# Polypharmacy, potentially inappropriate medications, and the vulnerability of older adults

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## Abstract

*Objective*: To analyze the frequency of polypharmacy and the prescription of Potentially Inappropriate Medications (PIM) according to the Beers Criteria and CBMPI in older adults with clinical-functional vulnerability. *Method*: This is a cross-sectional study where the medical records of 496 participants aged 60 and older, seen in their first appointment at a Gerontological Polyclinic, were analyzed. Sociodemographic data, medications, the Clinical-Functional Vulnerability Index-20 (IVCF-20), and falls were extracted from the medical records. Polypharmacy was defined as the simultaneous use of five or more medications. Participants were classified into three groups: robust, at risk, and vulnerable. *Results*: The analysis revealed that 69 (13.91%) participants were using polypharmacy. Among polypharmacy users, 40 (57.97%) were using at least one PIM. The most commonly found PIM were glibenclamide and omeprazole, respectively. Older adults with vulnerability were three times more likely to have polypharmacy (OR 3.59; 95% CI 2.109-6.092). *Conclusion*: The use of polypharmacy and PIM in this study was associated with the vulnerability of older adults, emphasizing the need for a thorough evaluation of medication prescriptions for this population.

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## INTRODUCTION

Longevity is a reality in the global population, and demographic changes resulting from a decrease in fertility rates, an increase in life expectancy, as well as advancements in diagnostic techniques, are precursors to the rise in population aging[1]. Although the words "illness" and "aging" are not synonymous, the growth of older population implies an increased prevalence of chronic diseases, necessitating a greater demand for healthcare assistance and elevating the likelihood of medication prescriptions[2,3].

Polypharmacy is defined as the simultaneous use of five or more medications, stemming from multiple comorbidities, consultations with different medical specialties, self-medication, and primarily the use of medications beyond those recommended in clinical care[4]. Polypharmacy increases the risk of consuming Potentially Inappropriate Medications (PIM)[5].

PIM are defined as drugs for which the probability of causing adverse effects is greater than that of providing health benefits. If used over an extended period and in excess, they can lead to pharmacological interactions, resulting in health impairments such as physical dysfunction, intoxications[6], hospitalizations[7], dementia[8], renal insufficiency[9] and the frailty of older adults[10].

Frailty is associated with the aging process and represents the degree of vulnerability of older adults to situations such as functional deficits, falls, fractures, hospitalizations, and even mortality[11]. Frailty has multifactorial causes that result in a reduction in resistance and muscle strength, leading to a state of physical, psychological, and social decline in older adults. This condition directly impacts the autonomy and functionality of the individual, increasing the risk of adverse outcomes. Older adults who use polypharmacy associated with PIM may exacerbate or develop greater clinical-functional vulnerability[12].

In 2012, the American Geriatrics Society (AGS) developed a list of Potentially Inappropriate Medications (PIM) that should be avoided, known as the Beers Criteria, which was updated in March 2023[13]. This list is based on a consensus among professionals in the fields of geriatric care, clinical pharmacology, and psychopharmacology, aiming to enhance the quality of prescriptions by identifying high-risk medications that should be generally avoided and under specific conditions[13,14]. The Beers Criteria 2012 were validated and served as the basis for the elaboration of the 2016 Brazilian Consensus of Potentially Inappropriate Medications (CBMPI) [15]. These national criteria classify PIM for older population, directing medication therapies and minimizing the risks of harmful adverse reactions for the Brazilian population.

Due to the health risks and impact on quality of life arising from the simultaneous use of medications, studies are necessary to investigate the association between polypharmacy and vulnerability in order to promote a risk-benefit analysis of usage, as well as the prescription of potentially inappropriate medications. The use of substances with greater safety helps avoid potential risks associated with PIM, thereby aiming to maintain functionality[16,17].

This study aimed to analyze the frequency of polypharmacy and the prescription of potentially inappropriate medications according to the Beers Criteria and CBMPI in older adults with clinical-functional vulnerability.

## METHOD

This is a cross-sectional study. The medical records of individuals attended at the Gerontological Polyclinic of the Open University of the Third Age Foundation (FUnATI) in the city of Manaus, Amazonas, were accessed and analyzed. FUnATI is an institution that focuses on education, research, and assistance for older adults. It also offers courses and workshops for the elderly, trains professionals, and provides care through its own Gerontological Polyclinic[18].

