

Review

Not peer-reviewed version

Prescribing Cascade as a Therapeutic Error: A Danger for Geriatric Patients with Multimorbidity

[Adrian Bryła](#)^{*}, Jarosław Woron, [Miłosz Miedziaszczyk](#), Barbara Lorkowska-Zawicka, [Beata Bujak-Giżycka](#), Daniel Orzechowski, Paulina Połetek, Wojciech Pałys

Posted Date: 27 November 2025

doi: 10.20944/preprints202511.2152.v1

Keywords: prescribing cascade; polypharmacy; chronic kidney disease; drug safety



Preprints.org is a free multidisciplinary platform providing preprint service that is dedicated to making early versions of research outputs permanently available and citable. Preprints posted at Preprints.org appear in Web of Science, Crossref, Google Scholar, Scilit, Europe PMC.

Copyright: This open access article is published under a [Creative Commons CC BY 4.0 license](#), which permit the free download, distribution, and reuse, provided that the author and preprint are cited in any reuse.

Disclaimer/Publisher's Note: The statements, opinions, and data contained in all publications are solely those of the individual author(s) and contributor(s) and not of MDPI and/or the editor(s). MDPI and/or the editor(s) disclaim responsibility for any injury to people or property resulting from any ideas, methods, instructions, or products referred to in the content.

Review

Prescribing Cascade as a Therapeutic Error: A Danger for Geriatric Patients with Multimorbidity

Adrian Bryła ^{1,2,*}, Jarosław Woron ^{1,3,4,5}, Miłosz Miedziaszczyk ⁶, Barbara Lorkowska-Zawicka ¹, Beata Bujak-Gizycka ¹, Daniel Orzechowski ², Paulina Połetek ² and Wojciech Pałys ⁷

¹ Department of Clinical Pharmacology, Chair of Pharmacology, Faculty of Medicine, Jagiellonian University Medical College, Krakow, Poland

² Clinical Pharmacy Team, Ludwik Rydygier Specialist Hospital, Krakow, Poland

³ University Hospital in Krakow, Clinical Department of Anesthesiology and Intensive Care and Clinical Pharmacology Consulting Office

⁴ University Center for Monitoring and Research on Adverse Drug Reactions, Kraków, Poland

⁵ Pharma Consult, Pharmacotherapy Safety Team, Zakopane, Poland

⁶ Department of Clinical Pharmacy and Biopharmacy, Poznan University of Medical Sciences, Poznan, Poland

⁷ Department of Anesthesiology and Intensive Care, SPZOZ Hospital in Sanok, Poland

* Correspondence: adrian.bryla@uj.edu.pl

Abstract

The aging of the population and the increasing prevalence of multimorbidity contribute to the widespread use of polypharmacotherapy, which in turn elevates the risk of adverse drug reactions and clinically significant drug–drug interactions. One of the key yet frequently underestimated issues in clinical practice is the prescribing cascade, which occurs when an adverse drug reaction is misinterpreted as a new medical condition, leading to the initiation of an additional medication. This phenomenon is particularly relevant in the elderly population, in whom altered pharmacokinetics and pharmacodynamics, together with reduced organ reserve, increase susceptibility to adverse drug events, including nephrotoxicity. The objective of this paper is to review current evidence on the mechanisms and clinical consequences of the prescribing cascade—with particular emphasis on renal function deterioration—as well as strategies for its prevention in the geriatric population. Analysis of the literature indicates that prescribing cascades remain insufficiently recognized in clinical practice, despite the availability of pharmacotherapy assessment tools such as the Beers Criteria and the STOPP/START criteria. Documented prescribing cascades have been shown to contribute to deterioration in health status and quality of life, an increased frequency of hospitalizations, and a greater burden on healthcare systems. Particularly concerning are cascades involving cardiovascular, neurological, and analgesic medications, which may induce or exacerbate renal injury, ultimately leading to chronic kidney disease and organ failure. Prescribing cascades represent a significant yet frequently underestimated threat to the efficacy and safety of pharmacotherapy in older adults. Their consequences may extend beyond reduced quality of life and increased treatment costs to include serious complications such as the development of renal failure. Enhancing clinicians’ awareness, conducting systematic medication reviews, and employing validated assessment tools are essential for the identification and prevention of prescribing cascades, thereby reducing the risk of renal injury and improving clinical outcomes.

