



# Prevalence and factors associated the use of potentially inappropriate medications by older adults in Rio Branco, Acre, Brazil: a population-based study

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## Abstract

**Objective:** To verify the prevalence and analyze the factors associated with the use of potentially inappropriate medications (PIM) in the older adults in Rio Branco, Acre, Brazil. **Method:** This is a cross-sectional population-based study. The dependent variable was the use of at least one PIM, according to the criteria of the Brazilian Consensus on Potentially Inappropriate Medicines for the older adults, regardless of clinical condition. In evaluating the association between the use of inappropriate medications and the independent variables, a crude and adjusted analysis was performed using logistic regression, using the hierarchical model by odds ratio (OR). **Results:** The prevalence of using at least one PIM among the 1,016 participants was 25.9% (95%CI 22.3; 29.8), positively associated with female sex (OR=1.38; 95%CI 1.01; 1.90), dependence on instrumental activities of daily living (OR=1.37; 95%CI 1.02; 1.83), negative self-rated health (OR=1.54; 95%CI 1.12; 2.11), hospitalization in the last 12 months (OR=1.79; 95%CI 1.19; 2.69) and presence of more than three comorbidities (OR=2.56; 95%CI 1.97; 3.33). The most used subcategory was proton pump inhibitors by 11.3% (9.2; 13.8). **Conclusion:** The prevalence of PIM use by elderly in this population was a quarter, being associated with female gender and health conditions. Awareness actions are necessary to guarantee the benefits of using medications.

**Keywords:** Potentially Inappropriate Medication List. Older Adults. Inappropriate Prescribing. Survey.

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## INTRODUCTION

Ensuring pharmacotherapeutic safety for older people is a major challenge, as, in addition to pharmacodynamic and pharmacokinetic changes, there may be barriers that interfere with their self-care. Among these, low health literacy, cognitive alterations, inadequate social support network, sensory deficiencies and other conditions that make it difficult to adhere to pharmacological treatments stand out<sup>1</sup>.

In the midst of this reality, the risk of adverse drug reactions (ADRs) with negative outcomes becomes greater, so it is necessary to properly identify potentially inappropriate medications (PIM) for older people<sup>2,3</sup>. In order to improve the safety of prescribing drugs in this group, over the last few years several tools have been developed for the assessment of PIM. The Beers criteria, initially proposed in the 1990s, have been regularly revised by the American Geriatrics Society and include drugs that should be avoided or used with caution by older people<sup>4,5</sup>.

Another widely used tool is the *Screening Tool of Older Person's Prescriptions (STOPP)* and *Screening Tool to Alert Doctors to Right Treatment (START)* criteria, which include a series of guidelines on drugs that should be avoided according to physiological systems, as well as those which should not cease to be prescribed under certain conditions<sup>6</sup>. In 2016, Galvão and colleagues developed a validated adaptation of the Beers and STOPP/START criteria called the Brazilian Consensus on Potentially Inappropriate Medications for Older People (CBMPII). This instrument plays an important role, since it only included drugs authorized by the National Health Surveillance Agency (ANVISA)<sup>3</sup>.

In Brazil, in recent years some studies were carried out that evaluated the use of PIM according to the Beers or STOPP criteria in different regions of the country. Of these, the Health, Well-being and Aging (SABE) study stands out, carried out with 1,254 older people in the city of São Paulo (SP), which obtained a PIM prevalence in 28% of the participants<sup>7</sup>; a study conducted in Pelotas (RS)<sup>8</sup> with 1,451 individuals, in which the prevalence was 42.4%; a longitudinal study carried out in Goiânia (GO), which followed

418 older people for 10 years, in which an incidence of PIM use was found to be 44.1 cases per 1,000 people-year<sup>9</sup>; in Viçosa (MG)<sup>10</sup> the prevalence was 43.8% and 44.8% in 621 interviewees, according to the Beers and STOPP criteria, respectively.

Factors associated with PIM use are polypharmacy, female sex, presence of comorbidities, low education, age greater than or equal to 80 years and non-white skin color<sup>9-12</sup>. Despite the great relevance of these publications, it is important to highlight that they did not use instruments validated for Brazil. In addition, it is necessary that the prevalence of PIM be evaluated in populations with different characteristics, since in the country there is great social inequality, low level of human development and heterogeneity in terms of educational and cultural levels and access to health services. In this sense, the objective of this study was to verify the prevalence and analyze the factors associated with the use of PIM in older people in Rio Branco, Acre, Brazil.

## METHOD

This is an observational, cross-sectional, population-based study with individuals aged 60 years or older, non-institutionalized and residing in urban and rural areas of the municipality of Rio Branco, Acre, from April to September 2014.

Rio Branco has a territorial unit of 8,834,942 km<sup>2</sup> and had approximately 21,620 older people, representing 6.4% of the population, of which 91.8% lived in the urban area. That same year, the Municipal Human Development Index (IDHM) was 0.727<sup>11</sup>.

Data previously collected within the scope of the Study of Chronic Diseases (EDOC) were used. Older people (from 60 years old) of both sexes, domiciled in Rio Branco, were eligible. Those identified by the interviewers with some cognitive impairment that made it difficult to communicate or understand the questions (or that such information was given by family members) were excluded from the study.