The sample was formed by convenience, and the completion of the medical records was carried out by the health team at FUnATI, consisting of nurses, during the participants' first consultation at the service. The medical records of individuals from the public healthcare system of both genders, aged 60 years or older, who sought care at the service (spontaneous demand) from January 2017 to December 2019, were included. Participants with

medical records containing incomplete information were excluded from the study.

The following data were collected from the medical records: gender (male/female), age (60 to 70 years/>70 years), and associated comorbidities. The medications collected from each medical record were those prescribed and used prior to the consultation at the polyclinic[19].

Vulnerability was assessed using the Clinical-Functional Vulnerability Index-20 (IVCF-20). The IVCF-20 is a reliable multidimensional assessment tool for evaluating the functionalities of older adults. This instrument covers questions related to age range, self-perception of health, activities of daily living, cognition, mood, mobility, communication, and multiple comorbidities. The questionnaire aims to identify the level of vulnerability in older adults, with a maximum score of 40 points. The scoring allows classification into three categories: robust, scoring 0 to 6 points; at risk of frailty if scoring 7 to 14 points; or vulnerable if scoring 15 or more points[20].

The presence of falls was assessed by the IVCF-20 question, "Have you had two or more falls in the last year?", allowing the creation of the Falls variable (yes/no).

Polypharmacy was characterized as the simultaneous use of five or more medications[4]. The Beers Criteria (Version 2023) and CBMPI (Version 2016) were employed to identify the presence and quantity of Potentially Inappropriate Medications (PIM) in the prescribed medications[13,15]. The use of PIM was considered when the medication was listed in either the AGS Beers 2023 or CBMPI 2016 criteria. The prescribed medications in the database were classified into therapeutic class and anatomical class according to the Anatomical Therapeutic Chemical (ATC) classification system for a better definition of their effects. The quantity of medications was analyzed to identify the presence or absence of polypharmacy, defined as the concomitant use of

five or more medications by older adults[21,22].

The frequency results were presented as percentages and analyzed using the chi-square test, considering a significant p-value < 0.05. The mean age among the groups was analyzed using a one-way Anova test, followed by the Tukey test.

The prevalence ratio (PR) was determined by the ratio between older adults with a prescription for polypharmacy and the total number of participants, with a 95% confidence interval[23].

The study was approved by the Research Ethics Committee of the Universidade Federal do Amazonas under the number 3,781,478.

## DATA AVAILABILITY

The dataset is not publicly available due to containing information that compromises the privacy of the research participants.

## RESULTS

Among the 496 participants, 344 (69.3%) were women, with an average age of 69 ± 76.8 years. Table 1 presents the sociodemographic characteristics of the participants. Hypertension was the most prevalent comorbidity among the participants (59.87%; n=297). Falls were more common among men compared to women (19.73%; n=30 versus 13.95%; n=48). The majority of participants were classified as robust (44.75%; n=222), followed by at risk of vulnerability (32.05%; n=159) and vulnerable (23.18%; n=115). The analysis revealed that 13.91% of older adults were using polypharmacy.

Table 2 presents the classification and frequency of the 298 prescribed medications. Gastrointestinal tract-acting medications (25.8%; n=77) and those affecting the nervous system (23.15%; n=69) were the most prevalent among older adults.

**Table 1.** Sociodemographic Characteristics of Participants, Polypharmacy, and Falls (n=496). Manaus, AM, Amazonas, 2019.

| Variables | Women n(%) | Men n(%) | Total n(%) |
|---|---|---|---|
| Sex | 344(69.35) | 152(30.64) | 496(100) |
| Age | | | |
| 60 to 70 years | 236(68.60) | 99(65.13) | 335(67.54) |
| >70 years | 108(31.39) | 53(34.86) | 161(32.45) |
| Comorbidities | | | |
| Hypertension | 214(62.20) | 83(54.60) | 297(59.87) |
| Diabetes Mellitus | 87(25.29) | 49(32.23) | 136(27.41) |
| Arthritis | 84(24.41) | 22(14.47) | 106(21.37) |
| Urinary incontinence | 84(24.41) | 20(13.15) | 104(20.96) |
| Other | 77(22.38) | 109(71.71) | 186(37.50) |
| Falls | | | |
| Yes | 48(13.95) | 30(19,73) | 78(15,72) |
| No | 296(86.04) | 122(80,26) | 418(84,27) |
| Vulnerability | | | |
| Robust | 157(45.63) | 65(42.76) | 222(44.75) |
| At risk of vulnerability | 110(31.97) | 49(32.23) | 159(32.05) |
| Vulnerable | 77(22.38) | 38(25.00) | 115(23.18) |
| Polypharmacy | 48(13.95) | 21(13.81) | 69(13.91) |

