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POLYPHARMACY IN AGEING POPULATIONS: NEUROLOGICAL RISKS, HEALTHCARE DETERMINANTS AND DIGITAL INTERVENTIONS IN EUROPE

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ABSTRACT

As Europe's population ages, managing polypharmacy has evolved from an individual clinical concern into a major public health priority [3, 4]. Broadly driven by multi-organ chronic diseases and uncoordinated specialist care, the accumulation of multiple drug prescriptions generates heavy clinical and economic costs [5, 6]. This narrative review maps the neurological risks linked to polypharmacy and evaluates the structural healthcare factors that shape prescribing habits across European nations [1, 12]. Gathering data published between 2010 and 2024, we synthesized evidence regarding regional prevalence, cumulative anticholinergic burden, and system-level weaknesses [4, 14]. Current statistics reveal that 40–50% of older Europeans aged ≥ 65 years face polypharmacy, though rates differ widely between countries [4, 24]. The central nervous system bears a disproportionate share of drug-induced harm; common outcomes include accelerated cognitive decline, acute delirium, motor instabilities, and the worsening of pre-existing psychiatric or epileptic conditions [13, 14, 19]. Much of this damage stems directly from an unmonitored anticholinergic burden, which tracks closely with elevated dementia rates and mortality [15, 16]. At the institutional level, fragmented communication between physicians, poor access to comprehensive geriatric assessments, and the absence of routine medication reviews act as primary drivers of unsafe prescribing [2, 26]. Mitigating these risks requires integrating targeted organizational shifts—such as mandatory deprescribing protocols and clinical pharmacist oversight—with digital infrastructure, including artificial intelligence platforms and clinical decision-support software [7, 31, 33, 34].

KEYWORDS

Polypharmacy; Ageing Population; Neurological Complications; Healthcare Systems; Digital Health; Public Health Policy

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1. Introduction

Modern medicine has successfully extended life expectancy, but the resulting rise in chronic multimoribity has left older adults exposed to highly complex drug regimens [3, 5]. While treating coexisting diseases often requires multiple therapies, the cumulative pharmacological burden frequently triggers unintended adverse outcomes [1, 11]. Among these, neurological complications stand out as particularly damaging, directly threatening patient autonomy and stripping years from an individual's independent life [9, 13].

The demographic landscape of Europe is shifting rapidly. For citizens aged ≥ 65 years, managing three or more chronic diagnoses has become the baseline reality rather than the exception [4, 12]. This demographic pressure strains conventional clinical frameworks [6, 7]. Polypharmacy cannot be dismissed as a simple series of isolated, poor prescribing choices by individual doctors. Instead, it is a structural byproduct of modern healthcare design, thriving wherever specialized care is siloed, electronic health records are fragmented, and primary care gatekeeping is weak [22, 23].

This narrative review examines how polypharmacy alters central nervous system function in older patients and details the systemic factors driving inappropriate drug accumulation [1, 12]. Additionally, we analyze the clinical value of structured deprescribing and evaluate how health policy and emerging digital tools might be leveraged to secure safer pharmacotherapy [2, 33].

2. Methodology

We designed this narrative review to synthesize contemporary evidence examining the intersection of polypharmacy, neurological complications, and European healthcare system structures. We executed a systematic literature search across PubMed, Scopus, and Web of Science covering papers published from January 2010 through December 2024. Our search strategy utilized targeted keyword strings, including polypharmacy, multimorbidity, older adults, neurological complications, anticholinergic burden, deprescribing, healthcare system, and Europe.

To ensure depth, we combed through the reference list of every retrieved paper to capture additional relevant data. We prioritized high-tier evidence, focusing on systematic reviews, meta-analyses, large-scale prospective cohort studies, and recent healthcare policy frameworks issued by international agencies [2, 3, 10]. Papers were selected if they evaluated populations aged $\geq$ 65 years and explicitly tracked clinical, cognitive, or system-level variables [11, 12]. We excluded non-English publications and studies lacking direct relevance to European health delivery models. Given the narrative scope of this synthesis, we did not deploy a formal, rigid quality-appraisal tool; instead, we filtered for methodological rigor, sample size, and chronological relevance. The final matrix comprises 35 pivotal references.

3. Polypharmacy as a Public Health Issue

The sheer scale of polypharmacy across Europe has transformed it into an expensive public health crisis [1, 3]. Epidemiological registries show that between 40% and 50% of Europeans over the age of 65 are on concurrent multiple drug regimens [4]. This baseline figure, however, hides deep geographic divides. While the Netherlands reports a relatively conservative prevalence of around 30%, Sweden climbs to 44%, and Greece exceeds 55% [4, 24]. These sharp regional disparities do not reflect differences in actual disease burden; rather, they point to deeper variations in national prescribing cultures, the strength of primary care models, and the local integration of geriatric medicine [6, 22].

