JHPHS
Journal of Hospital Pharmacy and Health Services

Original Paper

Open Access

Potentially inappropriate medication in older adults that have the capacity to induce cognitive impairment: prevalence and associated factors

Alaíde Matos SILVA[1], Laís Lessa PANTUZZA[2], Adriano Max REIS[1]

[1]Residência Multiprofissional em Atenção à Saúde do Idoso do Hospital das Clínicas da Universidade Federal de Minas Gerais, Belo Horizonte, Brasil; [2]Faculdade de Farmácia da Universidade Federal de Minas Gerais, Belo Horizonte, Brasil.

Corresponding author: Reis AM, amreis@outlook.com

Submitted: 07-03-2025 Resubmitted: 05-09-2025 Accepted: 26-09-2025

Double blind peer review

Abstract

Objective: To investigate the prevalence of use of potentially inappropriate medications for older adults that have the capacity to induce cognitive impairment (PIMs-cog) and associated factors. **Methods:** Cross-sectional study with quantitative approach. PIMs-cog include drugs with anticholinergic, sedative, hypnotic effects and others capable of inducing *delirium*. Older adults were interviewed in two outpatient clinics of teaching hospitals in Belo Horizonte and in homes in the metropolitan region. The independent variables were divided into sociodemographic, pharmacotherapeutic and clinical-functional variables. The descriptive analysis included determination of the frequency of proportion for categorical variables and measures of central tendency and dispersion for numerical variables. Normality was assessed by the Shapiro-Wilk test. Univariate analysis was performed by Pearson's chi-square test. Variables with $p<0.20$ were included in the multivariate analysis. In the final model, variables with $p<0.05$ remained. **Results:** A total of 344 older adults, with a median age of 67.5 years, participated in this study. PIMs-cog was used by 14.5% of older adults. The use of at least one PIM-cog was independently associated with the presence of polypharmacy (OR = 5.84, CI = 2.67–12.80, $p = 0.00$), cancer (OR = 5.07, CI = 2.18–11.76, $p = 0.00$), neuropsychiatric diseases (OR = 4.09, CI = 2.03–8.25, $p = 0.00$) and rheumatic disease (OR = 2.06, CI = 1.04–4.06, $p = 0.04$). **Conclusion:** The prevalence of PIM-cog use was 14.5% in the sample investigated and showed a positive and independent association with polypharmacy, cancer, neuropsychiatric diseases and rheumatic diseases.

Keywords: older adults, cognitive impairment, drug therapy, potentially inappropriate medication.

Medicamentos potencialmente inapropriados em idosos e que apresentam capacidade de induzir comprometimento cognitivo: prevalência e fatores associados

Resumo

Objetivo: Investigar a prevalência do uso de medicamentos potencialmente inapropriados em idosos e que podem induzir comprometimento cognitivo (MPIs-cog) e os fatores associados. **Métodos:** Estudo transversal de abordagem quantitativa. MPIs-cog abrangem fármacos com efeitos anticolinérgicos, sedativos, hipnóticos e outros capazes de provocar *delirium*. Idosos foram entrevistados em ambulatórios de dois hospitais de ensino de Belo Horizonte (MG) e em domicílios da região metropolitana. Dividiu-se as variáveis independentes em sociodemográficas, farmacoterapêuticas e clínico-funcionais. A análise descritiva compreendeu a determinação da frequência de proporção para as variáveis categóricas e medidas de tendência central e de dispersão para as variáveis numéricas. Avaliou-se a normalidade pelo teste de Shapiro-Wilk. Realizou-se a análise univariada pelo Teste Qui-quadrado de Pearson. Na análise multivariada incluíram-se variáveis com $p<0,20$. No modelo final, permaneceram variáveis com $p<0,05$. **Resultados:** Participaram do estudo 344 idosos, com mediana de idade de 67,5 anos. MPIs-cog foi utilizado por 14,5% dos idosos. O uso de pelo menos um MPI-cog esteve independentemente associado à presença de polifarmácia (OR = 5,84, IC = 2,67–12,80, $p = 0,00$), câncer (OR = 5,07, IC = 2,18–11,76, $p = 0,00$), doenças neuropsiquiátricas (OR = 4,09, IC = 2,03–8,25, $p = 0,00$) e doença reumática (OR = 2,06, IC = 1,04–4,06, $p = 0,04$). **Conclusão:** A prevalência do uso de MPIs-cog foi de 14,5% na amostra investigada e apresentou associação positiva e independente com polifarmácia, câncer, doenças neuropsiquiátricas e doenças reumáticas.