Sampling was complex, of the probabilistic type, by clusters in two stages, with 40 census sectors in the primary unit. 73 households were then drawn from each of these sectors, which constituted the

secondary unit, in which all residents aged 60 years or older and able to answer the questions were invited to participate in the study. The selection of sectors was made with probability proportional to their number and private households in the 2010 Demographic Census (CD2010) of the Brazilian Institute of Geography and Statistics (IBGE). To perform the sample calculation, a prevalence of alteration of kidney function among older people was adopted of 40.0%, confidence level of 95% and error of 3%. In order to cover probable losses and refusals, 20% were added, totaling a final sample of 1,016 individuals<sup>12</sup>.

After recruiting the participants, home interviews were carried out by properly trained researchers. The questionnaires included the application of an instrument structured in thematic modules with information on socioeconomic, demographic, behavioral and health conditions, in addition to physical assessments and medication use.

The variables surveyed included age (in years and categorized as 60-69; 70-79; 80 and over); sex (male; female); skin color (white; non-white (brown, black, yellow and indigenous)); marital status (with a partner; without a partner); education (no education (illiterate/never studied); elementary school; high school; higher education); practice of physical activity (yes; no); body mass index (eutrophic; underweight; overweight); smoking (yes; no); degree of dependence on the Instrumental Activities of Daily Living (IADL) scale (dependent; independent); degree of dependence on the Basic Activities of Daily Living (BADL) scale (dependent; independent); health self-assessment (positive (very good/good); negative (fair/poor/very poor)); hospitalization in the last 12 months (yes; no); more than three comorbidities (yes; no); and signs and symptoms of depression (GDS) (yes; no).

For the self-assessment of health, the question *In general, would you say that your health is: very good, good, fair, bad or very bad* was suggested. For the investigation of functional capacity, the IADL scale was used, consisting of seven items (doing housework, preparing food, going shopping, using the telephone, getting around using means of transport, managing money and using medication<sup>13</sup>), with reliability for

use in the country<sup>14</sup>; and the BADL scale modified by Katz and adapted to Brazilian Portuguese<sup>15</sup>, which includes the following items: eating, going to the bathroom, choosing your own clothes, getting ready and taking care of personal hygiene, keeping yourself continent, dressing and bathing. Based on the Katz scale, older people were classified as independent (6 to 5 points) and dependent (partial, with 4 to 3 points, and total, with less than 3 points). The questionnaires were applied directly to the study participants. For the IADL scale, those who reached 21 points were classified as independent, and those with 20 points and less were classified as dependent.

To screen the presence of symptoms of depression in older people, the Geriatric Depression Scale (GDS-15)<sup>16</sup> was used, which has a score between 0 and 15 points. For the analysis of this work, a cut-off point of 6 points was considered, in order to define symptoms suggestive of depression.

In the analysis of body mass index (BMI) - weight (kg) by height (in meters) squared ( $m^2$ ) -, the *Nutrition Screening Initiative* (NSI) cut-off points for older people being overweight ( $>27kg/m^2$ ) and underweight ( $<22kg/m^2$ )<sup>17</sup>. Anthropometric data were collected by a properly trained professional, using a Bal GI 200 *G-Tech*<sup>®</sup> digital scale and a *Sanny*<sup>®</sup> portable stadiometer.

Through self-report, the following chronic diseases were evaluated to describe comorbidities: systemic arterial hypertension, peripheral venous system diseases, diabetes mellitus, stroke, insomnia, cardiac arrhythmias, arthritis/arthrosis, osteoporosis, chronic kidney disease, congestive heart failure, acute myocardial infarction, anemia, autoimmune diseases, cirrhosis, dyslipidemia, cancer, depression, asthma, bronchitis, psoriasis, repetitive strain injury/tendinitis, and hepatitis. The morbidities listed were included because they were the most prevalent, each one being asked individually and answered as yes/no. The option of reporting those not previously listed and that entered the calculation of comorbidities was also added to "other morbidities".

The use of medication was verified through the questions *Do you use any medication?* and *If yes, which medications, dose and frequency?* The use of medications was verified by means of the active ingredient, dosage

and frequency, based on checking the prescription or packaging of those being used at the time. For the definition of polypharmacy<sup>18</sup>, the concept of the concomitant use of five or more drugs was chosen. The variable was dichotomized into yes (use of five or more drugs) and no (use of zero to four drugs). The characterization of the drugs was performed according to the *Anatomical Therapeutic Chemical Code* (ATC) adopted by the World Health Organization (WHO)<sup>19</sup>. To define PIM, the dependent variable of the study, the CBMPII3 was used. This variable was defined as the use of at least one PIM category, regardless of clinical condition.

For the quality control of the information, interviews and physical assessments were carried out with 30 older people in a pilot study carried out in a census sector not included in the sample<sup>12</sup> for training and calibration of procedures.

Frequency measures were estimated for the categorical data. In order to compare the proportion between the groups, Pearson's chi-square test was used. Then, univariate and multivariate logistic regression models were developed to estimate the association between the independent variables and the dependent variable.

In the logistic regression analysis, the variables that presented a  $p$  value lower than 0.10 in the crude analysis were selected for inclusion. In evaluating the association between the use of inappropriate medication and the independent variables, a crude and adjusted analysis was performed using logistic regression, using the hierarchical model by odds ratio (OR). At the distal level, PIM use was adjusted for sex and skin color; at the intermediate level, the variables degree of dependence (IADL), signs and symptoms of depression (GDS) and self-rated health were introduced; finally, at the proximal level, the variables hospitalization and presence of three or more comorbidities were incorporated, in order to control possible confounding factors. The adjustment was initially performed within each level of the model, including variables with  $p < 0.10$  in the

bivariate analysis; in the final model, the variables that reached  $p < 0.05$  were kept. A significance level of 5% was adopted, analyzed by the Wald test.

