European Geriatric Medicine (2019) 10:639–647
https://doi.org/10.1007/s41999-019-00181-5

RESEARCH PAPER

Potentially inappropriate prescribing to older adults in ambulatory care: prevalence and associated patient conditions

Dolores Mino-León[1] · Sergio Sánchez-García[2] · Liliana Giraldo-Rodríguez[3] · Hortensia Reyes-Morales[4]

Received: 11 December 2018 / Accepted: 8 March 2019 / Published online: 26 March 2019

Key summary points

Aim To analyze potentially inappropriate prescribing (PIP), its prevalence and patient conditions associated with this phenomenon, in a cohort of older adults receiving outpatient care.

Findings 41.8% of participants had at least one PIP. The most frequently identified PIPs involved nonsteroidal anti-inflammatory drugs (NSAIDs) and glibenclamide; clonazepam in patients with cognitive impairment; and interactions of warfarin with NSAIDs. Frailty, polypharmacy, lower educational levels, and taking hypoglycemics, antiasthmatics, nervous system or gastrointestinal disease drugs, anti-inflammatories-antirheumatics and analgesics were associated with PIP.

Message PIP, and association with medical and nonmedical factors in outpatient treatment highlights the need to take actions to improve drug treatment quality.

Abstract

Purpose To analyze potentially inappropriate prescribing (PIP), its prevalence and patient conditions associated with this phenomenon, in a cohort of older adults receiving outpatient care in Mexico.

Methods Data from 1252 adults ≥ 60 years of age, from primary care centers were analyzed. Information included sociodemographic data, medications, chronic diseases, polypharmacy (≥ 5 medications), functional dependence, cognitive impairment and frailty. Three logistic regression models were employed to identify associations between PIP (according to the Beers criteria) and different variable combinations.

Results A total of 41.8% of participants had at least one PIP. The most frequently identified PIPs involved nonsteroidal anti-inflammatory drugs (NSAIDs) and glibenclamide; clonazepam in patients with cognitive impairment; and interactions of warfarin with NSAIDs. In the multivariate analyses, Model 1 showed that frailty and polypharmacy were associated with PIP. In Model 2, only polypharmacy was associated with PIP. For Model 3, lower educational levels, taking hypoglycemics, nervous system disease drugs, antiasthmatics, gastrointestinal disease drugs and anti-inflammatories-antirheumatics and analgesics, were associated with PIP.

Conclusion PIP is common in outpatient treatment of health care services in Mexico. Its association with medical and nonmedical factors highlights the need to improve drug treatment quality focused on implementation of effective strategies, such as educative interventions, electronic medication safety alerts, and inclusion of pharmacists in the health team.

Keywords Inappropriate prescribing · Geriatric health services · Drug prescription · Quality of care

✉ Hortensia Reyes-Morales
hortensia.reyes@insp.mx

[1] Clinical Epidemiology Research Unit, Hospital de Especialidades, Centro Médico Nacional Siglo XXI, Instituto Mexicano del Seguro Social, Mexico City, Mexico

[2] Epidemiology and Health Services Research Unit, Aging Area, Centro Médico Nacional Siglo XXI, Instituto Mexicano del Seguro Social, Mexico City, Mexico

[3] Research Division, Demographic Epidemiology and Social Determinants Department, Instituto Nacional de Geriatría, Secretaría de Salud, Mexico City, Mexico

[4] Center for Health Systems Research, Instituto Nacional de Salud Pública, Avenida Universidad #655, Santa María Ahuacatitlán, 62100 Cuernavaca, Morelos, Mexico

Introduction

Between 2000 and 2050, the proportion of the global population that is 60 or older will double from 11% to 22%. In absolute numbers, this group will rise from 605 million people to two billion, representing an important demographic transformation [1]. Aging is a gradual and inevitable process that manifests itself primarily in morphological and physiological changes, making this transformation even more relevant. The International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) regards older adults as a special population "which differs of younger adults in terms of their comorbidity, polypharmacy and pharmacokinetics, as well as their increased vulnerability to adverse drug reactions" [2].

Multimorbidity leads to prescribing more medications, which favors polypharmacy and in turn raises the risk of potentially inappropriate prescribing (PIP) and adverse health events. Excess polypharmacy (≥ 10 medications) is considered a 5-year mortality predictor [3–5]. Inappropriate medications definition comprises those drugs for which the risk of suffering a resultant adverse event is higher than the clinical benefit. Inappropriate medications also include frequent use of medications, use of medications for longer than indicated, use of medications with a high-risk of drug–drug or drug–disease interactions, duplication of medications or prescribing drugs from the same therapeutic group, and not prescribing drugs that clinically should be prescribed [6–8].