Palavras-chave: idoso, declínio cognitivo, farmacoterapia, medicamentos potencialmente inapropriados.

Introduction

Aging is a physiological, irreversible, and universal process—although individualized and heterogeneous—resulting from the accumulation of biological changes that lead to functional decline of the organism with increasing age. It is the main risk factor for the development of neurodegenerative diseases[1,2]. The clinical syndrome of reduced physiological reserve associated with aging is known as frailty: the individual becomes more vulnerable to stressors and more susceptible to adverse health events, including those related to medication use[3-4]. Pharmacotherapy may exacerbate frailty and contribute to the occurrence of delirium, falls, anorexia, and functional and cognitive impairment[3].

Cognitive impairment involves alterations in memory, language, attention, learning, executive functioning, or visuospatial processing and can be assessed through neuropsychological tests. The more severe the cognitive decline, the greater the individual's dependence on others to perform daily activities, leading to increased caregiver burden, greater strain on the healthcare system, and higher rates of institutionalization[5-7].

Explicit criteria for identifying potentially inappropriate medications for older adults (PIMs) have been developed based on consensus methods and scientific evidence, resulting, for instance, in the AGS/Beers Criteria[8] and the STOPP/START lists[9]. These medications have an increased potential to cause adverse effects due to pharmacokinetic and pharmacodynamic changes specific to the geriatric population. It is noteworthy that PIMs with significant effects on the central nervous system may contribute to cognitive decline[10-12]. Potentially inappropriate medications for older adults associated with the risk of cognitive impairment (PIMs-cog) include drugs with anticholinergic, sedative, or hypnotic properties, among others capable of inducing delirium[12-13].

Preserving cognition is crucial for maintaining independence and autonomy among older adults[5-7,12]. This population frequently uses multiple medications to treat health conditions arising from aging[3-5,10,12]. Although pharmacological therapy is effective in restoring and maintaining health, some medications may interfere with cognition and induce other adverse events[3-6,8-13]. Therefore, the present study aims to investigate the frequency of PIM-cog use among older adults and the factors associated with it.

Methods

Study Design

This was a cross-sectional study with a quantitative approach. The data used in this research originated from the project "Development and validation of an instrument for measuring Medication Literacy in older adults"[14].

Data Collection

The target population consisted of community-dwelling older adults aged 60 years or older, residing in Belo Horizonte (MG), Brazil, and surrounding metropolitan areas. Interviews were conducted between November 2021 and June 2022 either in the waiting rooms of two teaching hospitals in Belo Horizonte or in the participants' homes. The outpatient clinics where the study was carried out specialized in older adult health care, women's health, and anticoagulation.

Information was collected through self-reports provided by older adults during interviews conducted by previously trained undergraduate pharmacy students. Data were recorded on printed forms developed specifically for research purposes and subsequently organized into a database using EpiInfo software, version 7.2.5.0 (Centers for Disease Control and Prevention, Atlanta, United States).

Participants were selected by convenience sampling through invitations. Inclusion criteria were: being aged 60 years or older, using at least one medication, having self-reported reading ability, and not presenting hearing, visual, or cognitive impairments. The exclusion of individuals with such impairments aimed to minimize bias related to the ability to recognize and accurately report medication use.

Dependent Variable

Use of at least one PIM-cog (potentially inappropriate medication associated with cognitive impairment).

Independent Variables

Sociodemographic variables: sex, marital status, occupation (retired or not), age (<70 or ≥70 years), years of education, and monthly family income (measured in minimum wages).

Pharmacotherapeutic variables: Polypharmacy was defined as the use of five or more medications[15]. PIMs-cog were defined according to Cross et al.[13] and Santos et al.[12], including anticholinergic, sedative, and hypnotic drugs, as well as other medications capable of causing delirium listed in the Beers Criteria[8] and STOPP/START criteria[9].

Clinical-Functional Variables:

(i) Self-perceived health, categorized as positive perception (excellent, very good, or good) and negative perception (fair or poor);

(ii) Self-reported diseases, classified as arterial hypertension, diabetes mellitus, heart disease (myocardial infarction, stroke, arrhythmia, thrombosis, angina, or congestive disease), rheumatic disease, neuropsychiatric disease (central nervous system or psychiatric dysfunction), chronic kidney disease, and cancer;

(iii) Multimorbidity, defined as the presence of three or more diseases; and

(iv) Cognition.