**Table 2.** Classification and Frequency of Prescribed Medications. Manaus, AM, Amazonas, 2019.

| Anatomical Group | n(%) |
|---|---|
| Gastrointestinal tract and metabolism | 77(25.83) |
| Nervous system | 69(23.15) |
| Cardiovascular system | 55(18.45) |
| Musculoskeletal system | 38(12.75) |
| Blood and hematopoietic organs | 19(6.37) |
| Anti-infectives for systemic use | 9(3.02) |
| Systemic hormones (excluding sex hormones and insulins) | 8(2.68) |
| Genitourinary System and Sex Hormones | 8(2.68) |
| Respiratory system | 7(2.34) |
| Antineoplastic Agents and Immunomodulating | 4(1.34) |
| Organs of Senses | 3(1.00) |
| Dermatological | 1(0.33) |
| Total | 298(100) |

As shown in Table 3, vulnerable older adults presented a more advanced age (71.10±7.35 years; p<0.001) compared to participants at risk of vulnerability (66.50±5.62) and robust individuals (67.03±5.65). The variable "falls" was more frequent in the at-risk group (41%; n=32) and the vulnerable group (42.3%; n=33) compared to the robust group (16.67%; n=13).

Among older adults not using polypharmacy, approximately 214 (50%) belonged to the robust group. In contrast, 46.5% (n=32) of vulnerable individuals were using polypharmacy. In the polypharmacy group,

40 (57.97%) had at least 1 potentially inappropriate medication in their medical records. Of these, more than half 25 (62.5%; n=25) of the participants were vulnerable older adults (p<0.001). Older adults with vulnerability had a 3.59 times higher risk of having polypharmacy (PR 3.59; 95% CI 2.109-6.092).

Within the group of older adults with polypharmacy, the analysis revealed 27 medications potentially inappropriate according to the Beers and/or CBMPI criteria, which are listed in Table 4. The most frequently encountered PIM was glibenclamide, followed by omeprazole and carvedilol.

**Table 3.** Association of Vulnerability with Potentially Inappropriate Medications and Falls. Manaus, AM, Amazonas, 2019.

| Variable | Robust (n=222) | At risk (n=159) | Vulnerable (n=115) | Total(%) (n=496) | p |
|---|---|---|---|---|---|
| Sex | | | | | |
| Women | 157(45.63) | 110(31.97) | 77(22.38) | 344(69.35) | 0.77 |
| Men | 65(42.76) | 49(32.23) | 38(25.00) | 152(30.64) | |
| Age (mean±SD) | 67.03±5.65* | 66.50±5.62* | 71.10±7.35 | 71.10±6.20 | <0.0001 |
| Falls (%) | | | | | |
| Yes | 13(16.67) | 32(41.02) | 33(42.31) | 78(15.72) | <0.0001 |
| No | 209(50.00) | 127(30.38) | 82(19.62) | 418(84.27) | |
| Polypharmacy (%) | | | | | |
| No | 214(50.11) | 130(30.44) | 83(19.43) | 427(86.08) | <0.0001 |
| Yes | 8(11.59) | 29(42.03) | 32(46.38) | 69(13.91) | |
| Polypharmacy with at least 1 PIM (%) | | | | | |
| No | 2(6.90) | 19(65.52) | 8(27.58) | 29(42.03) | 0.0027 |
| Yes | 6(15.00) | 10(25.00) | 25(62.50) | 40(57.97) | |

Frequencies were analyzed using the chi-square test. The mean age between groups was analyzed using a one-way ANOVA, followed by the Tukey test. A p-value less than 0.05 was considered significant. *versus vulnerable, considering a significant p-value < 0.05.