Several studies have documented high rates of inappropriate prescribing in older adults, such as prolonged use of psycholeptic medications and/or nonsteroidal anti-inflammatory drugs (NSAIDs), which can reach 40% [6, 9, 10]. In addition, recent data have shown that almost half of older adults may be at risk of polypharmacy, PIP, and drug–drug interactions [11]. However, it has also been reported that polypharmacy does not necessarily increase the risk of PIP and that strategies directed at reducing polypharmacy to decrease PIP have not been successful [12].

The identification of factors associated with PIP is relevant for designing strategies focused on ensuring patients' access to potentially beneficial treatments, and protecting patients from inappropriate prescribing and its potential harm [13]. To contribute to improving knowledge in this field for Mexico, the goal of this study was to analyze PIP, its prevalence and patient conditions associated with this phenomenon, in a cohort of older adults receiving outpatient care.

Methods

A secondary analysis was conducted using the database of the study "Cohort of obesity, sarcopenia and frailty of older Mexican adults" (COSFOMA) (Cohorte de obesidad, sarcopenia y fragilidad de adultos mayores Mexicanos) [14]. We analyzed data from 1252 adults aged 60 and older, who attended one of the 48 primary care centers known as Family Medicine Units (Unidades de Medicina Familiar [UMFs]) in Mexico City, during 2014. These centers are part of the Mexican Social Security Institute (Instituto Mexicano del Seguro Social [IMSS]), a public institution that provides medical care to over half of the country's population.

Variables

Based on the information contained in the original database through patients' self-reporting, the following data were extracted to integrate the variables for this study.

Sociodemographic data: sex, age, partnership status, and level of education (basic education ≤ 10 years, and higher education > 10 years).

Medications

Drugs regularly used for the treatment of chronic diseases. Medications were registered by the name of their active ingredient and then classified according to the anatomical therapeutic chemical (ATC) classification system [15].

Polypharmacy

Defined as the use of five or more medications [16].

Potentially inappropriate prescribing

From the list of medications, identification of drugs included in the 2015 Beers Criteria [17], and the application of the criteria for potential drug–disease or drug–syndrome interactions, based on the clinical information of each patient.

Chronic diseases

Hypertension, heart failure, type 2 diabetes, hypothyroidism, rheumatoid arthritis, psychosis, peptic ulcers, neoplasms, chronic obstructive pulmonary disease (COPD),

cerebrovascular disease, Parkinson's disease, neuritis, peripheral vascular disease, chronic kidney failure, anemia, and hepatopathy. Criteria for major depression were established using the center for epidemiologic studies depression scale-revised (CESD-R) [18].

Multimorbidity

Defined as the presence of two or more chronic diseases.

Other clinical conditions

Functional dependence, evaluated using the Lawton–Brody instrumental activities of daily living scale [19]; cognitive impairment determined by a mini-mental examination score of ≤ 23 [20]; and frailty, classified into three categories using the Fried frailty criteria (frail, pre-frail, and robust) [21].

Statistical analysis

A descriptive analysis of the sociodemographic variables, chronic diseases, medications, PIP and other clinical conditions was performed. Bivariate analysis was conducted by calculating the crude odds ratio (OR) and 95% confidence intervals (95% CI) to identify the association between the independent variables and PIP. A correlation matrix was used to detect collinearity among independent variables. Then, three multivariate binary logistic regression analyses with the significant variables from the bivariate analysis were conducted, employing the strategy of incremental variable inclusion into each model (forward step). First, sociodemographic variables were introduced, along with polypharmacy, multimorbidity and other clinical conditions (functional dependence, cognitive deterioration, and frailty) (Model 1). Next, the multimorbidity variable was replaced by the individual diseases that were statistically significant in the crude analysis (Model 2). Finally, the same variables from Model 2 were introduced, and medications that had significance in the crude analysis were incorporated, and the polypharmacy variable was removed (Model 3). A p value < 0.05 was considered statistically significant. The analyses were conducted using version 11 of the statistical software STATA (StataCorp, Texas).

Results

Women comprised 59.9% of the 1252 cases analyzed. The average age of the total sample was 68.4 ± 7.1. According to the Beers Criteria, 524 (41.8%) participants had at least one PIP. The subgroup of patients with PIP was characterized by higher proportion of women; higher age; more patients living alone; lower educational levels; higher proportion of patients with functional dependence, cognitive deterioration and frailty; and higher number of cases with multimorbidity and polypharmacy (Table 1).