Keywords: prescribing cascade; polypharmacy; chronic kidney disease; drug safety

1. Introduction

Population aging and the increasing prevalence of multimorbidity have led to a growing reliance on polypharmacotherapy, which substantially raises the risk of adverse drug reactions and clinically significant drug–drug interactions. Among the key yet still underappreciated challenges in clinical

practice is the phenomenon known as the prescribing cascade. This occurs when an adverse drug reaction is misinterpreted as a manifestation of a new disease, prompting the initiation of an additional medication. Such an approach may trigger a vicious cycle of subsequent pharmacological interventions, markedly amplifying the risk of further complications [1,2]. This problem is particularly pronounced in geriatric patients, in whom altered pharmacokinetics and pharmacodynamics, reduced organ reserve, and the coexistence of multiple chronic conditions significantly increase the risk of adverse drug events, their accumulation, and drug–drug interactions [2,3]. Of particular concern are cascades involving cardiovascular, analgesic, and anti-inflammatory agents, which may contribute to renal impairment and even the development of chronic kidney disease and renal failure. The consequences of prescribing cascades therefore extend beyond reduced quality of life and increased risk of hospitalization, encompassing serious organ complications that place an additional burden on healthcare systems. Despite the availability of tools supporting the evaluation of pharmacotherapy appropriateness, such as the Beers Criteria and STOPP/START criteria, prescribing cascades remain insufficiently recognized and often overlooked in clinical practice. The aim of this paper is to review the current evidence regarding the mechanisms and clinical consequences—particularly with respect to renal function deterioration—as well as strategies to prevent prescribing cascades in the geriatric population.

2. Risk Factors for Prescribing Cascades

Identification of risk factors for the occurrence of prescribing cascades is a key element in limiting the prevalence of this phenomenon. It reduces negative health consequences for the patient and enables verification and improvement of treatment standards, particularly in patients with multimorbidity. Preventing and eliminating prescribing cascades is therefore an important step toward improving the quality of care and clinical outcomes [4]. Risk factors for adverse prescribing cascades can be grouped into categories related to the medical status of the patient and those that are “non-medical,” associated with the current ease of access to medications and other medical products. In the first category, we include advanced age, multimorbidity, polypharmacy, and overprescribing, often linked to multispecialist treatment provided by several physicians without mutual verification of ongoing pharmacotherapy. Within this group, particular attention should be paid to the risk of renal injury-both acute kidney injury (AKI) and chronic kidney disease (CKD). Many drugs prescribed concurrently as part of cascades (e.g., nonsteroidal anti-inflammatory drugs, ACE inhibitors, diuretics, and nephrotoxic antibiotics) may exert cumulative renal burden, resulting in progressive renal impairment, especially in geriatric patients. [5–8]. The second group of risk factors includes obtaining prescriptions online without direct physician consultation, easy availability of over-the-counter drugs (OTC), and, consequently, the possibility of self-medication and unnecessary supplementation (pathosupplementation). Additional contributing factors are the widespread promotion of medications and supplements in pharmacies, mass media advertising (television, internet), and pharmacy-based sales promotions. Table 1 summarizes the risk factors for the occurrence of prescribing cascades [5,6,9].

Table 1. Risk factors for the occurrence of a prescribing cascade.

Risk factor	A mechanism promoting the prescribing cascade
Patient age	Age-related changes in drug metabolism and excretion (pharmacokinetics) as well as tissue responsiveness to drugs (pharmacodynamics) increase susceptibility to adverse drug reactions. Use of high-risk medications in geriatric populations.
Sex	In certain therapies, women have a higher likelihood of developing prescribing cascades, due to differences in drug absorption rates, hormonal regulation, and metabolic pathways.

Polypharmacy	A large number of concurrently used drugs increases the probability of drug–drug interactions and adverse events, which may be mistakenly interpreted as new diseases.
Multimorbidity	The coexistence of multiple comorbidities predisposes to multi-organ dysfunction of varying severity, which affects drug metabolism and elimination. Multiple diseases often require multiple medications.
Chronic use of multiple medications	Long-term therapies promote the accumulation (“overlapping”) of adverse effects and increase the risk of their misinterpretation.
Lack of comprehensive medication review	Lack of regular assessment of the appropriateness of a given therapy (the entire treatment regimen) perpetuates the use of unnecessary medications and fosters the development of prescribing cascades. Additionally, the absence of dose reassessment maintains adverse drug effects. Prescribing more drugs instead of minimizing doses, and the failure to consider non-pharmacological alternatives before initiating drug therapy, further contribute to the problem.
Overprescribing	Insufficient communication about pharmacological interventions implemented by various specialists involved in patient care, including primary care physicians.
Misinterpretation of symptoms	Adverse drug reactions are misinterpreted as new disease entities, and the patient receives additional medications instead of therapeutic modification.
Insufficient knowledge of prescribing cascades among healthcare professionals	Insufficient knowledge of the relationship between drugs and symptoms results in a failure to recognize that a new symptom is an adverse effect of a medication rather than a new disease.
Self-medication	The trend toward a “healthy lifestyle,” widespread availability of OTC drugs, and self-directed treatment, often reinforced by lack of trust in physicians and insufficient pharmacological knowledge.
Pathosupplementation (unnecessary supplementation without clinical indication)	Dietary supplements as part of alternative treatment approaches. Easy access to various supplements, combined with aggressive marketing, promotes their use. Supplements are often perceived as an element of a “healthy lifestyle” and part of pro-health trends.

