Pharmacoepidemiological profile and polypharmacy indicators in elderly outpatients

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This cross-sectional study was carried out with 1000 elderly outpatients assisted by a Basic Health District Unit (UBDS) from the Brazilian Public Health System (SUS) in the municipality of Ribeirão Preto. We analyzed the clinical, socioeconomic and pharmacoepidemiological profile of the elderly patients in order to identify factors associated with polypharmacy amongst this population. We used a truncated negative binomial model to examine the association of polypharmacy with the independent variables of the study. The software SAS was used for the statistical analysis and the significance level adopted was 0.05. The most prevalent drugs were those for the cardiovascular system (83.4%). There was a mean use of seven drugs per patient and 47.9% of the interviewees used ≥7 drugs. The variables that showed association with polypharmacy (*P* value < 0.01) were female gender, age >75 years, self-medication, number of health problems, number of medical appointments, presence of adverse drug events, use of over-the-counter drugs, use of psychotropic drugs, lack of physical exercise and use of sweeteners. The exposition to all these factors justified the high prevalence of polypharmacy amongst the interviewees. These results showed the need to adopt clinical intervention and educational and managerial measures to analyze and promote rationality in the use of drugs amongst the elderly users of SUS.

Uniterms: Pharmacoepidemiology. Elderly/use of drugs. Polypharmacy. Drugs/rational use. Public Health System.

Este estudo transversal foi realizado por meio de entrevistas com 1000 idosos atendidos em uma Unidade Básica Distrital de Saúde (UBDS) do Sistema Único de Saúde (SUS) no município de Ribeirão Preto. Analisou-se o perfil clínico, socioeconômico e farmacoepidemiológico a fim de identificar os fatores associados à polifarmácia nessa população. Utilizou-se um modelo binomial negativo truncado para análise da associação da polifarmácia com as variáveis independentes do estudo. O software SAS foi utilizado para a análise estatística. O nível de significância adotado foi de 0,05. Os fármacos com maior prevalência de uso foram do sistema cardiovascular (83,4%). Observou-se média de, aproximadamente, sete fármacos por paciente e 47,9% dos entrevistados usavam ≥7 fármacos. As variáveis que apresentaram associação com a polifarmácia (p< 0,01) foram: mulheres, idade (>75 anos), automedicação, quantidade de problemas de saúde, número de consultas médicas, uso de medicamentos isentos de prescrição médica, uso de psicotrópicos, não realização de exercícios físicos e uso de adoçante. A exposição a todos esses fatores justifica a alta prevalência de polifarmácia entre os entrevistados. Os resultados mostraram a necessidade de adotar medidas de intervenção clínica e educacional e gerencial para analisar e promover a racionalização do uso de fármacos entre os idosos usuários do SUS.

Unitermos: Farmacoepidemiologia. Idoso/uso de medicamentos. Polifarmácia. Medicamentos/uso racional. Sistema Público de Saúde.

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INTRODUCTION

Population ageing is a process common to all countries throughout the World. In most of the developed countries, this process occurred slowly and gradually, however in emerging countries such as Brazil, this change in the age structure is occurring rapidly (Carvalho, Garcia, 2003). This rapid change in the Brazilian aging process can be explained by improvements in the health conditions provided to the population in recent decades, which contributed to a significant reduction in overall mortality rates (IBGE, 2009). It has been estimated that by 2050, Brazil will be the fifth country in the World in the number of elderly citizens (United Nations, 2011), the elderly population representing 30% of the total population by that time in contrast to approximately 12% at the current moment (IBGE, 2010).

Although the change in the ageing process represents social development, it is important to consider that a lack of planning to deal with it can lead to social and economic problems in the health system (Chaimowicz, 1997). The elderly are considered special individuals from the pharmacotherapeutic point of view, showing physiological modifications that can alter the kinetics and/or dynamics of the drugs in the organism (Baldoni *et al.*, 2010). Beside this, due to several synergic factors like age, educational level, general state of health and the presence of specific morbidities, the number of drugs consumed by the general population tends to increase with age (Janchawee *et al.*, 2005).

