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Prevalence and impact of potentially inappropriate medication on community dwelling older adults

Prevalencia e impacto de la medicación potencialmente inapropiada en ancianos de la comunidad

Impact of inappropriate medication on older adults

Alejandra Fernández ¹, Fernando Gómez ¹, Carmen-Lucía Curcio ¹, Edison Pineda ¹, Juliana Fernandes de Souza ²

¹ Facultad de Ciencias para la Salud, Universidad de Caldas, Manizales, Colombia

² **Incluir sección institucional**, Universidad Federal de Río Grande del Norte, Natal, Brasil

Corresponding author:

Alejandra Fernández, Facultad de Ciencias para la Salud, Universidad de Caldas, Edificio Miguel Arango Soto, carrera 25 N°48-57, Manizales, Colombia.

alejandra.711611080@ucaldas.edu.co

Individual contribution of authors:

All authors participated in organizing and analyzing the data process, preparing and editing the article.

Introduction: Potentially inappropriate medication (PIM) is associated with adverse health and functional outcomes, and increased health care costs.

Objective: To estimate the prevalence and types of PIM according to the Beers criteria in community dwelling older persons and to identify the major clinical and functional consequences of PIM during two years of following.

Materials and methods: This was a longitudinal, descriptive and observational study that included 400 dwelling people 65 years and older (48% women) selected by simple random sampling in 2012; in 2014, 372 people were reevaluated and classified in two groups based on the presence or absence of PIM through the follow up period.

Results: In total, 31% had polypharmacy, (5-9 medications) and 1,8% had excessive polypharmacy (10 or more medications). A higher mean in the number of medications in the PIM group was found (3 vs 5.78 $p < 0.001$). Additionally, 21,9% held the PIM status at the follow up; of those, 75% had one PIM, and 23% had two PIMs. The presence of PIM was more frequent in frail, bad health self-assessment, depressed, and comorbid (especially Diabetes Mellitus and , Chronic Obstructive Pulmonary Disease, COPD) males. In the group with sustained PIM, deterioration of health self-assessment, increase in frailty, incidence of recurrent falls, and the prevalence of depression, as well as, a higher hospital admission rate, ambulatory medical consultation, and more prescribed medications were found. We did not find an impact on functional capacity.

Conclusions: We validate the negative effects of PIM in the long run in the health of older people, so we determined that PIMs must be monitored in primary attention in order to avoid greater risks.

Key words: Potentially inappropriate medication list; aged; comorbidity; frailty.

Introducción. La medicación potencialmente inapropiada (MPI) se asocia con consecuencias negativas clínicas, geriátricas, funcionales y fármaco-económicas.

Objetivo. Estimar la prevalencia y tipos de la MPI, según criterios Beers, en ancianos que viven en comunidad e identificar las principales consecuencias clínicas y funcionales de la MPI en dos años de seguimiento.

Materiales y métodos. Estudio descriptivo observacional longitudinal, el estudio base incluyó 400 mayores de 65 años (48% mujeres) que viven en la comunidad seleccionados mediante muestreo aleatorio simple en 2012, en el seguimiento a 2014 se reevaluaron 372, clasificados en dos grupos que permanecieron con y sin MPI durante los dos años.

Resultados. 31% tenían polimedicación, (5-9 medicamentos) y 1.8% polimedicación excesiva (10 o más medicamentos). Hay mayor promedio de consumo de medicamentos en el grupo de MPI (3 vs 5.78 $p < 0.001$). 21.9% permanecieron con MPI en el seguimiento, de ellos, 75% tenían 1 MPI y 23% 2 MPI. El uso de MPI fue más frecuente en hombres con mala autopercepción en salud, frágiles, con depresión, mayor número de comorbilidades, especialmente Diabetes Mellitus y Enfermedad-Pulmonar-Obstructiva-Crónica (EPOC). En el grupo que permaneció con MPI se encontró deterioro de la autopercepción de salud, incremento de la fragilidad, la presencia de caídas recurrentes, y depresión, con mayores ingresos hospitalarios y consultas médicas y mayor cantidad de medicamentos formulados. No se evidenció impacto en la capacidad funcional.