Prescribing cascades may occur in any patient experiencing health deterioration, but age-related physiological changes naturally predispose to worsening health status. Age is a parameter defining the biological and physiological aspects of aging and is associated with the natural predisposition to age-related diseases and their treatment. In this group, renal impairment is particularly prevalent, increasing susceptibility to adverse drug reactions from medications eliminated renally. Consequently, older adults are more likely to develop acute kidney injury as a result of prescribing cascades, and long-term exposure may even induce chronic kidney disease. Accurate data on the physiology and pathology of aging may help reduce unnecessary polypharmacy. However, clinical trials often exclude or insufficiently represent older adults with multimorbidity, resulting in a lack of evidence-based (EBM) guidelines for combination drug therapy in this population. This leads to suboptimal pharmacotherapeutic choices—frequently involving the use of “older” drugs with a high risk of adverse events, particularly nephrotoxic complications. The lack of data derived from clinical research also contributes to insufficient use of modern therapies in geriatric patients, often justified by concerns about poor tolerability due to age. On the other hand, unexpected cascades may occur when new medications are introduced without a thorough analysis of age-related pathophysiological changes. In summary, the underrepresentation of older adults with multimorbidity in clinical trials results in a lack of precise evidence-based pharmacotherapeutic guidelines for this population, fostering the occurrence of prescribing cascades and increasing the risk of renal insufficiency [5–7,10]. Verification of risk factors facilitates the recognition of prescribing cascades, yet practical tools to help physicians reliably identify cascades, assess them appropriately, and manage them effectively are

still lacking. Polypharmacy, although considered a risk factor for prescribing cascades, is undoubtedly an essential element of good prescribing practice in aging populations. At the same time, the lack of systematic evaluation of renal function during therapy selection further exacerbates the risk of cascades leading to acute kidney injury or progression of chronic kidney disease. The classification of cascades as appropriate or inappropriate (intended/unintended) may evolve over time depending on the clinical status of the patient. [7,8,12]. Therapeutic regimens, typically designed with a disease- and organ-specific focus, often overlook an interdisciplinary assessment of renal function. Failure to account for this aspect promotes therapeutic decisions that result in additive adverse drug effects and, consequently, increase the risk of prescribing cascades. Thus, a key question arises: Why does the risk of prescribing cascades increase in clinical practice? Table 2 presents cause-and-effect relationships of prescribing cascades, including their association with renal injury progression. [5–9,11,12,15].

Table 2. Why is the risk of prescribing cascades rising in clinical practice.

Treating the disease rather than the patient with the disease	<i>In the context of appropriately tailored pharmacotherapy, patient characteristics play a crucial role and may constitute significant risk factors for the occurrence of adverse drug reactions, including complex, multifactorial complications arising from the specific nature of the pharmacotherapy employed</i>
<i>Uncritical and context-free application of therapeutic guidelines</i>	<i>A therapeutic guideline must address not only individual diseases, but its appropriate application in a given patient should always be considered within the full spectrum of multimorbidity</i>
Assumption of a class effect within specific drug groups used in the patient	Within specific drug classes, a uniform class effect does not exist, which results from differences in pharmacokinetic and pharmacodynamic (PK/PD) parameters, as well as variability in adverse effect profiles and the associated risk factors for their occurrence.
Fragmentation of multimorbidity in pharmacological decision-making	Decisions regarding the initiation of pharmacotherapy for individual disease entities should always be guided by consideration of the overall spectrum of multimorbidity in the patient
Lack of benefit–risk assessment prior to initiation of pharmacotherapy	Before initiating any medication, the benefit–risk balance must be assessed, as it is influenced by patient-specific characteristics, coexisting risk factors for adverse events, concomitant pharmacotherapy, the use of complementary or alternative medicines, and dietary supplements. Equally relevant is the consumption of broadly defined recreational substances, as well as a history of prior drug-induced adverse reactions
<i>Self-medication and supplementation</i>	They may trigger drug interactions and complications, ultimately modifying the benefit–risk balance of the ongoing pharmacotherapy
<i>Lack of awareness of the adverse effect profiles of prescribed drugs</i>	In the context of polypharmacotherapy, clinicians must have a thorough understanding of the adverse effect profiles of prescribed agents and the risk factors predisposing to their development
Misinterpretation of drug-induced adverse effects as disease symptoms without consideration of ongoing pharmacotherapy	When new symptoms occur in a patient receiving pharmacotherapy, the primary consideration should be whether they are attributable to the treatment itself. If confirmed, appropriate modifications of the pharmacotherapy are required

