www.ijarp.com ISSN 2456-9992 Page: 01-32

International Journal Advanced Research Publications

Review Article

Volume: 02
Issue: 05

# POLYPHARMACY AND ITS IMPACT ON ELDERLY HEALTH A COMPREHENSIVE REVIEW OF PREVALENCE, RISKS, OUTCOMES, AND DEPRESCRIBING STRATEGIES

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**Article Received: 10 April 2026, Article Revised: 30 April 2026, Published on: 20 May 2026**

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DOI: https://doi-doi.org/101555/ijarp.6214

## ABSTRACT

The phenomenon of polypharmacy, involving the concomitant consumption of five or more medications, has emerged as a mounting concern in the domain of global health care, especially amongst individuals 65 years and older. In this extensive literature review, over 60 research articles, peer-reviewed and published within the timeframe of 1990 to 2024, have been collated to elucidate the underlying aspects related to the epidemiology, pharmacodynamics, clinical implications, and management strategies of polypharmacy within the elderly population. The incidence of polypharmacy within the elderly cohort spans between 20% and 67%, primarily fueled by the presence of several comorbidities, disjointed healthcare service delivery, and the lack of prescribing guidelines specific to geriatric medicine.Additional impacts related to the alterations in pharmacokinetics and pharmacodynamics in older patients result in an increased risk due to medication use. Potentially inappropriate medicines (PIMs), according to Beers criteria and STOPP/START screening tool, are frequently used regardless of the existing scientific evidence about their harmful effects on older adults' health. The practice of deprescribing, or systematic reduction or elimination of inappropriate medicines, has already been shown to be effective clinically and economically. Multidisciplinary approaches to medicines review, patient-oriented care, decision support technologies, and pharmacogenomics are prospective ways to optimize prescribing practices.

**KEYWORDS:** Polypharmacy, elderly, geriatric, adverse drug reactions, drug-drug interactions, deprescribing, Beers criteria, STOPP/START, pharmacokinetics,

multimorbidity, medication review, falls, cognitive decline, and inappropriate prescribing are all terms that can be used to describe this research.

## 1.INTRODUCTION

The rate at which the world's population is aging is unparalleled. Over 2.1 billion people will be 60 years of age or older by 2050, more than twice as many as in 2015, according to World Health Organization (WHO) projections [1]. Cardiovascular disease, diabetes mellitus, osteoporosis, chronic obstructive pulmonary disease (COPD), chronic kidney disease (CKD), and neurodegenerative illnesses are among the non-communicable chronic diseases that disproportionately affect older persons.

Polypharmacy is a phenomena that arises from the intrinsic need for concurrent pharmacotherapy due to the simultaneous management of numerous conditions, or multimorbidity. The most general definition of polypharmacy is when a single patient regularly takes five or more different drugs [2]. Nonetheless, there are many different criteria and conceptualizations in the literature, from simply quantitative (drug count) to qualitative evaluations of pharmaceutical appropriateness [3]. It is crucial to distinguish between "appropriate polypharmacy," which occurs when several medications are clinically warranted, and "problematic polypharmacy," which occurs when one or more medications are dangerous, redundant, or unnecessary [4].

Drug absorption, distribution, metabolism, and excretion are all significantly impacted by the basic physiological changes that the aging body experiences. Elderly people are significantly more vulnerable to medication-related damage than younger people due to reduced renal and hepatic function, altered body composition, decreased albumin levels, and increased receptor sensitivity [5]. Adverse drug responses (ADRs), drug-drug interactions (DDIs), drug-disease interactions, falls and fractures, delirium, cognitive impairment, nutritional deficiencies, and death are among the serious clinical outcomes that can occur when polypharmacy is piled onto this susceptible physiology .

Despite this, the fundamental physiological changes that the aging body goes through have a big impact on drug absorption, distribution, metabolism, and excretion. Due to changing body composition, lower albumin levels, impaired renal and hepatic function, and enhanced receptor sensitivity, elderly individuals are far more susceptible to medication-related harm than younger individuals When polypharmacy is added to this vulnerable physiology, significant clinical effects include adverse drug reactions (ADRs), drug-drug interactions

(DDIs), drug-disease interactions, falls and fractures, delirium, cognitive impairment, nutritional deficiencies, and mortality [6].inadequate worldwide. Clinical guidelines are frequently disease-specific rather than patient-centric, which leads to a paradox whereby prescribing for each unique ailment in accordance with guidelines unintentionally results in polypharmacy for the entire patient [7]. The issue is made worse by healthcare fragmentation, which occurs when several specialists independently write prescriptions without thorough oversight [8].

The goal of this review is to give a comprehensive, fact-based explanation of polypharmacy in older individuals. The epidemiology, definitions, pharmacological foundations, clinical outcomes, assessment instruments, deprescribing tactics, technological solutions, and the socioeconomic impact of polypharmacy are all covered. For scholars looking to delve deeper into this crucial area of geriatric pharmacology, the publication is organized to function as both a scholarly synthesis and a clinical reference.

## II.DEFINITION AND CLASSIFICATION OF POLYPHARMACY

The Greek words "polus" (many) and "pharmakon" (medication) are the origin of the term "polypharmacy." Although the idea has been acknowledged for many years, a consensus definition is still elusive. Direct comparison of outcome estimates and prevalence data is complicated by the variation in definitions among research [9].