**Table 4.** Presentation and classification according to the Beers 2023 and CBMPI 2016 criteria of each Potentially Inappropriate Medication prescribed for the participants. Manaus, AM, Amazonas, 2019.

| Name | n | Therapeutic Group According to ATC | Criteria |
|---|---|---|---|
| Glibenclamide (sulfonylureas) | 12 | Digestive Tract and Metabolism | CBMPI/BEERS |
| Omeprazole | 8 | Gastrointestinal Tract and Metabolism | CBMPI/BEERS<br>Recommendation: Avoid scheduled use for >8 weeks |
| Carvedilol | 8 | Cardiovascular System | CBMPI<br>In conditions of Chronic Obstructive Pulmonary Disease |
| Furosemide | 5 | Cardiovascular system | CBMPI |
| Ranitidine | 5 | Gastrointestinal Tract and Metabolism | CBMPI/BEERS<br>In clinical condition of Delirium |
| Pantoprazole | 3 | Gastrointestinal Tract and Metabolism | CBMPI |
| Nifedipine | 3 | Gastrointestinal Tract and Metabolism | CBMPI/BEERS |
| Aspirine | 2 | Blood and Hematopoietic Organs | CBMPI/BEERS<br>In conditions of bleeding disorders |
| Sertraline | 2 | Nervous System | CBMPI |
| Prednisone | 2 | Systemic Hormones | CBMPI |
| Ibuprofen | 2 | Musculoskeletal System | CBMPI/BEERS<br>In conditions of chronic kidney disease |
| Quetiapine | 2 | Nervous System | CBMPI<br>In conditions of a history of falls |
| Fluoxetine | 2 | Nervous System | CBMPI<br>In conditions of a history of falls |
| Enoxaparin | 1 | Blood and Hematopoietic Organs | BEERS<br>In dosages >30ml |
| Meloxicam | 1 | Musculoskeletal System | CBMPI/BEERS<br>In conditions of peptic ulcer |
| Pregabalin | 1 | Nervous System | CBMPI/BEERS<br>In conditions of a history of falls |
| Citalopram | 1 | Nervous System | CBMPI<br>In conditions of a history of falls |
| Escitalopram | 1 | Nervous System | CBMPI<br>In conditions of a history of falls |
| Amitriptyline | 1 | Nervous System | CBMPI/BEERS<br>In conditions of a history of falls |
| Gabapentin | 1 | Nervous System | CBMPI/BEERS |
| Hydralazine | 1 | Blood and Hematopoietic Organs | CBMPI<br>In conditions of postural hypertension |
| Spironolactone | 1 | Cardiovascular System | CBMPI/BEERS |
| Digoxin | 1 | Cardiovascular System | CBMPI/BEERS |
| Allopurinol | 1 | Blood and Hematopoietic Organs | CBMPI |
| Aceclofenac | 1 | Musculoskeletal System | CBMPI<br>In conditions of chronic kidney disease |
| Nimesulide | 1 | Musculoskeletal System | CBMPI<br>In conditions of chronic kidney disease |
| Diclofenac | 1 | Musculoskeletal System | CBMPI/BEERS<br>In conditions of chronic kidney disease |

ATC: Anatomical Therapeutic Chemical Classification; CBMPI: Brazilian Consensus on Potentially Inappropriate Medications.

## DISCUSSION

This study aimed to analyze the frequency of polypharmacy and the prescription of potentially inappropriate medications in older adults with clinical-functional vulnerability. Polypharmacy was found in 46.5% of individuals with vulnerability. Furthermore, individuals with polypharmacy exhibited a higher frequency of at least one potentially inappropriate medication prescribed.

The aging process predisposes individuals to higher risks of comorbidities, functional decline, and health conditions, increasing the likelihood of multiple medication prescriptions in an attempt to maintain quality of life and life expectancy[2,3]. Medications are necessary therapeutic resources, and when prescribed correctly, they help maintain the quality of life of older adults and control chronic illnesses. However, the assessment of risk/benefit is always essential.

In this study, more than half of the older adults using polypharmacy had at least one PIM. In a retrospective chart analysis study (n=406) of older adults receiving care in the secondary care setting of a Reference Center for Elderly Health Care, it was found that 66.8% of participants had at least one PIM in the presence of polypharmacy[20]. According to Neves et al.[9], who assessed individuals above 60 years old hospitalized (n=187), a similar percentage of 66.7% of participants with polypharmacy and PIM was observed. In both studies, the drug omeprazole was among the most prevalent. This result was consistent with the present study, where omeprazole was the second most prescribed.

Also, polypharmacy and the use of PIM were associated with higher levels of vulnerability. In a cross-sectional study conducted with an older population residing in urban areas in Minas Gerais, it was found that 51% of vulnerable older adults used at least one PIM, and 33% of participants classified as at risk of vulnerability used some PIM[22]. Furthermore, in a study conducted with an institutionalized older population in a geriatric residence in Spain, polypharmacy with PIM was prevalent in 92% of vulnerable individuals[10]. These results suggest that the higher the consumption of PIM, the higher the prevalence of vulnerability and the risk of vulnerability in older adults.