Uncritical use of electronic tools for assessing the risk of drug–drug interactions in polypharmacotherapy	Most drug–interaction prediction tools fail to indicate the dosage thresholds at which interactions become clinically relevant, and only a limited number report interactions arising from the additive adverse effects of concomitantly used medications
Cumulative adverse effects of drugs in polypharmacotherapy as a source of complications in patients with multimorbidity	The additive effects of adverse reactions represent one of the most frequent forms of drug interactions in clinical practice. The symptoms that emerge through this mechanism frequently initiate a prescribing cascade.

3. Examples of Prescribing Cascades and Their Clinical Significance

Prescribing cascades are a common but often underrecognized phenomenon in clinical practice, particularly among older adults. They occur when an adverse drug reaction is misinterpreted as a new medical condition, leading to the initiation of an additional drug rather than recognition of the underlying cause. In the long term, this process not only increases the risk of inappropriate polypharmacy but also heightens the likelihood of drug-related morbidity, hospitalizations, and healthcare costs [1,7,12]. The tables below summarize clinically important prescribing cascades described in recent consensus statements and systematic reviews. Table 3 and Table 4 presents cascades that are particularly relevant in older adults, identified through the *ThinkCascades* tool and the international list of potentially inappropriate prescribing cascades (PIPC) [1,7,12].

Table 3. Clinically important prescribing cascades.

Drug A	Adverse effect	Drug B
Calcium Channel Blocker	Peripheral edema	Diuretic
Diuretic	Urinary incontinence	Overactive bladder medication
Antipsychotic	Extrapyrimalidal symptoms	Antiparkinsonian agent
Benzodiazepine	Cognitive impairment	Cholinesterase Inhibitor or memantine
Benzodiazepine	Paradoxical agitation or agitation secondary to withdrawal	Antipsychotic
Selective Serotonin Reuptake Inhibitor (SSRI) / Serotonin-norepinephrine Reuptake Inhibitor (SNRI)	Insomnia	Sleep agent (e.g., Benzodiazepines, Benzodiazepine Receptor Agonists, Sedating antidepressant, Melatonin)
NSAID	Hypertension	Antihypertensive
Urinary Anticholinergics	Cognitive impairment	Cholinesterase inhibitor or memantine
Alpha-1 Receptor Blocker	Orthostatic hypotension, dizziness	Vestibular sedative (e.g., betahistine, Antihistamines, Benzodiazepines)

Table 4. Other prescribing cascades.

Drug A	Adverse effect	Drug B
Cardiovascular system		
Angiotensin converting enzyme inhibitor	Cough	Cough remedy
Antihypertensive	Orthostatic hypotension/dizziness	Antiemetic
Drug-induced hypertension	Hypertension	Antihypertensive drugs

Beta-blocker (particularly lipophilic e.g., propranolol)	Depression	Antidepressant
Beta-blocker (particularly lipophilic e.g., propranolol)	Erectile dysfunction	Phosphodiesterase-5 inhibitor, alprostadil
Calcium channel blocker, Gabapentin, Pregabalin	Peripheral edema	Diuretic
Calcium channel blocker	Constipation	Laxative
Diuretic	Gout or Hyperuricemia	Anti-gout agent
Diuretic	Urinary incontinence	Overactive bladder medication
Hydroxymethylglutaryl-coenzyme A (HMG Co-A) reductase inhibitor (statin)	Myalgia/myositis	Pain reliever
HMG Co-A reductase inhibitor	Myalgia/myositis	Mineral supplement, Quinine sulfate
HMG Co-A reductase inhibitor	Insomnia	Sleep agent
Digoxin	Nausea	Antiemetic
Midodrine	Hypertension	Antihypertensive
Central nervous system		
Anticonvulsant	Rash	Topical corticosteroid
Anticonvulsant	Nausea	Antiemetic
Antipsychotic	Extrapyramidal symptoms	Beta-blocker, Antiparkinsonian agent, Anti-tremor antimuscarinic
Antipsychotic	Akathisia or tardive movements	Sedative
Antipsychotic	Arrhythmia	Antiarrhythmic
Antipsychotic	Hyperglycemia	Antihyperglycemic
Benzodiazepine	Cognitive impairment	Cholinesterase Inhibitor
Cholinesterase inhibitor	Urinary incontinence	Overactive bladder medication
Cholinesterase inhibitor	Insomnia	Sleep agent
Cholinesterase inhibitor	Gastrointestinal upset	Antiemetic, Bismuth subsalicylate
Cholinesterase inhibitor	Diarrhea	Antidiarrheal
Cholinesterase inhibitor	Rhinorrhea	Antihistamine
Dopaminergic Antiparkinsonian agent	Psychotic symptoms, hallucinations	Antipsychotic
Selective serotonin reuptake inhibitor/Serotonin and norepinephrine reuptake inhibitor (SSRI/SNRI)	Urinary Incontinence	Overactive bladder medication
Tricyclic antidepressant	Cognitive Impairment	Cholinesterase Inhibitor
Tricyclic antidepressant	Constipation	Laxative
Tricyclic antidepressant	Urinary incontinence	Overactive bladder medication
Flunarizine	Depression	Antidepressant
Lithium	Extrapyramidal symptoms	Antiparkinsonian agent
Venlafaxine	Hypertension (dose-related)	Antihypertensive
Venlafaxine	Tremor	Benzodiazepine
Anticholinergics	Dyspepsia/reflux (gastroesophageal reflux disease – ‘GERD’)	Proton pump inhibitor
Drug-induced movement disorders	Movement disorders	Antiparkinsonian drugs
Endocrine system		

