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Association of age, frailty, polypharmacy, and multimorbidity with PIP in older adults according to the STOPP/START and Beers criteria in Colombia

Asociación entre la edad, la fragilidad, la polimedicación y la pluripatología con la PPI en adultos mayores según criterios STOPP/START y criterios Beers en Colombia

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Abstract

Introduction: Inappropriate prescription of medications in older adults can increase the risk of adverse drug reactions and interactions, causing higher numbers of consultations, hospital admissions, readmissions, and/or prolonged stays, all of which put well-being and quality of life at risk for these patients. **Objective:** To determine the association between potentially inappropriate prescriptions (PIPs) and factors such as frailty, sex, age, multiple pathologies, and polypharmacy. **Methodology:** A cross-sectional analytical study was carried out using the STOPP/START criteria and the Beers criteria. A total of 3,325 prescriptions for patients treated by a Health Care Provider (HCP) in Medellín during 2023 were analyzed. **Results**: The general PIP percentage in the patients studied was 31.5%, out of which 19.5% met any of the Beers criteria and 14.4% met any of the STOPP/START criteria. The main medications identified using the Beers criteria were proton pump inhibitors (PPIs), followed by diuretics, antipsychotics, and antidepressants. A significant association was found between PIP and the variables sex and number of medications, with a greater probability of PIP in women compared to men (OR: 1.80 95% CI 1.64–2.86) and those receiving a prescription with 8–9 medications (OR: 0.10 95% CI 0.06-0.24) or more than ten of them (OR: 0.21 95% CI 0.18-0.38). **Conclusions:** The safe use of medications among older adults requires tools that promote adequate prescription and contribute to achieving therapeutic objectives.

Keywords: Polypharmacy; Inappropriate Prescription; Older Adults

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Resumen

Introducción: La prescripción inadecuada de medicamentos en los adultos mayores puede aumentar el riesgo de aparición de reacciones adversas medicamentosas e interacciones, ocasionando el incremento de consultas, ingresos y reingresos hospitalarios o días de estancia prolongados, todo ello coloca en riesgo la salud y la calidad de vida de estos pacientes. **Objetivo:** Determinar la asociación entre factores como la fragilidad, el sexo, la edad, la pluripatología y la polimedicación y la prescripción potencialmente inadecuada (PPI). **Metodología:** Se realizó un estudio analítico transversal. Utilizando los criterios STOPP/START y los criterios Beers. Se estudiaron 3325 prescripciones de pacientes atendidos por un gestor farmacoterapéutico de la ciudad de Medellín durante el año 2023. **Resultados:** La PPI general en los pacientes estudiados fue del 31.52%. El 19.51% de estos cumplió algún criterio Beers y el 14.41% cumplió alguno de los criterios STOPP/START. Los principales medicamentos relacionados con los criterios Beers son los inhibidores de la bomba de protones (IBP), seguidos de los diuréticos, antipsicóticos y antidepresivos. Se encontró asociación significativa de la PPI con las variables: sexo y número de medicamentos, siendo las mujeres quienes presentan mayor probabilidad de PPI que los hombres (OR:1.80 IC95% 1.16-2.86) y, además, tener una prescripción entre 8 y 9 medicamentos o más de diez medicamentos (OR: 0.10 IC95% 0.06-0.24) (OR: 0.21 IC95% 0.18-0.38). **Conclusiones:** Es importante para un uso seguro de los medicamentos entre adultos mayores contar con herramientas que propendan a una prescripción adecuada y que aporten al logro de los objetivos terapéuticos.

Palabras Claves: Polifarmacia; Prescripción Inadecuada; Anciano

Introduction

Population ageing is associated with an increased prevalence of diseases[1,2]. Chronic and non-communicable diseases, in particular, lead to frequent emergency consultations and possible relapses, which places a significant burden on healthcare systems and leads to health costs[3–5]. To mitigate these challenges the STOPP/START (Screening Tool of Older Person's potentially inappropriate Prescriptions - Screening Tool to Alert doctors to the Right Treatment) and Beers criteria are used to provide the appropriate medications from a safe prescription adjusted to the needs of the patient[6]. Therefore, adequate and safe use of medications is necessary in older adult[7], who are more vulnerable due to their complexities[8].