Conclusiones. Se corroboran los efectos negativos a largo plazo de MPI en la salud de los ancianos, por lo cual se debe monitorizar MPI en la atención primaria para evitar mayores riesgos.

Palabras clave: lista de medicamentos potencialmente inapropiados; anciano; comorbilidad; fragilidad.

An accelerated increase in the proportion of older people implies great challenges for modern geriatrics (1). Up to 80% of people older than 65 have at least one chronic health condition (2). Usually, these patients are more vulnerable to worse out patient care quality, and especially, worse quality in the prescription of medications (3). There is a proportional relation between age and the number of prescribed medications, and with the development of problems related to medication (PRM) (4).

Within PRMs, polymedication or polypharmacy can be quantitatively described according to the number of medications, or in qualitative terms, keeping in mind the use of inadequate medications (5). Polymedication from a quantitative view is defined as the prescription of five or more medications per day, and excessive polymedication as the consumption of ten or more medications per day (6).

Qualitatively, polymedication is determined by a higher risk compared to the benefit when administering medication, regarding the characteristics of the drug and the individual characteristics of the patient, more widely known as Potentially Inappropriate Medication (PIM) (7). PIM is defined as the medications or a combination of them that should be avoided in older people because they may cause more harm than benefit when there are safer alternatives (8).

Explicit and implicit assessment strategies have been developed to detect PIM. Implicit strategies are based on judgement and require clinical information to be interpreted and assessed, as opposed to explicit strategies that are supported in predesigned lists for elderly population to determine which medication is more beneficial than harmful (9). In outpatient senior citizens, AGD Beers' criteria are more efficient to detect PIM (10,11). Polymedication and the use of inappropriate

drugs have direct consequences on adverse effects, interactions, frequency of consultation in health services, and functional outcomes; they are also associated to comorbidity, syndromes, and geriatric conditions, and they increase the risk of hospitalization, influence morbidity, mortality, and the quality of life of the senior patient (12).

The objectives of this study were to estimate the prevalence and types of PIM, according to Beers' criteria, in people older than 65 who live in the community, and to describe the main consequences of PIMs in relation to clinical conditions, functionality, syndromes and geriatric conditions, use of health services, and mental wellbeing during a two-year follow up (2012-2014).

Materials and methods

Study population

We carried out an analysis of the data obtained in the International Mobility in Aging Study (IMIAS), a longitudinal population study with 1995 people between 65 and 74 years old, who live in the community and whose origin was from five different cultural and social contexts: Kingston (Ontario, Canada), Saint-Hyacinthe (Quebec, Canada), Tirana (Albany), Manizales (Colombia), and Natal (Brazil). The objective of the IMIAS was to understand how the factors throughout the course of life affect mobility in old people. Its characteristics and details have been described elsewhere (13).

For this study, we used the data of the population of Manizales (Colombia), 200 males and 200 females in 2012, with a follow up of 372 senior citizens in 2014 (7% attrition). The selection procedure of the sample is shown in figure 1. After classifying the people with PIM in 2012 according to Beers' criteria, we followed

them up in 2014 and excluded those who did not comply with this condition.

Finally, 60 senior people continued to have PIM and 213 had no PIM, who were included in the longitudinal analysis.

Data collection

The information was obtained from house visits during which structured interviews were carried out by previously trained staff. Data regarding medications were obtained directly from the patients' prescriptions and from the boxes of drugs prescribed by a doctor or self-prescribed by the patient, taken during the previous 15 days. All medications were identified using the Anatomical Therapeutic Chemical (ATC) Classification suggested by WHO (14).

Main measurement

Potentially Inappropriate Medication (PIM). We used Beers' criteria, an explicit description strategy developed since 1991, which has regular updates by AGS according to new findings in the literature. It has been validated in various media, and has better performance for the detection of PIM in people living in communities compared with other strategies (15). We used version 2 – 2015 (tables 2, 3, 4) and those medications classified as inappropriate were taken into account (16,17).

