

# Potentially inappropriate medication use in hospitalized elderly patients

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## SUMMARY

**OBJECTIVE:** This study aimed to assess the prevalence of potentially inappropriate medication prescription in hospitalized elderly patients according to the 2019 American Geriatrics Society Beers Criteria.

**METHODS:** This study is a prospective analysis of electronic medical records of elderly patients admitted to the Department of Medicine, Hospital Central da Irmandade da Santa Casa de Misericórdia de São Paulo, between 1 September 2020 and 30 April 2021.

**RESULTS:** A total of 142 patients (85 women and 57 men) with a mean age of 74.5±7.3 years (65–99 years) were assessed. Of these, 108 (76.1%) were elderly (age ≥65 years and <80 years) and 34 (23.9%) long-lived (age ≥80 years). The average length of stay found in the sample was 25.3±28.7 days (between 2 and 235 days), and 102 out of the 140 patients assessed remained in the hospital for up to 29 days. Sixteen drugs considered potentially inappropriate medication were found in the patients' prescriptions, with at least one potentially inappropriate medication having been prescribed to 141 (99.3%) patients. Elderly patients had a mean of 2.57±0.94 potentially inappropriate medication prescribed versus 2.56±0.89 among long-lived patients. The most prescribed potentially inappropriate medication were as follows: regular human insulin as required (85.2%), and omeprazole (73.9%) and metoclopramide as required (61.3%).

**CONCLUSION:** The study sample showed significant percentages of potentially inappropriate medication prescriptions for the elderly admitted to the hospital.

**KEYWORDS:** Potentially inappropriate medication list. Inpatients. Side effects. Hospitalization. Aged. Iatrogenic disease. Inappropriate prescribing.

## INTRODUCTION

The number of elderly people and life expectancy worldwide have both increased significantly. This characterizes the phenomenon of aging, in which the population aged 65 years and older grows at a rate of about 3% per year, a rate that is higher than those in any other age group<sup>1,2</sup>.

Aging consists of a progressive inability to maintain the homeostatic balance and is associated with the decline of organic functions, which results in a predisposition of the elderly population to develop multiple comorbidities. In turn, the direct consequence of this scenario is a higher prevalence of older adults being hospitalized, in which a wide variety of drugs are used in addition to those chronically used by them<sup>3,4</sup>.

The elderly population, however, has a number of age-specific conditions that influence drug metabolism and pharmacokinetics thereof. Thus, both first-pass metabolism and hepatic clearance can be altered, which increases the bioavailability of

xenobiotics in the elderly. Furthermore, changes in body composition occur with age, and lipophilic drugs may have a greater distribution volume with a longer half-life, whereas hydrophilic drugs have a lower distribution volume. Finally, renal function is globally reduced, as the vast majority of elderly people have some degree of renal dysfunction<sup>5,6</sup>.

In this context, the concept of potentially inappropriate medication (PIM) use in the elderly must be taken into account<sup>7</sup>, and the use thereof represents greater risks of causing adverse reactions to patients due to the changes inherent to aging. Therefore, lists have been created in order to assist clinical practitioners in identifying PIM and preventing their prescription<sup>8-10</sup>.

The so-called "Beers criteria" of the American Geriatrics Society (AGS), developed by an American team of specialists, comprising, among others, geriatricians, pharmacologists, and clinical pharmacists, is one of those lists that are readily

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available and has become the most cited and used worldwide for detecting PIM<sup>11,12</sup>.

Refraining from using PIM in the elderly is an important public health strategy, since it optimizes the appropriate prescription for this population, thereby preventing potentially negative outcomes such as predictable adverse drug reactions, prolonged hospital stay, disabilities, and death<sup>13,14</sup>.

The goal of this study was to assess the prevalence of PIM use in hospitalized elderly patients according to the 2019 AGS Beers criteria<sup>15</sup>.

## METHODS

### Study design

This is a prospective analysis of electronic medical records of elderly patients admitted to the Department of Medicine at

Hospital Central da Irmandade da Santa Casa de Misericórdia de São Paulo (ISCMSP) between September 1, 2020 and April 30, 2021.

For analysis, patients aged  $\geq 65$  years, admitted to the internal medicine ward for 24 h or more and who were not receiving end-of-life palliative care or whose reason for admission was SARS-CoV-2 infection were included.

Those drugs listed in Table 1 (“Potentially Inappropriate Medication Use in Older Adults”) of the 2019 AGS Beers criteria were considered PIM. Such table was adapted according to the medications approved for use in Brazil as per data available from Brazil’s National Health Surveillance Agency (ANVISA, the Portuguese acronym for “Agência Nacional de Vigilância Sanitária”) website on October 28, 2021<sup>16</sup> (Table 2).

