. ‘Appropriate polypharmacy’ recognizes that a patient can benefit from multiple medications, while ‘inappropriate polypharmacy’ can occur when one or more medicines are prescribed unnecessarily, the indication has expired, or the dose is unnecessarily high. Studies using observational data have demonstrated the link between older adults’ polypharmacy and

potentially inappropriate prescription (PIP), as well as adverse clinical outcomes that could jeopardize patients’ safety and well-being [1,7]. Seniors’ pharmacological therapy is particularly challenging because of changes in metabolism caused by aging and the combination of multiple diseases that necessitate intricate medication schedules [2]. The first thing to be disturbed among the elderly is the pharmacokinetics as well as the pharmacodynamics [8]. First-pass metabolism, which is usually hepatic and occurs before a drug enters the systemic circulation, declines by roughly 1% annually after the age of 40. Therefore, older individuals may have higher circulatory medication concentration, such as propranolol or phenobarbital, for a given oral dose, which can increase the risk of hazardous consequences [9].

The principles of absorption, distribution as well as metabolism differ from a younger patient [8]. The decrease in the principle of absorption is caused by a number of factors. The main contributor is the decrease in the Hydrogen Potential of the gastric juices but it’s also caused by the decrease in blood supply as well as atrophy of the intestinal villi causing a decrease in the absorption area of the intestines [8,10]. The principle of absorption is impacted by the increase in the percentage of adipose tissue and the decrease in the level of hydration, while the distribution stage is affected by variations in the levels of protein bonds such as those with albumins [9,11]. Lipophilic drugs such as barbiturates, tricyclic antidepressants, amiodarone or certain cardiac specific potassium antagonists (Verapamil) are therefore dissolved in fat, leading to increased half-life or risk of its accumulation [11-12]. According to a 2021 publication, 4.1% of emergency room consultations among elderly Italians were reported to be linked to the negative effects of amiodarone, with a risk of hospitalization associated with cardiovascular issues. On the other hand, the so-called aquaphilic drugs tend to reach their maximum toxic concentration more quickly. This is the case of the common drugs used in cardiac pathologies, such as digoxin, propranolol, sotalol, and hydrochlorothiazide [13]. Due to the narrow therapeutic index of digoxin, even slight changes in plasma concentration can quickly lead to hazardous or subtherapeutic levels. Therefore, bioavailability consistency is crucial. Furthermore, even with normal digoxin concentrations, toxic symptoms may be present. Digoxin’s elimination half-life extends with age and the volume of distribution decreases. Digoxin is a commonly used medication for the treatment of congestive heart failure and arrhythmia,

despite its limited therapeutic index and potentially lethal toxicity, especially in older patients [14]. The principle of elimination is also affected – by the decline in hepatic metabolism and renal function. The latter is a major cause of elimination problems because most drugs are eliminated primarily through renal filtration, with very little elimination via the bile. Consequently, this can lead to drug accumulation and an increase in the half-life [8-9]. This affects, for example, drugs like biguanides, diazepam, lithiums, certain antibiotics like aminoglycosides – which forces the doctor to reduce the dose given to the patient [15-16]. Benzodiazepines (BZD), often used in the treatment of insomnia or anxiety disorders, tend to accumulate in the elderly due to their distribution. As a result, their toxicity increases. Additionally, repeated and prolonged use of benzodiazepine receptor agonists leads to modification of the type A γ -aminobutyric acid receptors. This modification decreases the potential for sedation but increases persistent amnesic effects, which can contribute to falls, accidents, fractures, and cognitive impairment [16]. Among patients with acute compound overdose, benzodiazepines accounted for the highest percentage of admissions to the emergency department (ED) and the second-highest percentage of admissions to the intensive care unit (ICU). Additionally, it was noted that among patients who experienced acute pharmaceutical overdoses, individuals with BZD overdoses were among those most frequently admitted to the emergency department (44%) and the intensive care unit (31%). Benzodiazepine's side effects and toxicity can lead to morbidity and even death in some patient groups, including the elderly, those with impaired lung function, and people with liver and renal problems [17]. More and more scientific publications conclude that polypharmacy is responsible for the sharp increase in fatal accidents among the elderly. As a result, polypharmacy patients are becoming more common in ED, which presents challenges for diagnosis and preventing the worsening of chronic illnesses during those visits [18]. Furthermore, polypharmacy is linked to death, incident disability, hospitalization, and ER visits in frail and prefrail older adults (but not in robust older people), according to a cohort study of 772 Spanish older adults [19]. A population-based cohort study conducted in Denmark revealed a link between mortality and the number of medications used. In summary, the fully adjusted model, which considered illnesses and the Barthel Index, demonstrated a mortality increase of more than 3% for each additional medicine [20]. In Poland, 38.6% of