Older adults at risk of frailty were 5 times more likely to use polypharmacy compared to robust participants. This risk increased to 7 times in vulnerable older adults. Similar results were found by Spekalski et al.[24] among individuals aged 60 to 85, residing in rural areas of Paraná. Potentially vulnerable or frail individuals had 3 times (3.73) more chances of using polypharmacy when compared to non-vulnerable ones[24].

The previously mentioned finding can be explained by the physiological changes of senescence that result in irregular drug absorption. Consequently, modifications in pharmacodynamics and pharmacokinetics related to the simultaneous use of medications potentiate harmful drug interactions that directly affect the functionality of older adults[5]. Functional impairment and the presence of multiple chronic diseases lead to an increasingly complex drug treatment for the elderly, making them even more vulnerable to harmful drug interactions that alter systemic body metabolism, contributing to increased functional decline, decreased muscle strength, resistance, and power – characteristics of vulnerability in older adults[23,25]. Vulnerable older adults have impairments in postural adjustments, proprioception, and gait. These deficits increase the risks of imbalances and falls. Therefore, it is necessary to analyze the harms and benefits of medication prescriptions and the impact that potentially inappropriate medications (PIM) have on the health of older adults[26].

All potentially inappropriate medications found in the medical records, such as glibenclamide and omeprazole, which act on the gastrointestinal system and metabolism, were the first and second most prescribed, respectively. Similar results were also found in a study conducted with elderly users of Primary Health Care, where the medication glibenclamide (25%) was the most prescribed among all potentially inappropriate medications, followed by omeprazole (23.4%)1. Glibenclamide is an oral hypoglycemic agent used in the treatment of diabetes mellitus[27,28], but it can be harmful to older adults as it can cause prolonged lowering of blood glucose, posing risks to metabolic stability.

Omeprazole is commonly indicated for the treatment of gastrointestinal disorders related to stomach acid secretion[7]. According to CBMPI, this drug should not be recommended for older adults as its prolonged use can lead to osteoporosis, dementia, and renal failure. However, it is common for professionals to prescribe omeprazole incorrectly to treat side effects resulting from the simultaneous use of many medications established for older adults[1,2,29].

In this study, 65.5% of older adults who exhibited polypharmacy and did not have any PIM were classified as at risk of frailty. This may be associated with the use of medications that act on the nervous system, as approximately 23% of all prescribed medications presented in Table 2 were agents affecting the nervous system. Central nervous system-acting cholinergic antidepressants are considered inappropriate due to their sedative effects, which increase the risk of falls and fractures in patients[1]. Benzodiazepines that act on the central nervous system have anxiolytic and anticonvulsant effects, and although suggested for anxiety and insomnia disorders—common issues faced by older adults—they may enhance the risks of falls, cognitive deficits, delirium, fractures, and further exacerbate the effects of depression[8,9,30].

The limitation of this study was its exclusive focus on an institution catering to individuals aged 60 and older. Additionally, the study design employed does not allow for the identification of a causal relationship between variables. Therefore, further studies are needed that address this topic and involve an older population attended to in different institutions within the city and state.

## CONCLUSION

The use of polypharmacy and Potentially Inappropriate Medications (PIM) has been associated with the vulnerability of older adults, emphasizing the need for a careful assessment of medication prescriptions for this population. Medications have a significant potential to improve the functionality of bodily systems, but they can also be harmful in equal measure.

The healthcare of older adults is highly complex, demanding a balance between the benefits and risks inherent in promoting care with the aim of enhancing and maintaining the life expectancy of older population. Patient safety must be a paramount consideration when recommending medications. Establishing therapeutic priorities and effectively managing the treatment of each health issue presented by elderly patients is crucial. A rational analysis is necessary to determine which interventions are more urgent and which can be addressed in the long term, thus avoiding the simultaneous use of many medications and reducing the risk of unnecessary harm.

## AUTHORSHIP

- Raquel Coelho de Andrade – Data analysis and interpretation, paper writing.

- Maira Mendes dos Santos – Contribution to data collection in the FUnATI Institution.

- Euler Esteves Ribeiro – Contribution to data collection in the FUnATI Institution.

- James Dean Oliveira dos Santos Júnior – Data analysis and interpretation.

- Hércules Lázaro Morais Campos – Supervision and guidance for article production. Approval of the version to be published.

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