Dipeptidyl peptidase 4 (DPP-4) inhibitor (e.g., sitag- liptin, saxagliptin)	Joint pain	Nonsteroidal anti-inflammatory drug
Sodium-glucose cotransporter-2 (SGLT-2) inhibitor	Mycotic genital infections	Antifungal
Metformin	Diarrhea	Antidiarrheal
Pioglitazone or Rosiglitazone	Edema	Diuretic
Rosiglitazone	Heart failure	Diuretic
Gastrointestinal system		
Anticholinergic antiemetic	Urinary retention	Alpha-1 receptor blocker
Antidopaminergic antiemetic	Extrapyramidal symptoms	Antiparkinsonian agent
Laxative	Diarrhea	Antidiarrheal agent
Proton pump inhibitor	Osteoporosis, fractures	Vitamin supplement
Proton pump inhibitor	Vitamin or Mineral Deficiency	Vitamin supplement
Musculoskeletal system		
Bisphosphonate	Gastritis	Gastroprotective agent
Nonsteroidal anti-inflammatory drug (NSAID)	Gastritis/gastric ulcer/gastrointestinal bleed	Gastroprotective agent
NSAID	Nausea	Antiemetic
NSAID	Hypertension	Antihypertensive
NSAID	Worsening of heart failure	Heart failure agent
Opioid	Depression	Antidepressant
Urogenital system		
Alpha-1 receptor blocker	Orthostatic hypotension, dizziness	Vestibular suppressant
Urinary anticholinergic	Dry mouth	Saliva substitute
Miscellaneous system		
Carbapenem (e.g., imipenem, meropenem, ertapenem)	Seizures	Anticonvulsant
Corticosteroid	Insomnia	Sleep agent
Corticosteroid	Psychosis	Antipsychotic
Corticosteroid	Hypertension	Antihypertensive
Acitretin	Vulvo-vaginal candidiasis	Antifungal
Erythromycin	Arrhythmia	Antiarrhythmic
Fludrocortisone	Hypertension	Antihypertensive
Iron supplement	Constipation	Laxative

The clinical significance of these cascades is multifaceted. First, they frequently contribute directly to deterioration in patients’ functional status. For example, calcium channel blocker–induced peripheral edema treated with diuretics may result in dehydration and falls. Similarly, benzodiazepine-related cognitive impairment treated with cholinesterase inhibitors only adds to the pharmacological burden without addressing the underlying cause. Second, an important yet often underestimated aspect of prescribing cascades is their impact on renal function. The use of diuretics in response to adverse effects of other medications (e.g., edema caused by calcium channel blockers or NSAIDs) may lead to dehydration, electrolyte disturbances, and accelerated decline in glomerular filtration. Consequently, the risk of nephrotoxicity from additional medications, accumulation of drug metabolites, and further progression of kidney disease increases. In older adults, whose renal reserve is already limited, such cascades can significantly increase the risk of acute kidney injury

(AKI) or accelerate the development of chronic kidney disease (CKD). Third, prescribing cascades often contribute to therapeutic inertia, as clinicians may attribute drug-related symptoms (such as dizziness, hypotension, or worsening renal function tests) to aging or disease progression rather than to adverse drug effects [7,12]. Recent systematic reviews emphasize that prescribing cascades are not random events but rather reproducible and predictable patterns observed across healthcare systems [1]. Recognition of these patterns is therefore critical for implementing preventive strategies such as medication review and deprescribing. In particular, the PIPC list developed by the international expert panel provides clinicians with a practical tool for identifying high-risk cascades, while the *ThinkCascades* tool offers a structured approach to evaluating drug-symptom associations in daily practice [7,12]. Ultimately, the presence of prescribing cascades highlights the importance of regular medication review, interdisciplinary collaboration, and patient education. Raising awareness of well-documented cascades such as those listed above may help clinicians distinguish adverse drug reactions from disease progression—including declining renal function and thereby reduce inappropriate polypharmacy and its associated risks.