Covariables

Sociodemographic: We included questions about general demographic aspects, such as, age in years, gender (male/female), educational level recorded as the number of formal education years finished 0-5, 6-11, or 12 or more. Marital status included single, married, widow/widower, and separated. Income was recorded according to the current legal minimum wage at the moment of the interview divided in two groups: less than 300 dollars or more than 300 dollars per month.

Self-Rated Health: It was assessed using the question 'Do you consider your health to be: good, very good, regular, bad, very bad' (18); for the analysis, it was dichotomized between good and very good vs. regular, bad, and very bad.

Presence of chronic illnesses: Participants were asked if a physician had ever told them they had one of the following chronic illnesses: high blood pressure, osteoarthritis/arthritis, heart disease, chronic obstructive pulmonary disease (COPD), diabetes, cancer, or osteoporosis. Additionally, we obtained the number of self-reported chronic conditions (19).

Medications: Refers to the total number of medications or active ingredients the person consumes regularly with a specific objective for at least two weeks, which have been prescribed by health personnel or self-prescribed. They were recorded according to the Anatomical Therapeutic Chemical (ATC) classification suggested by WHO (20). The boxes of the medications and their presentations were checked. Duplicate medications were not taken into account for the analysis. They were classified by quantity into no polymedication (0-4 medications), polymedication (5-9 medications), and excessive polymedication (10 or more medications) [3].

Visits to the doctor: Number of outpatient visits to the doctor in the last year, referred by the participant.

Hospitalization: Number of times the person was hospitalized in the last two years. This variable was analyzed only during follow up (year 2014).

Geriatric conditions: We took into account the following conditions: fragility, as defined by Fried et al. (21) and documented in previous publications of the IMIAS study (22).

Recurring falls: Refers to the self-report of two or more falls in the previous year (23,24).

Depression: We used the depression scale of the *Centro de Estudios Epidemiologicos* (CES-D) (25-27), which has 20 items related to depressive symptoms with a range between 0 and 60 points. Scores ≥ 16 were considered suggestive of depression (28).

Cognitive Impairment: We applied the Leganés cognitive test (LCT), which evaluates six cognitive areas: high scores mean adequate cognitive functioning and > 22 suggest Cognitive Impairment (28).

Activities of daily living (ADL): We asked the participants, 'Do you have any difficulty to independently perform one of the following activities: walking in a room, getting dressed, bathing, eating, climbing stairs, climbing into bed, and going to the toilet' (29,30). They were classified into two groups, those who had no difficulties when performing the activities vs. the rest.

It was endorsed by the University of Caldas Bioethics Committee.

Statistical analysis

We carried out a descriptive analysis (frequency distribution, averages, and standard deviation). We did a bivariate analysis using Student's t test for continuous variables, and the chi-squared test with Fisher's exact test for categorical variables. The normality of the continuous variables was evaluated using the Kolmogorov-Smirnov (KS) test. We used generalized linear models with robust Poisson regression models to estimate prevalence ratios (PR). Multivariate logistic regression was used to identify the correlations of maintaining a PIM after the adjustment of the demographic, health, and medication variables. $p < 0.05$ was

considered statistically significant. The data were analyzed using SPSS version 22.0.

Ethical considerations

This study was approved by the ethics committee of the *Universidad de Caldas*. All participants signed the informed consent. According to Resolution 8430/1993 from the *Ministerio de Salud* of Colombia, which rules studies with human beings, it is classified as minimal risk since the participants have a very low probability of suffering any harm as a consequence of the study.

Results

Table 1 shows the characteristics of the sample at the beginning of the study (2012) and during follow up (2014), according to sociodemographic and clinical variable, and geriatric conditions. There were significant differences regarding gender; from the total population with PIM, 66.7% were males. Concerning clinical status, self rated health was significantly better ($p=0.011$) in people without PIM. In regard to comorbidity, participants with PIM reported in average 2.02 chronic illnesses, while those without PIM only reported 1.31 ($p=0.000$).