Appropriate prescribing consists in the selection of the right medications according to the pathophysiology of each patient, who presents the lowest possibility of adverse reactions and interactions, and that is also cost-effective[7]. Consequently, there is a risk of potentially inappropriate medication (PIM) when the probability of adverse events is greater than the benefit of using of a medication and there are safer and more effective therapeutic alternatives[7].

PIM includes both potentially inappropriate prescribing (PIP) and potential prescribing omissions (PPO). The first is the inappropriate use of medications according to their dosage or due to therapeutic duplication or interactions. The second is the omission of necessary medications for the patient[2]. There are different alternatives for the assessment of PIM. For instance, the medication appropriateness index (MAI), one of the most reliable implicit criteria developed in the United States of America, has been validated for older adults, multi-pathological and polymedicated patients at all levels of care[9]. MAI evaluates each of the medications prescribed to a patient, assessing unnecessary medications and polypharmacy, but does not capture adverse effects, underutilization, and therapeutic non-compliance[10].

There are also explicit criteria that serve as an easy-to-apply tool, helping health professionals responsible for prescribing medication in this age group to review medication in a regulated and homogeneous manner. The Beers criteria are notable among them, especially the latest version from 2019[11]. In addition, the STOPP/START criteria, updated in 2023[7,12], constitute an effective tool for prescription review that has been shown to decrease polypharmacy, adverse events, and the use of health resources[13–15].

The Beers and STOPP/START criteria are applicable and suitable to be used in Colombia. In this validation, the experts deem these criteria to be important, useful, and applicable in Colombia[16].

The objective of this study was to describe PIP in chronic and polymedicated, multipathological older adults who are treated by a pharmacotherapy manager in the city of Medellin and to determine the association of said PIP with factors such as frailty, sex, age, number of diagnosed diseases, and number of medications prescribed

Methodology

This cross-sectional analytical study included a total population of 3,325 prescriptions for patients attending a secondary-level HCP in Medellín in 2023. The HCP sent the required prescription data, formatted as the researchers requested it and meeting two criteria:

- Inclusion criteria: prescription records and medical records of older adults, aged 65 or older, who had five or more medications per day and three or more chronic diseases with a diagnosis confirmed by medical history and according to the International Classification of Diseases Tenth Revision (ICD-10) at a HCP in Medellín during 2023.
- Exclusion criteria: medical records and prescriptions for older adults that did not have a diagnosis with an ICD-10 code and/or medical prescriptions for older adults who did not have the required information about the drugs, such as the dosage, name, strength, pharmaceutical form, and dosage range.

The format for the prescriptions database included the following information: sociodemographic data (age, sex), health conditions (diseases), medication prescription, all the information on their dosage (concentration, pharmaceutical form, dosage interval, and treatment time), and clinical assessments of potassium, creatinine, and glomerular filtration rate, among others.

Frailty data were gathered based on the pharmacotherapy manager's criteria, including age, polypharmacy, multimorbidity, hospitalizations, and emergency admissions. Patients were classified into low, medium, or high frailty levels.

All the prescriptions that were submitted and met the inclusion criteria were included in the analysis. The format and inclusion criteria were shared with the HCP, and a designated author was responsible for obtaining this data from the healthcare institution.

PIP was assessed in these prescriptions using the Beers and STOPP/START criteria, both of which have been previously validated for Colombia[16]. Additionally, the association between PIP and age, sex, number of diseases, and number of prescribed medications was evaluated using binary logistic regression. Therapeutic adherence and the utilization of clinical guidelines were not incorporated as variables in this study, a decision driven by the specific characteristics of this research and the scope of data investigation.