### A. Definitions of Quantitative

The concurrent use of five or more prescription drugs is the most commonly used criterion for polypharmacy, as recommended by the WHO and accepted by significant systematic reviews [10]. Although it doesn't differentiate between proper and inappropriate prescribing or take into consideration over-the-counter drugs, vitamins, or herbal supplements—all of which increase the likelihood of interactions—this threshold is useful for population-level surveillance and clinical research However, it does not differentiate between suitable and inappropriate prescribing, nor does it take into consideration over-the-counter drugs, vitamins, or herbal supplements, all of which increase the risk of interactions.

The literature is beginning to acknowledge subdivisions of severity. Major or severe polypharmacy (≥10 drugs) carries significantly elevated ADR and interaction risks; minor polypharmacy (2–4 drugs) is typically regarded as low-risk; moderate polypharmacy (5–9 drugs) is the standard research and policy benchmark; and hyper-polypharmacy (≥15 drugs)

is associated with the most complex clinical scenarios, frequently in institutionalized or terminally ill patients [11].

### B. Contextual and Qualitative Definitions

Qualitative frameworks acknowledge the importance of clinical appropriateness beyond drug count. "Appropriate polypharmacy" refers to regimens where each medicine is appropriately dosed, supported by evidence, and in line with patient preferences and care objectives [12]. In contrast, "problematic polypharmacy" refers to the use of one or more potentially inappropriate medications (PIMs), which are pharmaceuticals whose hazards outweigh their benefits in senior patients. It also includes prescription omissions, dosage errors, and complicated regimens that compromise adherence. Summary ofClassification Table I below compiles the primary classification groupings, thresholds, and contextual applicability in clinical and research settings.

**TABLE – I: Drug Threshold And Clinically Context Based POLYPHARMACY Classification.**

| Category | Drug Threshold | Common uses/ Context |
|---|---|---|
| Minor Polypharmacy | 2-4Drugs | Low Risk Frequently Supported by clinical Evidence |
| Moderate Polypharmacy | 5-9 Drugs | WHO Benchmark ; Standard Clinical Threshold |
| Severe/Major Polypharmacy | ≥10 Drugs | Drugs High Risk Linked to Frailty |
| Hyper- Polypharmacy | >15 Drugs | Critical Care and Complicated Chronic Illness |
| Problematic Polypharmacy | Inappropriate | Drug -Drug Interactions And PIMs |

## III. GLOBAL PREVALENCE AND EPIDEMIOLOGY

There is no doubt that polypharmacy is the norm rather than the exception in elderly populations globally, despite the fact that prevalence estimates differ significantly between nations, healthcare systems, and research approaches [13].

### A. United States

According to data from the National Health and Nutrition Examination Survey (NHANES), 39% of older individuals in the United States regularly take five or more prescription

medications; when over-the-counter pharmaceuticals and dietary supplements are taken into account, the number rises to 67% [14]. According to a groundbreaking 2015 study by Kantor et al., the prevalence of polypharmacy among American adults increased by 36% between 1988–1994 and 2009–2012, mostly due to increased usage of statins, antihypertensives, and antidiabetic medications.[15] According to Medicare data, more than 40% of beneficiaries who are 65 years of age or older fill prescriptions for ten or more drugs each year [16].

**B.Europe**

European prevalence rates vary from 51% in Swedish nursing home residents [18] to 26% in elderly people living in the community in Italy [17]. Over 45,000 people from 19 European countries participated in the SHARE (Survey of Health, Ageing and Retirement in Europe) study, which revealed a mean polypharmacy prevalence of 41% among those 65 and older [19]. According to the UK's Clinical Practice Research Datalink, polypharmacy among persons 65 and older nearly tripled over a 15-year period, rising from 12% in 1995 to 35% in 2010 [20].

**C. The Developing World and Asia**

The frequency of polypharmacy among older adults in Asia varies from 20% to 52% [21]. 23.9% of patients 60 years of age and more in geriatric outpatient departments were administered five or more medications at the same time, with cardiovascular pharmaceuticals, antidiabetics, and gastrointestinal agents being the most common classes, according to a multicenter study conducted across seven Indian states [22]. 52% of elderly outpatients in Shanghai hospitals in China had polypharmacy, with concomitant diabetes and hypertension being among the best predictors [23].

**D. Important Factors Increasing Prevalence**

Increased survival from acute events requiring long-term secondary prophylaxis; (1) population aging and the demographic shift toward longer-lived cohorts with multimorbidity; (2) disease-specific clinical practice guidelines that collectively recommend multiple medications; (3) growing pharmaceutical markets and direct-to-consumer advertising; and (5) insufficient systems for thorough medication review and coordination across specialists are all contributing factors to the rising prevalence of polypharmacy [24]. A comparative assessment of the prevalence of polypharmacy in various worldwide areas is shown in Table II.

**Table -II Global Prevalence Of Polypharmacy Among Elderly Adults.**

| Country | Prevalence (%) | Age | Source/ Year |
|---|---|---|---|
| United States | 42-67% | ≥65years | Kantor et al., 2015 |
| Eurpean Union | 38-55% | ≥65years | Alwhaibi et al., 2018 |
| United Kingdom | 35-51% | ≥65years | Guthrie et al., 2015 |
| India | 20-45% | ≥60years | Saraf et al., 2016 |
| China | 28-52% | ≥65years | Gu et al., 2010 |
| Australia | 30-48% | ≥65years | AIHW, 2018 |
| Brazil | 22-36% | ≥60 years | Netto et al., 2012 |

## IV. CHANGES IN PHARMACOKINETIC AND PHARMACODYNAMIC

Age-related physiological decline that modifies how drugs function in the body is a key factor in polypharmacy-related damage in older persons. These alterations are cumulative, progressive, and frequently underestimated by clinicians [25].