This high chemical exposure places immense pressure on hospital infrastructure [5, 23]. It drives up emergency admissions, lengthens hospital stays, and increases avoidable mortality [1, 13]. In practice, a vast portion of serious clinical events—ranging from sudden mechanical falls to acute delirium and rapid cognitive deterioration—can be traced back to drug-to-drug interactions or inappropriate prescriptions [9, 10].

The financial toll is equally severe [7]. Health budgets are drained not just by the procurement of medications, but by treating their downstream complications [12, 30]. Today, toxic drug reactions and adverse interactions trigger up to 10% of all acute medical admissions among older adults in several European states [1, 13]. To build effective countermeasures, healthcare planners must stop viewing polypharmacy as a private, isolated problem between a doctor and a patient, and start treating it as a failure of system coordination [6, 22].

4. Healthcare System Determinants of Polypharmacy

The design of a healthcare system directly dictates how many pills a patient takes [22, 23]. Fragmented delivery models are arguably the largest structural driver of drug inflation: an older patient routinely balances visits to a cardiologist, a urologist, and a pulmonologist [25, 26]. When these specialists operate in institutional siloes, they rarely cross-reference prescriptions, resulting in therapeutic duplications, conflicting drug mechanisms, and a total lack of centralized oversight [25, 26].

This vulnerability is worsened by a widespread shortage of geriatricians across Europe [5]. Without specialized physicians trained to manage multi-organ pathology holistically, care defaults to organ-specific specialists whose guidelines often mandate adding more drugs [3, 12]. Countries with structural exceptions, such as Denmark and the Netherlands—where geriatric protocols are embedded early into primary care paths—consistently demonstrate significantly lower rates of potentially inappropriate medication use [24, 26].

Furthermore, the lack of interoperable, real-time electronic health records strips general practitioners of the visibility needed to manage a patient's full medical history [6, 7]. This blind spot is widened by unrecorded self-medication and the unregulated use of over-the-counter dietary supplements [1, 5]. Across several EU nations, 20% to 35% of older adults regularly consume active supplements without informing their physicians, introducing unmonitored variables into their baseline therapies [3, 12]. Once a drug is introduced into an older person's routine, it is rarely removed; without mandatory, scheduled review intervals, prescriptions simply accumulate over time until a major clinical event occurs [7, 10, 22].

5. Mechanisms of Drug-Related Harm in the Elderly

Ageing fundamentally alters how the human body processes and responds to chemical compounds, making older adults uniquely vulnerable to adverse drug reactions [1, 9]. On the pharmacokinetic side, natural declines in glomerular filtration and hepatic blood flow slow down drug clearance, which raises steady-state plasma concentrations and extends half-lives [3, 12]. Concurrently, shifts in body composition—specifically an increase in adipose tissue relative to lean muscle mass and total body water—alter the distribution volumes of lipophilic and hydrophilic agents [5, 9].

Pharmacodynamically, structural changes within the central nervous system often increase receptor sensitivity, amplifying the sedative and cognitive side effects of psychotropic medications [1, 13]. The risk of harm increases exponentially with each added compound [1, 5]. Competitive inhibition or induction within the cytochrome P450 enzyme pathways represents a major pathway for toxicity [3, 12]. Furthermore, age-related drops in serum albumin can increase the unbound, free-floating fraction of highly protein-bound medications, elevating the risk of toxicity even when dosages remain within conventional therapeutic ranges [9, 13].

6. Neurological Consequences of Polypharmacy

The central nervous system is exceptionally sensitive to cumulative drug toxicity, making neurological dysfunction a primary consequence of polypharmacy [1, 13]. Regrettably, because these symptoms present as confusion, memory gaps, or balance issues, clinicians frequently misinterpret them as the inevitable effects of old age or the progression of primary dementia, delaying crucial adjustments [9, 12].

Cognitive impairment is a frequent byproduct of inappropriate polypharmacy, often causing notable deficits in working memory, sustained attention, and executive processing [14, 27]. On an acute level, drug toxicity is a leading cause of delirium, especially among hospitalized older adults [28]. This acute brain failure is linked to higher mortality, permanent cognitive decline, and prolonged institutionalization [13, 28].

In patients being treated for epilepsy, complex multi-drug regimens can backfire, inducing heavy sedation and paradoxically lowering the seizure threshold through competitive drug interactions [19]. Similarly, improper drug combinations can cause or worsen severe psychiatric symptoms, including treatment-resistant depression, severe anxiety, and drug-induced psychosis [1, 14]. Distinguishing between primary neurodegenerative diseases and drug-induced cognitive states remains a major diagnostic challenge; failing to make this distinction often leads to a delayed or missed opportunity for deprescribing [8, 9, 13].