These aspects place the elderly population as a group of patients vulnerable to negative pharmacotherapeutic outcomes. For example, the increased number of drugs consumed, referred to as polypharmacy, raises the risk of pharmacotherapeutic problems amongst the elderly, mainly those related to drug-drug interactions and adverse reactions (Obreli-Neto, 2012a; Nguyen *et al.*, 2006; Lai *et al.*, 2009; Buck *et al.*, 2009), with financial implications for the health system (Fulton, Allen, 2005).

In this context, pharmacoepidemiological studies are promising tools, which are accessible, low cost and obtain fast results for the planning and improvement of the quality of the health services. The results can be applied to promoting rational pharmacotherapy as well as making it feasible to direct possible technical interventions with respect to the health team, facilitating the adoption of structural and managerial measures to improve the public health system (Strom, 2000).

The aim of this study was to characterize the use of drugs and identify the clinical and socioeconomic-demographic factors that may be associated with the occurrence of polypharmacy amongst the elderly outpatients assisted by Brazilian Public Health System (SUS).

METHODOLOGY

Study design and setting

This cross-sectional study was carried out in the Brazilian city of Ribeirão Preto from November 20th, 2008 to May 20th, 2009. We collected information about the medications used by elderly outpatients assisted by SUS and attended by the pharmacy of the Basic Health District Unit (UBDS) in the western district of Ribeirão Preto at the Health Center School of the Faculty of Medicine of Ribeirão Preto of the University of São Paulo (CSE-FMRP-USP). The city of Ribeirao Preto has an estimated population of 605 thousand inhabitants, 12.6% of the individuals being over 60 years of age. The unit mentioned above covers an area with an estimated population of about 184 thousand inhabitants, with approximately 22,000 being elderly (IBGE, 2010; SEADE 2012).

Subjects

The study population represented 5.67% of the elderly patients attended by the public health service from the district previously mentioned. The inclusion criteria were patients aged 60 years or older, from both sexes, and who obtained their medications from the pharmacy of the Basic Health Unit during the study period. The exclusion criteria were elderly patients unable to express themselves and those who sent another person to the pharmacy to pick up their medication.

Data collection

The patients were invited to take part in the study when they come to the pharmacy to withdraw their medication. Patients who accepted the invitation were interviewed by a researcher in an individual room. The interview followed a structured form previously developed by our research team. During the interview the researcher collected socio-demographic data (age, gender, educational level and employment situation), clinical data (general state of health, morbidities, practice of physical exercise, ingestion of caffeinated beverages and alcoholic beverages and smoking) and data about the pharmacotherapy used (name and number of drugs being used at the moment of the interview and consumed in the previous thirty days, both with and without a medical prescription).

All the drugs consumed were classified according to the first level of the Anatomical-Therapeutical-Chemical Classification System (ATC) (WHO, 2011). Potential hazardous drug-drug interactions were investigated using the World Health Organization Model Formulary 2008 drug interaction guide (WHO, 2008a). The Over the Counter (OTC) and psychotropic medications were identified by Resolution nº 138/2003 (Brasil, 2003) and Decree 344/98 (Brasil, 1998) and its updates according to National Health Surveillance Agency (Anvisa), respectively.

Data analysis

Descriptive statistics were used to analyze most variables and the results presented in terms of the absolute and relative frequency, mean ± standard deviation (SD) with 95% confidence intervals (95% CI).

In the statistical analysis, the number of drugs used per person was considered as a dependent variable. The number of drugs used per person was modeled by means of a truncated negative binomial distribution (Hilbe, 2011) and a truncated Poisson distribution, considering that this variable is a count data without zero values (Long, 1997). Poisson and binomial negative distributions are frequently used to fit count data, but these models assume that the dependent variable is an integer number including zero, and in the present study, the number of drugs used per person is always equal or greater than 1. Therefore the statistical analysis assumed truncated distributions, that is, probability distributions which do not assume zero values.

The inclusion of independent variables (gender, age, practice of physical exercise, use of sweeteners, health problems, the number of medical appointments scheduled for a one year period, use of psychotropic and over the counter drugs (OTC), and self-medication) in the model allowed for comparisons between groups of interest. The SAS software (Morel, Neerchal, 2012) was used in the statistical analysis and the level of significance adopted was 0.05.