### (A) Pharmacokinetics

### 1.Absorption

Reduced stomach acid secretion (achlorhydria), delayed gastric emptying, decreased gastrointestinal motility, and decreased splanchnic blood flow are all significant changes in gastrointestinal drug absorption in elderly people, although most oral drugs do not significantly modify this process. These elements may hinder the absorption of pH-dependent medications such calcium carbonate and ketoconazole and prolong the time to peak plasma concentration (Tmax) for some medications [26].

### 2. Distribution

Age-related changes in body composition include a decrease in lean muscle mass (sarcopenia), an increase in body fat (from about 18% in young adults to about 36% in the elderly), and a 10–15% drop in total body water. These changes affect the volume of distribution (Vd) in predictable ways: hydrophilic drugs (like lithium and gentamicin) have lower Vd and higher peak concentrations, while lipophilic drugs (like diazepam and amiodarone) distribute more widely, leading to longer half-lives and accumulation risks [27]. Age and disease can cause a decrease in serum albumin levels, which increases the free (active) portion of highly protein-bound medications such phenytoin and warfarin, intensifying their toxic and pharmacological effects [28].

**3. Metabolism**

Age-related decreases in hepatic drug metabolism include decreased liver mass (20–40% decrease), decreased hepatic blood flow (25–40% reduction), and decreased activity of cytochrome P450 (CYP) enzymes, especially CYP3A4, CYP2C9, and CYP2D6 [29]. Compared to Phase II conjugation processes, Phase I reactions (oxidation, reduction, and hydrolysis) are more severely compromised. For many medications that are processed by the liver, this leads to decreased first-pass metabolism and longer half-lives. When CYP inhibitors and inducers are used concurrently in the context of polypharmacy, a complicated web of unanticipated drug interactions is created [30].

**4. Excretion**

The greatest clinically significant age-related reduction occurs in renal excretion. After age 40, the typical glomerular filtration rate (GFR) drops by about 1 mL/min/year; by age 75, it is about 50–60% of young-adult values [31]. Crucially, concurrent loss of muscle mass (which lowers creatinine production) means that serum creatinine alone cannot accurately reflect this reduction. For renally cleared medications such as digoxin, metformin, low-molecular-weight heparins, direct oral anticoagulants, and numerous antibiotics, renal clearance is consequently frequently overestimated, resulting in drug buildup, toxicity, and dose-related adverse drug reactions [32].

**B. Pharmacodynamics**

The elderly show increased or changed pharmacodynamic responses to numerous medication types in addition to altered kinetics. Due to neuronal loss, decreased receptor density, and compromised homeostatic processes, the central nervous system (CNS) becomes more susceptible to sedative, anticholinergic, and CNS-active drugs [33]. The cardiovascular system is more susceptible to orthostatic hypotension and bradyarrhythmias due to its increased susceptibility to vasodilators and negative chronotropes. A major cause behind polypharmacy-associated falls is decreased baroreceptor sensitivity, which makes it more difficult to adapt for blood pressure swings brought on by antihypertensives, diuretics, and alpha-blockers [34].

The effectiveness of sympathomimetics is decreased and reactions to beta-blockers are changed by alpha-1 adrenoceptor downregulation and compromised beta-adrenoceptor signaling. Anticoagulant-induced hemorrhagic risk is increased by the coagulation system's growing fragility. In the context of polypharmacy, renal tubular and glomerular sensitivity to

nephrotoxins (NSAIDs, aminoglycosides, contrast agents) is increased, increasing the risk of acute kidney injury [35].

Because of these combined pharmacokinetic and pharmacodynamic vulnerabilities, even "standard" dosage regimens created for younger adult populations may significantly overdose older people, especially those who are weak or have numerous comorbidities.

## V. POLYPHARMACY'S CLINICAL IMPLICATIONS

Polypharmacy affects almost every organ system and clinical area in older people. The repercussions might range from minor drug interactions that lessen the effectiveness of treatment to catastrophic, life-threatening incidents call for immediate Medical attention [36]

### A. Adverse Reaction

The most obvious clinical consequence of polypharmacy is adverse drug reactions (ADRs). The association between polypharmacy and the risk of adverse drug reactions (ADRs) is well-established and exhibits a near-exponential pattern: patients taking two medications have an ADR risk of about 13%, those taking five medications have an ADR risk of about 58%, and those taking seven or more medications have an ADR risk of about 82% [37].Up to 30% of hospital hospitalizations in older patients are due to adverse drug reactions (ADRs), with up to 70% of these being avoidable [38]. Anticoagulant-related bleeding, antidiabetic hypoglycemia, digoxin toxicity, NSAID-induced nephrotoxicity, and psychiatric medication-induced drowsiness and falls are the most frequent adverse drug reactions (ADRs) in older populations [39].

One well-established factor contributing to the persistence of polypharmacy is the idea of the "prescribing cascade," in which an adverse drug reaction (ADR) from one medication is mistaken for a new illness, leading to the administration of another medication. Allopurinol is used to treat gout caused by thiazides, levodopa is used to treat Parkinsonian characteristics caused by metoclopramide, and a diuretic is used to treat ankle edema caused by dihydropyridine calcium channel blockers [40].