people who had contact with emergency rooms and 19.6% of patients in ambulatory health care were people over 65 [21]. In Europe, it was estimated that nearly 5% of all hospital admissions were caused by ADEs (adverse drug event), and ADEs were responsible for 197,000 deaths annually. Better supervision of prescriptions and the doctor-patient relationship are a public health issue.

Patients with polypathology (or multimorbidity) living with two or more chronic illnesses – are typically older and taking multiple medications. Polypharmacy is present in 85% of cases, but it is not linked to higher survival rates [22]. Because polypathology is directly linked to polypharmacy, it is not surprising that polypharmacy is a major concern in this group of patients. Combining polypharmacy with the physiological changes brought on by aging raises the risk of drug-drug interactions (DDIs). When two or more pharmaceutical medicines are used concurrently, DDIs, which are anticipated adverse reactions can be attributable to pharmacokinetic or pharmacodynamic alterations [23]. According to research, individuals who take five to nine prescriptions have a 50% probability of experiencing a negative drug interaction; this risk rises to 100% when they take twenty or more medications [24]. Approximately 37% of patients with more than three chronic conditions takes five or more prescriptions each day, with 44% of patients taking at least one potentially inappropriate medication, according to a review of a random sample of patients aged 50 to 80 [23]. In 2019, high blood pressure and lower back pain or other chronic back problems affected almost $\frac{1}{4}$ of patients becoming the most frequent chronic illness and malady. Furthermore, at least 25% of those aged 70 or older had at least one illness such as diabetes or coronary heart disease [25].

In Poland there are 3.14 million of adults diagnosed with diabetes (according to data from 2022) [26]. Among people aged 60 and older one in four has diabetes [27]. When using corticosteroids with antidiabetic drugs it is necessary to monitor blood sugar regularly, as corticosteroid induce insulin resistance in the liver, adipocytes and skeletal muscle, as well as directly altering insulin secretion leading to hyperglycemia [28]. Some antipsychotic drugs such as olanzapine have a hyperglycemic value. They can provoke weight gain and hepatic glucose production and increase insulin resistance and plasma glucose concentration [29]. Some drug-drug interactions have a tendency to increase the risk of hypoglycemia (for instance sulfonylurea with fluconazole through CYP2C9 inhibition or clarithromycin through inhibition of

Table I. Percentages of indications of the most common diseases ailments by age groups in adults in 2019 [25]

Disease or ailment	15-29 years	30-39 years	40-49 years	50-59 years	60-69 years	70-79 years	80 years or more
High blood pressure	1.7 v	5.9	14.9	35.5	49.8	66.5	68.9
Lower back pain	6.1	13.6	24	35.6	38.5	45.2	51.3
Neck pain	3.3	7	13.8	23.3	25.8	29.7	31.4
Pain in the middle of the back	3.5	7.9	11.9	22.5	23.4	29.7	35.8
Osteoarthritis	–	1.1 v	7	18.9	29.3	44	52
Diseases of the thyroid gland	4.4	6.7	8.4	11.5	13.6	15.8	13
High lipid level	–	1.8 v	4.5	12.9	19.9	23.9	20.7
Allergy	9.1	8.3	7.5	8.5	8	10.5	7.6

