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Effectiveness and safety of deprescribing interventions in older adults with polypharmacy: a review of clinical trials from 2017 to 2026

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Abstract

Background. Population aging contributes to the rising prevalence of multimorbidity and polypharmacy, which increase the risk of adverse drug events and deterioration in quality of life among older adults. Deprescribing is a planned process of treatment optimization aimed at reducing unnecessary medication burden and improving patient well-being.

Aim. The objective of this study is to summarize current scientific evidence on the clinical effectiveness and safety of deprescribing interventions in older adults based on a review of clinical trials published between 2017 and 2026.

Material and methods. A review of English-language clinical trials published between 2017 and 2026 was conducted using the PubMed and Google Scholar databases, with the following search terms: “deprescribing,” “polypharmacy,” “inappropriate prescribing” and “potentially inappropriate.” Studies assessing the safety and clinical outcomes of deprescribing in individuals aged 65 years and older with polypharmacy were included.

Results. Deprescribing appears to have a neutral effect on mortality and hospitalizations, supporting the safety of this intervention. Its impact on the incidence of falls in older adults remains inconclusive. At the same time, improvements in quality of life, functional status, and selected cognitive functions are observed, particularly following the reduction of central nervous system–acting medications and drugs with anticholinergic properties.

Conclusions. Deprescribing is a safe treatment strategy that improves selected aspects of patient functioning. Rational medication selection, rather than the total number of medications,

is of key importance. Future studies should incorporate extended follow-up periods to better assess long-term health outcomes.

Key words: deprescribing, polypharmacy, aged, inappropriate prescribing.

1. Introduction

The progressive aging of societies and the systematic extension of average life expectancy lead to a rapid increase in multimorbidity, defined as the coexistence of two or more chronic conditions in a single patient. A direct consequence of treating numerous diseases is the rising prevalence of polypharmacy, which the World Health Organization defines as the concurrent use of five or more medications [1]. This phenomenon is intensifying globally; in Europe, polypharmacy affects an average of 32.1% of the geriatric population [2]. According to studies based on the Polish National Health Fund database, the prevalence of polypharmacy among individuals over 65 years of age in Poland ranges from 42.1% to 43.1%, while among seniors over 80 years of age, this percentage reaches 55.0–56.0%. When accounting for both reimbursed and non-reimbursed medications, the scale of the problem in Poland may involve as many as 62.9% of older adults [3].

This population is particularly vulnerable to adverse drug reactions due to age-related physiological changes and chronic conditions, which significantly alter the pharmacokinetics and pharmacodynamics of medications. The risk of adverse drug events and drug-drug interactions increases proportionally with the number of medications taken. A critical challenge in this population is the use of potentially inappropriate medications (PIMs), defined as drugs for which the potential clinical risks outweigh the expected benefits. Polypharmacy and PIMs burden are major risk factors for complications such as falls and fractures, cognitive impairment, delirium, diminished health-related quality of life, and increased rates of hospitalization and mortality [4].

In light of the increasing risks associated with excessive pharmacotherapy, deprescribing has become an essential component of care. This planned and professionally supervised process entails tapering, discontinuing, or substituting medications with safer alternatives in situations where clinical risks outweigh the expected benefits. Deprescribing should be viewed as a proactive, patient-centered element of the treatment continuum, aimed

at improving quality of life and reducing medication burden [5]. The objective of this study is to summarize current scientific evidence regarding the clinical effectiveness and safety of deprescribing interventions in patients aged 65 years and older, based on a review of clinical trials published between 2017 and 2026.

2. Research materials and methods

The analysis focused on individuals aged 65 years and older, evaluating the clinical outcomes of deprescribing interventions. A literature search was conducted in PubMed and Google Scholar using the following keywords: "deprescribing," "potentially inappropriate," "inappropriate prescribing," and "polypharmacy." Inclusion criteria encompassed clinical trials published between 2017 and 2026 that were available in full-text format and assessed the clinical effectiveness and safety of deprescribing in older adults. This review excluded non-clinical trial articles, non-English language publications, and studies for which full-text access could not be obtained. Furthermore, studies were excluded if, despite overlapping terminology, they lacked a substantive focus on the impact of deprescribing on patient health outcomes.