### B. Drug  Drug Interactions

One of the most complicated and possibly hazardous effects of polypharmacy is drug-drug interactions, or DDIs. There are ten potential pairwise drug combinations for a patient taking five drugs, compared to forty-five for a patient taking ten. In older patients who are heavily

medicated, the likelihood of at least one clinically relevant interaction is very certain [41]. Pharmacodynamic DDIs include additive or antagonistic pharmacological effects at shared receptor targets, whereas pharmacokinetic DDIs typically entail CYP enzyme inhibition or induction, changing the plasma amounts of impacted medicines[42].

Warfarin-NSAID (increased bleeding risk), ACE inhibitor-spironolactone (life-threatening hyperkalemia), clopidogrel-omeprazole (reduced platelet inhibition via CYP2C19 inhibition), clarithromycin-statin (rhabdomyolysis via CYP3A4 inhibition), and digoxin-amiodarone (digoxin toxicity via P-glycoprotein inhibition) are examples of clinically critical DDIs in older populations [43].

**C. Fractures and Falls**

One of the most dangerous effects of polypharmacy in the elderly is falls. Polypharmacy (≥4 medicines) independently increases fall risk by 24% (OR 1.24, 95% CI 1.07–1.43), according to a seminal meta-analysis of 79 studies [44]. Central nervous system medications (benzodiazepines, antidepressants, antipsychotics), antihypertensives (especially loop diuretics and alpha-blockers), antiepileptics, and hypoglycemic medications are examples of high-risk pharmacological classes. Due to drowsiness, orthostatic hypotension, diminished proprioception, decreased muscle strength, and hypoglycemia, these drugs
increase the risk of falls [45].

Elderly patients who fall suffer disproportionately serious consequences: roughly 5–10% of falls result in fractures, and 1-2% result in hip fractures, which have a 15–25% one-year mortality rate and are among the main causes of disability and institutionalization in older adults [46]. With adjusted odds ratios ranging from 1.4 to 2.8 across numerous large cohort studies, the association between the use of psychiatric medications and hip fracture has been particularly well-documented [47].

**D. Cognitive Impairment and Delirium**

In older individuals, polypharmacy is closely linked to both acute and chronic cognitive impairment. Numerous long-term studies have demonstrated that anticholinergic load, or the total anticholinergic activity of concurrently administered drugs, can independently predict incident dementia, cognitive decline, and delirium [48]. Central cholinergic deficit is increased by medications with strong anticholinergic activity, such as tricyclic antidepressants, first-generation antihistamines, antimuscarinics for overactive bladder, and

several antiemetics. Ten to thirty percent of senior inpatients experience hospital-acquired delirium, which is closely linked to polypharmacy, especially the use of anticholinergics, benzodiazepines, and opioids [49]. In addition to extending hospital stays by an average of five to ten days, delirium is independently linked to increased mortality, institutionalization, and cognitive decline. The introduction of any new psychoactive medicine in individuals with existing dementia requiresextra vigilance [50].

**E. Mortality and Hospitalization**

In older populations, polypharmacy is a strong independent predictor of hospitalization and mortality. A dose-response association between the number of medications and all-cause mortality was discovered in a Swedish registry study of 760,000 older people; patients on more than ten medications had a hazard ratio of 1.98 compared to those on fewer than three [51]. According to estimates, polypharmacy-related hospital admissions cost the US healthcare system more than $3.5 billion yearly, and 700,000 senior persons visit the ER each year due to avoidable medication-related incidents [52].

Elderly patients with polypharmacy have significantly higher readmission rates within 30 days. According to a major U.S. cohort research, the risk of 30-day readmission increased by 12% for every additional prescription at discharge [53]. Significantly, the relationship between polypharmacy, multimorbidity, and mortality is complicated—sicker patients are prescribed more medications—but numerous studies employing causal inference techniques verify that polypharmacy independently contributes to unfavorable outcomes beyond what multimorbidity alone would predict [54].

**F. Extra Clinical Damage**

In addition to the aforementioned areas, polypharmacy is linked to nutritional deficiencies (such as metformin-induced B12 depletion, PPI-induced hypomagnesemia and B12 deficiency), medication non-adherence because of complicated regimens, constipation (opioids, calcium channel blockers), urinary incontinence (diuretics, anticholinergics), poor wound healing, and decreased quality of life [55]. Patients and their caregivers, especially those with functional limitations or cognitive decline, experience considerable psychological and practical strain while managing complex pharmaceutical regimens, which include comprehending timetables, obtaining refills, and tolerating side effects [56].

## VI. COMMON DRUG CLASSES AND MEDICATIONS THAT MAY BE INAPPROPRIATE

Elderly patients' polypharmacy regimens are disproportionately composed of certain drug classes, which are associated with specific dangers.

### A.The Beers Criteria

The American Geriatrics Society (AGS) Beers Criteria, initially published by Dr. Mark Beers in 1991 and most recently updated in 2023 [57], are the most widely used paradigm for identifying potentially inappropriate medications (PIMs) in older adults. The criteria include avoiding drug-disease and drug-syndrome combinations, avoiding particular drugs and drug classes in individuals 65 years of age and older, and avoiding medications that may be inappropriate when combined (clinically significant DDIs). The 2023 update lists over 80 medications or drug classes and emphasizes patient options, shared decision-making, and clinician education [58].