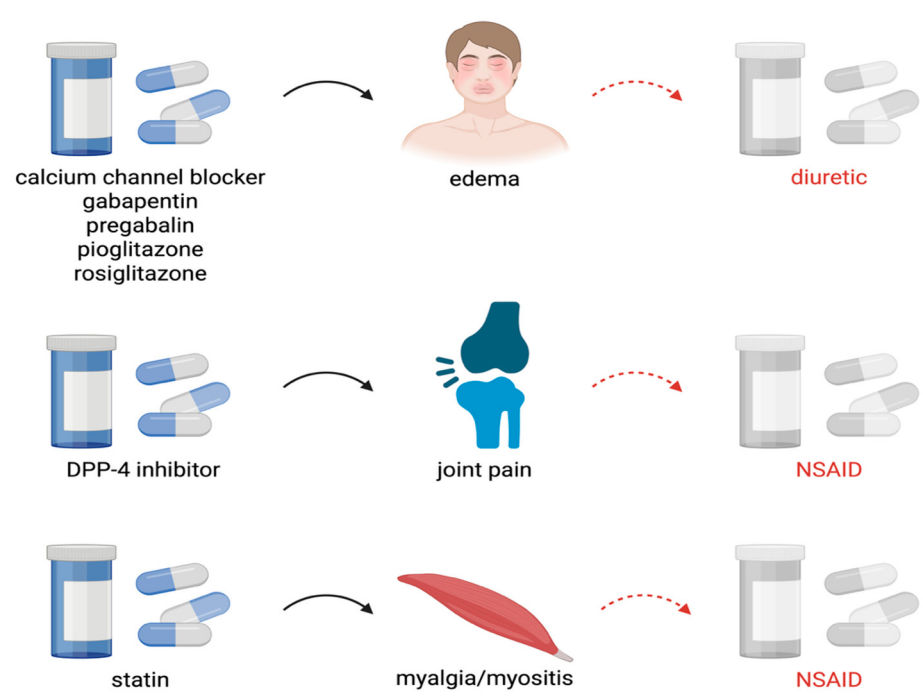


Figure 1. Examples of prescribing cascades affecting kidney function. DPP-4, Dipeptidyl peptidase 4; NSAID, Nonsteroidal anti-inflammatory drug. Created in BioRender. Miedziaszczyk, M. (2025) <https://BioRender.com/welwul>.

4. Consequences of Prescribing Cascades

A prescribing cascade can lead to serious health, social, and economic consequences. Although this phenomenon may appear to result from concern for the patient, it often worsens their clinical condition, leads to inappropriate treatment (so-called "therapeutic vicious circles") and polypharmacotherapy, which turns into polypragmasy. As a result, patients may experience intensified symptoms such as dizziness, drug-induced headaches, falls, delirium, cognitive impairment, balance disorders, orthostatic hypotension, or painsomnia. Importantly, some of these symptoms—such as delirium, balance disturbances, or hypotension—are often mistakenly attributed to the "natural" aging process or progression of the underlying disease, which further delays appropriate intervention. These are only some of the potential consequences of prescribing cascades, which negatively affect patients' quality of life, leading to reduced mobility and independence and, quite often, the need for hospitalization [12]. Findings from observational studies and systematic

reviews, as well as daily clinical practice, clearly indicate that prescribing cascades are a significant risk factor for hospitalization, especially in older adults, where the reason for hospital admission is not the primary disease but rather adverse drug reactions introduced in response to symptoms caused by previous pharmacotherapy. Examples include falls due to hypnotics or dehydration caused by diuretics prescribed in response to edema induced by NSAIDs or certain antidepressants. In the long term, prescribing cascades also contribute to rising healthcare costs, both direct (such as hospitalizations, diagnostics, and additional specialist consultations) and indirect (loss of independence, the need for continuous care). According to Farrell B and McCarthy LM, deprescribing and early identification of prescribing cascades can significantly reduce systemic expenditures as well as ease the burden on medical staff [7,14].