In all analyses, the effect of the sample design and the weights of the observations were taken into account, which were calculated by the inverse of the inclusion probabilities at each stage and later calibrated for extrapolation to the population by "estimate (n)", by sex and age groups, using a post-stratification estimator, in order to deal with typical household survey biases and correct for differential non-response. For that, the maximum pseudo-likelihood (MPL) method was used, considering the sample weights and the structural information of the sampling plan. The inferences were evaluated by Wald's statistics based on the sampling plan, together with the F distribution.

The study was approved by the Research Ethics Committee (CEP) of the Federal University of Acre, under protocol number 518,531 on 01/30/2014. Participants signed the Free and Informed Consent Term (ICF), guaranteeing the right to refuse and the confidentiality of the data collected.

## RESULTS

After evaluating the exclusion criteria, a final sample of 1,016 older people was obtained, with 59 individuals being eliminated. Subsequently, correction for weights was performed, reaching an estimated expanded population of 23,416 participants. The prevalence of use of at least one PIM in this population was 25.9% (95% CI: 22.3 – 29.8).

Most older people were female, that is, 53.5% (95% CI: 50.3 – 56.6), mean age of 71.1 years (95% CI: 69.7 – 70.6), non-white skin color, lived without a partner, illiterate, did not practice physical activities, was independent in terms of instrumental activities of daily living, had no symptoms of depression and was overweight, as shown in Table 1.

**Table 1.** Clinical and sociodemographic variables and bivariate association with the proportion of older people using PIM (n=1,016). Rio Branco, AC, 2014.

| Variables                                  | Total        |                    | PIM          |                    | <i>p-value</i> <sup>a</sup> |
|--|--------------|--------------------|--------------|--------------------|-----------------------------|
|  | Estimate (n) | % (95% CI)         | Estimate (n) | % (95% CI)         |                             |
| Sex  |              |                    |              |                    | 0.213                       |
| Male                                       | 10,554       | 46.5 (43.4 – 49.7) | 2,462        | 22.6 (18.0 – 27.9) |                             |
| Female                                     | 12,862       | 53.5 (50.3 – 56.6) | 3,597        | 28.7 (24.4 – 33.5) |                             |
| Age (years)                                |              |                    |              |                    | 0.048                       |
| 60-69                                      | 13,383       | 57.2 (54.7 – 59.6) | 3,383        | 25.3 (21.3 – 29.8) |                             |
| 70-79                                      | 6,698        | 28.6 (26.2 – 31.1) | 1,569        | 23.4 (18.6 – 29.1) |                             |
| 80 and over                                | 3,335        | 14.2 (12.2 – 16.6) | 1,106        | 33.2 (25.9 – 41.3) |                             |
| Skin color                                 |              |                    |              |                    | 0.416                       |
| Non white                                  | 17,802       | 76.0 (71.8 – 79.8) | 4,500        | 25.3 (21.5 – 29.5) |                             |
| White                                      | 5,614        | 24.0 (20.2 – 28.2) | 1,558        | 27.8 (22.1 – 34.2) |                             |
| Marital status <sup>b</sup>                |              |                    |              |                    | 0.513                       |
| With partner                               | 9,097        | 39.1 (35.8 – 42.6) | 2,490        | 27.4 (21.1 – 34.7) |                             |
| Without partner                            | 14,161       | 60.9 (57.4 – 64.2) | 3,545        | 25.0 (21.5 – 28.9) |                             |
| Education <sup>b</sup>                     |              |                    |              |                    | 0.789                       |
| No education                               | 17,471       | 75.2 (68.4 – 81.0) | 4,520        | 25.9 (21.8 – 30.4) |                             |
| Elementary School                          | 1,963        | 8.5 (6.2 – 11.5)   | 477          | 24.3 (17.3 – 33.1) |                             |
| High school                                | 2,802        | 12.1 (9.1 – 15.8)  | 801          | 28.6 (19.1 – 40.4) |                             |
| University education                       | 987          | 4.2 (2.7 – 6.7)    | 216          | 21.9 (12.0 – 36.6) |                             |
| Practice of physical activity <sup>b</sup> |              |                    |              |                    | 0.743                       |
| Yes  | 3,480        | 14.9 (11.9 – 18.4) | 865          | 24.9 (17.9 – 33.5) |                             |
| No   | 19,904       | 85.1 (81.6 – 88.1) | 5,193        | 26.1 (22.5 – 30.0) |                             |
| BMI <sup>b</sup>                           |              |                    |              |                    | 0.505                       |
| Eutrophic                                  | 8,449        | 38.3 (34.1 – 42.7) | 1,998        | 23.7 (18.3 – 30.0) |                             |
| Underweight                                | 2,789        | 12.7 (10.5 – 15.2) | 825          | 29.6 (20.8 – 40.1) |                             |
| Obese                                      | 10,797       | 49.0 (44.0 – 54.1) | 2,863        | 26.5 (21.8 – 31.8) |                             |
| Smoking                                    |              |                    |              |                    | 0.374                       |
| Yes  | 4,163        | 17.8 (15.4 – 20.4) | 980          | 23.5 (17.4 – 31.1) |                             |
| No   | 19,253       | 82.2 (79.6 – 84.6) | 5,078        | 26.4 (22.9 – 30.2) |                             |
| IADL dependence degree                     |              |                    |              |                    | 0.002                       |
| Independent                                | 11,907       | 51.1 (46.7 – 55.5) | 2,627        | 22.1 (18.6 – 26.0) |                             |
| Dependent                                  | 11,402       | 48.9 (44.5 – 53.3) | 3,432        | 30.1 (25.2 – 35.5) |                             |
| BADL dependence degree                     |              |                    |              |                    | 0.916                       |
| Independent                                | 17,550       | 75.3 (70.4 – 79.6) | 4,547        | 25.9 (22.5 – 29.6) |                             |
| Dependent                                  | 5,759        | 24.7 (20.4 – 29.6) | 1,512        | 26.3 (19.7 – 34.1) |                             |
| Health self-assessment                     |              |                    |              |                    | 0.001                       |
| Positive                                   | 8,598        | 36.7 (33.4 – 40.1) | 1,726        | 20.1 (16.1 – 24.7) |                             |
| Negative                                   | 14,818       | 63.3 (59.9 – 66.6) | 4,333        | 29.2 (24.9 – 34.1) |                             |

