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Polypharmacy in Elderly Patients: Clinical Risks, Drug Interactions and Strategies for Optimization – A Narrative Review

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Abstract

Background. Population aging and the growing prevalence of multimorbidity have led to an increasing number of older adults receiving multiple medications. Polypharmacy, commonly defined as the use of five or more medications, is associated with adverse drug reactions, drug interactions, functional decline, hospitalization, and mortality. Age-related physiological changes further increase susceptibility to medication-related harm.

Aim. To review the epidemiology, clinical risks, drug interactions, and optimization strategies associated with polypharmacy in elderly patients.

Material and methods. A narrative review of the literature was conducted using peer-reviewed articles, clinical guidelines, and consensus documents addressing polypharmacy in adults aged 65 years and older. Evidence related to epidemiology, pharmacological changes associated with aging, adverse drug events, assessment tools, potentially inappropriate medications, and optimization strategies was analyzed and synthesized narratively**.**

Results. Polypharmacy is highly prevalent among older adults, especially those with multimorbidity and frailty. Age-related pharmacokinetic and pharmacodynamic changes increase the risk of adverse drug reactions and clinically significant drug interactions. Common consequences include falls, delirium, cognitive impairment, hospitalization, and increased mortality. Tools such as the Beers Criteria, STOPP/START criteria, and Medication Appropriateness Index help identify inappropriate prescribing. Key optimization strategies include comprehensive geriatric assessment, medication review, deprescribing, and interdisciplinary care.

Conclusions. Polypharmacy remains a major challenge in geriatric care. Regular medication review, individualized treatment planning, and deprescribing interventions are essential to reduce medication-related harm and improve clinical outcomes in older adults.

Key words: polypharmacy, elderly patients, drug–drug interactions, deprescribing.

1. Introduction

Aging population is becoming one of the key challenges faced by modern healthcare systems across the globe. An increased lifespan, combined with a greater prevalence of chronic diseases, has led to the presence of more elderly patients requiring complicated and/or long-term medical treatment. It is within this context that the problem of polypharmacy – defined as concomitant administration of several drugs and usually characterized as frequent usage of five or more pharmaceutical preparations, both prescribed and over-the-counter (OTC) drugs, along with complementary medicines – has become highly relevant in contemporary healthcare practice [1,2,3]. Attention needs to be paid to two forms of polypharmacy: appropriate polypharmacy and inappropriate polypharmacy, which denotes unjustified and potentially harmful drug prescriptions [4,5].

The incidence of polypharmacy has been significantly increasing during the last decades, especially among individuals aged 65 years or more and patients suffering from multiple chronic conditions [6,7]. There are multiple reasons for such a tendency, including fragmented health services, disease-centered treatment guidelines, and the prescribing cascade, when patients are given more drugs in order to address adverse drug reactions, instead of treating their causes [7,8,9,10].

Older individuals are particularly prone to experiencing negative effects due to age-related alterations in pharmacokinetics and pharmacodynamics [11]. Decreased renal excretion, altered metabolism, and increased sensitivity to drugs make them more susceptible to toxicity, with additional complications being posed by their frailty status [11].

Some of the adverse consequences caused by polypharmacy include adverse drug reactions (ADRs), drug-drug interactions (DDIs), and drug-disease interactions [11]. They can result in impaired physical function and development of geriatric syndromes like falls, delirium, and cognitive decline [6]. Complicated treatment regimens can be tied to poor adherence, frequent hospitalization, and mortality [6,12].

The utilization of potentially inappropriate medications (PIMs) – drugs which may cause more harm than benefit in older adults – is considered one of the characteristics of inappropriate polypharmacy. PIMs are identified with the help of guidelines such as the Beers Criteria, STOPP/START criteria, and MAI; however, they are not consistently used in clinical practice [13,14].

To tackle the problem of polypharmacy in older people, certain interventions, such as CGA, structured medication review, and deprescribing, should be employed [12,15,16,17]. It is also important to engage multiple health professionals in the treatment process [18].

Given the growing impact of polypharmacy, understanding its risks and management is crucial. This narrative review provides an overview of polypharmacy in elderly patients, focusing on clinical risks, drug interactions, and optimization strategies.