7. Anticholinergic Burden and Cognitive Decline

The cumulative anticholinergic burden is a primary driver of drug-induced neurological decline in older adults [14, 16]. A wide range of commonly prescribed medications possess unexpected or secondary anticholinergic properties, including bladder stabilizers, older antihistamines, tricyclic antidepressants, and antipsychotics [16, 17]. When these medications are taken concurrently, their combined effect regularly causes memory deficits, confusion, and acute delirium [14, 15, 27].

Older adults are highly susceptible to these complications due to a natural decline in central cholinergic transmission and increased blood-brain barrier permeability [9, 14]. A critical issue in clinical practice is that even drugs with mild anticholinergic activity, which seem safe in isolation, can cause severe cognitive impairment when accumulated across a multi-drug regimen [16, 17]. Long-term cohort studies confirm that an unmonitored, elevated anticholinergic burden is strongly linked to an increased risk of developing formal dementia and higher overall mortality [15, 16].

While validated clinical tools like the Anticholinergic Cognitive Burden (ACB) scale can quantify these risks, their use outside of academic or specialized geriatric departments remains rare [17]. Systematically calculating and reducing this specific chemical burden is an essential step in protecting cognitive health in older populations [10, 18].

8. Clinical Implications and Deprescribing Strategies

Reversing the momentum of polypharmacy requires shifting clinical practice from a mindset of accumulation to one of continuous optimization [2, 7]. Regular, structured medication reviews must be established as a non-negotiable standard of care for complex older patients [10, 20]. Deprescribing—the planned, supervised tapering and cessation of medications that are no longer useful or cause active harm—is a highly effective clinical tool for improving cognitive and physical outcomes [8, 21].

To be successful, deprescribing requires clear, uninterrupted lines of communication across the healthcare continuum [6, 26]. Transition-of-care audits are vital: when a patient moves from a secondary hospital ward back

to primary care, clear accountability must be established to determine which physician is responsible for stopping outdated or temporary prescriptions [22, 23, 25]. Shared electronic health records and integrated care coordination can prevent the automatic renewal of redundant or dangerous medications [7, 23, 26].

Equally important is patient and caregiver education [2, 10]. When families understand that stopping certain medications reduces fall risks and clears confusion, adherence to deprescribing protocols increases significantly [3, 8]. This practical strategy is heavily supported by the STOPP/START criteria version 3 (2023), which provides clinicians with 190 updated, evidence-based recommendations for safely discontinuing inappropriate drugs and starting beneficial ones [35].

9. Future Directions and Technological Innovations

Despite clear evidence of the harms of polypharmacy, major implementation gaps remain [1, 6]. The literature still lacks large-scale, long-term randomized controlled trials that measure the direct impact of deprescribing on hard clinical outcomes, such as mortality rates or the reversal of cognitive decline [2, 10]. Future research must focus on real-world interventions while health systems work to embed clinical pharmacists directly into primary care teams [20, 21, 31].

Digital innovation provides highly scalable tools to support these efforts [6, 33]. Modern clinical decision-support systems (CDSS), when integrated directly into electronic prescribing networks, can instantly flag hazardous drug interactions, track cumulative anticholinergic scores, and alert physicians to age-inappropriate choices before a script is signed [32, 33]. These automated warnings can reduce prescribing errors by up to 40% in primary care environments [32].

Additionally, artificial intelligence and machine-learning algorithms can screen vast electronic health databases to identify high-risk patients by cross-referencing multi-morbidities with complex pharmacy records [34]. This predictive analytics capability allows clinicians to intervene and prevent adverse drug events before they occur [33, 34]. At the consumer level, digital health apps and connected electronic pill dispensers offer real-time tracking of medication use and early detection of adverse side effects [2, 7]. To maximize the benefit of these digital tools, health systems must prioritize software interoperability and build clear regulatory frameworks to govern AI use in daily clinical practice [33, 34].

10. Policy Recommendations for Healthcare Systems

Resolving the systemic issue of polypharmacy requires bold, coordinated policy interventions that go beyond individual clinical decisions [6, 7]. National health authorities should mandate structured, periodic medication reviews within primary care frameworks, targeting individuals aged ≥75 years or those managing multiple chronic conditions [10, 20]. Solid evidence shows that structured, interdisciplinary reviews can reduce inappropriate prescribing rates by 20% to 30% [29, 30].