3. Research results

3.1. Impact of deprescribing on key clinical outcomes

3.1.1. Falls and injuries. The impact of deprescribing on the incidence of falls and injuries in older adults remains a subject of inconclusive clinical findings, although analyses of selected studies indicate significant benefits in specific populations. Mahlknecht et al. [6] documented a statistically significant reduction in the number of falls requiring medical attention within an intervention group undergoing medication reviews. Findings from this study suggest that even a modest reduction in the burden of medications deemed inappropriate can lead to improved clinical stability for the patient. Conversely, in the multicenter OPERAM trial, pharmacotherapy optimization did not result in a statistically significant decrease in the risk of a first fall among older patients with multimorbidity [7]. However, secondary analysis of this trial's data identified a specific group of patients who derived substantial benefit from the deprescribing intervention. Among individuals with a history of previous falls, reducing antipsychotic use was associated with a significant 68% reduction in the risk of subsequent falls [8]. A secondary analysis of the MedSafer study [9] provides an important supplement to these data, focusing on the risks associated with sedative use (benzodiazepines and "Z-drugs") at the time of hospital discharge. Successfully deprescribing home sedatives was linked to a

61% reduction in the risk of adverse events during the 30-day post-hospitalization period. In contrast, new prescriptions for substances from this class at discharge resulted in more than a twofold increase in the likelihood of a fall during short-term follow-up. Such results suggest that the hospitalization period serves as an opportune window to reassess the appropriateness of continued sedative therapy to minimize subsequent accidents and injuries. Maintaining the patient's physical and functional independence is equally vital for the effective prevention of injuries. Although the FIMA study [10] observed no direct effect of deprescribing on the number of falls, it demonstrated that interprofessional medication assessment prevents the deterioration of mobility among older adults, as measured by the "Timed Up and Go" (TUG) test. Specifically, the intervention group showed a one-second improvement in TUG times, whereas the usual care group experienced a 2.4-second worsening. Previous research [11] indicates that increased TUG times are associated with declining physical performance, a higher risk of falls, and the onset of frailty syndrome. Despite these data, several large clinical trials have failed to demonstrate a statistically significant impact of deprescribing on fall rates in older populations with polypharmacy. The CHIPPS program [12], for instance, found no differences in fall frequency over a six-month follow-up period between the intervention and control groups. The authors attribute this to the multifactorial etiology of falls, in which medications represent only one of many risk components. Similar results were observed in studies involving nursing home residents in Germany (HIOPP-3-iTBX) [13] and Switzerland (QC-DeMo) [14]. In primary care settings, deprescribing interventions utilizing electronic clinical decision support systems also failed to reduce the number of falls compared to standard care. This was observed in both the Swiss OPTICA trial [15] and the multicenter PRIMA-eDS project, which included centers in Austria, Germany, Italy, and the United Kingdom [16]. While the actions undertaken in these studies proved safe - showing no increase in fall risk, mortality, or the frequency and duration of hospitalizations - they did not lead to statistically significant improvements over routine care. Notably, many of these projects were characterized by relatively short observation periods, which may have precluded a comprehensive assessment of the long-term clinical benefits resulting from reduced medication burden in older adults with polypharmacy.

3.1.2. Cognitive function and mental state. Pharmacotherapy optimization in older adults can contribute to improved cognitive functioning and mood stabilization, particularly through the reduction of sedative and anticholinergic medications. A study by Moga et al. [17] demonstrated that a patient-centered physician-pharmacist team intervention aimed at