to be continued

Continuation of Table 1

| Variables  | Total        |                    | PIM          |                    | <i>p</i> -value <sup>a</sup> |
|--|--------------|--------------------|--------------|--------------------|------------------------------|
|  | Estimate (n) | % (95% CI)         | Estimate (n) | % (95% CI)         |                              |
| Hospitalization in the last 12 months <sup>b</sup> |              |                    |              |                    | <0.001                       |
| Yes  | 3,746        | 16.6 (14.5 – 18.8) | 1,463        | 39.0 (31.5 – 47.2) |                              |
| No   | 18,868       | 83.4 (81.2 – 85.5) | 4,442        | 23.5 (19.8 – 27.7) |                              |
| More than three comorbidities                      |              |                    |              |                    | <0.001                       |
| Yes  | 6,845        | 29.2 (25.9 – 32.8) | 2,819        | 41.2 (35.8 – 46.7) |                              |
| No   | 16,571       | 70.8 (67.2 – 74.1) | 3,240        | 19.6 (16.1 – 23.6) |                              |
| Signs and symptoms of depression GDS <sup>b</sup>  |              |                    |              |                    | 0.002                        |
| Yes  | 7,546        | 32.5 (28.9 – 36.3) | 2,409        | 31.9 (26.3 – 38.1) |                              |
| No   | 17,601       | 67.5 (63.7 – 71.1) | 4,389        | 15.7 (13.3 – 18.5) |                              |
| Total  | 23,416       | 100.0              | 6,059        | 25.9 (22.3 – 29.8) |                              |

Results were shown in numbers, and percentages corrected for weight; Estimate (n): extrapolation to population; a: Pearson's chi-square test; 95%CI: 95% confidence interval; b: missing data in this variable due to non-response; IADL: instrumental activities of daily living; BADL: basic activities of daily living; BMI: body mass index; GDS: geriatric depression scale.

The most prevalent comorbidities found were: systemic arterial hypertension (61.2%), peripheral venous system diseases (37.5%), diabetes mellitus (18.1%), arthritis/arthrosis (16.6%), osteoporosis (16.5%), dyslipidemia (14.3%), depression (12.5%), insomnia (10.5%), anemia (7.8%) and bronchitis (7.7%).

Still in Table 1, it is possible to see that there was an association between the use of at least one PIM and the following variables: age, dependence for IADL, negative self-rated health, history of hospitalization in the last 12 months, presence of three or more comorbidities and depression symptoms.

In the logistic regression analysis adjusted by hierarchical level, there was an association between

the use of PIM at the distal level, sex, and at the intermediate level, dependence according to IADL and self-rated health ( $p < 0.05$ ). At the proximal level, there was an association with hospitalization in the last 12 months and the presence of three or more comorbidities ( $p < 0.05$ ), as shown in Table 2.

Table 3 describes the percentages of PIM categories in older people. According to the CBMPPII, the categories of drugs that should be avoided in these people, regardless of clinical condition, were the majority of the gastrointestinal system, followed by the central nervous system and psychotropic drugs and the cardiovascular system. The most used subcategory was use of proton pump inhibitors by 11.3% (9.2 – 13.8).

**Table 2.** Crude and adjusted hierarchical logistic regression model, having as dependent variable the use of at least one PIM by older people. Rio Branco, AC, 2014 (n=1,016).

