POLYPHARMACY IN OLDER ADULTS: BALANCING THERAPEUTIC BENEFITS AND MEDICATION-RELATED HARM

Bekim ISMAILI[1], Yllzana SINANI[1], Diellza MAZLLAMI[1], Maida VELI[1]

[1*]*Department of General Medicine, Faculty of Medical Sciences*
[*]*Corresponding author e-mail: bekim.ismaili@unite.edu.mk*

Abstract

This paper focuses on polypharmacy in older adults, defined as the use of five or more medications, and its increasing impact on public health. The aim is to highlight the clinical risks associated with polypharmacy, including adverse drug reactions, drug-related problems, hospital admissions, and mortality.
The study reviews current literature to evaluate the consequences of excessive medication use and the factors contributing to polypharmacy, such as multimorbidity and inappropriate prescribing. It also examines key strategies to reduce medication-related harm, including medication review, deprescribing, and improved communication among healthcare professionals.
While pharmacotherapy is essential in managing chronic diseases, the risks associated with multiple medications are significant, particularly in elderly populations. The paper emphasizes the importance of a multidisciplinary and patient-centered approach to optimize medication use and improve patient safety.

Keywords: polypharmacy, deprescribing, elderly patients, adverse drug reaction, drug-related problems, medication management, pharmacotherapy optimization

Introduction

The increasing use of multiple medications among older adults has become a major concern in modern healthcare. This condition, known as polypharmacy, is commonly defined as the use of five or more medications and is frequently associated with complex clinical management. As the population ages and the prevalence of chronic diseases rises, polypharmacy has become more widespread, leading to important safety challenges in pharmacotherapy.
The study aims to explore the clinical consequences associated with polypharmacy, including drug-related problems, hospital admissions, and mortality risk. It also seeks to highlight evidence-based strategies for optimizing medication use in older patients, with particular focus on medication review and deprescribing practices. Furthermore, the study emphasizes the importance of a multidisciplinary and patient-centered approach in medication management.
Effective collaboration between physicians, pharmacists, and patients is essential to ensure appropriate prescribing and to reduce the risks associated with inappropriate medication use. Overall, this research aims to underline the need for balancing therapeutic benefits with potential adverse effects in order to improve the safety and quality of pharmacological treatment in elderly populations.

Material and methods

This study was conducted as a narrative literature review focusing on polypharmacy in older adults and its associated clinical outcomes. A structured literature search was performed using PubMed, Web of Science, Scopus, and Google Scholar. The search included combinations of the following keywords: “polypharmacy”, “older adults”, “deprescribing”, “adverse drug reactions”, and “drug–drug interactions”. Studies published between 2015 and 2025 were prioritized.

Inclusion criteria were studies involving patients aged ≥65 years and addressing polypharmacy or deprescribing. Studies focusing exclusively on single diseases without relevance to polypharmacy or involving non-elderly populations were excluded.
Priority was given to high-quality evidence, including systematic reviews, meta-analyses, and large cohort studies. Data from selected studies were analyzed and synthesized descriptively, with emphasis on prevalence, clinical consequences, and strategies for optimizing medication use in older adults.

Results

Prevalence of Polypharmacy in Elderly Population

A large systematic review and meta-analysis conducted by Wang et al. [1] included 122 observational studies with a total population of over 57 million individuals. The authors reported that the global prevalence of polypharmacy in older adults was approximately 39.1% (95% CI: 35.5%–42.7%), while hyperpolypharmacy reached 13.3%. Higher prevalence rates were observed in Europe and North America compared to other regions. Factors such as advanced age (≥70 years) and residence in nursing homes were associated with an increased risk of polypharmacy. These findings highlight the significant global burden of polypharmacy and emphasize the need for appropriate medication management strategies in older populations. [1]

Adverse Drug Reactions

The risk of adverse drug reactions (ADRs) increases with the number of medications used, making polypharmacy a significant contributing factor. Older adults are particularly vulnerable due to age-related changes in pharmacokinetics and pharmacodynamics.
Studies report an incidence of approximately 5.7 ADRs per 100 elderly patients and a prevalence of 6.1 per 100 in general practice settings. Patients experiencing ADRs were found to use a higher number of medications compared to those without adverse effects.
Common drug classes associated with ADRs include antibiotics, antihypertensives, and non-steroidal anti-inflammatory drugs, which are frequently linked to gastrointestinal symptoms and dermatological reactions.
Although some studies suggest a direct correlation between the number of medications and ADR risk, findings remain inconsistent. This variability may be due to differences in study design, patient populations, and reporting methods.
Overall, polypharmacy remains an important risk factor for ADRs, emphasizing the need for careful medication review and monitoring in older patients. [2]

Potentially Inappropriate Medications

The Beers Criteria was developed by the late Mark Beers, MD, and colleagues at the University of California Los Angeles in 1991, with the purpose of identifying medications for which potential harm outweighed the expected benefit and that should be avoided in nursing home residents. (Table 2) The 1997 update, led by Dr. Beers, expanded the criteria to apply to all older adults. (Table 3) The criteria was updated by an interprofessional group in 2003 and the