An electronic form was created for receiving data taken from the patients’ medical records (Soul MV System, version

**Table 1.** Potentially inappropriate medicines identified in the sample.

Potentially inappropriate medication	Female patients and age		Male patients and age		Total (142)	Percentage of use
	Elderly (65)	Long-lived (20)	Elderly (43)	Long-lived (14)		
Regular human insulin AR	54	18	36	13	121	85.2
Omeprazole	48	15	32	10	105	73.9
Metoclopramide AR	41	12	26	8	87	61.3
Dimenhydrinate AR	4	2	3	1	10	7.0
Promethazine	3	–	2	1	6	4.2
Amiodarone	1	1	2	1	5	3.5
Diazepam AR	2	–	1	1	4	2.8
Dimenhydrinate	3	–	1	–	4	2.8
Phenobarbital	1	2	–	–	3	2.1
Amitriptyline	1	–	1	–	2	1.4
Clonazepam	1	–	1	–	2	1.4
Clonazepam AR	–	–	2	–	2	1.4
Scopolamine	1	–	1	–	2	1.4
Scopolamine AR	2	–	–	–	2	1.4
Hydroxyzine	2	–	–	–	2	1.4
Metoclopramide	2	–	–	–	2	1.4
Propantheline	–	–	2	–	2	1.4
Diazepam	–	–	1	–	1	0.7
Doxazosin	–	–	–	1	1	0.7
Methyldopa	–	1	–	–	1	0.7
Nifedipine	1	–	–	–	1	0.7

AR: as required.

**Table 2.** Medications licensed for use in Brazil listed in Table 2 of the 2019 American Geriatrics Society Beers criteria.

Therapeutic class				
<b>Central alpha-agonists</b> Clonidine (for first-line treatment of hypertension) Guanabenz Guanfacine Methyl dopa Reserpine (>0.1 mg/day)	<b>Antidepressants</b> Amitriptyline Amoxapine Clomipramine Desipramine Doxepin (>6 mg/day) Imipramine Nortriptyline Paroxetine Protriptyline Trimipramine	<b>First-generation antihistamines</b> Brompheniramine Carbinoxamine Chlorpheniramine Clemastine Cyproheptadine Dexbrompheniramine Dexchlorpheniramine Dimenhydrinate Diphenhydramine (oral) Doxylamine Hydroxyzine Meclizine Ppyrilamine or Mepyramine Promethazine Triprolidine	<b>Antiparkinsonian drugs</b> Benztropine (oral) Trihexyphenidyl	<b>Barbiturates</b> Amobarbital Butabarbital Butalbital Mephobarbital Pentobarbital Phenobarbital Secobarbital
<b>Genitourinary drugs</b> Desmopressin	<b>Hormones</b> Androgens Methyltestosterone Testosterone Other hormones Thyroid extract Estrogen with or without progesterone Growth hormone Megestrol	<b>Other anxiolytics</b> Meprobamate	<b>Peripheral alpha-1 blockers for hypertension treatment</b> Doxazosin Prazosin Terazosin	<b>Antispasmodics</b> Atropine ( <i>excludes ophthalmic use</i> ) Belladonna alkaloids Chlordiazepoxide-clidinium Dicyclomine Homatropine ( <i>excludes ophthalmic use</i> ) Hyoscyamine Methscopolamine Propantheline Scopolamine
<b>Nonsteroidal anti-inflammatory drugs</b> Acetylsalicylic acid (>325 mg/day) Mefenamic acid Ketoprofen Ketorolac (including parenteral) Diclofenac Diflunisal Etodolac Fenoprofen Ibuprofen Indomethacin Meclofenamate Meloxicam Nabumetone Naproxen Piroxicam Sulindac Tolmetin	<b>Antipsychotics</b> First generation (conventional) and second generation (atypical)	<b>Benzodiazepines</b> <i>Short or intermediate action:</i> Alprazolam Estazolam Lorazepam Oxazepam Temazepam Triazolam <i>Prolonged action:</i> Chlordiazepoxide (alone or in association with amitriptyline or clidinium) Clonazepam Clorazepate Diazepam Flurazepam Quazepam	<b>Nonbenzodiazepine hypnotics (Z-drugs)</b> Eszopiclone Zaleplon Zolpidem	<b>Muscle relaxants</b> Carisoprodol Chlorzoxazone Cyclobenzaprine Methocarbamol Orphenadrine
<b>Other cardiovascular action drugs</b> Amiodarone Disopyramide Dronedaron Digoxin (as first-line treatment for atrial fibrillation or heart failure) Nifedipine	<b>Antibiotics</b> Nitrofurantoin	<b>Antithrombotic drugs</b> Dipyridamole (oral, short-term)	<b>Gastrointestinal tract</b> Metoclopramide Mineral oil (oral) Proton-pump inhibitor	<b>Hypoglycemic drugs</b> <i>Sulfonylureas of prolonged action</i> Chlorpropamide Glibenclamide Glibenclamide <i>Short or fast-acting insulins</i> (in a scheme according to capillary glycemia)
	<b>Opioids</b> Meperidine	<b>Vasodilators of dubious efficacy</b> Ergoloid mesylates Isoxsuprine		

SMA-PEP.2019.006.LTS®). The following variables were collected: sex, age, ethnicity, comorbidities, prescription (at day 2 of hospital stay), and length of stay.

Elderly patients were those aged 65 years or older, and those aged 80 years or older were termed long-lived.

In addition, the Charlson index was also calculated<sup>17</sup> from the collected data.