Cognitive assessment was performed using the validated instrument Cognitive Abilities Screening Instrument – Short Form (CASI-S), developed by Teng et al.[16] and adapted to Brazilian Portuguese by Damasceno et al.[17]. According to the CASI-S, older adults with scores ≥23 were considered to have preserved cognition; for those aged over 70 years, preserved cognition was defined as scores ≥20.

Statistical Analysis

Descriptive analysis included determining frequency and proportion for categorical variables and measures of central tendency and dispersion for numerical variables.

The Shapiro–Wilk test was used to assess normality. Univariate analysis was performed using Pearson's Chi-square test or Fisher's Exact test, as appropriate, to determine the association between the use of PIM-cog and the independent variables. Variables with $p < 0.20$ were included in the multivariate analysis. The backward selection strategy was used to identify the best-fitting model. In the final model, variables with $p < 0.05$ were retained, adopting a 5% significance level. Model fit quality was evaluated using the Hosmer–Lemeshow test. The database was created using EpiInfo software.

Ethical Aspects

This research complies with Resolutions No. 466/2012 and No. 510/2016 of the Brazilian Ministry of Health. The study was approved by the Research Ethics Committee (CEP) of the Federal University of Minas Gerais (UFMG) (CAAE: 19835219.4.0000.5149). All data supporting the findings of this study are available upon request to the corresponding author. Only older adults who signed the Informed Consent Form (ICF) were included in the study.

Results

A total of 344 older adults participated in this study, with a median age of 67.5 years (interquartile range – IQR: 8.8), and 39.8% were aged ≥70 years. The sociodemographic, clinical-functional, and pharmacotherapeutic characteristics of the participants are presented in Table 1.

Regarding clinical-functional variables, 176 older adults (51.2%) presented multimorbidity, with a median of 3 diseases (IQR: 1.0). The most prevalent condition was arterial hypertension (69.8%), followed by heart disease (41.4%), rheumatic disease (35.5%), diabetes mellitus (28.7%), neuropsychiatric diseases (23.7%), cancer, and chronic kidney disease (13.0% each). Most participants had preserved cognition (80.0%) according to the CASI-S. Only 34.4% reported a negative self-perception of health (fair or poor).

The median number of medications used by participants was 5 (IQR: 3), and 42.7% met the criterion for polypharmacy. Older adults using at least one PIM-cog accounted for 14.5% of the sample, with the majority (80.0%) using only one PIM-cog. One participant reported the concomitant use of four PIMs-cog: diazepam, quetiapine, promethazine, and cyclobenzaprine. Table 2 presents the PIMs-cog used by older adults in the study.

The most commonly used medications among the participants belonged to the benzodiazepine (BZP) class (26.6%). However, the most frequently used PIM-cog was zolpidem, reported by eight participants (12.5%). Among anticholinergic agents, tricyclic antidepressants (15.6%) and antipsychotics (15.6%) were the most prevalent, particularly amitriptyline (n=6) and haloperidol (n=4), respectively. Prednisone was the corticosteroid used by five participants (7.8%).

Table 3 presents the univariate and multivariate analyses of the association between the use of PIM-cog and the sociodemographic, clinical-functional, and pharmacotherapeutic characteristics of the older adults. The use of at least one PIM-cog was independently associated with polypharmacy (OR = 5.84, CI = 2.67–12.80, $p = 0.00$), cancer (OR = 5.07, CI = 2.18–11.76, $p = 0.00$), neuropsychiatric diseases (OR = 4.09, CI = 2.03–8.25, $p = 0.00$), and rheumatic disease (OR = 2.06, CI = 1.04–4.06, $p = 0.04$) in the final logistic regression model.

Table 1. Sociodemographic, Clinical-Functional, and Pharmacotherapeutic Characteristics of Older Adults Included in the Study

Characteristics	Value[1]
Sociodemographic	
Age in years, median (IQR)	67.5 (8.8)
Age ≥ 70 years, *n* (%)	137 (39.8)
Sex: Female, *n* (%)	229 (66.6)
Marital status: Without partner, *n* (%)	175 (51.3)
Occupation: Retired, *n* (%)	204 (59.5)
Education: 0–8 years, *n* (%)	207 (60.2)
Income[2]: ≤ 2 minimum wages, *n* (%)	180 (55.2)
Clinical-functional	
Multimorbidity, *n* (%)	176 (51.2)
Number of diseases, median (IQR)	3 (1.0)
Hypertension, *n* (%)	236 (69.8)
Heart disease, *n* (%)	140 (41.4)
Rheumatic disease, *n* (%)	120 (35.5)
Diabetes mellitus, *n* (%)	97 (28.7)
Neuropsychiatric disorders, *n* (%)	80 (23.7)
Cancer, *n* (%)	44 (13.0)
Chronic kidney disease, *n* (%)	44 (13.0)
Cognition: Preserved, *n* (%)	278 (80.8)
Self-rated health perception: Negative, *n* (%)	117 (34.4)
Pharmacotherapeutic	
Number of medications, median (IQR)	5 (3.0)
Polypharmacy, *n* (%)	147 (42.7)
Use of PIM-cog, *n* (%)	50 (14.5)