### B. STOPP/START Criteria

The Screening Tool of Older Persons' Potentially Inappropriate Prescriptions (STOPP) and Screening Tool to Alert Clinicians to Right Treatment (START) criteria were created in response to the Beers Criteria's primary flaw, which was its exclusive emphasis on overtreatment at the expense of undertreatment. While START v3 has 38 criteria that indicate prescription omissions (medications that should be started for established conditions but have been withheld), the 2023 version of STOPP v3 has 187 criteria that identify PIMs [59]. Significant decreases in medication load and ADR incidence have been linked to the systematic use of these techniques in clinical practice, especially in hospital-based medication reviews [60].

A list of high-priority PIMs from the Beers Criteria, together with the issues they raise and suggested solutions, is shown in Table IV

**TABLE IV – Selected Drugs From the 2023 AGS.**

| Classes Of Drug | Concern | Alternative Recommended | Recommendation |
|---|---|---|---|
| Benzodiazepines (all) | Fall/fracture risk, cognitive impairment | Non-BZD cognitive-behavioral therapy | Avoid |
| First-gen | Anticholinergic | 2nd-gen antihistamines | Avoid |

| | | | |
|---|---|---|---|
| antihistamines | effects, sedation | (loratadine) | |
| NSAIDs (chronic use) | GI bleeding, peptic ulcer, renal injury | Topical NSAIDs; acetaminophen | Avoid unless alternatives fail |
| Muscle relaxants | CNS adverse effects, falls | Physical therapy | Avoid |
| Antipsychotics (dementia) | Stroke, mortality increase | Non-pharmacological behavioral interventions | Avoid unless non-pharm fails |
| Sliding-scale insulin | Hypoglycemia without benefit | Scheduled insulin regimens | Avoid |

## VII. PATIENT OUTCOMES AND MEDICATION ADHERENCE

Medication adherence, or how closely a patient follows the prescriber's recommended course of action, is severely hampered by polypharmacy [61]. Medication burden, complex dosing, side effects, cost, and cognitive decline are the primary barriers to adherence in older patients. WHO estimates that the average adherence rate for chronic conditions in affluent nations is 50%, and older patients on complex polypharmacy regimens frequently do not meet this benchmark [62].

Non-adherence in elderly polypharmacy patients can be either purposeful (planned omission due to perceived lack of benefit or adverse effects) or incidental (forgetting, inability to open packaging, unclear instructions). Both kinds carry a substantial clinical risk..Thromboembolic events, hyperglycemic emergencies, and hypertensive crises have all been directly associated with inadvertent non-adherence to antihypertensives, anticoagulants, and antidiabetics [63].

On the other hand, adherence is regularly improved by simplifying the regimen through deprescribing or formulation adjustments (e.g., combination tablets, once-daily dose). Simplifying dosage schedules from four times daily to once daily increased adherence by 26–30% across drug classes, according to a Cochrane systematic review of 62 randomized controlled trials [64]. A prospective study of 250 community-dwelling elderly individuals showed that medication adherence rates increased from 59% to 84% when polypharmacy was reduced from a mean of 9.2 to 5.1 drugs [65].

The quality of communication and the patient-provider connection have a big impact on adherence. Patients who receive prescriptions without sufficient justification are far less

likely to stick to their medication regimens than those who believe their concerns are acknowledged and addressed. In randomized trials involving older patients, structured medication counseling, pictographic medication regimens, pill organizers, and blister packaging have all shown moderate but significant adherence advantages [66]

## VIII. DEPRESCRIBING METHODS AND RESULTS

In order to manage polypharmacy and improve patient outcomes, deprescribing is described as the planned and supervised process of reducing the dosage or stopping the use of medications that are harmful or no longer beneficial [67]. It is a fundamental clinical skill in geriatric medicine, based on the idea that prescription choices need to be regularly reassessed as patient conditions, objectives, and physiology change over time.

### A Clinical Support for Deprescribing

Over the past ten years, the body of research supporting deprescribing has significantly expanded. A deprescribing strategy decreased the number of prescriptions by an average of 4.4 per patient in a seminal study by Garfinkel and Mangin including 119 nursing home residents (mean age 82, mean meds 7.7). When compared to controls, this intervention was linked to a 45% decrease in 12-month mortality [68]. A pharmacist-led deprescribing program decreased the number of prescriptions by 2.3 per patient, increased quality of life, and decreased healthcare expenses by $1,200 per patient over a 12-month period, according to a later randomized controlled trial conducted in community-dwelling elderly by Scott et al. [69].

Structured medication review and deprescribing interventions were linked to statistically significant decreases in the number of medications (mean reduction 1.4–4.4 drugs), falls, adverse drug reactions, and hospitalizations, without significant increases in adverse events attributable to discontinuation, according to a 2019 Cochrane Review of 38 deprescribing studies [70]. Crucially, evidence indicates that most medications, including long-term antidepressants, antihypertensives, proton pump inhibitors, and statins, can be safely stopped in suitable candidates with structured taper protocols [71]. However, fear of negative withdrawal effects frequently prevents clinicians from being willing to deprescribe.

**B.The Process of Deprescribing**

The clinical procedure for deprescribing to older individuals is organized as follows: (1) Complete medication reconciliation, which entails creating an accurate and comprehensive list of all prescription drugs, over-the-counter medications, supplements, and herbal products; (2) using standardized tools (Beers, STOPP, MAI) to identify medications for prioritized review; (3) evaluating each medication for continued appropriateness based on the patient's current conditions, goals of care, life expectancy, and functional status; (4) Using the harm-benefit ratio to determine targets for dose decrease or withdrawal; (5) carrying out a scheduled withdrawal under observation; and (6) A follow-up evaluation of patient experience and clinical results [72].