5. Identification and Prevention of Prescribing Cascades

Currently, there is a lack of practical tools to help physicians and pharmacists reliably detect, correctly assess, and manage prescribing cascades. *Ponte et al.* developed an 8-point (4 questions) scale to assess the prescribing cascade. Prescribing cascade is assumed to occur if the score is 4 or higher, reflecting the severity of the prescribing cascade. Table 5 presents a tool for assessing the occurrence of drug cascade prescription [15].

Table 5. Prescribing cascade assessment tool.

<i>Existence of ADR, either expected or unknown:</i>		
Doubtful	0	
Yes	1	
Yes, but misunderstood		2
<i>Action followed against the ADR:</i>		
Treatment discontinuation	0	
Continued with dose reduction		1
Continued unchanged or with another drug of the same group		2
<i>Existence of a second drug treatment for the ADR:</i>		
No	0	
Yes	1	
<i>Overall result of this new treatment:</i>		
Patient improves		0
Patient worsens or remains unchanged	1	
A new ADR appears	2	
The new ADR requires a third drug treatment		3

Dreischulte et al. proposed a tool that assesses whether the prescribing cascade is appropriate or inappropriate [6]. The tool is based on the following 6 questions. Although prescribing cascades are most often perceived as problematic, they may be appropriate and therapeutically beneficial in certain clinical situations. McCarthy et al. point out two important issues to consider when deciding on a prescribing cascade. First, consider whether the intentional initiation of a prescribing cascade aligns with the patient's treatment goals (patient well-being and improved quality of life). Second, consider whether the risks and benefits of the prescribing cascade have been discussed with the patient and whether the patient has been informed of the long-term effects [16]. Table 6 presents the Prescription Cascade Benefit Assessment Tool.

Table 6. Prescribing cascade benefit assessment tool.

Does/did the precipitating drug cause or pose a risk for a clinically relevant adverse drug reaction?
Is the precipitating drug still indicated?

Can a treatment adjustment of the precipitating drug prevent adverse drug reactions
Can switching the precipitating drug prevent adverse drug reactions?
Can the second drug have a beneficial effect on adverse drug reactions?
Is the benefit–risk balance of the prescribing cascade positive?

Analyzing everything that has been described, with particular emphasis on the risk factors for the occurrence of prescribing cascades, as well as clinical practices that increase the risk of their occurrence, we made an attempt to formulate general principles which, when implemented in clinical practice, may help prevent prescribing cascades. Table 7 presents the key points of clinical practice, which we can refer to as a list of good clinical practices [3].

Table 7. How to Prevent Prescribing Cascade – Table of Good Practice.

Area	Principle / Clinical Practice
Oligopharmacotherapy	Use only absolutely essential medications.
Zero tolerance for unnecessary drugs	Eliminate therapies without clinical indications.
Contextual pharmacotherapy	Take into account comorbidities and the individual situation of the patient.
Patient assessment	Before introducing a new drug, evaluate the entire pharmacotherapy, risk of interactions, and potential adverse effects.
Deprescribing	Regularly discontinue unnecessary or harmful medications.
Adverse drug reactions	- First, consider discontinuing dietary supplements; - Limit unnecessary self-medication; - Respond immediately to new symptoms.
Informed patient	Educate the patient: treatment goals, risks of polypharmacy, and the need to report adverse effects.

6. Conclusions

Prescribing cascades constitute a clinically significant yet underrecognized problem in geriatric pharmacotherapy. Their occurrence not only promotes inappropriate polypharmacy but also contributes to deterioration in patients’ functional status, an increased risk of hospitalization, and higher healthcare costs. Particularly alarming are cascades involving cardiovascular, analgesic, and neurological agents, which may accelerate the decline of renal function and predispose to acute kidney injury or chronic kidney disease. The findings of this review highlight the urgent need to raise awareness among healthcare professionals about the mechanisms and consequences of prescribing cascades. Regular medication reviews, systematic monitoring of renal function, and the use of validated assessment tools—such as the Beers Criteria, STOPP/START, and PIPC—are essential steps toward minimizing the risk of inappropriate prescribing and preventing renal complications. Interdisciplinary collaboration and patient education further strengthen preventive strategies. Ultimately, addressing prescribing cascades is not only a matter of improving medication safety but also a prerequisite for enhancing the quality of life and clinical outcomes in older adults.

Author Contributions: Conceptualization, A.B. and M.M.; formal analysis, A.B. and M.M.; data curation, A.B., J.W., M.M., B.L.Z., B.B.G.; writing—original draft preparation, A.B. J.W., M.M., B.L.Z., B.B.G., D.O., P.P., W.P.; writing—review and editing, A.B. and M.M.; visualization, A.B.; J.W.: M.M; supervision, A.B and M.M.; project administration, A.B. and M.M. All authors have read and agreed to the published version of the manuscript.