Ethical approval

This project was approved by the Ethics Committee of CSE-FMRP-USP, protocol n.285/2008.

RESULTS

Socio-demographic characteristics

From November 20th, 2008 to May 20th, 2009, 1227 elderly patients were invited to take part in the study. Of these 116 refused to take part and 111 did not attend the inclusion criteria. Thus 1000 patients were interviewed. The mean age of the study group was 69.8 (±6.5), with a higher prevalence of women (66.1%). The majority of the elderly patients had completed or nearly completed elementary school (70.2%) and were retired or pensioners (75.0%) (Table I).

TABLE I - Socio-demographic characteristics of the elderly outpatients, Ribeirão Preto-SP- Brazil, 2008/2009 (n= 1,000)

	Total (%)	Men (%)	Women (%)
Age (years)			
60 to 64	24.7	22.0	26.0
65 to 75	56.3	60.0	54.4
> 75	19.0	18.0	19.6
Educational level			
Illiterate	12.7	9.4	14.4
Literate	3.7	2.1	4.5
Completed all or part of elementary school	70.2	70.5	70.0
Completed high school or higher	13.4	18.0	11.1
Employment situation			
Retired/Pensioner	80.6	91.6	75.0
Housewife	14.3	1.7	20.7
Carry out some paid work	5.1	6.7	4.3

Clinical data

A mean of 3.4 morbidities/patient was observed, with 42.7% of the elderly outpatients presenting four or more health problems, the following standing out as more prevalent: hypertension (72.8%), dyslipidemia (42.2%), diabetes mellitus (24.3%), insomnia (12.2%), depression (12%), backache (11.6%) and osteoporosis (11.6%).

About one third of the elderly outpatients (31.1%) practiced physical exercise at least three times a week and 93.2% ingested caffeinated beverages, there being little difference between the genders for these variables. With respect to the ingestion of alcoholic beverages (33.9% *vs* 9.8%) and smoking (12.3% *vs* 6.5%), both were greater amongst the male gender.

Drug therapy data

A total of 6,856 medications were used in the previous 30 days, 5,475 being prescribed medications and 1,381 self-medications. A mean value of 6.85 (± 3.4) drugs (prescribed and self-medicated) was found per patient (Figure 1), and sixty one percent of the population used more than five medications. Drugs that act on the cardiovascular system (ATC code C) were the most commonly used, followed by drugs that act on the Alimentary Tract and Metabolism (ATC code A) and Nervous System (ATC code N) (Table II).

Self-medication was reported by 30.9% of the elderly outpatients, with a greater prevalence amongst the female gender (34.8% *vs* 23.3%). The drugs most used in self medication were dipirone (14.3%), followed by caffeine (9.5%), diclofenac (6.8%), orfenadrin (5.6%), paracetamol (4.2%), acetylsalicylic acid (2.6%) and carisoprodol (1.7%). An analysis of potential interactions between the drugs used by the elderly outpatients produced 243 potentially hazardous interactions, the majority being related to drugs that act on the cardiovascular system (ATC code C), the most prevalent being: enalapril and hydrochlorothiazide (n=127), enalapril and furosemide (n=29), nifedipine and propanolol (n=12) and acetylsalicylic acid and warfarin (n=11).

The statistical analysis provided evidence that the use of polypharmacy by the elderly was influenced by socio-demographic, clinical and pharmacotherapeutic factors (Table III).