2. Research materials and methods

This narrative review was conducted to summarize current evidence regarding polypharmacy in elderly patients, with particular emphasis on clinical risks, drug interactions, potentially inappropriate medications, and optimization strategies. Relevant literature published in peer-reviewed journals, clinical guidelines, and consensus documents was identified through a non-systematic search of major biomedical databases, including PubMed

and Google Scholar. The search focused on publications addressing polypharmacy, adverse drug reactions, drug–drug interactions, deprescribing, comprehensive geriatric assessment, and medication appropriateness in adults aged 65 years and older. Priority was given to recent reviews, clinical practice guidelines, and validated assessment tools, including the Beers Criteria, STOPP/START criteria, and Medication Appropriateness Index. The selected publications were analyzed narratively to provide an up-to-date overview of the epidemiology, risks, assessment methods, and management approaches related to polypharmacy in geriatric populations.

3. Research results

3.1. Aging and Pharmacology

Aging brings physiological changes that alter drug disposition and response, heightening interindividual variability and adverse outcome risk in older adults. These involve both pharmacokinetics (PK) and pharmacodynamics (PD), further modified by frailty, which complicates pharmacotherapy [6].

Key PK changes affect distribution and elimination most. Increased body fat with reduced lean mass and total body water prolongs the half-life of lipophilic drugs and raises plasma concentrations of hydrophilic ones [8,19]. Hepatic metabolism is largely preserved, though reduced first-pass effect can increase bioavailability of some agents [8]. Renal function declines progressively and represents the most clinically significant change, promoting drug accumulation and toxicity; thus, dosing must be adjusted according to estimated glomerular filtration rate [8].

PD alterations increase drug sensitivity at similar concentrations. Older adults show heightened responses to centrally acting drugs (sedatives, opioids, anticholinergics) and to agents affecting blood pressure or coagulation [8]. This translates into greater risk of sedation, falls, hypotension, and bleeding, even at standard doses.

Frailty—a distinct syndrome of diminished physiological reserve, marked by weakness, weight loss, low activity, and poor resilience to stressors—amplifies these risks and reduces medication tolerance [6,20]. Unlike chronological age alone, frailty demands individualized prescribing, slow dose titration, and frequent reassessment.

In summary, age-related PK/PD changes combined with frailty necessitate a cautious, patient-specific approach to prescribing in older adults.

3.2. Epidemiology and Drivers of Polypharmacy

Polypharmacy, which has been defined by the regular intake of five or more medications, becomes highly prevalent with advancing age and is seen in 30–50% of older community-residents aged 65 and above (and 50% or even greater percentages in nursing home settings, among multimorbid patients) [3,19].

Multimorbidity appears to be the key factor: the presence of another chronic condition typically results in another prescription and rapid complication of regimens [21]. Care fragmentation contributes to the phenomenon as well since several prescribers can prescribe without adequate collaboration, causing duplicative therapy [22]. Prescribing cascades refer to cases where adverse reactions to medications are misdiagnosed as separate diseases and treated with more medications [10]. Over-the-counter (OTC) drugs and dietary supplements, which are frequently left off the list of prescribed medicines, present a potential for dangerous interactions [23].

The system factors that contribute to the development of polypharmacy include ineffective communication between prescribers, lack of routine medication reviews, guidelines that focus on a single disease and overlook multimorbidity, and prescribing inertia—the failure to deprescribe when clinical circumstances change [8].

To conclude, polypharmacy in geriatric patients is very frequent and multidimensional and is associated with various factors.

3.3. Clinical Risks and Drug Interactions in Polypharmacy

Polypharmacy substantially elevates medication-related harm in older adults through additive effects of multimorbidity, age-related PK/PD changes, and complex regimens. Adverse drug reactions (ADRs) rise with medication count and often present atypically, mimicking underlying disease and triggering further prescribing [11].

Drug–drug interactions (DDIs) occur when a substance modifies the pharmacokinetics and pharmacodynamics of another substance through absorption, distribution, metabolism, or excretion processes [24]. Pharmacokinetic DDIs are amplified by reduced hepatic and renal function; cytochrome P450 inhibition (e.g., CYP3A4, CYP2D6) increases drug levels and toxicity, while induction may diminish efficacy [25,26]. Transporters such as P-glycoprotein also play a role, particularly for cardiovascular and central nervous system drugs [27]. Pharmacodynamic interactions add risk when drugs with similar effects are combined.

High-risk combinations warrant particular caution: anticoagulants with NSAIDs heighten bleeding risk; renin–angiotensin system inhibitors combined with potassium-sparing diuretics can cause hyperkalemia; and multiple CNS depressants (e.g., benzodiazepines, opioids, sedatives) markedly increase respiratory depression, delirium, and falls [28]. Drug–disease interactions may worsen preexisting cardiovascular, renal, or cognitive conditions.