For the study, an older adult was considered to be any person over 65 years of age[17]. This variable was categorized into 65 to 75 years, 76 to 86 years, and more than 86 years of age. Moreover, polypharmacy was considered the prescription of 5 or more medications for over 3 months. The number of medications prescribed was categorized into 5 to 7 medications, 8 to 9 medications, and more than 10 medications. Multimorbidity was defined as the presence of three or more different clinical diagnoses, coded according to the ICD-10. The number of diseases diagnosed was categorized into two groups: three diseases and four diseases or more.

Two types of analysis were carried out: bivariate and multivariate. In the first analysis, the relationship between the two variables was determined, with the dependent variable defined as PIP, based on the different independent variables. Quantitative variables were recoded into qualitative variables, and crude ORs were calculated with a 95% confidence interval, with a standard error of 5%. For the second analysis, a binary multiple logistic regression model was developed for explanatory purposes. This model was used to assess the relationship between the dichotomous dependent variable (PIP) which took values of 0 and 1 (presence or absence of PIP) and the set of qualitative independent variables. The candidate variables to enter the model were assessed using a bivariate analysis, considering the Hosmer–Lemeshow criterion for a value of $p \leq 0.25$. The measure of strength of association was the prevalence ratio (OR adjusted) with 95% confidence intervals and a standard error of 5%.

For data analysis, descriptive biostatistical techniques were applied to identify the relative and absolute frequencies of the main characteristics of the study population and to characterize the dependent variable, PIP. Subsequently, a binary logistic regression model was used to evaluate the strength of the association between the study variables and PIP. Odds Ratios (ORs) and their respective 95% confidence intervals (95% CI) were calculated. This approach allowed the determination of the magnitude and direction of the associations.

Results

A population of 3,325 polymorbid and polymedicated older adults assisted by a pharmacotherapy manager in Medellín was studied. **Table 1** shows that 64.70% of the patients were women, the overall mean age was 77 years old, and the predominant age group was between 65 and 75 years old (48.30%). Additionally, 20.90% had high frailty, and 79.1% had medium frailty. The examined population had a mean of 3.80 diseases per patient, with 55.30% having three clinical diagnoses and 44.70% having more than four. Regarding the number of medications, 40.10% of the individuals took between 5 and 7, and 32.40% took more than ten. In total, sixty diverse types of prescribed medications were identified across 469 different diagnoses (**Table 1**).

Table 1. Characteristics of the population studied in a HCP in Medellín, Colombia, in 2023. (n: 3,325)

Independent variable	%(n)
Sex	
Man	35.30 (1175)
Woman	64.70 (2150)
Frailty	
Medium	79.10 (2630)
High	20.90 (695)
Age. Years	
65-75	48.30 (1605)
76-85	36.50 (1214)
≥ 86	15.20 (506)
Number of medications	
5-7	40.10 (1333)
8-9	27,50 (914)
≥ 10	32.40 (1078)
Número of Diseases	
3	55.30 (1838)
≥ 4	44.70 (1487)

HCP: Health Care Provider

Table 2 presents the top ten diseases recorded in this population. It can be observed that essential (primary) hypertension is the most common disease, affecting 34.88% of individuals. The second most frequent pathology is unspecified Chronic Obstructive Pulmonary Disease (COPD), present in 8.12% of the population, followed by non-insulin-dependent diabetes mellitus, affecting 8.05%.

Other significant diseases include insulin-dependent diabetes mellitus (4.32%), unspecified asthma (2.31%), and prostatic hyperplasia (1.98%). Additionally, chronic renal failure and congestive heart failure affect 1.97% and 1.86% of the population, respectively, indicating a considerable burden of cardiovascular and renal diseases. Unspecified hypothyroidism and postmenopausal osteoporosis without pathological fracture were also present, though in smaller proportions (1.61% and 1.58%, respectively).