American Geriatrics Society took over stewardship in 2010. The 2023 American Geriatrics Society (AGS) Beers Criteria (AGS Beers Criteria) for Potentially Inappropriate Medication (PIM) Use in Older Adults is the seventh overall update and fourth since AGS became the criteria's steward. As with previous updates, the AGS and its expert panel have attempted to preserve the spirit and intent of the original Beers Criteria by providing an explicit list of PIMs that are best avoided by older adults in most circumstances or under specific situations, such as certain diseases, conditions, or care settings. The AGS Beers Criteria® comprises drugs and drug classes that the AGS and its expert panel consider to be potentially inappropriate medications (PIMs) for use in older adults. The expert panel organized the criteria into the same five general categories that were used in the 2019 update:

1. Medications considered as potentially inappropriate (Table 2);
2. Medications potentially inappropriate in patients with certain diseases or syndromes (Table 3);
3. Medications to be used with caution (Table 4);
4. Potentially inappropriate drug–drug interactions (Table 5); and
5. Medications whose dosages should be adjusted based on renal function (Table 6).

Table 2: Medications to Avoid in Older Adults (General)

Drug/Class	**Examples**	**Main Risk/Rationale**	**Recommendation**
First-generation antihistamines	Diphenhydramine, Hydroxyzine	Strong anticholinergic effects → confusion, dry mouth, constipation, falls, delirium	**Avoid**
Aspirin (primary prevention)	—	High bleeding risk, no net benefit	**Avoid initiating**
Rivaroxaban	—	Higher GI & major bleeding vs alternatives	**Avoid for long-term use**
Benzodiazepines	Diazepam, Lorazepam	Cognitive impairment, delirium, falls, fractures	**Avoid**

Z-drugs	Zolpidem	Similar risks to benzodiazepines, minimal benefit	**Avoid**
Long-acting sulfonylureas	Glyburide, Glimepiride	Prolonged hypoglycemia	**Avoid**
Proton Pump Inhibitors (PPIs)	Omeprazole	*C. difficile*, fractures, bone loss	**Avoid >8 weeks** (unless indicated)

Table 3: Drugs to Avoid with Specific Diseases

Condition	**Avoid**	**Why**
Heart failure	NSAIDs, COX-2 inhibitors, Diltiazem, Verapamil	Fluid retention, HF exacerbation
Syncope	AChE inhibitors, Alpha-1 blockers, TCAs	Orthostatic hypotension, bradycardia
Dementia	Anticholinergics, Benzodiazepines, Z-drugs	Delirium, cognitive decline
Falls/fractures history	Antiepileptics, Antipsychotics, SSRIs	Ataxia, impaired balance, syncope

Table 4: Medications to Use with Caution

Drug/Class	**Concern**	**Clinical Note**
Amiodarone	Multiple toxicities	May be used in HF for rhythm control
Dabigatran, Edoxaban	Increased GI bleeding (≥75 yrs)	Compare with warfarin
SGLT2 inhibitors	Urogenital infections, euglycemic DKA	Monitor closely
Diuretics	SIADH, hyponatremia	Monitor sodium levels

Table 5: Clinically Significant Drug–Drug Interactions

Combination	**Risk**
ACEIs + Spironolactone	Hyperkalemia
Anticholinergic + Anticholinergic	Cognitive decline, falls
Corticosteroids + NSAIDs	Peptic ulcer, GI bleeding
Warfarin + NSAIDs	Major bleeding
Opioids + Benzodiazepines/Gabapentinoids	Sedation, respiratory depression, overdose

Table 6: Renal Dose Adjustment / Avoidance

Drug	**Issue in Renal Impairment**	**Recommendation**
Ciprofloxacin	CNS toxicity (seizures)	Avoid/reduce if CrCl <30 mL/min
Gabapentin, Pregabalin	CNS depression, sedation	Dose reduction required
Enoxaparin	Bleeding risk	Reduce dose if CrCl <30
Trimethoprim-SMX	Hyperkalemia, renal worsening	Use cautiously

[3],[4]

Potential Drug-Drug Interactions

Polypharmacy is a common finding among hospitalized patients and is closely associated with an increased risk of potential drug–drug interactions (pDDIs). In the analyzed cohort, more than half of patients were receiving five or more medications, and the vast majority were exposed to at least one interaction. Most identified interactions were classified as moderate in severity and typically required monitoring rather than immediate discontinuation of therapy. Although pharmacokinetic interactions accounted for a smaller proportion of all detected interactions, they remain clinically important, particularly those involving drug metabolism via cytochrome P450 enzymes such as CYP3A4. Notably, the number of prescribed medications

was the strongest predictor of interaction risk, with significantly higher odds observed in patients receiving more than seven drugs.