Table 1 Characteristics of study population

Characteristics	All n = 1252 n (%)	Non-PIP** n = 728 n (%)	PIP n=524 n (%)
Sex*			
Female	750 (59.9)	410 (56.3)	340 (64.9)
Male	502 (40.1)	318 (43.7)	184 (35.1)
Age* (years)	68.4 ± 7.1	68.0 ± 7.0	69.1 ± 7.4
Partnership status*			
Does not live alone	744 (59.4)	459 (63.0)	285 (54.4)
Lives alone	508 (40.6)	269 (37.0)	239 (45.6)
Education (years)*			
≤ 10 years	646 (51.6)	348 (47.8)	298 (56.9)
> 10 years	606 (48.4)	380 (52.2)	226 (43.1)
Functional dependency*			
Yes	437 (34.9)	227 (31.2)	210 (40.1)
No	815 (65.1)	501 (68.8)	314 (59.9)
Cognitive impairment*			
Yes	304 (24.3)	157 (21.6)	147 (28.1)
No	948 (75.7)	571 (78.4)	377 (71.9)
Frailty*			
Robust	482 (38.5)	306 (42.0)	176 (33.6)
Pre-frail	630 (50.3)	364 (50.0)	266 (50.8)
Frail	140 (11.2)	58 (8.0)	82 (15.6)
Multimorbidity*			
Yes	233 (18.6)	112 (15.4)	121 (23.1)
No	1019 (81.4)	616 (84.6)	403 (76.9)
Polypharmacy*			
Yes	142 (11.3)	26 (3.6)	116 (22.1)
No	1110 (88.7)	702 (96.4)	408 (77.9)

*p < 0.05

***PIP* potentially inappropriate prescribing

Patients with PIP had higher rates of depression (35.5%), hypertension (24.6%) and type 2 diabetes (18.9%). These patients more frequently reported taking medications across all of the groups of drugs analyzed in this study, especially anti-inflammatory-antirheumatic and analgesic drugs (75.4%), antihypertensive drugs (50.6%), and hypoglycemic agents (29.6%) (Table 2). Of the medications to be avoided according to the Beers Criteria, nonsteroidal anti-inflammatory drugs (NSAIDs) and glibenclamide were the most frequently prescribed. The main drug–disease interaction was the use of clonazepam in patients with cognitive impairment (3.2%), and the principal drug–drug interaction was the use of warfarin together with NSAIDs (Table 3). The crude odds ratio

Table 2 Chronic diseases and drugs by self-reporting

Diseases and drugs (ATC classification)	Non PIP* $n=728$ n (%)	PIP $n=524$ n (%)	p
Depression	186 (25.5)	186 (35.5)	0.001
Hypertension	142 ((19.5)	129 (24.6)	0.031
Type 2 diabetes	87 (11.9)	99 (18.9)	0.001
Rheumatoid arthritis	24 (3.3)	28 (5.3)	0.085
Hypothyroidism	18 (2.5)	13 (2.5)	> 0.05
Neoplasia	4 (0.5)	9 (1.7)	0.051
Peptic ulcers	6 (0.8)	8 (1.5)	> 0.05
Heart failure	4 (0.5)	5 (1.0)	> 0.05
Chronic pulmonary disease	6 (0.8)	5 (1.0)	> 0.05
Peripheral vascular disease	6 (0.8)	5 (1.0)	> 0.05
Anemia	4 (0.5)	4 (0.8)	> 0.05
Cerebrovascular disease	6 (0.8)	4 (0.8)	> 0.05
Chronic kidney failure	5 (0.7)	4 (0.8)	> 0.05
Parkinson´s disease	2 (0.3)	3 (0.6)	> 0.05
Neuritis	3 (0.4)	1 (0.2)	> 0.05
Liver diseases	5 (0.7)	1 (0.2)	> 0.05
Psychosis	1 (0.1)	1 (0.2)	> 0.05
Drugs			
Anti-inflammatories-antirheumatics and analgesics (M01, N02)	21 (2.9)	395 (75.4)	0.000
Antihypertensives (C02)	219 (30.1)	265 (50.6)	0.000
Medications used for diabetes (A10)	104 (14.3)	155 (29.6)	0.000
Drugs used for nervous system diseases (N03, N05, N06)	23 (3.2)	103 (19.7)	0.000
Lipid modifying agents (C10)	82 (11.3)	97 (18.5)	0.000
Antianemic preparations (B03)	29 (4.0)	55 (10.5)	0.000
Alimentary tract and metabolism drugs (A02, A03)	24 (3.3)	45 (8.6)	0.000
Drugs used for bone diseases (A11, G03, M05)	22 (3.0)	28 (5.3)	0.041
Drugs for obstructive airways diseases (R03)	7 (1.0)	22 (4.2)	0.000
Antithrombotic agents and vasoprotectives (B01, C01, C05)	11 (1.5)	21 (4.0)	0.010
Antineoplastic and immunomodulating agents (H02, L01, L04, M01)	10 (1.4)	18 (3.4)	0.019