[1]Total varies according to unanswered questions (N ≠ 344). [2]Value of the minimum wage (MW) in the year of the survey: R$ 1,100.00.

Table 2. Potentially Inappropriate Medications for Older Adults That May Induce Cognitive Impairment (PIMs-cog), by Drug Class

PIMs-cog	Older adults using the medication, *n* (%)
Anticholinergics (n)	**31 (48.4)**
Antipsychotics: haloperidol (4); quetiapine (3); risperidone (2); chlorpromazine (1)	10 (15.6)
Tricyclic antidepressants: amitriptyline (6); nortriptyline (3); imipramine (1)	10 (15.6)
First-generation antihistamines: dexchlorpheniramine (2); promethazine (2); diphenhydramine (1)	5 (7.8)
Antispasmodics: scopolamine butylbromide (2)	2 (3.1)
Muscle relaxants: carisoprodol (1); cyclobenzaprine (1)	2 (3.1)
Antiparkinsonian agents: biperiden (1)	1 (1.6)
Other antidepressants (with anticholinergic activity): paroxetine (1)	1 (1.6)
Sedatives and hypnotics (n)	**26 (40.6)**
Benzodiazepines (BZDs): clonazepam (7); diazepam (7); alprazolam (2); bromazepam (1)	17 (26.6)
Non-BZD hypnotics: zolpidem (8)	8 (12.5)
Barbiturates: phenobarbital (1)	1 (1.6)
Other medications that may cause delirium (n)	**7 (10.9)**
Systemic corticosteroids: prednisone (5); dexamethasone (2)	7 (10.9)

Table 3. Univariate and Multivariate Analysis of the Association Between the Use of PIM-cog Among Older Adults and Their Sociodemographic, Clinical-Functional, and Pharmacotherapeutic Characteristics

Variables	Use of PIM-cog		Univariate analysis[1]		Multivariate analysis[2]	
	Yes *n* (%)	No *n* (%)	OR (95% CI)	P value	OR (95% CI)	P value
Sex			1.71 (0.86–3.41)	0.13		
Female	38 (16.6)	191 (83.4)				
Male	12 (10.4)	103 (89.6)				
Age			0.60 (0.32–1.16)	0.12		
≥ 70 years	15 (10.9)	122 (89.1)				
< 70 years	35 (16.9)	172 (83.1)				
Education			0.90 (0.49–1.65)	0.73		
0–8 years	29 (14.0)	178 (86.0)				
> 8 years	21 (15.3)	116 (84.7)				
Income[3]			1.26 (0.66–2.38)	0.49		
> 2 MW	27 (15.0)	153 (85.0)				
≤ 2 MW	18 (12.3)	128 (87.7)				
Self-rated health			1.96 (1.06–3.59)	0.03		
Negative	24 (20.5)	93 (79.5)				
Positive	26 (11.7)	197 (88.3)				
Cognition			0.78 (0.34–1.74)	0.54		
Cognitive im-pairment	8 (12.1)	58 (87.9)				
Preserved cognition	42 (15.1)	236 (84.9)				
Multimorbidity			3.66 (1.72–7.81)	0.00		
Yes	41 (20.1)	163 (79.9)				
No	9 (6.4)	131 (93.6)				
Polypharmacy			6.99 (3.36–14.54)	0.00	5.84 (2.67–12.80)	0.00
Yes	40 (27.2)	107 (72.8)				
No	10 (5.1)	187 (94.9)				
Hypertension			1.13 (0.58–2.20)	0.72		
Yes	36 (15.3)	200 (84.7)				
No	14 (13.7)	88 (86.3)				
Diabetes mellitus			1.20 (0.63–2.30)	0.58		
Yes	16 (16.5)	81 (83.5)				
No	34 (14.1)	207 (85.9)				
Heart disease			1.03 (0.56–1.89)	0.93		
Yes	21 (15.0)	119 (85.0)				
No	29 (14.6)	169 (85.4)				
Rheumatic disease			2.46 (1.34–4.52)	0.00	2.06 (1.04–4.06)	0.04
Yes	27 (22.5)	93 (77.5)				
No	23 (10.6)	195 (89.4)				
Neuropsychiatric disorders			4.24 (2.26–7.93)	0.00	4.09 (2.03–8.25)	0.00
Yes	25 (31.3)	55 (68.8)				
No	25 (9.7)	233 (90.3)				
Cancer			3.34 (1.62–6.90)	0.00	5.07 (2.18–11.76)	0.00
Yes	14 (31.8)	30 (68.2)				
No	36 (12.2)	258 (87.8)				
Chronic kidney disease			1.59 (0.71–3.54)	0.26		
Yes	9 (20.5)	35 (79.5)				
No	41 (13.9)	253 (86.1)				