reducing anticholinergic burden resulted in a significant improvement in the mental health domain of the SF-36 questionnaire within the intervention group, whereas these parameters worsened in the control group. Benefits regarding intellectual performance were further confirmed by van der Meer et al. [18], who documented that patients undergoing medication reviews achieved significantly higher scores on the Digit Symbol Substitution Test (DSST), a validated measure of cognitive function. Patients in this group also reported significantly fewer side effects associated with sedative medications. Substantial evidence concerning the safety of psychotropic deprescribing was provided by the COSMOS trial conducted in Norwegian nursing homes [19]. This research established that medication reviews and systematic clinical evaluations led to an effective reduction in psychotropic prescriptions, which neither exacerbated behavioral and psychological symptoms of dementia nor lowered patient mood. Instead, these interventions led to improvements in activities of daily living (ADL). Reductions most frequently involved antidepressant and sedative medication burden, resulting in enhanced physical function for the patients. These findings align with observations by Harnisch et al. [20], who highlighted the prevalence of quetiapine overprescribing by primary care physicians for patients with dementia. While frequently prescribed off-label for behavioral symptoms such as agitation or aggression, its use is often characterized by an unfavorable benefit-harm balance due to potential adverse outcomes. Results from this large study, involving 84,881 individuals with dementia, revealed that reducing quetiapine usage did not worsen behavioral symptoms, impair cognitive functions, or lead to a decline in mood. Furthermore, no impact was observed regarding the frequency of urgent hospitalizations or mortality rates. Such outcomes confirm the overall safety of this deprescribing intervention. In contrast to the preceding data regarding psychotropic medications, findings from the DANTON trial [21] provide significant insights concerning the modification of medications from other therapeutic classes. This study demonstrated that in individuals with moderate-to-severe dementia, discontinuing antihypertensive therapy was associated with a significant risk of serious adverse events compared to the group continuing treatment. Specifically, a marked increase in the risk of delirium and falls was observed, and usual care proved more beneficial in terms of reducing neuropsychiatric symptoms and maintaining quality of life. Although previous research [22, 23] suggested that antihypertensive deprescribing is safe for older adults without substantial cognitive deficits, the DANTON data indicate an unfavorable benefit-harm balance for such an intervention in patients with moderate-to-severe dementia. Taken together, these findings underscore that

deprescribing decisions must be individually tailored, accounting for each patient's specific clinical profile and the pharmacological characteristics of the medication being discontinued.

3.1.3. Hospitalizations and mortality. Most large clinical trials of deprescribing have failed to demonstrate a statistically significant impact on hard endpoints, such as hospitalization rates or mortality. Authors frequently attribute these results to the multifactorial etiology of such events, as well as the advanced age and multimorbidity of the study populations. Nevertheless, analysis of recent data from 2017–2026 provides evidence that precisely targeted interventions can improve these parameters in specific patient groups. Substantial clinical benefits regarding the reduction of major adverse events were documented by Kua et al. [24] in a study conducted in Singaporean nursing homes. A five-step deprescribing intervention led by an interdisciplinary team was associated with a significant decrease in mortality and the number of hospitalized residents in that setting. At the conclusion of a 12-month follow-up, researchers also noted a reduced medication burden, the substantial elimination of PIMs and daily cost savings of approximately $11.42. These findings suggest that active deprescribing focused on the elimination of inappropriate drugs can prevent severe clinical events, even if the total number of medications remains relatively high due to the patient's multimorbidity. Kornholt et al. [25] also observed a significant improvement in survival during a short-term follow-up of geriatric outpatients. Within the intervention group, which received an additional consultation and medication review, a significant reduction in mortality was noted after four months, alongside an improved quality of life compared to usual care. This effect was not sustained at the 13-month follow-up, at which point the differences between groups were no longer statistically significant. Given the progressive nature of multimorbidity in older adults, pharmacotherapy optimization processes may require regular repetition to exert a lasting influence on patient prognosis. Despite these promising results, several high-quality clinical trials continue to show no distinct impact of deprescribing on mortality and hospitalizations. In the multicenter OPERAM trial [7], pharmacotherapy optimization in hospitalized patients failed to reduce drug-related hospital readmissions, despite a successful reduction in polypharmacy. Similar neutral results were reported in the SENATOR study [26], where the authors identified poor implementation of the software-generated recommendations by physicians as a primary reason for the lack of impact on readmissions and mortality. Furthermore, a long-term, 4-year follow-up of the OPTiMISE trial [27] demonstrated that antihypertensive medication reduction in non-demented individuals with controlled blood pressure did not influence hospitalization or mortality rates;