| Variables   | OR <sub>Brute</sub> (95%CI) | p-value | OR <sub>Adjusted</sub> (95%CI) | p-value |
|---|-----------------------------|---------|--------------------------------|---------|
| <b>Distal level<sup>a</sup></b>                   |                             |         |                                |         |
| Sex   |                             | 0.049   |                                | 0.046   |
| Male  | 1                           |         | 1                              |         |
| Female  | 1.38 (1.00 – 1.91)          |         | 1.38 (1.01 – 1.90)             |         |
| Age (years)                                       |                             | 0.049   |                                | 0.065   |
| 60-69   | 1                           |         | 1                              |         |
| 70-79   | 0.90 (0.69 – 1.19)          |         | 0.90 (0.69 – 1.18)             |         |
| 80 and over                                       | 1.47 (0.99 – 2.17)          |         | 1.47 (0.99 – 2.17)             |         |
| <b>Intermediate level<sup>b</sup></b>             |                             |         |                                |         |
| IADL dependence degree                            |                             | 0.002   |                                | 0.015   |
| Independent                                       | 1                           |         | 1                              |         |
| Dependent   | 1.52 (1.17 – 1.97)          |         | 1.39 (1.07 – 1.81)             |         |
| Health self-assessment                            |                             | 0.001   |                                | 0.011   |
| Positive  | 1                           |         | 1                              |         |
| Negative  | 1.65 (1.23 – 2.21)          |         | 1.50 (1.10 – 2.04)             |         |
| Signs and symptoms of depression GDS <sup>b</sup> |                             | 0.002   |                                | 0.053   |
| No  | 1                           |         | 1                              |         |
| Yes   | 1.54 (1.18 – 2.03)          |         | 1.31 (0.99 – 1.73)             |         |
| <b>Proximal level<sup>c</sup></b>                 |                             |         |                                |         |
| Hospitalization in the last 12 months             |                             | <0.001  |                                | 0.007   |
| No  | 1                           |         | 1                              |         |
| Yes   | 2.08 (1.42 – 3.05)          |         | 1.79 (1.19 – 2.69)             |         |
| More than three comorbidities                     |                             | <0.001  |                                | <0.001  |
| No  | 1                           |         | 1                              |         |
| Yes   | 2.88 (2.23 – 3.72)          |         | 2.56 (1.97 – 3.33)             |         |

95%CI: 95% confidence interval; OR – Odds Ratio; p – Wald test value; a: distal level (adjusted for sex and age); b: intermediate level (adjusted for significant variables at the distal level plus self-rated health, signs of depression symptoms (GDS) and degree of dependence (IADL)); c: proximal level (adjusted for significant variables at the intermediate level, plus hospitalization in the last 12 months and presence of three or more comorbidities).

**Table 3.** Frequency of use of potentially inappropriate medication categories in the assessed older people (n= 1,016), regardless of clinical condition. Rio Branco, AC, 2014.

| Category  | N     | % (95%CI)         |
|---|-------|-------------------|
| Gastrointestinal system   | 2,684 | 11.5 (9.4 – 14.0) |
| Proton pump inhibitors (omeprazole, pantoprazole, esomeprazole)   | 2,647 | 11.3 (9.2 – 13.8) |
| Gastrointestinal antispasmodics (scopolamine)   | 52    | 0.2 (0.1 – 1.0)   |
| Metoclopramide  | 93    | 0.4 (0.1 – 1.1)   |
| Mineral oil (orally)  | 18    | 0.1 (0.0 – 0.6)   |
| Central nervous system and psychotropic medications   | 1,795 | 7.7 (5.8 – 10.0)  |
| First-generation antihistamines (bronpheniramine, cyproheptadine, chlorpheniramine, dexchlorpheniramine, dimenhydrinate, doxylamine, meclizine, promethazine) | 319   | 1.4 (0.8 – 2.4)   |

to be continued

Continuation of Table 3

| Category   | N     | % (95%CI)       |
|--|-------|-----------------|
| First-generation (chlorpromazine, haloperidol, levomepromazine) and second-generation (quetiapine, risperidone) antipsychotics for behavioral problems in dementia | 261   | 1.1 (0.6 – 2.0) |
| Barbiturates (phenobarbital)   | 129   | 0.6 (0.2 – 1.4) |
| Benzodiazepines (alprazolam, bromazepam, clonazepam, cloxazolam, diazepam, flunitrazepam, lorazepam, midazolam, nitrazepam)  | 1,163 | 5.0 (3.5 – 6.9) |
| Tertiary tricyclic antidepressants (amitriptyline, imipramine, nortriptyline, maprotiline) alone or in combination   | 338   | 1.4 (0.8 – 2.5) |
| Cardiovascular system  | 1,104 | 4.7 (3.5 – 6.3) |
| Alpha-1 blockers for the treatment of hypertension (doxazosin)   | 117   | 0.5 (0.2 – 1.2) |
| Centrally acting alpha agonists for routine treatment of hypertension (methyldopa)   | 128   | 0.5 (0.2 – 1.7) |
| Class Ia, Ic, III antiarrhythmic drugs (amiodarone)  | 84    | 0.4 (0.1 – 0.9) |
| Aspirin at a dose > 150 mg/day   | 291   | 1.2 (0.6 – 2.4) |
| Digoxin > 0.125 mg/day   | 243   | 1.0 (0.6 – 1.8) |
| Loop diuretics (furosemide) as first-line monotherapy for hypertension   | 55    | 0.2 (0.1 – 0.7) |
| Nifedipine, immediate-release capsule  | 267   | 1.1 (0.7 – 1.9) |
| Endocrine system   | 1,335 | 5.7 (4.3 – 7.5) |
| Estrogens (with or without progestones). Avoid oral forms and transdermal patches  | 24    | 0.1 (0.0 – 0.8) |
| Glibenclamide  | 1,311 | 5.6 (4.2 – 7.4) |
| Musculoskeletal system   | 331   | 1.4 (0.9 – 2.3) |
| Muscle relaxants (carisoprodol, cyclobenzaprine, orphenadrine)   | 331   | 1.4 (0.2 – 2.3) |
| Several  | 18    | 0.1 (0.0 – 0.6) |
| Theophylline as monotherapy for chronic obstructive pulmonary disease  | 18    | 0.1 (0.0 – 0.6) |

## DISCUSSION

In this study, a prevalence of 25.9% (95%CI: 22.3 – 29.8) of the use of at least one PIM was observed, regardless of the clinical condition. There was also an association between PIM use and the following variables: female sex, IADL dependence, negative self-rated health, hospitalization in the last 12 months and more than three comorbidities. Among PIM, proton pump inhibitors were the most used (11.3%, 95%CI: 9.2 – 13.8), followed by drugs acting on the central nervous system (7.7%, 95%CI: 5.8 – 10.0) and on the cardiovascular system (4.7%, 95%CI: 3.5 – 6.3).