**PIP* Potentially inappropriate prescribing

for all variables showed significant association with PIP, except for rheumatoid arthritis or neoplasms (Table 4). Multivariate models with adjusted associations resulted in the following: in Model 1, polypharmacy (OR 6.88, CI 95% 4.38–10.81, $p<0.001$) and the clinical condition of frailty (OR 1.60, CI 95% 1.03–2.47, $p=0.037$) were statistically associated with PIP. In Model 2, only the polypharmacy variable (OR 6.81, CI 95% 4.33–10.75, $p<0.001$) was associated with PIP. Model 3 demonstrated several variables that were statistically associated with PIP, including lower educational levels (OR 1.56, CI 95% 1.03–2.43 $p=0.047$) and taking hypoglycemic agents (OR 9.27, CI 95% 5.06–16.98, $p<0.001$), nervous system disease drugs, including psycholeptics, psychoanaleptics and antiepileptics (OR 25.66, CI 95% 13.54–48.63, $p<0.001$); antiasthmatic drugs (OR 5.18, CI 95% 1.35–19.80, $p=0.016$); gastrointestinal disease-related drugs (OR 4.92, CI 95% 2.10–11.56, $p<0.001$); and anti-inflammatories, antirheumatics and analgesics (OR 278.07, CI 95% 152.61–505.66, $p<0.001$) (Table 5).

Discussion

The use of inappropriate medications in older patients is a public health problem that affects the morbidity and mortality of this population. The results of this study show that certain groups of drugs have higher probabilities of being inappropriately prescribed to elderly patients, regardless of clinical conditions such as frailty, cognitive impairment or

Table 3 Potentially inappropriate prescribing, according to Beers criteria (2015)

Beers criteria	$n=524$ n (%)
Chronic use of NSAIDs*	388 (74.0)
Glibenclamide**	84 (54.2)
Clonazepam	47 (9.0)
Proton-pump inhibitors for > 8 weeks unless for high-risk patients	38 (7.3)
Cognitive impairment/clonazepam	17 (3.2)
History of gastric or duodenal ulcer/NSAIDs without gastroprotective agent	8 (1.5)
Heart failure/NSAIDs	4 (0.8)
Cognitive impairment/imipramine	4 (0.8)
Cognitive impairment/paroxetine	4 (0.8)
Oral or parenteral corticosteroids/NSAIDs without gastroprotective agent	3 (0.6)
Chronic kidney disease/NSAIDs	2 (0.4)
Warfarin/NSAIDs	2 (0.4)
Cognitive impairment/diazepam	1 (0.2)

**NSAIDs* nonsteroidal anti-inflammatory drugs

**Denominator corresponds to all patients receiving hypoglycemic agents ($n=155$)

Table 4 Risk factors for having a potentially inappropriate prescription

Risk factor (reference)	OR (CI 95%)	p*
Sex: female (male)	1.43 (1.14–1.81)	0.002
Age	1.02 (1.01–1.04)	0.008
Partnership status: lives alone (does not live alone)	1.43 (1.14–1.80)	0.002
Education (years): ≤ 10 (> 10)	1.44 (1.15–1.81)	0.002
Functional dependency: yes (no)	1.48 (1.17–1.87)	0.001
Cognitive impairment: yes (no)	1.42 (1.09–1.84)	0.008
Frailty: (robust)		
Pre-frail	1.27 (1.00–1.62)	0.054
Frail	2.46 (1.67–3.61)	0.000
Multimorbidity: yes (no)	1.65 (1.24–2.20)	0.001
Polypharmacy: yes (no)	7.68 (4.93–11.95)	0.000
Diseases: yes (no)		
Hypertension	1.35 (1.03–1.77)	0.031
Type 2 diabetes	1.72 (1.26–2.35)	0.001
Rheumatoid arthritis	1.66 (0.95–2.89)	0.076
Neoplasia	3.16 (0.97–10.33)	0.056
Depression	1.60 (1.26–2.05)	0.000
Medications: yes (no)		
Medications used for diabetes	2.52 (1.91–3.33)	0.000
Antianemic preparations	2.83 (1.78–4.50)	0.000
Antihypertensives	2.38 (1.88–3.00)	0.000
Drugs used for bone diseases	1.81 (1.02–3.20)	0.041
Drugs used for nervous system diseases	7.50 (4.70–11.97)	0.000
Lipid modifying agents	1.79 (1.30–2.46)	0.000
Drugs for obstructive airway diseases	4.51 (1.91–10.65)	0.001
Alimentary tract and metabolism drugs	3.11 (1.90–5.07)	0.000
Antineoplastic and immunomodulating agents	2.55 (1.17–5.58)	0.019
Antithrombotic and vasoprotective agents	2.72 (1.30–5.69)	0.008
Anti-inflammatories-antirheumatics and analgesics	103.09 (63.96–166.16)	0.000

*$p < 0.05$ = Statistical significance

Table 5 Multivariate logistic regression analyses for having a potentially inappropriate prescription