Table 2. Description of the top ten pathologies that occur in the population studied (n: 3,325)

Pathology	% (n)
Essential hypertension (primary)	34,88 (1160)
Chronic obstructive pulmonary disease, unspecified	8.12 (266)
Non-insulin-dependent diabetes mellitus with no mention of complication	8.05 (232)
Insulin-dependent diabetes mellitus with no mention of complication	4.32 (124)
Asthma, unspecified	2.31 (60)
Prostate hyperplasia	1.98 (55)
Chronic renal failure, unspecified	1.97 (54)
Congestive heart failure	1.86 (52)
Hypothyroidism, unspecified	1.61 (46)
Postmenopausal osteoporosis, without pathological fracture	1.58 (44)

Table 3 presents the ten most frequently prescribed medications in the study population that met the Beers criteria for PIP. Proton Pump Inhibitors (PPIs) were the most common, with esomeprazole (18.12%) and omeprazole (6.13%) ranking highest. Among diuretics, furosemide (11.30%), hydrochlorothiazide (6.71%), and spironolactone (6.34%) were the most prominent.

Furthermore, a considerable use of antipsychotics and antidepressants was observed, with quetiapine (5.72%), sertraline (5.42%), and escitalopram (5.30%) being the most frequently prescribed. Insulin glulisine (3.11%) and pregabalin (2.83%) also appeared on the list, indicating a trend toward prescribing medications that require a careful risk-benefit evaluation in this population.

The medications that meet the STOPP/START criteria are presented below in **Table 4**, where the most frequently identified are acetaminophen/codeine (7.45%), followed by tramadol (7.12%), and levomepromazine and hydrocodone/acetaminophen (both with a frequency of 6.30%). Also noteworthy are olanzapine and furosemide, each with 5.22%, risperidone with 5.16%, lorazepam with 4.45%, IHAC with 3.92%, and calcium/vitamin D with 3.80%. These data indicate a significant variety of prescription-associated medications that may require a revision of established clinical standards.

The presence of opioid analgesics such as tramadol and combinations like hydrocodone/acetaminophen draws attention to pain management in geriatric patients, while the inclusion of antipsychotics such as levomepromazine and olanzapine suggests a broad consideration of psychiatric disorders in this demographic. Furosemide, a diuretic, is also identified as a standard drug under the Beers criteria, suggesting cardiovascular and renal conditions among the older adults in this study.

Table 3. Top ten medicines that meet the Beers Criteria for potentially inappropriate prescribing (n: 3,325)

Medicament	% (n)
Esomeprazole	18.12 (1076)
Furosemide	11.30 (669)
Hydrochlorothiazide	6.71(397
Spirinolactone	6.34 (375)
Omeprazole	6.13 (360)
Quetiapina	5.72 (336)
Sertraline	5.42 (323)
Escitalopram	5.30 (313)
Insulin Glulisine	3.11 (181)
Pregabalin	2.83 (166)

Table 4. Top ten medicines that meet the STOPP/START criteria for potentially inappropriate prescribing (n: 3,325)

Medication	%(n)
Acetaminophen/codeine	7.45(64)
Tramadol	7.12(61)
Levomepromazine	6.30(54)
Hydrocodone/Acetaminophen	6.30(54)
Olanzapine	5.22(45)
Furosemide	5.22(44)
Risperidone	5.16(38)
Lorazepam	4.45(34)
IHAC[a]	3.92(33)
Calcium/Vitamin D	3.80(32)

[a] Acetylcholinesterase inhibitors

Regarding PIP, **Table 5** shows that 31.50% of prescriptions meet at least one of the two criteria: Beer or STOPP/START. Regarding the association analysis of the distinct characteristics of the studied population, a statistically significant association was found between sex and PIP; women appear to be 1.82 times more likely to experience PIP than men in the initial analysis. In addition, the number of medications prescribed showed a statistically significant relationship, with a reduction in PIP in those with 8-9 medications and more than 10 compared to those receiving 5–7.

This study also explored the association of PIP through a multivariate analysis using binary logistic regression with variables such as age, number of diseases, and frailty. Although age and the presence of more than four diseases did not show statistically significant associations with PIP, a higher probability of PIP was observed in individuals over 85 years of age. Furthermore, frailty did not show a significant association, with an OR of 1.34, for those with high frailty compared to those with a medium level in the raw analysis (see **Table 5**).