these findings serve as an indicator of the long-term safety of antihypertensive deprescribing in this population. Neither the COFRAIL [28] nor the MPEG [29] trial found statistically significant differences in hospitalization rates; however, the authors of both studies emphasized that the interventions were clinically safe. Nevertheless, these interventions did not yield the anticipated clinical benefit of reducing the number of hospitalizations. Considering the collective evidence, deprescribing rarely serves as an independent factor for reducing hospitalizations or mortality in older adults with polypharmacy. It does, however, generally represent a safe clinical intervention that does not worsen patient prognosis. Achieving more sustainable health outcomes may require regular medication reviews, as a single intervention may only produce short-term effects.

3.1.4. Quality of life and functional status. The impact of deprescribing on the quality of life and functional independence of older adults is a crucial aspect from the patient's perspective, as it directly influences their physical autonomy and daily well-being. Recent research provides evidence that systematic pharmacotherapy optimization can lead to measurable improvements in these domains. One such study by Romskaug et al. [30] examined the impact of a comprehensive geriatric assessment and medication review, conducted through geriatrician and family physician collaboration, on health-related quality of life (HRQoL). This study demonstrated that after 16 weeks of follow-up, HRQoL scores were significantly higher in the intervention group compared to the usual care group. Furthermore, the findings suggested positive effects on selected physical and cognitive performance parameters. Similar observations were reported in the DREAMeR trial [31], where medication reviews tailored to individual health goals and patient preferences were associated with improved quality of life, as measured by the EQ-VAS visual analogue scale. The intervention group experienced both a reduction in the number of long-term medications and a significant decrease in the number of health problems impacting their daily functioning. A vital element affecting the quality of life in older adults with polypharmacy is reducing the excessive burden of central nervous system active medications, to which this age group exhibits increased sensitivity. Research by Farhat et al. [32] indicates that deprescribing these medications is a primary factor facilitating improvement in ADL, such as eating, bathing, dressing, toileting, transferring, and continence. The authors demonstrated that discontinuing just two central nervous system drugs could enable the near-complete recovery of one ADL. Given that the degree of functional autonomy directly impacts the quality of life of older adults and reduces the burden on their caregivers, regular medication reviews aimed at

eliminating unnecessary neuropsychotropic therapy are well-justified. Their utility is further supported by the analysis of Salm et al. [33], which identified a strong correlation between inappropriate prescribing and a higher degree of functional disability. This analysis considered both the overuse of PIMs and potential prescribing omissions. The study revealed that the number of PIMs was a stronger predictor of functional disability than multimorbidity itself. These results provide compelling evidence that for the well-being of seniors with polypharmacy, the appropriate selection of medications and the avoidance of PIMs are more critical than the total number of drugs prescribed.

3.2. Safety of deprescribing interventions. Evidence from numerous clinical trials supports the conclusion that deprescribing is a safe intervention that, in most cases, does not lead to a deterioration in the clinical status of older adults with polypharmacy. This safety was demonstrated in the OPTiMISE trial [27], where a four-year follow-up of individuals aged 80 and older found no increase in mortality or hospitalization rates following the rational reduction of antihypertensive medications. A critical component of safety assessment involves monitoring adverse drug withdrawal events, such as the recurrence of underlying symptoms or physiological withdrawal reactions. The SPPiRE study [34] established that these events are relatively rare; out of 826 instances of medication discontinuation, only 15 such episodes were reported, representing less than 2% of all deprescribing attempts. Pivotal evidence in this regard was also provided by the MedSafer trial [35], which utilized electronic clinical decision support systems to facilitate deprescribing interventions among hospitalized patients. Within the 30-day post-discharge period, researchers observed no increase in adverse drug events, nor were there significant differences in the rates of falls, mortality, or readmissions between the intervention and control groups. Similar outcomes were achieved in the large-scale OPTIMIZE project [36, 37], conducted among primary care patients with dementia or mild cognitive impairment. The educational intervention, designed to encourage discussions regarding medication appropriateness and the discontinuation of unnecessary or potentially harmful drugs, proved safe despite not significantly reducing the overall medication burden. During a 4-month follow-up, researchers noted no significant increase in mortality, hospitalization frequency, or intervention-related adverse events following medication withdrawal. Pharmacotherapy changes preceding any hospitalizations typically resulted from routine responses to fluctuating chronic disease symptoms rather than the deprescribing process itself. These findings are supplemented by results from the FIMA study [38], which evaluated the impact of interprofessional medication assessments among residents of Finnish