Risk factor (reference)	Model 1 OR (CI 95%)	p*	Model 2 OR (CI 95%)	p*	Model 3 OR (CI 95%)	p*
Sex: female (male)	1.25 (0.96–1.62)	0.099	1.24 (0.95–1.61)	0.112	0.98 (0.62–1.54)	0.914
Age	1.00 (0.98–1.02)	0.989	1.00 (0.98–1.02)	0.897	0.99 (0.96–1.02)	0.525
Partnership status: lives alone (does not live alone)	1.24 (0.95–1.60)	0.115	1.25 (0.96–1.63)	0.095	1.06 (0.68–1.68)	0.789
Education (years) ≤ 10 (> 10)	1.23 (0.96–1.58)	0.100	1.20 (0.94–1.55)	0.148	1.56 (1.03–2.43)	0.047
Functional dependency: yes (no)	1.13 (0.86–1.47)	0.379	1.12 (0.86–1.47)	0.392	1.04 (0.65–1.67)	0.874
Cognitive impairment: yes (no)	1.13 (0.84–1.51)	0.423	1.11 (0.83–1.49)	0.473	1.63 (0.99–2.70)	0.056
Frailty: (robust)						
Pre-frail	1.03 (0.79–1.33)	0.838	0.99 (0.76–1.30)	0.961	1.06 (0.67–1.68)	0.793
Frail	1.60 (1.03–2.47)	0.037	1.45 (0.91–2.30)	0.115	0.88 (0.40–1.92)	0.741
Multimorbidity: yes (no)	1.23 (0.90–1.68)	0.189	–	–	–	–
Polypharmacy: yes (no)	6.88 (4.38–10.81)	0.000	6.81 (4.33–10.71)	0.000	–	–
Diseases: yes (no)						
Hypertension			0.98 (0.72–1.33)	0.893	0.88 (0.50–1.57)	0.671
Type 2 diabetes			1.40 (0.98–1.98)	0.064	0.92 (0.48–1.77)	0.800
Depression			1.21 (0.91–1.61)	0.194	0.73 (0.44–1.20)	0.213
Medications: yes (no)						
Medications used for diabetes					9.27 (5.06–16.98)	0.000
Antianemic preparations					0.84 (0.36–1.94)	0.676
Antihypertensives					0.94 (0.59–1.49)	0.777
Drugs used for bone diseases					2.22 (0.79–6.26)	0.131
Drugs used for nervous system diseases					25.66 (13.54–48.63)	0.000
Lipid modifying agents					1.28 (0.74–2.24)	0.382
Drugs for obstructive airway diseases					5.18 (1.35–19.80)	0.016
Alimentary tract and metabolism drugs					4.92 (2.10–11.56)	0.000
Antineoplastic and immunomodulating agents					0.27 (0.07–1.09)	0.065
Antithrombotic and vasoprotective agents					1.00 (0.29–3.48)	0.997
Anti-inflammatories-antirheumatics and analgesics					278.07 (152.61–505.66)	0.000

*$p < 0.05$ = Statistical significance

functional dependence, conditions that make patients more vulnerable to suffering negative clinical outcomes (falls, hospitalizations, disabilities, and death) [21]. In addition, the strong association of polypharmacy with PIP documented raises this risk even more.

A relevant finding is that almost half of the patients were exposed to PIP, which is higher than the rate reported by other authors [22, 23]. Therefore, avoiding inappropriate medications should be a primary objective of medical attention for the elderly [3–5]; selection, dose and duration of pharmacological treatments should be carefully evaluated in clinical practice, particularly in patients suffering cognitive impairment (including the use of central action drugs that often produce chronic or acute behavioral and cognitive alterations) [24].

Regarding specific medications the results also showed that, according to the Beers Criteria, prescriptions for NSAIDs and glibenclamide are the most frequently identified PIPs. This pattern differs slightly from other reports that have found that hypnotic, sedative and anxiolytic drugs are the most frequently identified, present in more than two-thirds of PIP [22, 23, 25–30]. In Mexico, glibenclamide is included in the reference drug list of the IMSS; as a result, it is frequently prescribed to vulnerable elderly patients. Something similar occurs in Brazil, where this drug is included in the list of essential medicines, and the Brazilian government distributes it in primary care facilities [31]. Therefore, improving practitioners' prescription quality should include actions related to the medications that are sold or included in health institutions' medication formularies or the reference drug list.

Proton-pump inhibitors are high-risk medications that were found associated to PIP. The belief that these drugs are simply "gastric protection" has increased their use, and their treatment is often prolonged. Appropriate evaluation for bleeding risk factors before prescribing these drugs should be essential, as well as continuing periodic clinical and prescription review to define the need to discontinue

their use. The risk of serious adverse events, such as community-acquired pneumonia, bone fractures, *Clostridium difficile* infection, hypomagnesemia and kidney damage, is well known [32]. This finding is consistent with the global increase in the prescription of these medications, and points to a clear need to create strategies that guide doctors in their correct use, such as technology and multifaceted educative interventions, among others [33–36].

