









# Polypharmacy and drug classes in fall risk among older adults

Polifarmácia e uso de classes medicamentosas no risco de quedas em pessoas idosas

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## Abstract

**Objective:** To identify polypharmacy, including drug classes that, when used concomitantly, increase fall risk in older adults.

**Methods:** This cross-sectional quantitative study included noninstitutionalized individuals aged  $\geq 60$  years living in Rio Branco, Acre, Brazil. In the descriptive data analysis, the frequency distributions were evaluated and multiple logistic regression was used to identify factors associated with fall risk. The ROC curve was used to determine the logistic model's accuracy.

**Results:** The fall rate was higher among women (73.30%) and the 70–79 year age group (42.50%). A total of 80.70% of the participants used  $\geq 1$  medication and 32.60% used 2–3 medications. According to the odds ratio calculation, use of medications with possible drug interactions increased the occurrence of falls by 47.00% in the last 12 months. The model's accuracy was 55.00%.

**Conclusions:** The results indicate that polypharmacy and the use of certain drug classes in older adults can lead to potential drug interactions, making them more susceptible to adverse events, such as postural hypotension, vertigo, dizziness, and loss of balance, all of which increase fall risk. Educational measures for older adults on correct medication use are needed.

**Keywords:** falls; polypharmacy; elderly.

## Resumo

**Objetivo:** Identificar o uso da polifarmácia e de classes medicamentosas que, quando usadas concomitantemente, elevam os riscos de quedas em pessoas idosas.

**Metodologia:** Trata-se de um estudo quantitativo, com delineamento transversal, com indivíduos de 60 anos ou mais, não institucionalizados, residentes em área urbana do município de Rio Branco, capital do estado do Acre. Na análise descritiva dos dados, avaliaram-se as distribuições de frequências e, para identificação dos fatores associados, utilizou-se o modelo de regressão logística múltipla. Para verificar a qualidade do modelo logístico na identificação da acurácia, utilizou-se a curva de característica de operação do receptor.

**Resultados:** Pessoas idosas do sexo feminino (73,30%) e de faixa etária de 70 a 79 anos (42,50%) obtiveram maiores ocorrências de quedas; 80,70% das pessoas idosas que apresentaram queda faziam a utilização de, no mínimo, um medicamento; 32,60% dos indivíduos idosos faziam uso de dois ou três medicamentos. Pela tabela de razão de chances, constatou-se que o uso de determinada medicação aumentou em 47,00% a ocorrência de quedas nos últimos 12 meses. O modelo apresentou uma acurácia de 55,00%.

**Conclusão:** Tendo em vista os aspectos observados, conclui-se que a prática de polifarmácia e o uso acentuado de determinadas classes medicamentosas em pessoas idosas podem gerar potenciais interações medicamentosas e deixá-las mais suscetíveis a eventos adversos, como hipotensão postural, vertigem, tontura, perda do equilíbrio e vulnerabilidade, que propiciam o risco de quedas. Isto posto, é fundamental que os profissionais de saúde implementem medidas educativas favoráveis à correta utilização dos fármacos pelos indivíduos idosos.

**Palavras-chave:** quedas; polimedicação; pessoas idosas.



## INTRODUCTION

Falls are defined as abrupt unintentional displacements of the body to a lower level. They can be caused by intrinsic or extrinsic factors, corroborating the occurrence of physical, psychological, or social damage. They increase the costs associated with hospitalization, can lead to functional disabilities, and can increase in the risk of addiction and death.<sup>1</sup>

Older adults are more vulnerable to falls due to the aging process, as well as to physical and metabolic compromise from bone and muscle injuries.<sup>2</sup> Their functional independence and quality of life can be directly impaired by falls.<sup>3</sup>

Falls are one of the main causes of hospitalization for people aged  $\geq 60$  years in Brazil, accounting for approximately 134 932 hospitalizations in 2021.<sup>4</sup> These episodes lead to lower quality of life and well-being<sup>5</sup> and have deleterious effects on the health of older adults.<sup>6</sup>

One extrinsic factor involved in falls is polypharmacy. Most older adults with comorbidities must take several medications concomitantly.<sup>6</sup> Some therapeutic classes, such as benzodiazepines, antidepressants, non-steroidal anti-inflammatory drugs, vasodilators, and antihypertensives, increase the risk of postural instability and fall risk.<sup>7</sup>

Associating these drug groups contributes to potential drug interactions (PDIs), which also increase fall risk. There is a PDI when 2 or more drugs are administered simultaneously to a patient: they can act independently or interact synergistically (increasing desirable effects), antagonistically (counteracting desirable effects), or neutralize each other.<sup>8</sup>

A drug's effects can also be altered by food, drink, or chemical agents in the environment. Thus, fall risk in older adults increases according to the number of medications they are prescribed.<sup>9</sup>