(the symbol „v” means a number of between 20 and 50 answers; (dot) means a number of less than 20 answers

P-glycoprotein and CYP enzymes), and intensify reactions between metformin anticholinergics increasing the oral bioavailability of metformin modifying gastrointestinal motility [30]. The other aspect of common drug-to-drug interactions in Polish society is hypertension, affecting 9.94 million patients. According to the findings of the NATPOL 2011 research, Poland is expected to have almost 14 million more hypertension patients between the ages of 18 and 79 by 2035 [31]. There are many drugs that can raise blood pressure (BP), such as steroids or nonsteroidal anti-inflammatory drugs (NSAIDs). Additionally, several other variables commonly referred to as food-drug interactions, including alcohol, caffeine, grapefruit juice, and over-the-counter medicines may also impact blood pressure [32-33]. Corticosteroids may be the medications most strongly correlated with hypertension. In Japanese research, individuals receiving large doses of exogenous corticosteroids had elevated levels of renin substrate and decreased action of several vasodepressor mechanisms. As a result, blood pressure became difficult to manage [33]. While glucocorticoid-induced hypertension is a well-known problem, the exact mechanism underlying the blood pressure increase remains unclear [32], some speculate that this is a sign of 11β -hydroxysteroid dehydrogenase inhibition in the presence of cortisol or its analogs [33]. The other interactions can be caused by using NSAIDs, which raise the chance of starting antihypertensive medication (1.5–1.8 times higher than non-users) [32]. NSAIDs reduce renal perfusion and raise systemic blood pressure by inhibiting both COX-1 and COX-2's synthesis of prostaglandins. The diminished natriuresis caused by NSAIDs' COX-2 inhibitory action increases salt and water retention (which might exacerbate hypertension

patients' edema and blood pressure) and NSAIDs also modify the metabolism of arachidonic acid and/or raise blood pressure via inducing the synthesis of endothelin-1 [32,34]. Another example of drug interaction present among the elderly are anticoagulants. Vitamin K antagonists have constituted the mainstay of anticoagulation therapy for many years, despite of the number of patients treated with NOACs (novel oral anticoagulants) increasing significantly in the past few years. The use of antibacterials such as sulfamethoxazole-trimethoprim or even amoxicillin plus clavulanic acid, in combination with acenocoumarol leads to an over-coagulation, therefore resulting in a higher risk of bleeding [35]. Use of amiodarone reduces the action potential of warfarin (leading to a reduction in its anticoagulant function), which means the dosage of the latter must be adjusted [36]. Drug-drug interaction between verapamil and dabigatran (or macrolide interaction with NOAC) increase the risk of bleeding [35]. The patients should be aware of the risk of drug-drug interactions and what symptoms can appear. Understanding how medications interact with other substances is essential to preventing or minimizing side effects, including hospital stays. To prevent polypharmacy negligence, novel strategies like the use of a fixed-dose combination pill or medical audits should be put into practice [32].

Another contributor to the adverse drug effects is self-medication, which could be defined as: using medicine that friends or family recommends, not following a treatment plan, or altering the dosage of prescription drugs [37]. Based on data from the 2020 French Health Barometer, (a cross-sectional poll with data representative of the entire country) 48.7% of elderly people reported practicing self-medication. The most

commonly self-medicated non-prescription drugs were painkillers and antipyretics, followed by, drugs for cough and sore throat and drugs for heartburn and indigestion. Vitamins and minerals and drugs for stress or insomnia are often also self-medicated.

Nonsteroidal anti-inflammatory drugs are a highly popular class of drugs used for self-medication, particularly for pain relief. However, because they may cause gastrointestinal bleeding or peptic ulcers in high-risk individuals (those who are aged 75 and older or use oral, parenteral corticosteroids, anticoagulants, or antiplatelet agents), they are not advised as a first line of treatment for chronic pain. Nephrotoxicity has also been linked to NSAID usage in some cases.