[1]Chi-square test. [2]Logistic regression. [3]Family monthly income measured in minimum wages (MW). Hosmer–Lemeshow test: $\chi^2 = 4.33$, degrees of freedom = 6, $p = 0.63$. *Note*. OR = odds ratio; CI = confidence interval (95%).

Discussion

In the present study, polypharmacy and diagnoses of cancer, neuropsychiatric disorders, and rheumatic diseases showed a positive and independent association with the use of PIM-cog among the older adults investigated. These results provide important insights for older adult care and highlight the risks associated with medication use at this stage of life.

A pharmacovigilance study conducted in South Korea[6] investigated voluntary reports of adverse reactions related to medication-induced cognitive impairment. The comorbidities most frequently associated with this phenomenon were cancer and neuropsychiatric disorders, followed by vascular and musculoskeletal diseases. These findings are consistent with those of the present study. Medication-related cognitive disturbances were mainly reported with zolpidem, tramadol, and morphine. It is noteworthy that zolpidem was also the most commonly used PIM-cog among older adults in this study. The use of this medication in geriatric patients is discouraged, and when effective alternatives are unavailable, it should be prescribed for a limited duration[8,9]. Further research—particularly with prospective designs—is needed to clarify the quality and strength of the evidence regarding the association between zolpidem use and the induction of cognitive impairment.

The frequency of PIM-cog use reported in previous studies ranged from 7% to 37.5%[12,13,18]. Higher prevalence rates (21.4% and 37.5%) were reported in Australia in studies limited to elderly patients diagnosed with mild cognitive impairment or dementia[13,18]. A Brazilian study conducted with a cohort of university employees aged over 60 years reported a lower prevalence of PIM-cog use (7%)[12]. In the present study, although the use of PIM-cog was higher, it was closer to the Brazilian study mentioned above, which also included community-dwelling older adults with various health conditions. The clinical predictors of medication-induced cognitive impairment identified in the South Korean pharmacovigilance study[6] included patient demographic data, use of drugs capable of causing cognitive decline, comorbidities, and the number of concomitant medications. These factors may explain the variability in PIM-cog use frequencies across studies.

Polypharmacy is positively associated with the use of PIMs and with the risk of cognitive decline[19,20], which explains the magnitude of the association between PIM-cog use and polypharmacy found among the older adults in this study. However, it is important to emphasize that the use of multiple medications is not always inappropriate. Therefore, pharmacotherapy in the geriatric population should be reviewed regularly to ensure that all medications being used are necessary and appropriate for the patient's health condition.

Older adults with cancer are frequently exposed to polypharmacy and to the use of PIMs-cog, especially benzodiazepines (BZPs), first-generation antihistamines, muscle relaxants, and anticholinergic antispasmodics[21-23]. The use of PIMs-cog may vary according to the type of neoplasm and is not always contraindicated, as these medications can play an important role in managing symptoms such as pain, nausea, and mood instability. Older adults with cancer who use multiple medications and PIMs may be more likely to experience psychological distress, including anxiety and depression[23]. However, PIMs may increase chemotherapy-related adverse effects and negatively impact survival, although evidence remains limited[22].

The use of multiple medications in this population increases the risk of drug–drug interactions, adverse reactions, and hospitalizations, while PIMs may reduce tolerance to oncologic therapy and are associated with functional decline in older adults. Therefore, it is essential to assess the necessity and safety of each medication at the onset of cancer treatment[24]. When the use of a PIM-cog is identified, a safer therapeutic alternative should be sought, or the duration of use should be minimized, with ongoing monitoring of cognitive changes in the patient.