The average number of consumed medications was 3.67 (SD 2.66), with higher consumption in people with PIMs compared to those that did not have them (3 vs 5.78 $p < 0.001$). In total, 31% had polymedication (5-9 medications), and 1.8% had excessive polymedication (10+ medications). At the two-year follow up, 21.9% of participants maintained the PIM. From them, 75% had one PIM, 23% had two PIMs, and 0.4% had three PIMs. The use of PIM was more frequent in males with bad self rated health, a higher number of comorbidities, especially diabetes mellitus and COPD, more fragile, and who had depression. The most frequent

PIMs in order were: 33% prazosin (alpha blocker), 17% proton pump inhibitors (PPIs), 12% Non-Steroidal Anti-Inflammatory Drugs (NSAIDs), and 7.5% antihistamines, which continued to be prescribed two years later (figure 2).

During follow up, people with PIMs were found to suffer from a deterioration of their self rated health, and an increase in the number of comorbidities, especially diabetes mellitus. In the group with PIM, fragility increased significantly from 11% to 17% after two years. The number of recurring falls was significantly higher in the PIM group (18.3% vs 8.5%). Likewise, depression, number of hospitalizations, medical consultations, and the total prescribed medications were significantly higher in the group that maintained PIM after two years.

Regarding outcomes in both populations after two years, we did not find statistically significant differences among the sociodemographic characteristics. On the other hand, from the people with good and very good self rated health in 2014, 84.3% belonged to the group without PIM since 2012. From 2012 to 2014 there was an increase in the mean of chronic illnesses, with higher significance in the PIM group.

The prevalence of diabetes mellitus increased 5% in the population with PIM compared to 0.9% in the population without them. Fragility increased significantly in both groups at the two-year follow up, but it was more significant in the group with PIM, with 16.7% of people with PIM in 2012 being fragile in 2014, compared to 4.7% of those without PIM. The percentage of participants with depression was significantly higher in the group with PIM. The number of hospitalizations, doctor consultations, and total prescribed medications were higher in the group of patients with PIM since 2012.

Table 2 shows the logistic regression analysis that we used to analyze the associated characteristics in the group of subjects who persisted with MPI in the two years studied. We found an association between PIM persistence and consequences such as self rated health, number of chronic illnesses, especially diabetes mellitus, fragility, recurring falls, depression, and more use of health care services. We did not evidence a significant impact on functional capacity.

Discussion

This study analyzed PIM longitudinally, established its prevalence, and assessed comorbidity and functionality outcomes, and geriatric syndromes in elderly population in the community. Quantitative polymedication (five or more medications) occurs in 31% of senior citizen, and from them, 21% had PIMs, especially heart medication (prazosin), PPIs and NSAIDs. PIM was more frequent in males with bad self rated health, a higher number of comorbidities, especially diabetes mellitus and COPD, more fragile, and depressed. At the two-year follow up, PIM was associated with adverse health outcomes like worse self rated health, increase in comorbidities, especially diabetes mellitus, increase in fragility, recurring falls, and variables associated with adverse health events, including hospitalizations, medical consultations, and the total number of prescribed medications.

Regarding the found prevalence in quantitative polymedication and PIM, it is within the ranges reported in the literature. Similar to this study, approximately one third of the elderly population living in the community consumes five or more medications (12), and from them, at least one fourth had PIM (31). A Spanish study that included senior citizens older than 85 living in the community (5) reported a

prevalence of PIM of 69%, while a Colombian report (11) showed 6.9% in outpatient elderly population. Additionally, a Brazilian longitudinal study on PIM (32) found a prevalence of 43.8%, and it was associated with bad self rated health, but contrary to our study, it was more frequent in females.

Both at the beginning and at follow up, the most frequently prescribed PIMs were cardiovascular ones, specifically alpha blockers (around 30%), followed by PPIs without clear indication, and lastly by drugs with a direct effect on the central nervous system, as documented in other studies (33). More recent studies show a high proportion of hypnotic and anticholinergic medication.