When these medications are self-medicated and used without first being evaluated by a healthcare provider, the risk of those adverse effects occurring is higher. [37]. More than 30% of the elderly use NSAIDs like diclofenac. Diclofenac in combination with warfarin increases the INR (International Normalized Ratio) on average from 1 to 4 [39], causing an increase beyond the therapeutic range linked to pharmacokinetics. This reduction in clearance of warfarin leads to an increase

in its concentration and consequently influences the INR. Another example is ibuprofen in combination with an SSRI (selective serotonin reuptake inhibitor), which increases the prevalence of gastro-duodenal adverse effects. The risk is 10 times higher for SSRI alone and 4 times higher for NSAIDs alone, potentially leading to prolonged or even fatal bleeding. Commonly prescribed antidepressants like paroxetine and fluoxetine are also examples of selective serotonin reuptake inhibitors that may increase the risk of gastrointestinal bleeding because they prevent serotonin from being reabsorbed by thrombocytes [40].

The over-the-counter (OTC) medicine business is a dynamically growing one, mostly driven by self-medication. In addition to pharmacies, other places to obtain these medications include supermarkets, convenience stores and online retailers. Self-medication will undoubtedly be a major factor in the development of this industry in the years to come [41]. A survey performed by Suliga et al, found that 64.2% of Poland's senior population consumed dietary supplements. The most often utilized supplement ingredients among the senior population were magnesium (28.5%) and vitamin

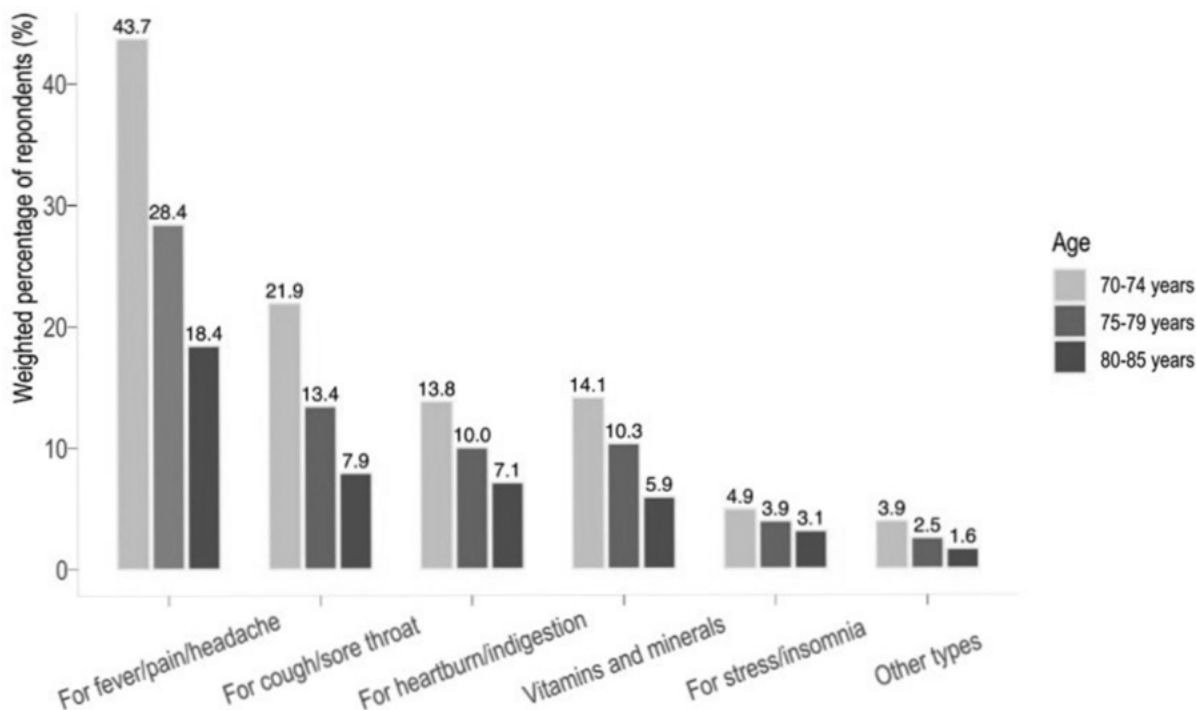


Figure 1. Nonprescription medication use by age groups (N=862) [38]