Funding: This research received no external funding.

Data Availability Statement: Not applicable.

Conflicts of Interest: The authors declare no conflict of interests.

Abbreviations

The following abbreviations are used in this manuscript:

AKI	Acute Kidney Injury
CKD	Chronic Kidney Disease
ACEI	Angiotensin Converting Enzyme Inhibitors
OTC	Over The Counter
EBM	Evidence Based Medicine
PIPC	Potentially Inappropriate Prescribing Cascades
GERD	Gastroesophageal Reflux Disease
DDP-4	Dipeptidyl Peptidase 4
SGLT-2	Sodium Glucose Cotransporter 2
NSAID	Nonsteroidal Antiinflammatory Drug
ADR	Adverse Drug Reaction

References

1. Adrien, O.; Mohammad, A.K.; Hugtenburg, J.G.; et al. Prescribing Cascades with recommendations to Prevent or Reverse Them: A Systematic Review. *Drugs and Anging*. **2023**, *40*, 1085-1100.
2. Shahid, F.; Moriarty, F.; Boland, F.; et al. Prescribing cascades in ambulatory care: A structured synthesis of evidence. *Pharmacotherapy*, **2024**, *44*, 87-96.
3. Woron, J.; Tyminski, R.; Drygalski, T.; et al. Farmakoterapia nieprawidlowo dobrana, co to znaczy w praktyce, a takze w Oddziale Intensywnej Terapii. *Anestezjologia i Ratownictwo*, **2023**, *17*, 42-48.
4. Rochon, P.A.; Gurwitz, J.H. The prescribing cascade revisited. *Lancet*, **2017**, *6*, 1778-1780.
5. Doherty, A.S.; Shahid, F.; Moriarty, F.; et al. Prescribing cascades in community-dwelling adults: A systematic review. *Pharmacol. Res. Perspect.* **2022**, *10*, 1-32.
6. Dreischulte, T.; Shahid, F.; Muth, C.; et al. Prescribing Cascades: How to Detect Them, Prevent Them, and Use Them Appropriately. *Dtsch. Arztebl. Int.* **2022**, *119*, 745-752.
7. McCarthy, L.M.; Savage, R.; Dalton, K.; et al. A Tool for Identifying Clinically Important Prescribing Cascades Affecting Older People. *Drugs Aging*. **2022**, *39*, 829-840.
8. Shahid, F.; Doherty, A.; Wallace, E.; et al. Prescribing cascades in ambulatory care: A structured synthesis of evidence. *Pharmacotherapy*. **2024**, *44*, 87-96.
9. Chen, Z.; Liu, Z.; Zeng, L.; et al. Research on prescribing cascades: a scoping review. *Front. Pharmacol.* **2023**, *14*, 1-10.
10. Jennings, A.A.; Doherty, A.S.; Clyne, B.; et al. Stakeholder perceptions of and attitudes towards problematic polypharmacy and prescribing cascades: a qualitative study. *Age Ageing*. **2024**, *53*, 1-12.
11. O'Mahony, D.; Rochon, P.A. Prescribing cascades: we see only what we look for, we look for only what we know. *Age Ageing*. **2022**, *51*, 1-4.
12. Rochon, P.A.; O'Mahony, D.; Cherubini, A.; et al. International expert panel's potentially inappropriate prescribing cascades (PIPC) list. *Eur. Geriatr. Med.* **2025**, 1-12.
13. American Geriatrics Society Beers Criteria. Update Expert Panel. American Geriatrics Society 2023. Updated Beers Criteria for Potentially Inappropriate Medication Use in Older Adults. *J. Am. Geriatr. Soc.* **2023**, *71*, 923-947.
14. Farrell, B.; Tsang, C.; Raman-Wilms, L.; et al. What are priorities for deprescribing for elderly patients? Capturing the voice of practitioners: a modified Delphi process. *PLoS One*. **2015**, *10*, 1-16.
15. Ponte, M.L.; Wachs, L.; Wachs, A.; Serra, H.A. Prescribing cascade. A proposed new way to evaluate it. *Medicina (B Aires)*. **2017**, *77*, 13-16.
16. McCarthy, L.M.; Visentin, J.D.; Rochon, P.A. Assessing the Scope and Appropriateness of Prescribing Cascades. *J. Am. Geriatr. Soc.* **2019**, *67*, 1023-1026.

Disclaimer/Publisher's Note: The statements, opinions and data contained in all publications are solely those of the individual author(s) and contributor(s) and not of MDPI and/or the editor(s). MDPI and/or the editor(s) disclaim responsibility for any injury to people or property resulting from any ideas, methods, instructions or products referred to in the content.