Such harms contribute to geriatric syndromes—including falls, delirium, and cognitive decline—leading to functional loss, reduced adherence, higher healthcare utilization, and increased mortality [6,4]. Prescribing cascades perpetuate the cycle.

In summary, polypharmacy drives adverse outcomes largely via interactions and inappropriate use. Timely recognition of high-risk combinations and routine medication review are essential for harm reduction [15].

3.4. Assessment and Identification of Polypharmacy

Assessment should be done systematically by taking into account clinical, functional, and social aspects. Comprehensive Geriatric Assessment (CGA) helps in identifying the functional status of patients, cognition, and social support system which indicates factors responsible for increasing ADRs or poor adherence, along with the role of polypharmacy in causing a decline in the functional status of elderly people [11].

Medication review is a crucial component of deprescribing. Prescription review focuses on technical aspects like dosing, and clinical medication review considers patient-related aspects such as comorbidities, frailty, and goals of care. Clinical medication review becomes relevant when considering deprescribing in the geriatric population [16].

Tools are used in risk stratification in medication use. Medication Regimen Complexity Index (MRCI) helps in estimating the regimen complexity that can lead to non-adherence. Drug Burden Index (DBI) estimates the total burden of anticholinergics and sedatives which cause problems in physical and cognitive functioning [12]. Information obtained through CGA and systematic medication review along with use of tools like MRCI or DBI would guide clinicians towards medications that need deprescribing and adjustment of dose which is the first step towards optimizing the treatment [3].

In summary, combining CGA, structured medication review, and targeted tools enables identification of high-risk patients and informs targeted optimization.

3.5. Potentially Inappropriate Medications (PIMs)

Potentially inappropriate medications (PIMs) are defined as drugs where risks might outweigh benefits particularly in older individuals. Their use correlates with higher ADR rates, hospitalization, functional decline, and mortality [29,30]. Several tools can be used to identify such medications.

The 2023 American Geriatrics Society Beers Criteria is one of the most widely used explicit tools. It provides a list of medications that are potentially inappropriate for older adults, categorized based on their risk profiles, drug–disease interactions, and required dose adjustments [28].

The STOPP/START version 3 (2023) (Screening Tool of Older Persons' Prescriptions / Screening Tool to Alert to Right Treatment) offer a complementary approach. The STOPP component identifies medications that should potentially be discontinued, while the START criteria highlight common prescribing omissions where beneficial medications may be underused [14].

The Medication Appropriateness Index (MAI) is an implicit tool that assesses the appropriateness of individual medications based on clinical judgment. It considers factors such as indication, effectiveness, dosage, directions, drug–drug and drug–disease interactions, and duplication. Although more time-consuming, it allows for a more individualized evaluation [13].

High-risk classes include centrally acting agents (benzodiazepines, anticholinergics) linked to sedation, delirium, cognitive impairment, and falls; NSAIDs associated with gastrointestinal bleeding, renal injury, and cardiovascular events; and long-term proton pump inhibitors without clear indication, which may increase fracture and infection risk [8].

In summary, PIMs represent a modifiable contributor to harm. Systematic screening with validated tools promotes safer, more appropriate prescribing.

3.6. Strategies for Optimization

Optimizing pharmacotherapy in older patients necessitates a comprehensive approach, with due consideration of the medication burden as well as the medical needs of the patient. Essential components consist of deprescribing, individualized care, interdisciplinary collaboration, and system-level support.

Deprescribing involves systematic identification and discontinuation of drugs that are no longer indicated, ineffective, or harmful [3,5,7]. The process includes: (1) identifying candidates based on adverse effects, interactions, limited efficacy, or mismatch with life expectancy and goals; (2) prioritizing agents according to risk–benefit ratio and withdrawal potential; and (3) close monitoring for symptom recurrence or withdrawal effects, with timely follow-up and adjustment as needed [5,31].

Personalized prescribing goes beyond guideline-based care by taking into consideration the multiple conditions of a patient, their frailty, functionality, life expectancy, and values [32]. In most situations, improving the quality of life, relief from symptoms, and functional independence should be prioritized over achieving a therapeutic target.

The collaboration among an interdisciplinary team consisting of physicians, pharmacists, and nurses improves results by means of joint assessment and education related to medications [18]. Effective communication reduces duplication and errors across care transitions.