When evaluating similar studies carried out in other countries in South America, the Middle East, Asia and Africa, a heterogeneous prevalence of PIM use according to the Beers and STOPP criteria can be

seen, ranging from 15.7%, as that observed in Nigeria among individuals aged 65 years and over according to the STOPP criterion and from 30.3% according to the Beers criterion, up to 72.7% in Argentina in 2,231 individuals aged 65 years and over according to the Beers criterion<sup>20-22</sup>. It is believed that this variability is related to the type and place of study, sample conditions such as older age, socioeconomic and other conditions of each population, since several factors can lead to a greater use of PIM<sup>20-22</sup>.

Comparing the results of this study with Brazilian population studies, there is a lower prevalence of PIM use, since other authors found a frequency that ranged from 28% to 44.8% in different regions of the country<sup>7-10,23</sup>. Considering that the population in this study has less education, access to medication use may be impaired, which partly explains these findings.

Our work stands out for being the first national, population-based study that used PIM criteria adapted to the Brazilian reality, in accordance with ANVISA<sup>3</sup> regulation. In 2018, a study evaluated the same criteria as the CBMPIO in a cross-sectional survey carried out with 227 older people from two basic health units and found a higher prevalence of PIM: 55.9%<sup>24</sup>. However, it is important to highlight that the study by these authors includes a convenience sample, regularly seen in primary care centers, which probably may have influenced the results. No other population-based studies were found that used the same criteria for PIM.

As already described, this study evidenced an association between several variables and the use of PIM. As in other studies carried out in Brazil, in the final adjusted model it was observed that the female gender was related to the dependent variable<sup>7-10</sup>. A possible explanation would be that, in our country, older women culturally tend to seek health services more, which can lead to a higher risk of PIM use. In addition, there is a greater life expectancy in female individuals, which, consequently, may be associated with a higher prevalence of chronic diseases that require continuous pharmacological treatment<sup>25</sup>.

It was also observed that older people with dependence for at least one instrumental activity of daily living were more likely to use PIM. This association can be explained by the fact that these individuals, with loss of functional capacity, demand more from health services, which, therefore, would lead to an increase in the frequency of consultations and pharmacotherapeutic follow-up. This follow-up, however, is essential, since individuals with loss of functional capacity need more intense attention with the aim of rehabilitation and loss reduction.

Another important issue is that these individuals with greater vulnerability are often assisted by caregivers with low education, inadequate training and work overload, and this can amplify the negative impacts of polypharmacy<sup>26,27</sup>. Therefore, it is important to develop formal training programs for caregivers of older people, who are often responsible for their medication.

Individuals who rated their health as negative were also at higher risk of using PIM. Currently, the concept of health is seen in a complex way, since it involves multiple dimensions, and self-assessment is a global indicator based on subjective perception, which encompasses physical, emotional, social and well-being components<sup>28</sup>. Other authors had already pointed out that self-rated health can be a marker associated with the use of PIM, being useful even as a prognostic tool<sup>29,30</sup>.

There are some hypotheses that could explain this finding. First, it is believed that older people with a negative health perception tend to seek greater support in health services, therefore, they would have greater exposure to different medications. Another possible explanation would be that the indiscriminate use of drugs can increase the chances of adverse events, which impacts self-rated health. However, these hypotheses cannot be explained by the design of the present study.

Hospitalization in the last 12 months was also a factor associated with PIM use. It is important to emphasize that it can be configured both as a complication of the use of these drugs and as a risk factor for their use at hospital discharge. In an Italian population-based retrospective cohort that followed 1,480,137 older people between 2003 and 2013, it was observed that 15.6% of hospitalizations during this period occurred in the context of using at least one PIM<sup>31</sup>.

Additionally, a cross-sectional study carried out with older people hospitalized in medical clinic and geriatric units of a Brazilian public hospital showed, at the time of hospital discharge, a frequency of 58.4% of PIM use, according to the CBMPIO criteria. The authors also observed that hospitalization in the geriatrics ward proved to be a protective factor for the use of these drugs, suggesting that specialists in the care of older people are better prepared for quaternary prevention of iatrogenic diseases, which highlights the importance of global and multidisciplinary care for older people<sup>32</sup>.

The presence of more than three comorbidities was associated with the use of PIM. Similar results

were found in other studies, such as the one carried out in Pelotas (RS)<sup>8</sup>, and the SABE study, developed in the city of São Paulo (SP)<sup>7</sup>. These data indicate the importance of primary care for older people, avoiding the fragmentation of care, since the figure of the generalist and the multidisciplinary team play a fundamental role in the evaluation of the patient as a whole. In this way, care centered on older people with multimorbidities facilitates an approach aimed at deprescription and prevention of iatrogenic events<sup>33</sup>.

In the present study, the most common PIM categories were from the gastrointestinal system. The most used subcategory was the use of proton pump inhibitors, and the most used PIM was omeprazole. This same drug was also the most found in a population-based study carried out in the city of Viçosa (MG), which showed a frequency of use of 20%<sup>12</sup>. In a study carried out in two primary care centers located in the city of Belo Horizonte (MG), the main class of PIM found was also the prolonged use of proton pump inhibitors (30.1%)<sup>24</sup>.