Brazilian publications on the association between polypharmacy, PDIs, and falls among hospitalized patients and outpatients are scarce. Studies, mainly in psychiatry, have assessed PDIs<sup>10</sup> in drugs that act on the central nervous system.<sup>11</sup> Pediatric studies on PDIs have also been published, but no studies have assessed susceptibility to PDIs due to polypharmacy in older adults.<sup>12</sup>

Thus, it is understood that polypharmacy and the concomitant use of certain drug classes can damage the health of older adults through increased toxicity, counteracting the desired effect, and adverse events that are closely related to increased fall risk.<sup>13</sup> Thus, the objective of this study was to identify polypharmacy and drug classes that, when used concomitantly, increase fall risk older adults.

## METHODS

This study was part of a larger research project called "Multicenter study on the association between cardiometabolic

risk factors and falls, social support, and multimorbidity in older adults", funded by the Acre Research Support Foundation in association with the Brazilian Unified Health System. It was approved by the Hospital das Clínicas do Acre Research Ethics Committee (opinion 2.319.053; certificate 76889417.3.1001.5009). The project followed ethical principles for research involving human beings, including the resolution 466/2012.

This cross-sectional quantitative study included non-institutionalized adults aged  $\geq 60$  years who lived in an urban area of Rio Branco, capital of the state of Acre, Brazil. The probabilistic sample consisted of 441 older adults; the sample size was calculated considering a proportion estimate of 0.5, a sampling error of 10.00%, a 95% confidence level, and a design effect of 1.17.

Data were collected in 2019 through individual interviews with the participants at the nearest health unit to their residence or, for older adults unable to travel to the health unit, at their residence. A form was used to record data on age, sex, medication use, types, and amounts, in addition to any effects that could contribute to fall risk, such as dizziness, vertigo, postural hypotension, or drowsiness.

Individuals aged  $\geq 60$  years who provided written informed consent were included in the sample. Those with neurological or cognitive conditions that might prevent them from answering the questionnaire were excluded.

The information collected during the interview was managed in Microsoft Excel 2.60, including all medications used by the participants. The pharmacological groups were then classified and the National Health Surveillance Agency (ANVISA)<sup>14</sup> was consulted to determine whether the drugs had adverse events, such as postural hypotension, dizziness, etc., that could contribute to fall risk.

The literature was then consulted to determine PDIs when these drugs are associated with other drugs from the same group or different groups, and whether their main adverse events could increase fall risk. The data were analyzed in R version 1.3.1093.

A multiple logistic regression model was used in a backward stepwise variable selection process to identify factors associated with fall risk. The receiver operating characteristic curve (ROC) curve was used to determine the logistic model's accuracy, obtaining an area under the curve ranging from 0 to 1. Values approaching 1 indicate greater accuracy for detecting patients with the selected characteristics.

A significance level of 5% was used in all analyses. Variables with  $p < 0.2$  in the univariate analysis were included in the multiple regression model.

## RESULTS

A total of 441 older adults aged  $\geq 60$  years were included in the sample. The collected data included sex, age, medication use (including those that increase fall risk), and the number of falls in the last 12 months. The pharmacological groups found are described in Table 1: 254 (45.60%) drugs that act on the cardiovascular system (CVS), 110 (19.80%) drugs that act on the genitourinary system, 62 (11.10%) drugs for pain and inflammation, 54 (9.70%) drugs that act on the central nervous system, 44 (7.90%) drugs that act on the gastrointestinal system, 23 (4.10%) drugs that act on metabolism, 8 (1.40%) antimicrobials, and 2 (0.40%) drugs that act on the respiratory tract.

**TABLE 1.** Distribution of the main pharmacological groups associated with fall risk used by interviewed older adults in Rio Branco, AC, Brazil, 2019 (n = 557).

Pharmacological groups	n	%
Drugs that act on the CVS	254	45.60
Drugs that act on the GUS	110	19.80
Drugs for pain and inflammation	62	11.10
Drugs that act on the CNS	54	9.70
Drugs that act on the GIS	44	7.90
Drugs that act on metabolism	23	4.10
Antimicrobials	8	1.40
Drugs that act on the respiratory tract	2	0.40

CVS: cardiovascular system; GUS: genitourinary system; CNS: central nervous system; GIS: gastrointestinal system.

The CVS group included 221 (66.40%) antihypertensive drugs, 73 (21.90%) antiplatelet drugs, 27 (8.10%) hypotensive drugs, 4 (1.20%) vasodilators, 3 (0.90%) anti-vertigo drugs, 3 (0.90%) beta-blockers, and 2 (0.60%) anti-hemorrhagic drugs.