Making decisions together is crucial to this process. Patients frequently have strong opinions about the drugs they take, including attachment to those they feel are necessary and a wish to stop taking others that they find burdensome. It has been demonstrated that a patient-centered approach improves both willingness to participate in deprescribing and successful long-term medication reduction when clinical evidence is communicated openly and the patient's preferences and priorities are explicitly incorporated into the deprescribing plan [73].

**Frameworks and Tools for Deprescribing**

In clinical practice, the deprescribing process is supported by a number of approved techniques and frameworks. An overview of the main tools that doctors can use is given in Table V

**TABLE V – MAJOR DEPRESCRIBING TOOLS AND FRAMEWORKS IN GERIATRIC PRACTICE**

| Framework | Description | Applicability |
|---|---|---|
| Beers Criteria | AGS list of PIMs for ≥65; updated 2023 | US clinical settings; widely adopted |
| STOPP/START | STOPP: 114 criteria to stop; START: 31 criteria to start | European focus; includes undertreatment |
| Medication Appropriateness Index (MAI) | 10-question scoring tool per medication | Research & quality improvement |
| STOPPFrail | Simplified tool for end-of-life / frail patients | Frail elderly; palliative contexts |

| | | |
|---|---|---|
| NPS Deprescribing Guidelines | Algorithm-based drug-specific protocols (e.g., PPIs, BZDs) | Australia/NZ; drug-class specific |
| Patient-Centered Outcomes | Shared decision-making aligned to patient goals | Geriatric care; outpatient settings |

## IX. MULTIDISCIPLINARY METHODS FOR MANAGING POLYPHARMACY

Physicians, pharmacists, nurses, geriatricians, care coordinators, and patients themselves must all work together to effectively manage polypharmacy in older patients [74]. The biggest organizational obstacle to polypharmacy resolution is fragmented care, which is a structural norm in the majority of healthcare systems where hospital teams, subspecialists, and primary care physicians work in informational silos [75].

### A. Thorough Geriatric Evaluation

A multifaceted, interdisciplinary diagnostic and therapeutic procedure called Comprehensive Geriatric Assessment (CGA) assesses an aged patient's functional, social, psychological, and medical capacities. Systematic medication review is a fundamental component of CGA, which has continuously shown its capacity to detect and address problematic polypharmacy [76]. Ellis et al.'s seminal meta-analysis of 29 CGA RCTs revealed that CGA enhanced cognitive function, decreased mortality, and raised the likelihood of staying at home at 12 months—outcomes that were probably partially mediated by medication optimization [77].

### B. Involvement of Clinical Pharmacists

Because of their specific expertise in pharmacokinetics, pharmacodynamics, and medication interactions, clinical pharmacists are in a unique position to treat polypharmacy. Pharmacist-led medication reviews have been shown to be beneficial in both community and institutional settings. A systematic evaluation of 20 RCTs revealed that pharmacist interventions significantly decreased the frequency of ADRs, PIMs, and medication-related issues (OR 0.41, 95% CI 0.27–0.61) [78]. Collaborative drug therapy management (CDTM) models between pharmacists and physicians have been linked to increased patient satisfaction, less polypharmacy burden, and better prescribing quality [79].

### C. Care Coordinator and Nursing Roles

In polypharmacy management, nurses and care coordinators play crucial roles in medication administration and monitoring, patient education, early detection of adverse drug reactions (ADRs), prescriber communication, and adherence support. Formal medication optimization

in geriatric settings is becoming more common among advanced practice registered nurses (APRNs) with prescriptive authority [80]. 30-day readmission rates linked to drug-related adverse events have been shown to be significantly reduced by transitional care models, especially those that incorporate nurse-led post-discharge medication reconciliation [81].

### C. Information Technology for Health

Electronic Health Records (EHRs) that incorporate Clinical Decision Support Systems (CDSS) are a quickly developing tool for managing and detecting polypharmacy in real time. Significant decreases in prescription errors have been reported when doctors receive alerts for newly discovered DDIs, PIM prescriptions, dosage errors in patients with renal impairment, or duplicate therapy during prescription submission [82]. However, "alert fatigue"—a condition in which doctors ignore or override the majority of signals due to excessive alert volume, insufficient specificity, and workflow disruption—undermines the efficacy of CDSS alerts. It is still a top research priority to optimize alarm systems for clinical relevance and actionability [83].

## X. PHARMACOGENOMICS AND NEW TECHNOLOGIES

Beyond what conventional clinical tools can do, the integration of emerging technologies and precision medicine techniques holds great promise for improving polypharmacy management in senior patients [84].

### A. Pharmacogenomics

The study of genetic variants that affect drug response, known as pharmacogenomics (PGx), offers the possibility of customizing medicine selection and dosage in ways that lower the risk of adverse drug reactions (ADRs) in senior polypharmacy patients. CYP2C19 (clopidogrel activation, PPI metabolism), CYP2D6 (codeine, tricyclics, tamoxifen), CYP2C9 (warfarin, NSAIDs), and SLCO1B1 (statin myopathy risk) are clinically actionable PGx variations that have an impact on geriatric treatment [85]. Evidence-based recommendations for PGx-guided prescribing for 24 gene-drug pairings are provided by the RIGHT protocol and CPIC guidelines, which are especially pertinent for older patients on complicated polypharmacy regimens [86].