The use of proton pump inhibitors for more than eight weeks is a common finding, and their use should be cautious in the geriatric population, as it is associated with the development of osteoporosis, fractures, dementia and kidney failure. The physician should always weigh its use for long periods and think about non-pharmacological strategies to avoid prolonged use<sup>4,5</sup>.

In this study, a high frequency of use of PIMs that act on the central nervous system and cardiovascular system was also observed. These same categories were also found in other Brazilian population-based surveys. In the one carried out in Pelotas (RS), the most common PIM category was that of the central nervous system, which corresponded to 48.9% of inappropriate medications<sup>10</sup>; in the SABE study, most PIM found belong to drugs acting on the cardiovascular system<sup>9</sup>. Therefore, there is a heterogeneity of PIM classes found in the main population-based studies carried out in Brazil, but also a visible predominance among drugs acting on the digestive system.

This work had some limitations. First, as it is a cross-sectional observational study, it was not possible to infer causality. Second, no cognitive test was performed to exclude patients with cognitive decline, which may have interfered with the assessment of some patients. This may also influence the application of questionnaires to assess activities of daily living, since individuals with unidentified cognitive deficits may not adequately report such activities. Finally, it was not possible to assess the duration of use of proton pump inhibitors, as this information was not available.

Population-based studies that aim to assess associated factors and frequency of PIM use, using the CBMPII as a criterion, are scarce and do not encompass all Brazilian regions. This data is important for the development of public policies and identification of patients at iatrogenic risk, as well as to reinforce teaching about the particularities of pharmacotherapy for older people for professionals able to prescribe medication.

## CONCLUSION

The prevalence of PIM use among older people in Rio Branco, Acre, Brazil was 25.9%, being associated with female gender, IADL dependence, negative self-rated health, hospitalization in the last 12 months and presence of more than three comorbidities.

Data on the use of PIM using a national criterion are important for the standardization of this measurement and for adapting to the particularities of pharmaceutical care in Brazil. This is justified by the fact that there are medicines registered here that are not available in other countries, and vice versa. In addition, information on PIM use is heterogeneous across the country according to the criteria adopted by the studies. Therefore, carrying out this investigation will be one more piece that will make it possible to understand the particularities of pharmacotherapeutic care in Brazil.

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## REFERENCES

1. Johansson T, Flamm M, Sönnichsen A, Schuler J. Interventions to reduce inappropriate polypharmacy: Implications for research and practice. *Maturitas*. 2017;97:66-8.
2. Fick DM, Semla TP, Steinman M, Beizer J, Brandt N, Dombrowski R, et al. American Geriatrics Society 2019 Updated AGS Beers Criteria® for Potentially Inappropriate Medication Use in Older Adults. *J Am Geriatr Soc*. 2019;67(4):674-94.
3. Oliveira MG, Amorim WW, Borja-Oliveira CR, Coqueiro HL, Gusmão LC, Passos LC. Consenso Brasileiro de Medicamentos Potencialmente Inapropriados para Idosos. *Geriatr Gerontol Aging*. 2016;10(4):168-81.
4. Beers MH, Ouslander JG, Rollingher I, Reuben DB, Brooks J, Beck JC. Explicit criteria for determining inappropriate medication use in nursing home residents. UCLA Division of Geriatric Medicine. *Arch Intern Med*. 1991;151(9):1825-32.
5. Fick DM, Semla TP, Beizer J, Brandt J, Dombrowski R, DuBeau CE, et al. American Geriatrics Society 2015 Updated Beers Criteria for Potentially Inappropriate Medication Use in Older Adults. *J Am Geriatr Soc*. 2015;63(11):2227-46.
6. O'mahony D, O'sullivan D, Byrne S, O'connor MN, Ryan C, Gallagher P. STOPP/START criteria for potentially inappropriate prescribing in older people: Version 2. *Age Ageing*. 2015;44(2):213-8.
7. Cassoni TCJ, Corona LP, Romano-Lieber NS, Secoli SR, Duarte YA de O, Lebrão ML. Use of potentially inappropriate medication by the elderly in São Paulo, Brazil: SABE Study. *Cad Saúde Pública*. 2014;30(8):1708-20.
8. Lutz BH, Miranda VIA, Bertoldi AD. Potentially inappropriate medications among older adults in Pelotas, Southern Brazil. *Rev Saúde Pública*. 2017;51:52. Disponível em: <https://doi.org/10.1590/S1518-8787.2017051006556>
9. Araújo NC, Silveira EA, Mota BG, Mota JPN, Silva AEBC, Guimarães RA, et al. Potentially inappropriate medications for the elderly: Incidence and impact on mortality in a cohort ten-year follow-up. *PLoS One*. 2020;15(10):e0240104. Disponível em: <https://doi.org/10.1371/journal.pone.0240104>. eCollection 2020
10. Martins GA, Acurcio FA, Franceschini SCC, Priore SE, Ribeiro AQ. Use of potentially inappropriate medications in the elderly in Viçosa, Minas Gerais State, Brazil: a population-based survey. *Cad Saúde Pública*. 2015;31(11):2401-12.
11. Programa das Nações Unidas para o Desenvolvimento. Atlas do Desenvolvimento Humano no Brasil 2013. 2013. Disponível em: [http://www.pnud.org.br/IDH/Atlas2013.aspx?indiceAccordion=1&li=li\\_Atlas2013](http://www.pnud.org.br/IDH/Atlas2013.aspx?indiceAccordion=1&li=li_Atlas2013)
12. Amaral TLM, Amaral CA, Portela MC, Monteiro GTR, Vasconcellos MTL. Study of Chronic Diseases (Edoc): Methodological aspects. *Rev Saúde Pública*. 2019;53:8. Disponível em: <https://doi.org/10.11606/S1518-8787.2019053000847>
13. Lawton MP, Brody EM. Assessment of Older People: Self-Maintaining and Instrumental Activities of Daily Living. *Gerontologist*. 1969;9(3):179-86.
14. Santos RL, Virtuoso JS Jr. Confiabilidade da versão brasileira da Escala de Atividades Instrumentais da Vida Diária. *RBPS*. 2008;21(4):290-6.
15. Lino VTS, Pereira SRM, Camacho LAB, Ribeiro ST Filho, Buksman S. Cross-cultural adaptation of the Independence in Activities of Daily Living Index (Katz Index). *Cad Saúde Pública* 2008;24(1):103-12.
16. Almeida OP, Almeida SA. Short versions of the geriatric depression scale: a study of their validity for the diagnosis of a major depressive episode according to ICD-10 and DSM-IV. *Int J Geriatr Psychiatry*. 1999;14(10):858-65.
17. Nutrition Screening Initiative. Nutrition Interventions Manual for Professionals Caring for Older Americans. Washington, DC: Nutrition Screening Initiative; 1992.
18. Pereira KG, Peres MA, Lop D, Boing AC, Boing AF, Aziz M, et al. Polifarmácia em idosos: um estudo de base populacional. *Rev Bras Epidemiol*. 2017;20(2):335-44.
19. WHO Collaborating Centre for Drug Statistics Methodology. Guidelines for ATC classification and DDD assignment 2018. Oslo, Norway: WHO, 2017.
20. Chiapella LC, Montemarani MJ, Marzi M, Mamprin ME. Prevalence of potentially inappropriate medications in older adults in Argentina using Beers criteria and the IFAsPIAM List. *Int J Clin Pharm*. 2019;41(4):913-9.
21. Saboor M, Kamrani AAA, Momtaz YA, Sahaf R. Prevalence and associated factors of potentially inappropriate medications among Iranian older adults. *Med Glas*. 2019;16(1):121-7.
22. Fadare JO, Desalu OO, Obimakinde AM, Adeoti AO, Agboola SM, Aina FO. Prevalence of inappropriate medication prescription in the elderly in Nigeria: A comparison of Beers and STOPP criteria. *Int J Risk Saf Med*. 2015;27(4):177-89.