The enter method used in the logistic regression model shows that the observed probabilities match their expected counterparts (Hosmer–Lemeshow test, $P > 0.05$). The variables sex, number of medications, number of diseases, and frailty collectively explain 22.70% of the variability in PIP, according to the value of Wald's statistic: >3.84. Moreover, we can say that the independent variables explain the dependent variable, so the null hypothesis is rejected, and it can be stated that sex, number of medications, number of diseases and frailty explain the probability of having PIP (see **Table 5**).

Table 5. Bivariate and multivariate analysis to describe the association of PIP with age, sex, number of medications, number of pathologies, and frailty in the population studied (n: 3,325).

Independent variable	OR (CI 95%) (cr)	*p* value (cr)	OR (CI 95%) (tight)	*p* value (tight)
Sex				
Man	1		1	
Woman	1.82 (1.16–2.86)	0.009	1.21 (1.04–1.43)	0.025
Age (in years)				
65–75	1		1	
76–85	0.87 (1.74–1.02)	0.104	0.93 (0.77–1.11)	0.426
≥86	1.00 (0.81–1.24)	0.972	1.15 (0.91–1.46)	0.225
Number of medications				
5–7	1		1	
8–9	0.10 (0.0–0.13)	<0.001	0.10 (0.08–0.12)	<0.001
≥10	0.21 (0.18–0.38)	<0.001	0.20 (0.17–0.25)	<0.001
Number of diseases				
3 diseases	1		1	
≥4 diseases	1.32 (1.14–1.53)	<0.001	1.16 (1.07–1.38)	0.035
Frailty				
Middle	1		1	
High	1.34 (1.15–1.62)	0.002	1.26 (1.07–1.58)	0.028

OR(cr): crude odds ratio, OR(tight): tight odds ratio, CI: confidence interval, *p* value (cr): crude *p* value crude, *p* value (tight): tight *p* value.

Discussion

This study found a 31.50% prevalence of PIP in older adults. Besides, according to the 2019 update of the Beers criteria, the prevalence was 19.50%; and, when using the STOPP/START criteria (version 2), the prevalence was found to be 14.4%. In recent studies of PIP in hospitalized older adults, PIP was estimated at 66.30% and 26.50% using the same versions of the Beers and STOPP/START criteria. Moreover, other studies have estimated PIP in intensive care units at 80.60% according to the 2019 Beers Criteria and 59.70% according to STOPP/START (version 2). Likewise, another study, with patients from a geriatric institution, reported a prevalence of 68.80% applying the Beers criteria and 57.40% with the STOPP/START criteria, all using the same versions[18–20]. The high prevalence of PIP highlights the complexity of the issue and the urgent need to improve prescribing practices in this population.

Although the study by Zhu et al. involved a smaller population, the variables they analyzed are comparable to those presented in this study, including age, number of diseases, and number of medications, all of which were similarly categorized. The average age of their patients, studied using the Beers criteria (2019 updated version) and the STOPP/START criteria (2014 version), is similar to that in the present study. However, the percentage of PIP meeting both criteria was higher in this study[18]. Zhu et al. found that 27.30% of prescriptions met the Beers criteria, while 23.70% met the STOPP criteria and 21.10% met the START criteria. These findings highlight the variability of PIP across different populations and clinical settings. The higher prevalence of PIP in our study could be influenced by factors specific to the local environment and prescribing practices in Medellín's population, which emphasizes the importance of contextualizing intervention strategies to improve prescribing quality in polymorbid and polymedicated older adults.

The results of this study show that being a woman increases the likelihood of PIP by 1.82 times compared to men (95% CI: 1.16–2.86). This is in line with Pastor Cano et al.'s study, which showed that women have a 17% higher risk of receiving PIP for at least one active ingredient (95% CI: 1.12-1.23)[21]. The similarity in results from both studies suggests that sex is a significant factor in the probability of receiving PIP, which may be related to differences in chronic disease prevalence, healthcare service utilization patterns, and prescribing practices between men and women.