A 30% decrease in clinically significant adverse drug reactions (ADRs) was observed in the PGx-guided group (HR 0.70, 95% CI 0.59–0.83) in the PREPARE research, a seminal pragmatic RCT that randomly assigned 6,944 European patients to receive PGx-guided

versus standard dosing [87]. Preemptive PGx testing could be a major advancement in the treatment of individualized polypharmacy for older individuals beginning high-risk drugs.

### B. Machine Learning & Artificial Intelligence

The potential of machine learning (ML) and artificial intelligence (AI) systems to identify, forecast, and avoid the negative effects of polypharmacy is being investigated more and more. When applied to EHR data, natural language processing (NLP) algorithms have proven to identify complicated DDIs, adverse drug reactions (ADRs), and potentially inappropriate prescribing trends with greater accuracy than rule-based systems [88]. ML-based predictive modeling has demonstrated potential in identifying patients most at risk for hospitalization due to polypharmacy, allowing for focused preventive intervention [89].

When it comes to predicting adverse drug events in elderly patients, deep learning models trained on extensive prescription claims datasets have outperformed conventional logistic regression techniques with AUC values of 0.82–0.91 [90]. Prospective validation, interpretability, and smooth integration into current clinical workflows are necessary for translating these models into clinical practice; these issues are still being researched.

### C Tools for Mobile Health and Digital Adherence

Digital companion tools, smart pill dispensers, and smartphone-based medication management apps provide useful ways to increase medication safety and adherence among older patients living in the community. Across populations with chronic illnesses, systematic studies of smartphone medication reminder apps consistently demonstrate gains in adherence of 10–20% [91]. A potential approach to proactive polypharmacy management is the integration of these tools with prescriber EHR systems, which allows for real-time adherence monitoring and automated notifications for non-adherence [92].

## XI. POLYPHARMACY'S ECONOMIC BURDEN

The enormous healthcare expenses linked to adverse outcomes caused by polypharmacy constitute a mostly avoidable burden on the resources of the global healthcare system [93]. Key economic estimates from the published literature are shown in Table VI

**ECONOMIC BURDEN OF POLYPHARMACY**

| Economic Outcomes | Estimated Cost | Refrences |
|---|---|---|
| ADE-related hospitalizations (USA, annual) | > $3.5 billion | Budnitz et al., NEJM 2011 |
| Preventable ADRs in elderly (USA) | ~$30 billion/year | Ernst & Grizzle 2001 |
| Polypharmacy-linked falls (EU annual) | €2–3 billion | WHO Falls Report 2021 |
| Unnecessary medication costs per patient | $300–$1,200/year | Scott et al., 2017 |
| Hospitalizations avoided by deprescribing | $1,000–$5,000 savings per patient | Garfinkel & Mangin, 2010 |

ADRs in elderly polypharmacy patients accounted for a disproportionate amount of the $177 billion yearly cost of medication-related morbidity and mortality in the US, according to a landmark study by Ernst and Grizzle [94]. Anticoagulants, antidiabetics, and digoxin accounted for 66% of emergency hospitalizations for ADEs in older Americans, totaling over $3.5 billion yearly, according to a more cautious but methodologically robust 2011 review by Budnitz et al. [95].

According to a 2018 NHS review, 6.5% of all unscheduled hospital admissions in the UK were linked to adverse drug reactions (ADRs), which resulted in an annual direct cost of almost £2.5 billion. Of these, 70% might have been avoided through optimized prescribing [96]. ADR-attributable hospitalization costs range from €1–4 billion per country yearly, according to studies from Germany, the Netherlands, and Australia [97].

The financial impact of polypharmacy extends beyond direct medical expenses and includes lost productivity (for caretakers), out-of-pocket drug prices, and the costs to society of early death and institutionalization. The cost-effectiveness of deprescribing and medication review initiatives is regularly demonstrated by pharmacoeconomic analyses, with incremental cost-effectiveness ratios (ICERs) far below typical willingness-to-pay thresholds in a variety of healthcare systems [98].

## XII. PARTICULAR POPULATIONS IN POLYPHARMACY FOR ELDERLY

### A. Weak Elderly

Polypharmacy hazards are significantly raised by frailty, a clinical state of diminished physiologic reserve and heightened susceptibility to stresses. Due to compounding pharmacokinetic deterioration, frail elderly patients are more likely to develop adverse drug reactions (ADRs), falls, and drug accumulation [99]. The STOPPFrail criteria, which emphasize stopping preventative drugs (statins, bisphosphonates, and antihypertensives in patients with normotension) and vigorous symptom treatment, were created especially to direct medication reviews in frail elderly patients with short life expectancies [100].

### B. Dementia Patients

Dementia patients pose special polypharmacy challenges. Pharmacological treatment for behavioral and psychological symptoms of dementia (BPSD) is common, despite the substantial risk of harm and the paucity of data supporting its effectiveness. The U.S. FDA has issued a black-box warning on the increased mortality risk associated with antipsychotics used for BPSD in older dementia patients [101]. When anticholinergic drugs and anticholinesterase inhibitors (donepezil, rivastigmine) are taken together, a pharmacological antagonistic reaction occurs that lowers the effectiveness of treatment. It is clinically necessary to do a systematic medication review in individuals with dementia, paying special attention to anticholinergic burden, psychotropic rationalization, and the withdrawal of drugs of dubious efficacy [102].

### C. Elderly People in Institutions

The elderly cohort with the highest prevalence and severity of polypharmacy—and possibly the most susceptible to its negative effects—are those who live in long-term care facilities, or nursing homes. Research regularly shows that at least 50% of people in nursing homes use ten or more drugs per day [103]. A cluster-randomized study by Furniss et al. reported that a pharmacist-led evaluation of 330 nursing home residents decreased drug-related problems by 53% over a 12-month period [104]. Systematic medication review programs have shown significant benefits in long-term care settings.