To support this, healthcare payers should fund the integration of clinical pharmacists into primary care networks and geriatric teams [31]. Pharmacist-led interventions have consistently demonstrated success in driving deprescribing initiatives, lowering medication errors, and reducing drug-related hospitalizations [2, 31].

Policymakers must also invest in unifying digital infrastructure [25]. National health strategies must mandate the use of shared electronic health records and centralized prescribing networks to eliminate the data siloes between medical specialists [23, 26]. Finally, public health agencies should launch targeted educational campaigns to warn the public about the risks of unmonitored over-the-counter self-medication and supplement use, empowering older adults to co-manage their treatment plans safely [3, 8, 10].

11. Discussion

The findings of this review show that polypharmacy in Europe is no longer just an individual clinical side effect; it is a structural challenge built into modern, fragmented healthcare delivery models [4, 6, 23]. With prevalence rates among older adults stuck between 40% and 50% across the continent, the issue sits at the intersection of demographic changes, rigid guidelines, and fragmented medical care [4, 6, 23].

The high rate of drug-induced neurological injuries shows how vulnerable the ageing brain is to multi-drug regimens [9, 13]. Our synthesis highlights that a significant portion of cognitive decline, acute confusion, and motor instability is driven by medication side effects rather than non-modifiable neurodegenerative diseases [13, 14, 27]. This distinction is critical for clinicians. Misdiagnosing a drug-induced cognitive state as primary dementia triggers a dangerous "prescribing cascade," where more medications are added to treat side effects, missing an important opportunity to deprescribe [8, 10].

Central to these neurological risks is the unmonitored accumulation of an anticholinergic burden [14, 16]. The data linking cumulative anticholinergic exposure to long-term cognitive decline and mortality are clear and concerning [15, 16]. Our review emphasizes that even drugs with low anticholinergic scores can cause significant cognitive harm when combined across a long prescription list [16, 17]. This reveals a clear gap in routine care: while objective tools like the Anticholinergic Cognitive Burden scale are well-validated, they are rarely used outside of academic geriatric wards [17].

The wide variations in polypharmacy rates across Europe—from 30% in the Netherlands to over 55% in Greece—prove that health system design shapes prescribing habits [4, 24]. Countries that rely on strong primary care gatekeeping and integrated electronic coordination achieve structurally safer prescribing profiles [25, 26]. Conversely, fragmented, specialist-heavy systems without a central point of clinical accountability naturally encourage therapeutic duplication and dangerous drug interactions [22, 26].

Addressing this problem requires shifting from passive awareness to active intervention, supported by modern clinical guidelines. The publication of the STOPP/START criteria version 3 (2023) is a major step forward, expanding actionable indicators to 190 and giving clinicians a clear framework to stop inappropriate prescribing [35]. However, guidelines alone will not solve the issue without institutional backup. The digital health transition—specifically deploying AI-driven clinical decision-support systems (CDSS) and interoperable electronic health records—offers a practical, proven way to reduce prescribing errors by up to 40% [32, 33].

11.1 Limitations of the Current Evidence

Several limitations in the current literature should be noted. First, as a narrative review, this paper did not utilize a formal systematic scoring tool for study quality, introducing potential selection bias. Second, there is a clear shortage of high-quality, long-term randomized controlled trials that measure the direct impact of deprescribing on hard clinical endpoints, such as reduced mortality or the reversal of cognitive decline [2, 10]. Most available studies focus on short-term process metrics, like counting the number of pills removed, rather than tracking long-term patient health. Finally, accurate epidemiological data on over-the-counter self-medication and dietary supplement use among older Europeans remain scarce, leaving a significant source of drug-related harm unmeasured in national health registries [1, 5].

12. Conclusions

Polypharmacy remains a major, unresolved threat to public health across Europe's ageing populations [3, 4]. While adding medications is often clinically necessary, inappropriate multi-drug use carries severe risks, particularly to the central nervous system, where it can cause delirium, accelerate cognitive decline, and worsen psychiatric conditions [13, 14, 19].

These prescribing patterns are heavily driven by institutional flaws, including siloed specialist care, a shortage of geriatric resources, and a lack of routine medication reviews [22, 26]. Addressing these structural root causes is essential to protecting older patients [7, 23].

Emerging technologies, such as AI-backed decision-support software and integrated electronic health networks, provide powerful tools to improve medication safety [32, 34]. However, turning these digital tools into routine care requires sustained policy updates, targeted infrastructure funding, and deep interdisciplinary teamwork [6, 33]. Ultimately, health systems must integrate clinical, organizational, and technological strategies to successfully reduce the burden of polypharmacy and safeguard independent living for older adults across Europe [10, 21, 35].

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