Regarding age, there is a trend towards a higher probability of PIP in individuals over 85 years of age (OR = 1.15). The confidence interval (95% CI: 0.91–1.46) includes the unit (1.0), and its p value is > 0.05. This indicates that the association is not statistically significant in our study. Therefore, we cannot state with 95,0% confidence that there is a real difference in PIP between this age range and the reference category. This does not rule out a genuine association, as suggested by other studies [18–20]. It is likely that our study (with its current sample size and design) was not sufficiently powered to identify an effect that might be subtle or subject to high variability in the data. Studies with larger sample sizes or designs with greater capacity are required to confirm this association and determine its true magnitude.

Since this was a census study, the prevalence of 1.50% of PIP accurately represents the real value in the population studied, thereby presenting high internal validity. However, when analyzing associations, it is important to consider statistical power. The absence of statistically significant associations for some variables, such as age, despite having censused the entire population, suggests several possibilities: the size of the actual effect could be minimal; the variability in the data could have limited the detection of significant differences; or the presence of uncontrolled residual confounding (e.g., unmeasured variables such as health system affiliation, socioeconomic status, or medication habits) was able to mask true associations.

Polymedication, defined in this study as the prescription of five or more medications, was grouped into three categories and showed a statistically significant association with PIP in the 8–9 and ≥10 medications groups, with polypharmacy rates of 23.50% and 32.0%, respectively. Although the OR values for this variable appear to indicate a protective factor in this study, this is possibly because the HCP does pharmacotherapeutic follow-up of patients with a higher probability of prescription errors, which may explain the result of polymedication as a protective factor for this population. In other studies, polymedication is mentioned as a factor associated

with PIP, as seen in the paper by Albarracín et al., which found a direct proportional relationship between PIP and polypharmacy, as well as the number of comorbidities[22]. Similarly, in the systematic review by Bohórquez et al., polypharmacy was reported as a factor associated with PIP in 62.00% of the studies analyzed[23]. For the specific case of the present study, a decrease in PIP was observed with an increase in the number of prescribed medications, which could be explained by the protocols for follow-up, therapy support, and risk management in patients with a higher number of medications.

The current study found no significant association between frailty and PIP. Most patients presented a medium frailty value, which may have contributed to the lack of a significant association. These results are in contrast with findings from previous studies, such as that by Martinot et al. in a French population, where a significant association was found between frailty in the elderly and the use of a potentially inappropriate medication like non-steroidal anti-inflammatory drugs (NSAIDs)[24]. Furthermore, the authors of the GAZEL cohort also noted an association between polypharmacy and frailty in the early stages of old age, suggesting that the accumulation of multiple medications can exacerbate vulnerability in this population [24]. These findings underscore the importance of constant and critical review of prescriptions in older adults to minimize the risk of PIP and optimize therapeutic management [24].

According to the STOPP/START criteria, this study showed that the most common medications associated with PIP were opioid analgesics, benzodiazepines, and antipsychotics. These findings are consistent with existing literature, which highlights the long-term use of opioids and benzodiazepines as problematic due to their side effects and dependence risks, especially in older patients. Similarly, the use of antipsychotics is associated with an increased risk of adverse events, such as falls and cognitive impairment, emphasizing the need for vigilance in their prescription.

Concerning the Beers criteria, PPIs (such as esomeprazole) and loop diuretics (like furosemide) stood out due to their high frequency of PIP. While these medications are effective for their specific indications, they can be inappropriate when used long-term or without a clear indication. In line with the above, the study by Machado-Alba et al. reported that loop diuretics are not the first-line medication of choice or monotherapy for arterial hypertension, given the risk of electrolyte imbalance in older adult patients[25]. Their study also highlights the inappropriate prescription of furosemide in geriatric patients, which is consistent with our findings and reinforces the importance of regularly reviewing and adjusting medication in this population to avoid complications associated with these medicines.

Similarly, in the study by Pastor Cano et al., PPIs used for more than eight weeks, benzodiazepines, and antipsychotic medications were identified to have elevated risk of PIP. The present study underlines that the prolonged use of PPIs can lead to adverse effects such as increased risk of fractures and vitamin B12 deficiency in older adults, reinforcing the importance of limiting their use to the minimum necessary time. Benzodiazepines, in turn, are highlighted for their association with a significant increase in the risk of falls, drowsiness, and cognitive impairment factors that can significantly affect the health and quality of life of older adults[21].