### D End-of-Life Support

Treatment objectives for patients nearing the end of their lives drastically change from illness prevention and modification to symptom management and quality of life. In patients who are dying, continuing preventive drugs (statins, bisphosphonates, aspirin, and antihypertensives)

has no discernible benefit and increases pill load, side effects, and prescription costs without improving outcomes. Palliative deprescribing, which involves systematically stopping non-beneficial or potentially hazardous prescriptions for patients nearing the end of their lives, is an ethically sound and evidence-based strategy that can enhance patient comfort, lower costs, and better align care with patient values [105].

## XIII. POLICY AND HEALTH SYSTEM ACTIONS

Interventions at the health system and policy levels are necessary to address polypharmacy as a systemic issue that goes beyond the scope of individual clinician-patient interactions [106].

Mandatory medication reconciliation at all care transitions (hospital admission, discharge, transfer), pharmacist review requirements for patients receiving five or more concurrent prescriptions, reimbursement frameworks that provide financial incentives for thorough medication review, and integration of real-time prescription monitoring programs to identify PIM prescribing and hazardous combinations are among the regulatory measures implemented in several countries [107].

In order to incorporate geriatric pharmacology, deprescribing techniques, and multidisciplinary medication management into undergraduate and graduate training programs, medical education reform is needed. Polypharmacy and geriatric prescribing are not given enough attention in comparison to their clinical significance, according to surveys of medical school curricula [108].

Polypharmacy is specifically identified as a high-priority safety concern by the WHO's Medication Without Harm initiative, which is a part of the Global Patient Safety Challenge. The initiative calls for national action plans to implement medication review programs, patient empowerment tools, and electronic medication management systems across member states [109]. Measurable improvements in prescribing quality, patient safety, and healthcare cost reduction have been reported by nations that have implemented national polypharmacy reduction programs, such as Scotland (Polypharmacy Guidance, 2015, updated 2018), Australia (National Medicines Policy), and Canada (Deprescribing Guidelines) [110].

## XIV. DISCUSSION

Polypharmacy is unquestionably one of the biggest and most unappreciated risks to the health of senior citizens globally, according to the evidence compiled in this analysis. The

combination of disease-specific prescription practices, increasing multimorbidity, and unprecedented demographic aging has produced a perfect storm where the very drugs meant to promote health are causing significant iatrogenic harm [111].

This synthesis yields several important findings. First off, polypharmacy is not intrinsically harmful; rather, the objective is to maximize pharmaceutical use rather than reduce it. Clinicians should aim for appropriate polypharmacy, where each medicine is appropriately dosed, genuinely indicated, and consistent with patient goals. Differentiating healthy polypharmacy from problematic polypharmacy and addressing the latter by systematic, evidence-based drug optimization are clinical imperatives [112].

Second, every prescription decision must take into account the fundamental, non-negotiable clinical reality that older patients are pharmacologically vulnerable due to age-related pharmacokinetic and pharmacodynamic alterations. One systematic source of avoidable damage is the continuous use of dose guidelines from younger adult populations for older patients [113].

Third, a multilayered, coordinated approach is needed to handle polypharmacy; a single intervention is insufficient. Health information technology, pharmacogenomics, patient empowerment, multidisciplinary team collaboration, individual clinician competence and awareness, and supportive policy frameworks must all be used in concert [114].

Fourth, there is a strong financial argument for funding polypharmacy management. There is a clear economic case for investing in the health system because the costs of avoidable adverse drug reactions (ADRs), hospital stays, falls, and fractures are significantly higher than those of organized medication reviews and deprescribing initiatives [115].

There are still a number of important research gaps, including the need for high-quality RCTs on deprescribing in particular elderly subgroups (frail, dementia, end-of-life), prospective studies on the long-term effects of pharmacogenomics-guided prescribing in elderly polypharmacy patients, more research on the best CDSS alert design to minimize fatigue while maximizing clinical impact, and standardization of patient-reported outcome measures specific to polypharmacy burden across international research settings [116].

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## XV. CONCLUSION REVIEW

Polypharmacy is an exceptionally significant and significant global geriatric health issue. Up to two-thirds of older persons in high-income countries and a rapidly growing number in poor countries are prescribed five or more prescriptions at the same time, which leads to a series of largely avoidable pharmacological, clinical, economic, and humanistic consequences.

Medication-related dangers are significantly increased by the physiological vulnerabilities associated with aging, and improper prescribing is sustained by the structural dispersion of healthcare systems. The Beers Criteria, STOPP/START, comprehensive geriatric evaluation, and multidisciplinary drug review are just a few of the clinical strategies that have been proven to be effective in identifying and treating inappropriate polypharmacy. Implementation, education, and cultural transformation in healthcare delivery are the challenges.

Pharmacogenomics, artificial intelligence, and digital health tools are examples of emerging technologies that have revolutionary potential for improving and customizing medicine administration for senior citizens. Sustained investment in workforce development, equitable access, regulatory support, and research is necessary to realize this potential.

The ultimate objective of polypharmacy management is to match pharmacotherapy with the priorities of each unique older patient—maximizing quality of life, maintaining function, and promoting dignity throughout the aging process—rather than counting pills. To improve clinical practice and patient outcomes, the research community, healthcare institutions, and politicians must collaborate swiftly and methodically.

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