DISCUSSION

Awareness of the pharmacoepidemiological profile of elderly patients can help in the development of health policies to guarantee patient safety. A high number of drugs consumed per patient were verified in our study, most of them acting on the cardiovascular system, with a high prevalence of potentially hazardous drug interactions. The practice of self-medication and the use of psychotropic drugs were common in our sample. The variables that showed association with polypharmacy (*P* value < 0.01) were female gender, age >75 years, self-medication, number of health problems, number of
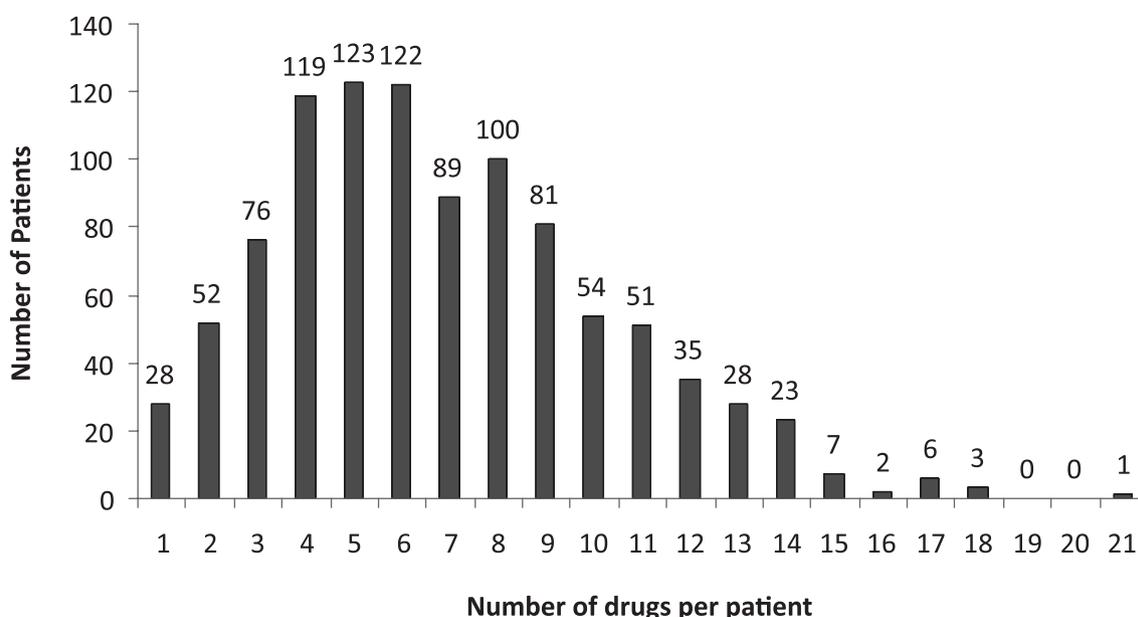
FIGURE 1 - Distribution of the total number of drugs used by the elderly outpatients interviewed, contained in prescriptions and self-medicated, Ribeirão Preto-SP-Brazil, 2008/2009, (n=1000).

TABLE II - Frequency of drugs with greater prevalence of use amongst the elderly outpatients interviewed, Ribeirão Preto-SP, Brazil, 2008/2009 (n= 1,000)

First level ATC WHO		Drugs (prescribed & self-medicated)	Frequency (%)
C	Cardiovascular system	Hydrochlorothiazide (C03AA03) - 37.7% Sinvastatin (C10AA01) - 36.2% Enalapril (C09AA02) - 27% Captopril (C09AA01) - 18.8% Propranolol (C07AA05) - 17.2%	83.4
A	Alimentary tract and Metabolism	Omeprazole (A02BC01) - 34.4% Metformin (A10BA02) -17.8% Calcium carbonate (A12AA04) - 17%	64.3
N	Nervous system	Dipyrone (N02BB02) - 23.9% Paracetamol (N02BE01) - 19.7% Fluoxetine (N06AB03) - 9.1%	62.3
M	Musculo-skeletal system	Diclofenac (M01AB05) - 20.3%	50.1
B	Blood and blood forming organs	Aspirin (100mg) (B01AC06) - 37.2%	37.2
R	Respiratory system	Dexchlorpheniramine (R06AB02) - 9.6%	18.8
H	Systemic hormonal preparations, except sex hormones and insulin	Levotyroxine (H03AA01) - 11.0%	11.6

medical appointments, use of over-the-counter drugs, use of psychotropic drugs, lack of physical exercise and the use of sweeteners. This pharmacoepidemiological profile indicates the need for developing health care practices to guarantee patient safety.