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### Statistical analysis

Statistical analysis of the study population was based on the presence or absence of PIM in the patient's prescription.

The Charlson index was also compared between groups of male and female patients, as well as between elderly and long-lived patients, for whom Pearson's  $\chi^2$  test was used with a significance level (alpha value) of 0.05.

## RESULTS

A total of 142 patients (85 females and 57 males) with a mean age of  $74.5 \pm 7.3$  years (65–99 years) were analyzed. Of them, 108 (76.1%) were elderly and 34 (23.9%) were long-lived. The mean length of stay in the sample was  $25.3 \pm 28.7$  days (from 2 to 235 days), with 102 of the 142 analyzed patients having stayed at the hospital for up to 29 days.

Sixteen drugs considered PIM were found in the patients' prescriptions (Table 1).

The elderly had a mean of  $2.57 \pm 0.94$  PIMs prescribed, whereas the long-lived patients had  $2.56 \pm 0.89$ , with at least one PIM having been prescribed for 141 (99.3%) patients.

The Charlson index was calculated according to sex (female or male) and age (elderly or long-lived) of the sample (Table 3).

**Table 3.** Study population's Charlson index.

Charlson index	Sex (F/M) $p=0.047^*$	Age (E/L) $p=0.049^*$	Total
Absence of comorbidity	33 (39)/18 (32)	37 (35)/14 (41)	51 (36)
Low comorbidity	32 (38)/14 (25)	31 (29)/15 (44)	46 (33)
High comorbidity	20(23)/24 (43)	39 (36)/5 (15)	44 (31)

F: female; M: male; E: elderly; L: long-lived.

## DISCUSSION

With aging, there occur losses to the functional reserve of multiple organs, which affects drug metabolism. PIMs for the elderly, therefore, are those whose use represents a greater potential risk than benefit for this population.

This, along with the global trend of an increasing number of elderly people, makes not only the identification but also the avoidance of PIM use in health institutions essential for preventing potentially negative outcomes, such as predictable adverse drug reactions, prolonged length of stay, and disabilities.

Literature data on PIM use, especially in developing countries, remain scarce, as does the analysis of the prevalence of these drugs in an in-hospital environment, since a significant portion of the studies focuses on institutionalized elderly patients or in outpatient care. This study, therefore, aims to address this gap.

Our sample showed significant percentages of PIM prescriptions, with 99.3% of them making use of at least one PIM. The prescription of some PIMs "as required" was also noted, which does not minimize their harmful risk, since in an in-hospital environment their use can become daily rather than episodic.

The drugs that were prescribed in our series are considered inappropriate due to the exacerbation of their mechanism of action in the elderly population. Thus, changes that are inherent to aging, such as reduced activation of enzymatic systems, lower concentration of plasma proteins, impaired renal function, and changes in body composition (in which case, the liposubstitution process alters the expected distribution of lipophilic drugs), contribute to greater bioavailability of such drugs and may result in actual doses exceeding the therapeutic dose that would be desired, therefore causing toxic effects<sup>15,18</sup>.

Among the drugs identified, regular human insulin, omeprazole, and metoclopramide stand out as those most prescribed ones. The first is considered inappropriate when it is not used concomitantly with long-acting insulin, due to the increased risk of hypoglycemia and inappropriate management of hyperglycemia, which contributes to its long-term consequences<sup>15</sup>.

It is noteworthy, however, that the health care service where our study was carried out began to implement a protocol for insulin prescription after our data collection had finished. Such a protocol eliminates the status of this drug as PIM, which can result in a significant reduction in its prescription.

In relation to metoclopramide, its contraindication is due to the risk of extrapyramidal symptoms. Dystonia and akathisia are symptoms that can occur following administration of a single dose of this drug, whereas conditions such as Tardive dyskinesia and secondary Parkinsonism tend to occur with sustained use<sup>15</sup>.

The use of omeprazole, in turn, was associated with an increased risk of bone loss, falls and fractures, infection by *Clostridium difficile*, dementia, vitamin B12 deficiency, and kidney disease. It is worth mentioning that such effects have been reported when it was used in a chronic manner (at least one daily dose for 8 weeks)<sup>19</sup>, with its use being more relevant in the in-hospital environment for prolonged stays.

The Charlson index is a method for categorizing patients' comorbidities that can be used as a prognostic tool for hospital mortality. The fact that in our study population, female and long-lived patients had better rates coincides with the tendency of these populations to have healthier lifestyle habits, in addition to seeking primary health care services more often, which allows for the prevention of diseases or screening thereof with an early treatment and hence better progression.

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## CONCLUSIONS

This work has contributed to identifying the indiscriminate prescription of PIMs for the elderly population in tertiary health care centers. It thus serves as an alert to health care professionals about the importance of recognizing such indiscriminate use, assisting clinical practice, and optimizing patient care.

## AUTHORS' CONTRIBUTIONS

**RMAFO:** Data curation, Formal Analysis, Writing – original draft. **MLG:** Conceptualization, Writing – review & editing. **RFR:** Conceptualization, Methodology, Writing – review & editing.