Practical tools include conducting frequent structured reviews of medications (prescription, OTCs, and supplements), using clinical decision support systems (carefully to prevent alert fatigue), medication reconciliation during transition phases of care, and engaging patients through effective communication and shared decision-making [8,33].

In summary, successful optimization integrates deprescribing, patient-centered planning, team-based care, and systematic review to minimize harm and align therapy with individual needs.

3.7. Future Directions and Research Gaps

Despite the growing awareness of the dangers associated with polypharmacy, several significant issues still exist. The application of precision medicine, through the use of pharmacogenomics, might be useful in creating personalized therapy according to the individual's genetic constitution, presence of comorbid diseases, and degree of frailty; the detection of CYP2D6 or CYP2C19 gene mutations may aid clinicians in adjusting medication doses or making informed decisions to avoid adverse effects in patients taking multiple drugs [34,35]. Artificial intelligence could examine a patient's complicated regimen, detect interactions between the prescribed medications, and provide immediate decision-making assistance to healthcare providers; recent research utilizing artificial intelligence has demonstrated success in automatic generation of deprescribing recommendations by applying

Beers or STOPP criteria [36]. Additional research is necessary to develop effective and clinically relevant deprescribing tools and algorithms for implementation into clinical practice among different patient populations. Future studies should adopt inclusive designs that better reflect real-world geriatric populations and evaluate implementation strategies in diverse healthcare settings.

4. Discussion

The implications of the research studies covered in this review demonstrate that polypharmacy in elderly patients is a complex and multidimensional problem that is influenced by physiological aging, the shortcomings in the health care system, and the use of medications. The changes in pharmacodynamics and pharmacokinetics associated with aging and the presence of chronic diseases contribute to the heightened vulnerability to toxic reactions to medications and geriatric syndromes. Frailty also poses an additional challenge in managing patients' conditions, calling for more sophisticated approaches than chronological age alone.

One of the critical problems linked with polypharmacy in older people is the prevalence of adverse drug reactions and adverse interactions that are caused by prescribing cascades. Such effects usually result in a decrease in functionality, greater hospitalization rate, and death. The effective management of this issue involves a systematic identification of people at risk with the use of such strategies as geriatric assessment and medication reviews.

Any optimization strategy should always focus on the patient as the center of any care plan, taking into account evidence-based practices along with personal goals, longevity, and quality of life. The practice of deprescribing, when used in conjunction with collaboration among interdisciplinary professionals, proves to be an important step as long as the right monitoring is applied. Despite many accomplishments in recent years, most clinical guidelines still do not address issues of multimorbidity and frailty, and frail elderly patients are underrepresented in clinical trials. New methods of management, such as pharmacogenomics and artificial intelligence assistance, are considered promising.

In conclusion, addressing polypharmacy demands a comprehensive, individualized, and system-oriented approach. By combining careful assessment, evidence-based tools, deprescribing strategies, and interdisciplinary collaboration, clinicians can mitigate risks and better align pharmacotherapy with the needs of the aging population.

5. Conclusions

Polypharmacy in elderly patients is, by nature, not inherently dangerous, but can become dangerous if not optimized. There are several reasons for the negative effects that come along with polypharmacy in elderly patients, but most of them can be changed. Taking a narrative approach focused on optimizing the four key areas of polypharmacy optimization will provide the best chance of success in providing safe medication management to these vulnerable patients. By tailoring treatment options to fit the needs of each person according to their preferences, functional abilities, and life expectancy, clinicians can help these patients live healthier lives.

Disclossure

All authors have read and approved the final version of the manuscript for publication.

Author Contributions

Conceptualization, R.W. and K.W.; methodology, S.W.; software, F.K.; validation K.W. and S.W.; formal analysis W.W.; investigation, M.D.; resources J.O.; data curation W.W.; writing—original draft preparation R.W.; writing—review and editing H.L. and M.D.; visualization W.W.; supervision M.P.; project administration, F.K.; funding acquisition R.W. All authors have read and agreed to the published version of the manuscript.

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The authors declare no conflicts of interest.

Declaration of the Use of Generative AI and AI-Assisted Technologies in the Writing Process

During the preparation of this work, the authors used ChatGPT for the purpose of language editing and grammar correction of the English text to improve readability and linguistic accuracy. After using this tool, the authors reviewed and edited the content as needed and take full responsibility for the substantive content of the publication.

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