In Spain, in patients over 85 years old, high prescription of hypnotics (benzodiazepine-type), and cardiovascular medication such as loop diuretics and NSAIDs was reported (5). A French study showed that approximately 12% of all PIMs were hypnotic (benzodiazepines), and almost 10% anticholinergics (tricyclic antidepressants-type) (34). In Taiwan, around 21% of all PIMs were benzodiazepines (35). In the Brazilian study mentioned previously, prescribing methyl dopa and clonazepam corresponded to 25% of the total prescribed PIMs. In Colombia, the pharmacological group which was the most frequently associated with PIM were NSAIDs, with almost 12% of prescriptions in this age group (11). PPIs without clear indication represented almost 17% of all PIM prescriptions in our study, similar to other studies, like in Pakistan, where they accounted for 25% (36). The number of prescribed PIM stayed the same with a small tendency to increase during the two follow-up years, which according to the literature could be associated with an increase in the medication-medication and medication-comorbidity interactions (37). Additionally, in our study there was an increase in the

number of comorbidities during follow-up, suggesting the need for more medications to be managed, as evidenced at the two-year mark. This is the tendency reported in longitudinal studies with an increase in comorbidities, and as such, in polypharmacy and PIM (23,38).

Diabetes mellitus was associated in the PIM group during follow-up. It has been previously stressed that specific chronic conditions (for instance, mental health conditions or diabetes mellitus) could increase the risk of PIM since the medications that are usually used for their management are linked to adverse effects in the elderly population (19). On the other hand, the association between PIM and depression has been mentioned before (25,38), and is it likely that in our case, they are collateral effects of PIM or medications that promote depressive symptoms (38). Along those lines, the observed deterioration in self-perceived health during follow-up could be due to the fact that senior patients with the worst self-perceived health think of themselves as sicker and using health care services a lot more (32). Likewise, the association of self rated health with illnesses, disability, and functional limitations is clear (39).

In regard to the consequences of geriatric conditions and syndromes and PIMs, they have been mostly reported in transversal studies (34). Concerning the increase in fragility in elderly people with PIMs during follow up and its link to PIM, the contributing role of medications has been strongly stressed, especially those with anticholinergic effects in the development of fragility (40). In a transversal study including French population older than 65 years, they found a proportional association between fragility with excessive poly medication and PIM (34), which are findings that support the recommendation to reduce polypharmacy as part of

the interventions to manage fragility. As shown in various studies (41), the role of PIM in recurring falls through drowsiness, deterioration of postural reflexes, myorelaxant effects, and extrapyramidal symptoms is clear (24).

Regarding the use of health care services, we corroborated the association between PIM and the increase in hospitalization rates, a higher number of doctor visits (35), and an increase in polymedication. In a recent metanalysis of observational studies on PIM, it was found that it was significantly associated with emergency room visits, drug adverse reactions, and hospitalizations. Additionally, the Albacete study recently showed that polypharmacy is linked to mortality, incident disability, hospitalization, and visits to the emergency room in fragile and pre-fragile elders. These findings indirectly indicate that physicians are prescribing these medications in great proportion in this age group, and as such, are responsible for most of the PIMs and the impact they have on people's health.

Among the strengths of this study, we can find the documentation of long-term PIM associations with sociodemographic factors, clinical characteristics, and geriatric conditions in a group of elderly citizens in the community. Usually, longitudinal studies are done with quantitative polypharmacy, while this one used qualitative polypharmacy. Another strength is the direct review of patient prescriptions and medication boxes by the health personnel who collected the data, which affords more reliability to our results. Finally, we can also list including self-prescribed medications in our work as part of this category, since it is infrequent in PIM studies.

Similarly, various limitations ought to be mentioned. Given the selection filters of the participants, sample size might not have been enough to find a significant

association among some variables. Another limitation was the inclusion of senior citizens in the community within a narrow age range, 65-74 years old. Hence, the results may not be generalized to populations that might present higher PIMs, such as very old or institutionalized people.