23. Pinto MCX, Ferré F, Pinheiro MLP. Potentially inappropriate medication use in a city of Southeast Brazil. *Braz J Pharm Sci.* 2012;48(1):79-86.
24. Almeida TA, Reis EA, Pinto IVL, Ceccato MGB, Silveira MR, Lima MG, et al. Factors associated with the use of potentially inappropriate medications by older adults in primary health care: An analysis comparing AGS Beers, EU(7)-PIM List, and Brazilian Consensus PIM criteria. *Res Social Adm Pharm.* 2019;15(4):370-7.
25. Baldoni ADO, Ayres LR, Martinez EZ, Dewulf NDLS, Santos V, Pereira LRL. Factors associated with potentially inappropriate medications use by the elderly according to Beers criteria 2003 and 2012. *Int J Clin Pharm.* 2014;36(2):316-24.
26. Novaes PH, Cruz DT, Lucchetti ALG, Leite ICG, Lucchetti G. The “iatrogenic triad”: polypharmacy, drug-drug interactions, and potentially inappropriate medications in older adults. *Int J Clin Pharm.* 2017;39(4):818-25.
27. Figueiredo MDLF, Gutierrez DMD, Darder JJT, Silva RF, Carvalho ML. Formal caregivers of dependent elderly people in the home: Challenges experienced. *Cienc Saúde Coletiva.* 2021;26(1):37-46.
28. Organisation for Economic Cooperation and Development (OECD). *Health at a Glance 2019: OECD Indicators.* OECD Publishing: Paris; 2019.
29. Nothelle SK, Sharma R, Oakes A, Jackson M, Segal JB. Factors associated with potentially inappropriate medication use in community-dwelling older adults in the United States: a systematic review. *Int J Pharm Pract.* 2019;27(5):408-23.
30. Suemoto CK, Ueda P, Beltrán-Sánchez H, Lebrão ML, Duarte YA, Wong R, et al. Development and validation of a 10-year mortality prediction model: Meta-analysis of individual participant data from five cohorts of older adults in developed and developing countries *J Gerontol A Biol Sci Med Sci.* 2017;72(3):410-6.
31. Varga S, Alcusky M, Keith SW, Hegarty SE, Del Canale S, Lombardi M, et al. Hospitalization rates during potentially inappropriate medication use in a large population-based cohort of older adults. *Br J Clin Pharmacol.* 2017;83(11):2572-80.
32. Magalhães MS, Santos FS, Reis AMM. Factors associated with the use of potentially inappropriate medication by elderly patients prescribed at hospital discharge. *Einstein.* 2019;18:eAO4877. Disponível em: [http://dx.doi.org/10.31744/einstein\\_journal/2020AO4877](http://dx.doi.org/10.31744/einstein_journal/2020AO4877)
33. Mehta RS, Kochar BD, Kennelty K, Ernst ME, Chan AT. Emerging approaches to polypharmacy among older adults. *Nat Aging.* 2021;1(4):347-56.