Older adults have high rates of pain syndromes and osteoarticular disease, for which anti-inflammatory-antirheumatic and analgesic medications (ATC M01 and N02) are frequently prescribed. The elevated proportion of patients with PIP who were prescribed these medicines is noteworthy in this study, and the proportion identified is higher than that mentioned in the literature (e.g., 18% in Brazil [37] and 31.4% in Portugal [22]) The overprescribing of NSAIDs among the patients in Mexico is a problem that has been repeatedly reported in the literature [10, 38]. It is also a problem for which the health system has not yet incorporated strategies to contain, regardless of the existing evidence of effective interventions in this context [39, 40].

Antiasthmatic drugs (R03) were also associated with PIP, with theophylline being one of the most frequently prescribed drugs of this group. This PIP illustrates the risk to which patients are exposed: theophylline affects the central nervous system (insomnia) and raises the risk of arrhythmias. Finally, other examples of PIPs identified in this study include the use of anticholinergic drugs that reduce urine flow and cause urinary retention, the use of nonselective beta-blockers in patients with chronic obstructive pulmonary disease (COPD), and the use of systemic corticosteroids instead of inhaled corticosteroids for the treatment of patients with moderate-to-severe COPD [14, 41].

Among sociodemographic characteristics that showed association with PIP, low educational level has also been described in other studies [26–28]. This finding suggests that patients' levels of awareness of their health and treatment, as well as their expectations, may play relevant roles in the prescriptions they receive. Patients with higher educational levels may have better access to information about medications and thus be more active in doctor-patient communication, exercising an influence over their prescription. Our results confirmed that even when controlling for the number of diseases, the effect of education level with respect to PIP held steady, as another study also showed [26]. This suggests that patients' educational levels can influence the quality of the medications they receive, independent of their clinical conditions, and highlights the importance of considering educational levels when designing intervention strategies to improve drug prescription to older adults.

A strength of this study is that the findings show the need in Mexico for having an updated reference drug list containing drugs that have been shown to be effective, safe and at reasonable costs; furthermore, the inclusion of the pharmacist in the health teams, and the modernization of the clinical record with electronic alerts for enhance medication use should be considered as part of the national drug policy.

Some limitations must be recognized. The secondary data analysis did not allow the application of more sensitive PIP criteria such as STOPP/START [42]. In addition, although these results are not generalizable to other contexts, they are representative of primary care users in a public institution that covers nearly 50% of the population of Mexico [43].

Conclusion

This study complement information regarding the potentially inappropriate use of medications in ambulatory healthcare provided to elderly patients. The significant association of medical and nonmedical factors with PIP highlights the need to take actions to improve the quality of drug treatment, through strategies directed both at the education of patients and the training of doctors in geriatric pharmacotherapy. Including the participation of the pharmacist in the care of elderly patients, computer support for decision-making in clinical practice should also be considered in those Countries in which these strategies have not been implemented. Additional actions must seek to reduce the risks of adverse health events by strengthening effective, educational communication with elderly patients.

Acknowledgements We thank the authorities and staff of the South and North Delegations of the Mexican Institute of Social Security (IMSS) of Mexico City for their support for this study.

Funding This work was funded by the Sector Fund Health Research and Social Security SS/IMSS/ISSSTE/CONACYT (México) SALUD-2013-01-201112, and the Fund for the Promotion of Health Research, IMSS, FIS/IMSS/PROT/PRIO/13/024. The funders had no role in the design, execution, analysis and interpretation of data, or writing of the study.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval The original study was approved by the National Scientific Research Committee (*Comité Nacional de Investigación Científica*) and the Health Research Ethics Committee (*Comité de Ética en Investigación en Salud*), both part of the IMSS, with registry number 2012-785-067. This article does not contain any studies with human participants performed by any of the authors.

Informed consent Informed consent was obtained from all individual participants included in the original study (COSFOMA). The data used in this study were anonymous.