In conclusion, to the group of patients included in the sample polymedication occurs in a third of the elderly population that lives in the community, and from them, a fifth have PIMs, especially heart and gastrointestinal medications, and anti-inflammatories. We corroborated the negative long-term effects of PIM in elderly health, especially regarding deterioration in self rated health, higher comorbidities like diabetes mellitus and depression, multiple geriatric conditions, including fragility, recurring falls, and more use of health care services. It is important for the health care team to constantly monitor their presence to avoid the risks that polymedication and inappropriate use of medication entail.

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Conflicts of interest:

None declared.

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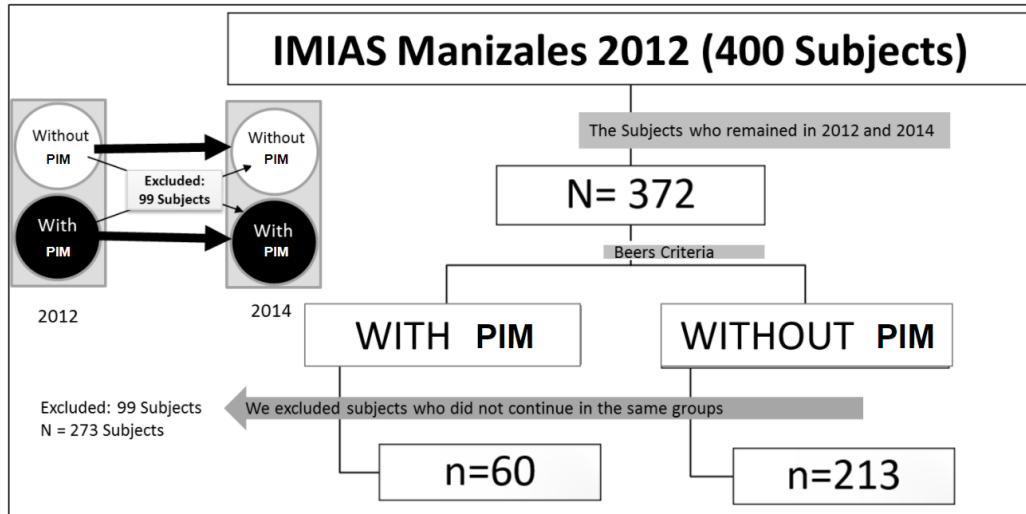
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Characteristics	2012				2014			
	Total n=273	PIM (no) n=213	PIM (yes) n=60	p value	Total n=273	PIM (no) n=213	PIM (yes) 1 n= 60	p value
Sociodemographic								
Age, average (SD)	69.3(2.96)	69.1(2.89)	69.9 (4.15)	0.075	71.4 (3.00)	71.2(2.95)	72.3 (3.146)	0.081
Gender, n (%)				0.010				0.010
Female	131 (48.0)	111(52.1)	20 (33.3)		131(48.0)	111 (52.1)	20 (33.3)	
Male	142 (52.0)	102(47.9)	40 (66.7)		142 (52.0)	40(47.9)	40(66.7)	
Marital status, n (%)				0.613				0.389
Single	37 (13.6)	30 (14.1)	7(11.7)		40 (14.7)	34 (16.0)	6 (10.0)	
Married	127 (53.8)	111 (52.1)	36 (60.0)		147 (53.8)	109 (51.2)	38 (63.3)	
Widow/Widower	60 (22.0)	50 (23.5)	10 (16.7)		63 (23.1)	51 (23.9)	12 (20.0)	
Separated	29 (10.6)	22 (10.3)	7 (11.7)		23 (8.4)	19 (8.9)	4 (6.7)	
Education				0.838				0.700
0-5 years n (%)	180 (65.9)	139 (65.3)	41 (68.3)		167 (64.8)	137 (64.3)	40 (66.6)	
6-11 years	43(15.8)	35 (16.4)	8 (13.3)		59 (21.6)	47 (22.1)	12 (20.0)	
12 years or more	50 (18.3)	39 (18.9)	11 (18.3)		37 (13.6)	29 (13.6)	8 (13.0)	
Income, n (%)				0.678				0.609
Less than US\$300	219 (80.2)	172 (80.8)	47 (78.3)		167 (61.2)	132 (62.0)	35 (58.3)	
More than US\$300	54 (19.8)	41 (19.2)	13 (21.7)		106 (38.8)	81 (38.0)	25 (41.7)	
Clinical characteristics								
Self Rated Health				0.011				<0.001
Excellent / Very good	153 (56.0)	128 (60.1)	25 (41.7)		185 (67.8)	156 (73.2)	29 (48.3)	
Regular/ Bad / Very bad	120 (44.0)	85 (39.9)	35 (58.3)		88 (32.2)	57 (26.8)	31 (51.7)	
Chronic illnesses								
Average (SD)	1.47(1.27)	1.31 (1.14)	2.02 (1.52)	<0.001	1.62 (1.31)	1.47 (1.21)	2.16 (1.50)	<0.001
High blood pressure, n (%)	158 (57.9)	118 (55.4)	40 (66.7)	0.247	162 (59.0)	120 (56.3)	41 (68.3)	0.095
Osteoarthritis, n (%)	75 (27.5)	54 (25.4)	21 (35.0)	0.266	83 (30.4)	60 (28.2)	23 (38.3)	0.131
Heart disease, n (%)	49 (17.9)	35 (16.4)	14 (23.3)	0.219	60 (22)	46 (21.6)	14 (23.3)	0.774
COPD, n (%)	32 (11.7)	20 (9.4)	12 (20.0)	0.024	38(13.9)	25 (11.7)	13 (21.7)	0.050
Diabetes Mellitus, n (%)	32 (11.7)	17 (8.0)	15 (25.0)	<0.001	37 (13.6)	19 (8.9)	18 (30.0)	<0.001
Osteoporosis, n (%)	35(12.8)	26 (12.2)	9 (15.0)	0.525	39 (14.3)	30 (14.1)	9 (15.0)	0.858
Cancer, n (%)	12 (4.4)	6 (2.8)	6 (10)	0.017	16 (5.9)	8 (3.8)	8 (13.3)	0.050
Medications								
Total, average (SD)	3.67 (2.66)	3.08 (2.3)	5.78 (2.54)	<0.001	4.01 (3.149)	3.35 (2.80)	6.38 (3.195)	<0.001
Prescribed medications	3.0 (2.41)	2.47 (2.14)	4.88(2.38)	<0.001	3.49 (2.88)	2.87 (2.56)	5.72 (2.90)	<0.001
Self-prescribed Medications	0.67 (1.03)	0.60 (0.94)	0.90 (1.27)	0.048	0.47 (0.818)	0.44 (0.797)	0.57 (0.89)	0.295
Visits to the doctor in the last year, average (SD)	4.48 (4.03)	4.0 (3.65)	6.18 (4.80)	<0.001	4.7 (4.34)	4,23 (4,29)	6.35 (4.14)	0.001