Furthermore, Pastor Cano et al. emphasize that antipsychotic medications, when inappropriately prescribed, can cause anticholinergic effects that exacerbate confusion and cognitive dysfunction, as well as increase the risk of mortality in patients with dementia. The findings of our study are consistent with those results, as we also identify a high prevalence of PIP with these medications. These results highlight the need for constant and careful medication review in older adults to avoid the risks associated with prolonged and inappropriate use of these medicines. In this regard, implementing medication review strategies and providing ongoing education to healthcare professionals is crucial for minimizing risks and enhancing the quality of life for patients in this age group [21].

One of the main limitations of this study is its cross-sectional design because, due to it, causal relationships cannot be established between the analyzed variables and PIP. Additionally, the sample was obtained from a single HCP, which may limit the generalizability of the results to other populations or settings. Another limitation is the potential lack of detailed information on the precise clinical indications for each prescription, which could

impact the evaluation of medication appropriateness according to the STOPP/START and Beers criteria. Similarly, reliance on medical records and patient self-reports may introduce information biases. Finally, socioeconomic and cultural aspects that could influence prescribing, medication use, self-medication, and adherence were not evaluated, representing an essential dimension for future studies.

As mentioned above, an essential element to consider in interpreting our results is the measure of association used here, given that this is a cross-sectional study. The prevalence of the outcome of interest was 31.50%. We are aware that the Odds Ratio (OR) may overestimate the true magnitude of the Prevalence Ratio (PR). Although PR would be the ideal measure to directly reflect the dimension of the effect in studies with frequent outcomes, it was decided to present the ORs due to their concurrence with the multivariate logistic regression models used to control for multiple variables; their wide prevalence in the scientific literature, which facilitates comparability with other studies; and their capacity to manage errors for these models. This possibility of overestimation must be considered when interpreting the strength of the associations presented here. For a more precise understanding of the magnitude of the impact in terms of prevalence, future research could explore the direct estimation of PR using alternative models.

This study identified three potential types of bias: selection bias, information bias, and confusion bias[26-28]. Selection bias could arise from using data exclusively from a single healthcare institution. To address this, we acknowledge that this institution is a secondary-level facility, serving patients with high-cost chronic diseases. Furthermore, it actively manages health risks for these patients, including follow-up for those on multiple medications, a factor linked to PIP. Additionally, the findings in this study will be compared with other relevant research in the discussion section to provide context for the results. However, we acknowledge that this single-facility limitation may affect the generalizability of our findings to broader populations.

Concerning information bias, PIP assessment may be affected by relying on the HCP's data system. In this regard, limitations in the completeness of the electronic health records were noted (reflecting the national context rather than specific institutional practices). Concerning information bias, PIP assessment may be affected by dependence on institutional data. Limitations in EHR completeness were observed in this area, mirroring national trends. Clinical records and/or prescriptions were evaluated based on how they were administered by various physicians, and documentation practices (e.g., diagnosis selection, completeness) could vary. To control this bias, medical staff were requested to correct or complement any inconsistencies identified before data entry. Furthermore, the institution's existing audit criteria for this process were taken into consideration. Importantly, the consistency of PIP assessment across all patients, using both Beers and STOPP/START criteria, was deemed sufficient, especially given the study's substantial sample size, which provides considerable statistical power[26-28].

Confusion bias occurs when an unmeasured (or inadequately measured) variable is associated with both the exposure and the outcome, distorting the true relationship between them. Although this study was adjusted for variables such as sex, age, number of medications, number of pathologies, and frailty, other elements, not included in the model, may influence the observed associations. For example, the affiliation with the health system, the socioeconomic status of patients, or their medication use habits were not measured in this study[26-28]. These factors, not considered here, could be related to the number of medications and the number of pathologies, as well as to PIP, which can generate spurious associations or obscure authentic relationships.