References

1. World Health Organization (2014) Ageing and life-course. Facts about ageing. http://www.who.int/ageing/about/facts/es/. Accessed 13 Nov 2018
2. International Conference on Harmonisation ICH Harmonised tripartite guideline studies in support of special populations: Geriatrics E7 (1993). http://www.ich.org/fileadmin/Public_Web_Site/ICH_Products/Guidelines/Efficacy/E7/Step4/E7_Guideline.pdf. Accessed 13 Nov 2018
3. Field TS, Gurwitz JH, Avorn J, McCormick D, Jain S, Eckler M, Benser M, Bates DW (2001) Risk factors for adverse drug events among nursing home residents. Arch Intern Med 161:1629–1634
4. Herr M, Robine JM, Pinot J, Arvieu JJ, Ankri J (2015) Polypharmacy and frailty: prevalence, relationship, and impact on mortality in a French sample of 2350 old people. Pharmacoepidemiol Drug Saf 24:637–646
5. Jyrkkä J, Enlund H, Korhonen MJ, Sulkava R, Hartikainen S (2009) Polypharmacy status as an indicator of mortality in an elderly population. Drugs Aging 26:1039–1048
6. Beers MH, Ouslander JG, Fingold SF, Morgenstern H, Reuben DB, Rogers W, Zeffren MJ, Beck JC (1992) Inappropriate medication prescribing in skilled-nursing facilities. Ann Intern Med 117:684–689
7. World Health Organization (2011) Teacher's guide to good prescribing. France: World Health Organization. http://apps.who.int/medicinedocs/documents/s15940e/s15940e.pdf. Accessed 13 Nov 2018
8. Hamilton HJ, Gallagher PF, OMahony D (2009) Inappropriate prescribing and adverse drug events in older people. BMC Geriatr 9:5
9. Ble A, Masoli JA, Barry HE, Winder RE, Tavakoly B, Henley WE, Kuchel GA, Valderas JM, Melzer D, Richards SH (2015) Any versus long-term prescribing of high risk medications in older people using 2012 Beers Criteria: results from three cross-sectional samples of primary care records for 2003/4, 2007/8 and 2011/12. BMC Geriatr 15:146
10. Doubova SV, Torres-Arreola LP, Rosas-Carrasco O, Pérez-Cuevas R (2007) Quality of medication prescribing for elderly patients with non-malignant pain syndrome attending family medicine clinics. Rev Invest Clin 59:428–436
11. Novaes PH, da Cruz DT, Lucchetti ALG, Leite ICG, Lucchetti G (2017) The, "iatrogenic triad": polypharmacy, drug-drug interactions, and potentially inappropriate medications in older adults. Int J Clin Pharm 39:818–825
12. Carey IM, De Wilde S, Harris T, Victor C, Richards N, Hilton SR, Cook DG (2008) What factors predict potentially inappropriate primary care prescribing in older people? Analysis of UK primary care patient record database. Drugs Aging 25:693–706
13. Davies EA, O´Mahony MS (2015) Adverse drug reactions in special populations—the elderly. Br J Clin Pharmacol 80:796–807
14. Sánchez-García S, García-Peña C, Salvà A, Sánchez-Arenas R, Granados-García V, Cuadros-Moreno J, Velázquez-Olmedo LB, Cárdenas-Bahena Á (2017) Frailty in community-dwelling older adults: association with adverse outcomes. Clin Interv Aging 12:1003–1011
15. World Health Organization (2018) Collaborating centre for drug statistics methodology. Structure and principles. https://www.whocc.no/atc/structure_and_principles/. Accessed 13 Nov 2018
16. Hovstadius B, Petersson G (2012) Factors leading to excessive polypharmacy. Clin Geriatr Med 28:159–172
17. American Geriatrics Society (2015) Beers criteria update expert panel. American geriatrics society 2015 updated beers criteria for potentially inappropriate medication use in older adults. J Am Geriatr Soc 2015(63):2227–2246
18. Eaton W, Muntaner C, Smith C, Tien A (1998) Revision of the center for epidemiologic studies depression (CES-D) scale. Johns Hopkins University, Prevention Center, Baltimore
19. Lawton MP, Brody EM (1969) Assessment of older people: self-maintaining and instrumental activities of daily living. Gerontologist 9:179–186
20. Folstein MF, Folstein SE, McHugh PR (1975) Mini-mental state: a practical method for grading the cognitive state of patients for the clinician. J Psychiatr Res 12:189–198
21. Fried LP, Tangen CM, Walston J, Newman AB, Hirsch C, Gottdiener J, Seeman T, Tracy R, Kop WJ, Burke G, McBurnie MA (2001) Cardiovascular health study collaborative research group. Frailty in older adults: evidence for a phenotype. J Gerontol A Biol Sci Med Sci 56:M146–M156
22. Eiras A, Teixeira MA, González-Montalvo JI, Castell MV, Queipo R, Otero Á (2016) Consumption of drugs in over 65 in Porto (Portugal) and risk of potentially inappropriate medication prescribing. Aten Primaria 48:110–120
23. Parodi-López N, Villán-Villán YF, Granados-Menéndez MI, Royuela A (2014) Potentially inappropriate prescribing in patients over 65 years-old in a primary care health centre. Aten Primaria 46:290–297
24. Robles-Bayón A, Gude-Sampedro F (2014) Inappropriate treatments for patients with cognitive decline. Neurologia 29:523–532
25. Gnjidic D, Hilmer SN, Blyth FM, Naganathan V, Cumming RG, Handelsman DJ, McLachlan AJ, Abernethy DR, Banks E, Le Couteur DG (2012) High-risk prescribing and incidence of frailty among older community-dwelling men. Clin Pharmacol Ther 91:521–528
26. Haider SI, Johnell K, Weitoft GR, Thorslund M, Fastbom J (2009) The influence of educational level on polypharmacy and inappropriate drug use: a register-based study of more than 600,000 older people. J Am Geriatr Soc 57:62–69
27. Lechevallier-Michel N, Gautier-Bertrand M, Alpérovitch A, Berr C, Belmin J, Legrain S, Saint-Jean O, Tavernier B, Dartigues JF, Fourrier-Réglat A (2005) 3C study group. Frequency and risk factors of potentially inappropriate medication use in a community-dwelling elderly population: results from the 3C study. Eur J Clin Pharmacol 60:813–819
28. Laurier C, Moride Y, Kennedy WA (2002) Health survey data on potentially inappropriate geriatric drug use. Ann Pharmacother 36:404–409
29. United Nations Political declaration and Madrid international plan of action on ageing (2002) New York: United Nations. https://www.un.org/development/desa/ageing/madrid-plan-of-action-and-its-implementation.html. Accessed 13 Nov 2018
30. Chang CB, Yang SY, Lai HY, Wu RS, Liu HC, Hsu HY, Hwang SJ, Chan DC (2015) Application of three different sets of explicit criteria for assessing inappropriate prescribing in older patients: a nationwide prevalence study of ambulatory care visits in Taiwan. BMJ Open 5:e008214
31. Oliveira MG, Amorim WW, de Jesus SR, Heine JM, Coqueiro HL, Passos LC (2015) A comparison of the Beers and STOPP criteria for identifying the use of potentially inappropriate medications among elderly patients in primary care. J Eval Clin Pract 21:320–325
32. Hernández-Arroyo MJ, Díaz-Madero A, Enríquez-Gutiérrez E, Teijeiro-Bermejo MC, Sáez-Rodríguez E, Gutiérrez-Martín MR (2018) Analysis of the use of proton pump inhibitors in primary health care. Semergen 44:316–322
33. Savarino V, Dulbecco P, de Bortoli N, Ottonello A, Savarino E (2017) The appropriate use of proton pump inhibitors (PPIs): need for a reappraisal. Eur J Intern Med 37:19–24
34. Dalton K, O'Brien G, O'Mahony D, Byrne S (2018) Computerised interventions designed to reduce potentially inappropriate