Hospitalized in the two last years, n (%)	----	----	----	----	73 (26.7)	48 (22.5)	25 (41.7)	0.003
Number of times, average (SD)	----	----	----	----	1.55 (1.00)	4,23 (4,29)	1.96 (1.27)	0.010
Activities of daily living, without difficulties	212 (77.6)	170 (79)	42 (70)	0.031	200 (78)	165 (77.4)	35 (58.3)	0.042
Activities of daily living, one or more difficulties	61 (22.4)	43 (21)	18 (30)	0.031	73 (22)	48 (22.6)	25 (41.7)	0.042
Geriatric conditions								
Recurring falls, n (%)	45 (16.5)	32(15.0)	13 (21.7)	0.221	29 (10.6)	18 (8,5)	11 (18.3)	0.028
Fragility				0.004				0.003
Vigorous	136(49.8)	112(52.6)	24(40.0)		133 (48.7)	111 (52,1)	22(36.7)	
Pre-fragile	125 (45.8)	96(45.1)	29 (48.3)		120 (44.0)	92 (43.2)	28 (46.7)	
Fragile	12 (4.4)	5(2.3)	7 (11.7)		20 (7.3)	10 (4.7)	10 (16.7)	
Fragile (yes), n (%)	12 (4.4)	5 (2.3)	7 (11.7)	0.002	20 (7.3)	10 (4.7)	10(16.7)	0.002
Depression n (%)	63 (23.1)	43(20.2)	20 (33.3)	0.033	51(18.7)	30 (14.1)	21 (35.0)	<0.001
Cognitive Impairment n (%)	13 (4.7)	10 (4.6)	3 (5.9)	0.90	15 (5.5)	11 (5.1)	4 (6.7)	0.46