The gastrointestinal group included 103 (99.00%) diuretic drugs, and 1 (1.00%) anti-prostate cancer agent. The pain and inflammation group included 55 (82.10%) non-steroidal anti-inflammatory drugs, 11 (16.40%) corticosteroids, and 2 (3.00%) antirheumatic drugs.

The central nervous system group included 54 (90.00%) antidepressants, 10 (16.70%) muscle relaxants, 5 (8.30%) anticonvulsants, 3 (5.00%) mood modulators, 2 (3.30%) alpha-adrenergic antagonists, 2 (3.30%) antipsychotics, 1 (1.70%) anti-Parkinson drug, and 1 (1.70%) anticholinergic drug.

The antimicrobial group included 5 (41.70%) antiprotozoal drugs, 4 (33.30%) antifungal drugs, 2 (16.70%) antibiotics, and 1 (8.30%) anthelmintic drug. The gastrointestinal group included 41 (87.20%) antiulcer drugs, 4 (8.50%) antiemetic drugs, and 2 (4.30%) antispasmodic drugs.

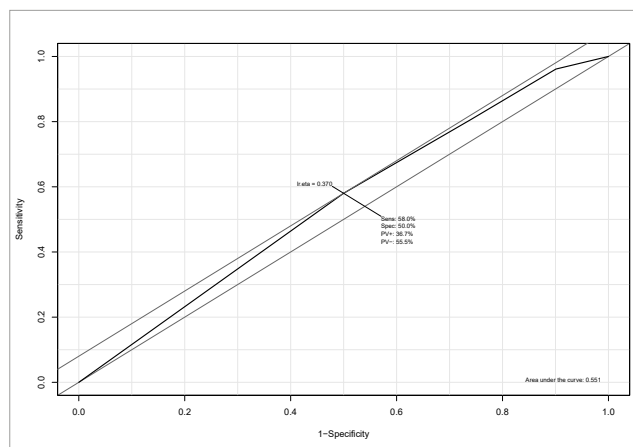
The metabolic group included 94 (88.70%) oral hypoglycemic agents, 7 (6.60%) bisphosphonates, 4 (3.80%) hormones, and 1 (0.90%) antiestrogen drug. Finally, the respiratory tract group included 11 (78.60%) antihistamines, 2 (14.30%) bronchodilators, and 1 (7.10%) mucolytic drug.

As shown in Table 2, the fall rate was higher among women (133, 73.30%) than men (48, 26.70%), and in the 70 – 79 year-old age group (77, 42.50%).

**TABLE 2.** Univariate association between falls in the last 12 months, patient characteristics, and medication use in Rio Branco (AC), Brazil, 2019 (n = 557).

	Have you fallen in the last 12 months?						OR	p-value
	No		Yes		Total			
	n	%	n	%	n	%		
Sex								
Female	172	66.00	132	73.30	304	69.00		
Male	89	34.00	48	26.70	137	31.00	0.701	0.094
Aged (years)								
60 – 69	98	37.70	70	38.70	168	38.10		
70 – 79	123	47.30	77	42.50	200	45.40	0.876	0.538
$\geq 80$	39	15.10	34	18.80	73	16.60	1.219	0.483
Are you on medication?								
No	68	26.20	35	19.30	103	23.40		
Yes	192	73.90	146	80.70	338	76.60	1.47	0.096
Do you use drugs that increase fall risk?								
No	89	34.20	56	30.90	145	32.90		
Yes	171	65.80	125	69.10	296	67.10	1.160	0.469
How many of these drugs?								
0 – 1	137	52.70	93	51.40	230	52.10		
2	45	17.30	40	22.10	85	19.30	1.332	0.276
3	78	30.00	48	26.50	126	28.60	0.917	0.670

OR: odds ratio; p-value: descriptive level or probability of significance.



**FIGURE 1.** Receiver operating characteristic curve from the logistic regression model.

A total of 80.7% of the population who fell used at least one medication, and 48.60% ( $n = 88$ ) used 2 or 3 medications.

Figure 1 shows the ROC curve of the logistic regression model, with variables selected by backward stepwise elimination. Thus, we obtained a model that, with relative accuracy, detected patients who fell in the last 12 months.

According to the logistic multiple regression model results (Table 3), using a medication with a PDI increased the odds of a fall in the last 12 months by 47.00%, with women having a 41.00% higher odds of falling than men. Therefore, sex and medication use were risk factors for falls. With an accuracy of 55.00%, the model indicated that, for every 100 patients, 55 with these characteristics had a fall in the last 12 months.

## DISCUSSION

This study, whose sample consisted of older adults registered with the municipal health department of Rio Branco, found high use of medications with adverse events that included vertigo, dizziness, postural hypotension, and blurred vision,<sup>15</sup> all of which increase fall risk. The most prevalent drug groups were CVS, genitourinary, and anti-inflammatory.