Regarding the design of this study, the time between exposure and outcome makes it difficult to rule out residual confounding, as it is not possible to ensure that the cause precedes the effect. Therefore, it is essential to consider that the observed associations occur at a point in time, rather than as definitive causal relationships. While our findings are vital for hypothesis generation and identifying risk groups, future studies with longitudinal designs, such as cohort studies, are needed to explore the causal nature of these associations and mitigate this type of bias. In this research, said bias was controlled through multivariate analysis using binary logistic regression[26-28], which allowed for the control of all variables in the study.

On the other hand, both STOPP/START and Beers criteria were used in this evaluation, providing a robust and reliable assessment of PIP in the analyzed population. Furthermore, the inclusion of a large patient population, such

as the one in this study, can produce relevant results for clinical practice. The detailed comparison with previous studies and the identification of specific risk factors, such as polypharmacy and sex, add value to the existing body of knowledge and can guide future interventions to improve prescribing in multimorbid and polymedicated older adult populations. Lastly, this study emphasizes the need for continuous vigilance and personalized strategies to minimize PIP, thereby contributing to the improvement of the quality of life and safety of older patients.

Conclusion

In conclusion, this study emphasizes the importance of using explicit criteria, such as STOPP/START and Beers, to identify and prevent potentially inappropriate prescribing (PIP) in older adults. Being female and prescribed more than seven medications were found to be significant risk factors for PIP, findings consistent with previous studies. Although frailty did not show a significant association in this study, other research has demonstrated its relevance, suggesting the need for further research.

Using the STOPP/START criteria, the most frequently identified medications were opioid analgesics, benzodiazepines, and antipsychotics. In turn, using the Beers criteria, proton pump inhibitors and loop diuretics stood out. These findings, consistent with previous research by Machado-Alba and Pastor Cano, underscore the need for vigilant and tailored prescribing in this population.

Appropriate medication in older adults is fundamental for improving their health status and quality of life. Certain conditions, such as frailty, increased emergency department visits, and hospitalization, can increase PIP and, consequently, the risk of adverse drug events. Therefore, having tools like explicit criteria for PIP is highly valuable to guide medical personnel when prescribing, ensuring safer and more effective care.

This study provides valuable evidence that can guide future strategies and interventions to improve medication prescribing in older adults—despite its limitations, such as lack of longitudinal measurement and focus on a single population. The inclusion of updated and validated criteria reinforces the applicability of the results, providing a solid foundation for enhancing the quality of life and safety of older patients through more informed and careful prescribing practices. However, it is essential to continue with longitudinal or intervention studies (such as clinical or community trials) and/or studies that collect primary data on therapeutic adherence, self-medication, and adverse event reporting to the Colombian system.

Ethical responsibilities

The authors declare that the present study was conducted in accordance with the ethical principles established by the Human Ethics Committee at Universidad CES. The research received approval from this committee, recorded in Minute 148 dated May 28th, 2020, under project code number 898. The confidentiality of the collected data was ensured using identification codes instead of real names in all documents and databases. The information obtained was used exclusively for research purposes and was protected under strict security measures, always ensuring the participants' privacy. The research team was rigorously committed to maintaining scientific and ethical integrity at all stages of the project, ensuring that the results were presented with objectivity and transparency, thus contributing ethically and responsibly to the advancement of scientific knowledge.

Author contributions

OA: Substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work. The same applies to writing the paper or critically reviewing important intellectual content. In addition, be responsible for all aspects of the work to ensure that questions relating to the accuracy or completeness of any part of the work are properly investigated and resolved. ASC: Substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work. The same applies to writing the paper or critically reviewing important intellectual content, and final approval of the version to be published. JMC: Substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work. The same applies to writing the paper or critically

reviewing important intellectual content, and final approval of the version to be published. EAG: Substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work. The same applies to writing the paper or critically reviewing important intellectual content, and final approval of the version to be published.

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Ethical considerations

The authors declare that they have no conflicts of interest.

Competing interests

None of the authors has any conflicts of interest in carrying out this research.

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