prescribing in hospitalised older adults: a systematic review and meta-analysis. Age Ageing 47:670–678
35. Straand J, Fetveit A, Rognstad S, Gjelstad S, Brekke M, Dalen I (2006) A cluster-randomized educational intervention to reduce inappropriate prescription patterns for elderly patients in general practice–the prescription peer academic detailing (Rx-PAD) study [NCT00281450]. BMC Health Serv Res 6:72
36. Gray SL, Hart LA, Perera S, Semla TP, Schmader KE, Hanlon JT (2018) Meta-analysis of interventions to reduce adverse drug reactions in older adults. J Am Geriatr Soc 66:282–288
37. Lutz BH, Miranda VIA, Bertoldi AD (2017) Potentially inappropriate medications among older adults in Pelotas, Southern Brazil. Rev Saude Publica 51:52
38. Luna-Medina MA, Peralta-Pedrero ML, Pineda-Aquino V, Durán-Fernández YC, Avalos-Mejía A, Aguirre-García Mdel C (2013) Inappropriate prescribing in older adults with chronic-degenerative disease. Rev Med Inst Mex Seguro Soc 51:142–149
39. Doubova SV, Mino-León D, Reyes-Morales H, Flores-Hernandez S, del Torres-Arreola LP, Pérez-Cuevas R (2010) Effects of two educational programmes aimed at improving the utilization of non-opioid analgesics in family medicine clinics in Mexico. J Eval Clin Pract 16:716–723
40. Doubova SV, Reyes-Morales H, Jiménez-Balderas FJ, Camargo-Coronel A, Navarro-Pureco S, del Torres-Arreola LP, Mino-León D, Olivares-Santos RA (2008) Guide for appropriate using of the non-opioid analgesics in the management of pain. Rev Med Inst Mex Seguro Soc 46:523–532
41. Poudel A, Ballokova A, Hubbard RE, Gray LC, Mitchell CA, Nissen LM, Scott IA (2016) Algorithm of medication review in frail older people: focus on minimizing the use of high-risk medications. Geriatr Gerontol Int. 16:1002–1013
42. O'Mahony D, O'Sullivan D, Byrne S, O'Connor MN, Ryan C, Gallagher (2015) STOPP/START criteria for potentially inappropriate prescribing in older people: version 2. Age Ageing 44:213–218
43. Gutiérrez JP, Rivera-Dommarco J, Shamah-Levy T, Villalpando-Hernández S, Franco A, Cuevas-Nasu L, Romero-Martínez M, Hernández-Ávila M (2012) Encuesta nacional de salud y nutrición. Resultados nacionales. Instituto Nacional de Salud Pública (MX), Cuernavaca