Falls are multifactorial in nature and have high therapeutic complexity.<sup>16</sup> The present study showed that women had a higher fall risk, especially when using medications with the above-mentioned adverse events. This corroborates the literature, which shows that sex is an intrinsic factor in falls.

Considering that the sample was predominantly older women and that the use of  $\geq 2$  medications by the same individual can contribute to a higher occurrence of adverse effects with advancing age,<sup>17</sup> this group becomes more susceptible to problems directly linked to declining health.

**TABLE 3.** Multiple logistic regression model for fall risk according to use of a medication with potential drug interaction and sex. Rio Branco (AC), Brazil, 2019 ( $n = 441$ ).

Risk factors	$\beta$	p-value	OR	95%CI
Use of a medication with a PDI	0.3861	0.107	1.47	0.92 – 2.34
Sex	0.3450	0.101	1.41	0.93 – 2.15

p-value: descriptive level or probability of significance; OR: odds ratio; CI: confidence interval.

Most of our population used  $\geq 2$  medications simultaneously, and those who fell in the 12 months prior to the interview used at least 1 medication that increased fall risk. This demonstrates that polypharmacy increases the risk of falls, hospitalization, use of health resources, and death.<sup>18</sup>

Some of the most frequent pathological conditions in older adults are cardiovascular diseases, gait changes, ocular, auditory, and cognitive impairment, inadequate mobility, and a history of falls.<sup>19</sup> Older adults can be affected by these conditions individually or simultaneously, which results in ongoing therapy, polypharmacy, PDIs, adverse events, health problems, and a higher fall risk.<sup>20</sup> This suggests that PDIs due to polypharmacy are common among older adults and can lead to serious and even fatal outcomes for susceptible individuals.<sup>21</sup>

Based on the sensitivity and specificity of the ROC curve in this study, drugs in different pharmacological groups can contribute to worsening health in older adults through adverse events associated with fall risk, considering that of every 100 participants, 55 were at risk of falling.

This study has some limitations linked to its cross-sectional design: not all the medications the participants reported using could be proven with a prescription, the participants were not followed up regarding medication use, and many patients reported self-medicating.

Moreover, because this study design entails a situational diagnosis, it cannot be stated that PDIs are responsible for falls, but rather that polypharmacy may be an extrinsic factor contributing to fall risk in older adults, mainly because drugs that act on the CVS and central nervous system, in addition to involving adverse events, contribute to fall risk, as described in the literature.

In view of the above, this population urgently requires pharmaceutical care that provides guidance about medications that can aggravate their health and damage their quality of life, physically, mentally, and emotionally.<sup>22</sup>

## CONCLUSIONS

Our results show that polypharmacy and the preponderant use of certain drug classes in older adults entails PDIs, making

them more susceptible to adverse events, such as postural hypotension, vertigo, dizziness, loss of balance, and hence fall risk.

Health professionals must increase educational measures for older adults about correct medication use, discouraging self-medication and recommending medications that reduce PDIs and fall risk.

Despite the importance of the association between polypharmacy, PDIs, and falls, little research on it has been published, especially among older adults. Our results highlight the need for improved pharmacovigilance in Brazil, including new studies to deepen our understanding of this phenomenon, leading to interventions that increase the safety of older adults on medication, either at home or in primary, secondary, or tertiary care, thus minimizing the risks of mortality and serious and disabling injuries.

### Conflict of interest

The authors declare no conflicts of interest.

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### Authors' contribution

CFS: data curation, formal analysis, investigation, project administration, supervision, writing – original draft, writing – review & editing. GSR: conceptualization, data curation, formal analysis, software, supervision, writing – review & editing. FLJ: conceptualization, data curation, formal analysis, writing – review & editing. KSA: data curation, investigation, resources. VEMC: data curation, investigation, resources. RRL: data curation, validation, visualization. TRPB: data curation, validation, visualization.

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## ERRATUM

In the manuscript “Polypharmacy and drug classes in fall risk among older adults,” DOI: 10.53886/gga.e0230017, published in *Geriatr Gerontol Aging*. 2023;17:e0230017, pages 4 and 5:

Page 4

### Where it read:

Table 3.

Risk factors		p-value	OR	95%CI
Use of a medication with a PDI	0.3861	0.107	1.47	0.92 – 2.34
Sex	0.3450	0.101	1.41	0.93 – 2.15

### It should read:

Table 3.

Risk factors		p-value	OR	95%CI
Use of a medication	0.4862	0.038	1.47	1.06-3.08
Female sex	0.3957	0.041	1.41	1.04-2.77

Page 5

### Where it read:

Funding: This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

### It should read:

Funding: The research was funded by the Research Program for the SUS: shared management in health - PPSUS/AC. Call FAPAC-SESACRE-Decit/SCTIE/MS-CNPq under process No. 33376.512.21332.21092017.