Psychotropic drugs occupy a significant place in the explicit PIM criteria of the AGS/Beers and STOPP/START lists, due to their high anticholinergic burden and the risk of falls, dependence, cognitive decline, and mortality in older adults[8,9]. The occurrence of PIM use is common among patients with neuropsychiatric disorders[10]. The cross-sectional study by Sharma et al.[24] conducted in an outpatient psychiatric clinic for older adults found that more than 70% of participants were using potentially inappropriate psychotropics (PIPs) according to the two aforementioned lists. The most commonly used PIPs were long-acting BZPs and atypical antipsychotics. In psychogeriatrics, it is important to consider that aging increases sensitivity to drugs that act directly on the central nervous system, particularly anticholinergics[10-12]. Cholinergic neuronal activity is associated with attention processes and cerebral perfusion. Thus, the effects of anticholinergic medications have been investigated in certain cognitive domains—such as memory and language—as well as in relation to dementia risk. The concomitant use of more than one drug with anticholinergic burden over a prolonged period may cause saturation of cholinergic antagonism in the brain; therefore, this class should be used with caution in older adults[25].

The increase in life expectancy has also contributed to a growing proportion of older adults with rheumatic diseases. Polypharmacy affects at least half of this population and is associated with greater morbidity and mortality[26,27]. Among those with rheumatoid arthritis and systemic lupus erythematosus, chronic pain, anxiety, depression, and insomnia are common, increasing the likelihood of exposure to opioids, antidepressants, BZPs, and non-BZP hypnotics[26,27]. Another PIM-cog class widely used by patients with rheumatic diseases is glucocorticoids, which are strongly associated with polypharmacy. This occurs because these drugs contribute to comorbidities that also require pharmacological management, such as hypertension, diabetes mellitus, osteoporosis, and gastrointestinal ulcers. In addition, lupus flares and long-term prednisone use can trigger anxiety and insomnia, which are often treated with sedative medications[27]. For well-controlled rheumatoid arthritis, guidelines already contraindicate long-term glucocorticoid therapy and recommend gradual deprescription[26]. Prolonged glucocorticoid therapy has been associated with cognitive impairment characterized by memory deficits, reduced mental processing speed and concentration, and even "steroid-induced psychosis"[28]. Another important consideration is the increased risk of cancer—particularly lung cancer and lymphomas—among individuals with rheumatoid arthritis[26]. As mentioned earlier, oncologic diseases are also risk factors for the use of PIMs-cog.

One of the consequences of global population aging will be the increased occurrence of cognitive impairment among older adults[6]. Senescence itself brings cognitive consequences due to the reduction of brain volume, atrophy of white and gray matter,

decreased hippocampal neurogenesis, cerebral hypoperfusion, increased blood–brain barrier permeability, and disturbances in neurotransmission mechanisms[1,2]. The present study contributes to the discussion of factors associated with these phenomena, with special attention to the influence of medications on cognition. These effects are still underestimated, as cognitive decline is often attributed primarily to the progression of underlying diseases rather than to adverse drug reactions[6]. Moreover, the number of PIMs used by older adults may be higher than estimated, since analyses are generally based on prescribed medications, disregarding self-medication practices[23].

The use of PIM-cog may represent a modifiable factor in the risk of cognitive decline among older adults. However, observational studies such as this one do not allow causal inference. Randomized clinical trials and/or prospective observational studies are needed to establish causality. Selection bias represents one limitation of this study, as older adults treated in outpatient settings may present more complex clinical conditions and use more medications, including PIM-cog. Recall bias is also possible, as medication use was self-reported by participants without cross-validation through medical records or prescriptions, which may compromise the accuracy of exposure data. Additionally, no information was collected on medication duration or dosage, including whether the medication was used continuously or only as needed. It is important to highlight that the study was conducted in two outpatient clinics in Belo Horizonte and in the homes of older adults from a single metropolitan area. Therefore, the findings cannot be generalized to the broader older population.

Several studies have identified that different drug classes may increase the risk of cognitive impairment, including antiparkinsonian agents[6,11], antineoplastic drugs[5,6], statins[5,6], corticosteroids[28], proton pump inhibitors[5,29,30], opioids[5,6,11], antiepileptics[5,11,30], and antimicrobials[5,31]. Thus, it becomes evident that the current PIM-cog lists only partially capture medications associated with cognitive decline, as they focus on those deemed potentially inappropriate. This highlights the need to develop assessment instruments encompassing the use of drugs from different pharmacological classes with evidence, supported by high-quality clinical studies, of increasing the likelihood of cognitive disorders.