C (32.5%). While older people are the demographic that is most vulnerable to dietary deficits, it does not imply that there should be no limitations on the use of dietary supplements [42]. When medications and micronutrients share metabolic and transport routes, they might directly compete with one another, changing the pharmacokinetics or micronutrient status (absorption, distribution, metabolism, excretion) [43]. As a result, a micronutrient may negatively impact a drug's activity, for example: magnesium, calcium, and zinc can obstruct the gastrointestinal absorption of tetracycline antibiotics [44]. Given the intricate and potentially life-threatening interactions that exist between magnesium and certain cardiovascular medications (for instance, digoxin's ability to slow the ventricular response in atrial fibrillation is enhanced by magnesium) [45]. Patients taking these medications should have their magnesium status closely monitored. Because the negative consequences very often outweigh the positive ones, the increased use of possibly unnecessary medicaments for self-medication is concerning. In order to protect older people, lower the risk of side effects, and maintain their quality of life, it is crucial to limit self-medication of unnecessary drugs. Using dietary supplements and over-the-counter pharmacological substances without a doctor's advice may not be medically necessary and could even be dangerous [2]. The elderly require extra consideration when it comes to self-medication – due to the typical changes associated with aging, there is a higher risk of medication interactions, leading to a potential increase in adverse drug reactions (ADRs), which can be harmful to patients. Additionally, there is a possibility of an inaccurate or delayed diagnosis, which could prolong the patient's suffering from the illness [37]. More than 40 percent of medication errors are the result of inadequate reconciliation in admission, transfer or a discharge of patients handoffs [47]. In order to avoid mistakes, it's critical for healthcare professionals to communicate effectively with one another, as well as with their patients. Medication reconciliation is a structured procedure where healthcare providers collaborate with patients to guarantee the precise and comprehensive transmission of prescription information at the point of service [1]. This process should be based on creating lists of the drugs that are currently being taken, those that should be administered, and the pharmaceuticals that are currently available. Next, compare the lists, evaluate the medications, make clinical judgments based on the comparison and inform the patient and relevant care-

givers of the updated list [47]. Medication reviews and reconciliation have been shown to be beneficial, although widespread adoption of these practices is still challenging. These processes do require a significant amount of time and specialized knowledge, as well as effective organization and collaboration among various healthcare providers [46]. Some organizations have recognized STOPP (Screening Tool of Older Persons' Prescriptions) and START (Screening Tool to Alert to Right Treatment) as best practices. These criteria are used by doctors to examine possibly inappropriate drugs in older persons [48]. Preventing administration of potentially unsuitable drugs and ensuring the initiation of appropriate medications are crucial when prescribing for older individuals. The STOPP/START criteria provide a detailed list of medications. Approximately 70% of the criteria pertain to drugs that should either no longer be administered to older individuals or, if prescribed, should be discontinued due to concerns about polypharmacy and overprescribing for this population [49]. The increased body of published research between 2014 and 2022 on the use of medications to treat prevalent conditions that older adults face (such as diabetes, heart disease, and chronic obstructive pulmonary disease (COPD)), is reflected in the much higher number of STOPP/START criteria in version 3 [48].