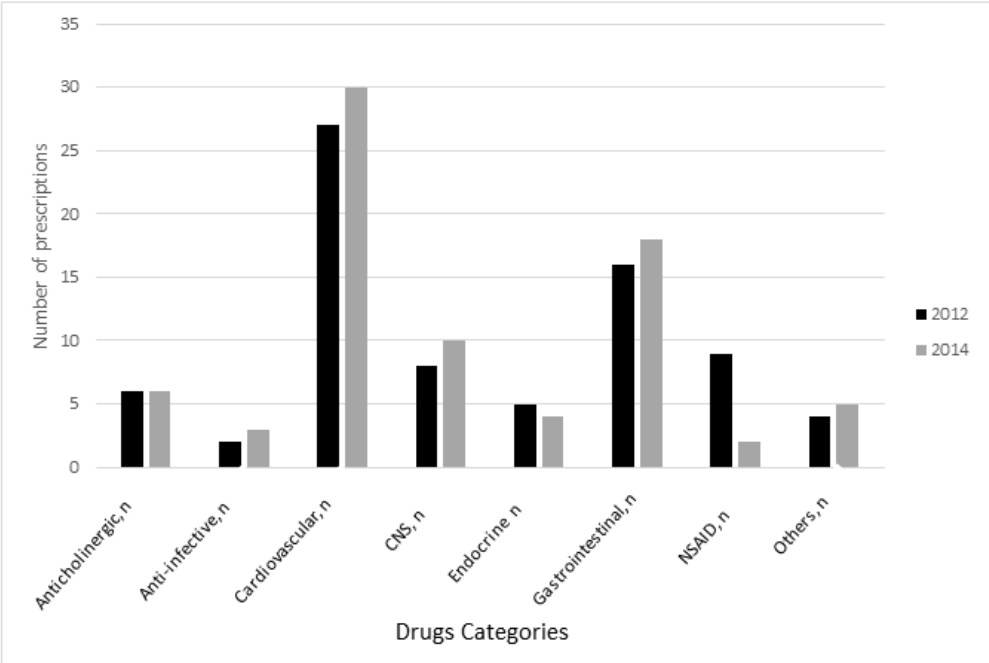
Table 2. Prevalence ratio for various consequences among the subjects with PIM 2012-2014 (n=60)		
Characteristic	Significance (p<0.05)	PR (CI)
Self Rated Health	p<0.001	2.93 (1.62-5.27)
Number of chronic diseases (two or fewer vs three or more)	p<0.001	2.50 (1.34-4.69)
Diabetes Mellitus	p<0.001	4.38 (2.11-9.04)
Fragility	0.004	4.06 (1.60-10.28)
Recurring falls	0.028	2.43 (1.08-5.84)
Depression CES-D scale >16 points	p<0.001	3.28 (1.70-6.33)
Hospitalizations in the last two years	p<0.001	2.45 (1.34-4.50)
Number of hospitalizations in the last two years	0.010	3.75 (0.82-17.24)
Number of doctor consultations in the last year	0.001	4.22 (1.73-10.29)
Total prescribed medications (Polymedication vs no polymedication)	p<0.001	8.93 (4.67-17.08)
*PR (CI): Prevalence ratios (Confidence interval). CI=95%		

Figure 1. Sample selection process



*PIM: Potentially inappropriate medications

Figure 2. Prescribed potentially inappropriate medication categories (2012-2014).



*CNS: Central Nervous System drugs. NSAID: Non-Steroidal Anti-Inflammatory Drugs.