Drug Combination	**Mechanism**	**Risk**	**Clinical Recommendation**
Omeprazole + Cefuroxime	↑ gastric pH → ↓ absorption	Moderate (X)	Avoid combination
Levofloxacin + Calcium	Chelation → ↓ absorption	Moderate (D)	Separate by ≥2 hours
Clopidogrel + Omeprazole	CYP2C19 inhibition	Major (D)	Avoid; use alternative PPI
Amlodipine + Simvastatin	CYP3A4 inhibition	Moderate	Limit simvastatin ≤20 mg
Amiodarone + Acenocoumarol	CYP2C9 inhibition	Major (D)	Reduce anticoagulant dose
Methotrexate + NSAIDs	↓ renal excretion	Moderate	Avoid, especially high doses
Dabigatran + Amiodarone	P-gp inhibition	Moderate	Monitor for bleeding
Fluconazole + Apixaban	CYP3A4 inhibition	Major	Monitor bleeding risk

[5], [6], [7], [8]

The Role of Lack of Coordination Among Healthcare Providers

Polypharmacy management is often complicated by poor coordination among healthcare providers, leading to duplication of therapy, inappropriate prescribing, and increased risk of adverse drug events. [9]

Patients frequently experience confusion and non-adherence due to complex medication regimens, while fragmented care can result in prescribing cascades, where additional medications are introduced to manage side effects of existing therapies.

Improving communication between physicians, pharmacists, and other healthcare professionals is essential to minimize these risks. Interprofessional collaboration has been shown to enhance medication review processes, support deprescribing, and improve patient outcomes. [15]

Evidence suggests that deprescribing interventions can reduce potentially inappropriate medications by up to 30–60% and improve adherence to remaining therapies. [11-14]

Discussion

Overall Burden of Polypharmacy in Older Adults

The findings of this review demonstrate that polypharmacy in older adults is a widespread and clinically significant issue, strongly associated with increased risk of adverse drug reactions (ADRs), drug–drug interactions, and reduced quality of life. These findings are consistent with large-scale epidemiological data reporting a high global prevalence of polypharmacy, particularly in older populations. [1,19,20]

Adverse Drug Reactions and Inappropriate Prescribing

The results presented in section 3.2 highlight that ADRs increase with the complexity of medication regimens, with commonly implicated drug classes including antibiotics, antihypertensives, and NSAIDs. Although the relationship between number of medications and ADR incidence is not always linear, patients receiving multiple drugs were consistently found to have higher overall exposure to adverse outcomes. [2,6,7]

Furthermore, the analysis of potentially inappropriate medications using the Beers Criteria (Tables 2 and 3) demonstrates that several commonly prescribed drugs in older adults, including benzodiazepines, anticholinergics, and long-acting sulfonylureas, significantly increase the risk of cognitive impairment, falls, and hypoglycemia. [3,4] These findings emphasize the importance of regular medication review and avoidance of high-risk drug classes in geriatric populations.

Drug–Drug Interactions and Clinical Complexity

Drug–drug interactions (Tables 5 and 6) further illustrate the clinical complexity of polypharmacy. Pharmacokinetic interactions involving CYP450 enzymes, as well as clinically relevant combinations such as ACE inhibitors with spironolactone or opioids with benzodiazepines, contribute significantly to morbidity in older patients. [5,8] In addition, renal impairment further increases drug toxicity risk, requiring dose adjustments or avoidance of specific medications such as gabapentin and enoxaparin.

A major contributing factor identified in this review is poor coordination among healthcare providers (section 3.5), which leads to duplication of therapy, prescribing cascades, and fragmented care. These cascades often result in additional medications being prescribed to treat adverse effects of existing therapy, further increasing medication burden and risk of harm. [9]

Importantly, deprescribing strategies and interprofessional collaboration have been shown to significantly reduce inappropriate polypharmacy. Evidence indicates that structured medication review and coordinated deprescribing can reduce potentially inappropriate medication use by 30–60%, improve adherence, and decrease hospitalization rates. [11-15] The findings from the included studies (Table 4 and deprescribing literature) strongly support a multidisciplinary approach involving physicians, pharmacists, and nurses to optimize pharmacotherapy.

Despite these findings, this review has limitations, including its narrative design, heterogeneity of included studies, and lack of quantitative synthesis, which may limit generalizability. [16-18]

Conclusion

This review highlights that polypharmacy in older adults is a significant and growing clinical problem associated with adverse drug reactions, drug–drug interactions, inappropriate prescribing, and reduced quality of life. Findings from this study demonstrate that the risk of medication-related harm increases with the number and complexity of prescribed drugs, particularly in the presence of high-risk medications identified by the Beers Criteria and clinically significant drug–drug interactions. Renal impairment further exacerbates this risk, requiring careful dose adjustment and medication selection.

Poor coordination among healthcare providers contributes to duplication of therapy and prescribing cascades, which further increase medication burden and adverse outcomes. This emphasizes the need for structured communication and coordinated care in managing older patients.

Deprescribing, supported by interprofessional collaboration between physicians, pharmacists, and other healthcare professionals, has been shown to significantly reduce inappropriate medication use and improve patient outcomes.

Overall, optimal management of polypharmacy requires a patient-centered, multidisciplinary approach that balances therapeutic benefits with potential harms, supported by regular medication review and evidence-based prescribing tools.

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