The AGS Beers criteria are also commonly used by patients, study researchers, pharmacists, dispensers, and other professionals. They can be used to choose medications more effectively, educate patients and healthcare professionals, and lower the incidence of adverse drug events in older adults. This measure is also used to assess the cost, quality, and drug-use trends among the elderly [50]. These standards are becoming more and more prevalent in research into potentially inappropriate prescription which should generally be avoided in order to reduce the risk of medication-related damage in the elderly [48]. Moreover, adherence to therapies is a primary determinant of treatment success. The World Health Organization (WHO) defines medication adherence as 'the degree to which a person's behavior corresponds with the agreed recommendations from a healthcare provider'. Compliance, on the other hand, refers to how well a patient's behavior aligns with the prescriber's advice. Poor adherence and compliance can lead to serious health consequences, as supported by various studies (for instance, hospitalization rates were more than double in patients with hypertension, hypercholesterolemia, and diabetes mellitus). Simplifying

medication regimens, providing key information during prescribing, and scheduling appropriate follow-ups can all contribute to improving medication adherence [51].

Introduced in Poland on October 1, 2021 „Coordinated care” (OK – Opieka Koordynowana) programme (also known as integrated health care, entire or comprehensive care, or a patient-centered approach) [52] is a long-standing idea that has been implemented in many different forms throughout several health care systems globally. The primary objective of this solution is to offer health promotion, illness prophylaxis, diagnosis, treatment and management of diseases, as well as rehabilitation, through the execution of interconnected activities. Patients are being treated by a single physician, who oversees the full diagnostic and therapeutic process (or who has changed their pharmaceutical regimen during a hospital stay), which ensures continuity of care. The majority of the programme’s patients are chronically sick, older, and more likely to suffer from multimorbidity. A sizable fraction of them require medication optimization – that’s why the programme includes drug review referrals to a pharmacist [53]. Encouraging patients to bring all of their medications and supplements to their appointment and evaluating them is known as the “Brown Bag Review” of medications. The aim is to find out what medications individuals are taking and how they are taking them [53-54]. Comprehensive strategies carried out in collaboration with a pharmacist and a doctor present opportunities to enhance compliance generally and to lower the number of hospital admissions caused by improper prescription usage [53].

Summary

The average human lifespan has been unprecedentedly extended thanks to effective curative treatments (such as antibiotics) and preventative measures (such as immunizations and lipid-lowering medications) discovered in the previous century. The astounding advancement of modern medicine has had an unanticipated impact on the global demographic shift that is currently evident [55]. The aging of the world’s population will place a heavy burden on the healthcare system. In 2019, there were 703 million people globally who were 65 years of age or older, and by 2050, that number is predicted to rise to 1.5 billion [56]. Because pharmacotherapy is typically used to prevent and cure chronic illnesses that affect older individuals, senior patients are almost always

at a higher risk of requiring combination medication [55]. Patients with dementia may use medications more intricately if they experience communication difficulties due to cognitive decline and ongoing mental symptoms. Additionally, dementia is associated with an increased likelihood of having other chronic conditions, such as diabetes and hypertension, which further raises the risk of polypharmacy compared to individuals without dementia [56]. However, research indicates that polypharmacy is not exclusive to the elderly. As more and more illnesses (such as ADHD) can be effectively treated with medication, this phenomenon may be observed in people of various ages, including children. In addition to age, several other factors have been found to significantly impact the likelihood of polypharmacy. These factors include being female, having lower education levels, smoking, obesity, and institutionalization. Nevertheless, the senior population in Polish society remains the primary target of polypharmacy programmes due to the increasing prevalence of polypharmacy with age and the population aging [55].

This issue is supported by a new WHO study on polypharmacy, which calls for all nations to act quickly to safeguard patients from the negative consequences by putting in place specialized programmes. In an effort to control and minimize incorrect prescriptions, a number of clinical recommendations and algorithms have been developed thus far. Beers and STOPP/START criteria are among the most widely recognized tools. The WHO study lists many feasible solutions for lessening the impact of the polypharmacy issue and highlights numerous European initiatives aimed at achieving this objective. With the goal of maximizing the use of pharmaceuticals and enhancing health outcomes, the WHO study specifically promotes the use of medication reviews or systematic assessments of a patient’s prescription regimen [1,55].

Conflict of interest

None

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