nursing homes. These interventions led to a statistically significant reduction in the risks of renal impairment, bleeding, and constipation over 6 months of follow-up. Furthermore, the risk of anticholinergic effects - which predispose seniors to adverse outcomes such as falls, cognitive decline, and confusion - was also diminished. While the FIMA intervention did not significantly lower the total number of medications, it successfully reduced the burden of PIMs and improved overall pharmacotherapy quality. Additionally, the study by Wong et al. [39] confirmed the safety of weekly multidisciplinary team-led deprescribing rounds in a Singaporean rehabilitative hospital. After a 28-day follow-up, mortality and hospitalization rates did not differ significantly from the usual care group. However, the intervention group experienced a significantly higher incidence of constipation and a more frequent need to re-initiate laxative therapy following attempted withdrawal. Other adverse events did not occur more frequently than in usual care. The authors noted that intervention safety was ensured through patient education, gradual dose tapering, and the assurance that medications could be promptly reinstated if symptoms recurred.

4. Discussion

The synthesis of current scientific evidence establishes that pharmacotherapy optimization is a safe and clinically feasible strategy for managing older adults with polypharmacy. Most large-scale trials consistently report a neutral impact on hard endpoints such as mortality and hospital readmission rates, confirming that proactive medication cessation does not worsen patient prognosis. This lack of statistical significance in survival outcomes is often attributed to the high baseline mortality and the progressive, multifactorial nature of illness in this population, where medications represent only one of many risk factors. However, specialized multidisciplinary interventions, particularly those integrated into long-term care settings, have demonstrated substantial benefits in reducing both the medication burden and severe clinical events. Beyond survival metrics, the evidence confirms a significant positive impact on patient-centered outcomes, including health-related quality of life and functional independence. Reducing the burden of central nervous system-active medications emerges as a critical driver of functional recovery, as these drugs are strongly associated with cognitive decline and falls. Despite these advantages, the clinical effectiveness of such programs is frequently constrained by implementation barriers, including clinician reluctance to alter therapies initiated by specialists, time constraints, and insufficient interprofessional communication.

5. Conclusions

The evidence synthesized in this review mandates a fundamental transition toward systematic, evidence-based, and patient-centered deprescribing as a foundation of modern geriatric care. It is essential to redefine medication management as a continuous "prescription continuum," moving away from incidental, one-off reviews toward models of longitudinal monitoring and iterative re-evaluation. The success of these interventions should be measured not merely by the quantitative reduction in drug counts but by the qualitative optimization of functional autonomy and alignment with individual health goals. Institutional support for robust multidisciplinary collaboration involving family physicians and geriatricians is a prerequisite for identifying high-risk medication profiles and ensuring safe withdrawal. Furthermore, future healthcare policies must address systemic barriers by providing the necessary infrastructure, technological communication channels, and financial incentives to sustain these practices in routine clinical workflows. Future research directions should focus on extending observation periods, which is essential for a reliable assessment of the long-term health benefits derived from polypharmacy reduction. Ultimately, while aging involves a natural decline in health, the stabilization or enhancement of functional parameters through individualized pharmacotherapy management offers a vital pathway to preserving independence and improving well-being in the growing geriatric population.

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