Conclusion

The frequency of PIM-cog use was 14.5% in the studied sample and showed a positive and independent association with polypharmacy, cancer, neuropsychiatric disorders, and rheumatic diseases. This study contributes to the ongoing discussion of factors associated with cognitive decline in older adults. Further research is needed to better understand the role of medications in this process.

Funding

This research did not receive any funding for its execution.

Author Contributions

AMS: project conception; data analysis and interpretation; manuscript drafting; critical review. LLNP: project conception; data analysis and interpretation.

AMMR: project conception; data analysis and interpretation; manuscript drafting; critical review. All authors approved the final version of this article and take responsibility for the information contained herein.

Conflict of Interest Statement

The authors declare that there are no conflicts of interest related to this article.

References

1. Dziechciaż M, Filip R. Biological psychological and social determinants of old age: bio-psycho-social aspects of human aging. Ann Agric Environ Med. 2014;21(4):835-838. doi:10.5604/12321966.1129943
2. Kritsilis M, V Rizou S, Koutsoudaki PN, et al. Ageing, Cellular Senescence and Neurodegenerative Disease. Int J Mol Sci. 2018;19(10):2937. doi:10.3390/ijms19102937
3. Randles MA, O'Mahony D, Gallagher PF. Frailty and Potentially Inappropriate Prescribing in Older People with Polypharmacy: A Bi-Directional Relationship?. Drugs Aging. 2022;39(8):597-606. doi:10.1007/s40266-022-00952-z
4. Reallon E, Chavent B, Gervais F, et al. Medication exposure and frailty in older community-dwelling patients: a cross-sectional study. Int J Clin Pharm. 2020;42(2):508-514. doi:10.1007/s11096-020-01007-2
5. Do D, Schnittker J. Utilization of Medications With Cognitive Impairment Side Effects and the Implications for Older Adults' Cognitive Function. J Aging Health. 2020;32(9):1165-1177. doi:10.1177/0898264319895842
6. Sunwoo Y, Eom SH, Yun JS, et al. Real-World Data-Derived Pharmacovigilance on Drug-Induced Cognitive Impairment Utilizing a Nationwide Spontaneous Adverse Reporting System. Medicina (Kaunas). 2024;60(7):1028. doi:10.3390/medicina60071028
7. Taylor-Rowan M, Kraia O, Kolliopoulou C, et al. Anticholinergic burden for prediction of cognitive decline or neuropsychiatric symptoms in older adults with mild cognitive impairment or dementia. Cochrane Database Syst Rev. 2022;8(8):CD015196. doi:10.1002/14651858.CD015196.pub2em

8. American Geriatrics Society Beers Criteria Update Expert Panel. American Geriatrics Society 2023 updated AGS Beers Criteria for potentially inappropriate medication use in older adults. J Am Geriatr Soc. 2023;71(7):2052-2081. doi:10.1111/jgs.18372

9. O'Mahony D, Cherubini A, Guiteras AR, et al. STOPP/START criteria for potentially inappropriate prescribing in older people: version 3. Eur Geriatr Med. 2023;14(4):625-632. doi:10.1007/s41999-023-00777-y

10. Hefner G, Hahn M, Toto S, et al. Potentially inappropriate medication in older psychiatric patients. Eur J Clin Pharmacol. 2021;77(3):331-339. doi:10.1007/s00228-020-03012-w

11. Kristensson JH, Zahirovic I, Londos E, et al. Medications causing potential cognitive impairment are common in nursing home dementia units - A cross-sectional study. Explor Res Clin Soc Pharm. 2021;3:100054. doi:10.1016/j.rcsop.2021.100054

12. Dos Santos ANM, Farias-Itao DS, Benseñor IM, et al. Potentially inappropriate medications and cognitive performance: cross-sectional results from the ELSA-Brasil study. Eur J Clin Pharmacol. 2023;79(7):927-934. doi:10.1007/s00228-023-03504-5

13. Cross AJ, George J, Woodward MC, et al. Potentially Inappropriate Medication, Anticholinergic Burden, and Mortality in People Attending Memory Clinics. J Alzheimers Dis. 2017;60(2):349-358. doi:10.3233/JAD-170265

14. Pantuzza LLN. Desenvolvimento e validação de um instrumento para mensuração do *Medication Literacy* em idosos [tese]. UFMG: Belo Horizonte;2022.

15. Masnoon N, Shakib S, Kalisch-Ellett L, et al. What is polypharmacy? A systematic review of definitions. BMC Geriatr. 2017;17(1):230. doi:10.1186/s12877-017-0621-2

16. Teng EL, Hasegawa K, Homma A, et al. The Cognitive Abilities Screening Instrument (CASI): a practical test for cross-cultural epidemiological studies of dementia. Int Psychogeriatr. 1994;6(1):45-62. doi:10.1017/s1041610294001602

17. Damasceno A, Delicio AM, Mazo DF, et al. Validation of the Brazilian version of mini-test CASI-S. Arq Neuropsiquiatr. 2005;63(2B):416-421. doi:10.1590/s0004-282x2005000300010

18. Cross AJ, George J, Woodward MC, et al. Potentially Inappropriate Medications and Anticholinergic Burden in Older People Attending Memory Clinics in Australia. Drugs Aging. 2016;33(1):37-44. doi:10.1007/s40266-015-0332-3

19. Caçador C, Teixeira-Lemos E, Oliveira J, et al. The prevalence of polypharmacy and potentially inappropriate medications and its relationship with cognitive status in Portuguese institutionalized older adults: a cross-sectional study. Int J Environ Res Public Health. 2022;19(5):2637. doi:10.3390/ijerph19052637

20. Niikawa H, Okamura T, Ito K, et al. Association between polypharmacy and cognitive impairment in an elderly Japanese population residing in an urban community. Geriatr Gerontol Int. 2017;17(9):1286-1293. doi:10.1111/ggi.12862

21. Bandidwattanawong C, Rattanaserikulchai P, Jetsadavanit N. Polypharmacy and potentially-inappropriate medications are prevalent in the elderly cancer patients receiving systemic cancer therapy and they co-relate with adverse outcomes. BMC Geriatr. 2023;23(1):775. doi:10.1186/s12877-023-04471-3

22. Ozkan M, Karahan I, Yalcin S, et al. Effects of Potentially Inappropriate Medications in Older Patients with Gastrointestinal System Cancer. Medeni Med J. 2023;38(4):284-290. doi:10.4274/MMJ.galenos.2023.03063

23. Ramsdale E, Ramsdale E, Mohamed M, Yu V, et al. Polypharmacy, potentially inappropriate medications, and drug-drug interactions in vulnerable older adults with advanced cancer initiating cancer treatment. Oncologist. 2022;27(7):e580-e588. doi:10.1093/oncolo/oyac053

24. Sharma R, Bansal P, Sharma A, et al. Prevalence and predictors of Potentially Inappropriate Psychotropic Medication in older adults with psychiatric illness. Asian J Psychiatr. 2021;66:102872. doi:10.1016/j.ajp.2021.102872

25. Hong CT, Chan L, Wu D, et al. Antiparkinsonism anticholinergics increase dementia risk in patients with Parkinson's disease. Parkinsonism Relat Disord. 2019;65:224-229. doi:10.1016/j.parkreldis.2019.06.022

26. Lee J, Singh N, Gray SL, et al. Optimizing Medication Use in Older Adults With Rheumatic Musculoskeletal Diseases: Deprescribing as an Approach When Less May Be More. ACR Open Rheumatol. 2022;4(12):1031-1041. doi:10.1002/acr2.11503

27. Séguin DJ, Peschken CA, Dolovich C, et al. Polypharmacy and potentially inappropriate medication use in older adults with systemic lupus erythematosus. Arthritis Care Res (Hoboken). 2023;75(2):356-364. doi:10.1002/acr.24766

28. De Alcubierre D, Ferrari D, Mauro G, et al. Glucocorticoids and cognitive function: a walkthrough in endogenous and exogenous alterations. J Endocrinol Invest. 2023;46(10):1961-1982. doi:10.1007/s40618-023-02091-7

29. Khan Z, Mehan S, Saifi MA, et al. Proton Pump Inhibitors and Cognitive Health: Review on Unraveling the Dementia Connection and Co-morbid Risks. Curr Alzheimer Res. 2024;20(11):739-757. doi:10.2174/0115672050289946240223050737

30. Nevado-Holgado AJ, Kim CH, Winchester L, et al. Commonly prescribed drugs associate with cognitive function: a cross-sectional study in UK Biobank. BMJ Open. 2016;6(11):e012177. Published 2016 Nov 30. doi:10.1136/bmjopen-2016-012177

31. Zerah L, Bihan K, Kohler S, et al. Iatrogenesis and neurological manifestations in the elderly. Rev Neurol (Paris). 2020;176(9):710-723. doi:10.1016/j.neurol.2019.11.010