The socio-demographic characteristics (age, gender, educational level and employment situation) of our sample were similar to those observed in other Brazilian population studies involving non-institutionalized elderly outpatients. Obreli-Neto *et al.* (2011), found a mean age of 65.8 ± 5.8 years (range 60-88 years) and a high prevalence of woman (65.9%) in a study carried out in the Ourinhos microrregion, Sao Paulo State. In a study developed in Marília, Sao Paulo State, 42.9% of the elderly patients were between 60-69 years, 61.8% were female, most of them were illiterate or had incomplete elementary schooling (68.1%), and the basic health units were the health service most used (62.4%) (Marin *et al.*, 2008). A study carried out in the city of Rio de Janeiro found a total of 41.1% elderly patients between 60-69 years, 60.6% being female, most of them had some elementary schooling (50.8%) and no private health coverage (56.9%) (Rozenfeld, Fonseca, Acurcio, 2008). It is important to consider the low educational level of the Brazilian elderly, since this is one of the factors interfering in adherence to a pharmacological treatment (Vermeire *et al.*, 2001), in the use of inappropriate drugs and in polypharmacy (Haider *et al.*, 2009).

Similar to previous Brazilian studies, our sample presented a high prevalence of chronic diseases, with hypertension, diabetes and dyslipidemia being the most common ones (Rozenfeld, Fonseca, Acurcio, 2008, Obreli-Neto *et al.*, 2011, Obreli-Neto *et al.*, 2012b). The high prevalence of chronic diseases is onerous for the health system, a fact also encountered in other studies with elderly patients (Leite-Cavalcanti *et al.*, 2009; Crentsil *et al.*, 2010), and should serve as an alert for health service planning due to the process of population ageing, since chronic diseases require continuous treatment and monitoring (Abegunde, Stanciole, 2006). For example, it is estimated that more than US$ 471 billion were spent worldwide on healthcare for diabetes in 2012 for all age groups, with the greatest diabetes mellitus–associated health resource use attributed to the population aged ≥ 65 (Hagan, Dall, Nikolov, 2003; IDF, 2012). Our study also verified a lack of practice of physical activities and an elevated ingestion of caffeinated and alcoholic beverages, and smoking. The use of these social drugs can influence negatively in the search for positive therapeutic outcomes for these chronic diseases.

The mean number of drugs used by the elderly outpatients was higher than that found in other studies carried out with patients in the same age range (Flores, Mengue, 2005; Danilow *et al.*, 2007; Barry *et al.*, 2006; Gallagher, Mahony, 2008). It was notable that

TABLE III - Mean number of drugs used per elderly outpatient with its respective 95% confidence interval (95%CI), estimates of the mean difference between groups (with 95%CI), and crude and adjusted *P* values obtained using truncated negative binomial models

| | Mean | 95%CI | Difference between means | | |
			Estimate (95%CI)	Crude *P* value	Adjusted *P* value
Gender					
Males	5.62	(5.32,5.93)	1.84 (1.43,2.25)	<.01	<.01 [a]
Females	7.48	(7.20,7.75)			
Age Range (years)					
60 to 64	6.56	(6.14,6.97)	Reference		
65 to 69	6.69	(6.30,7.09)	0.13 (-0.43,0.71)	0.64	0.54 [b]
70 to 74	6.98	(6.54,7.41)	0.42 (-0.17,1.02)	0.17	0.05 [b]
75 or older	7.23	(6.75,7.71)	0.67 (0.04,1.30)	0.04	<.01 [b]
Self-medication					
No	6.24	(6.01,6.48)	1.95 (1.47,2.44)	<.01	<.01 [c]
Yes	8.20	(7.77,8.63)			
Health problems					
Up to 3	5.29	(5.08,5.49)	3.66 (3.38,4.05)	<.01	<.01 [c]
More than 3	8.95	(8.62,9.28)			
Medical appointments made					
Up to 4	6.36	(6.12,6.60)	1.64 (1.14,2.13)	<.01	<.01 [c]
More than 4	8.00	(7.57,8.43)			
Use of OTC					
No	4.14	(3.83,4.14)	3.38 (3.00,3.77)	<.01	<.01 [c]
Yes	7.52	(7.29,7.75)			
Takes physical exercise					
No	7.11	(6.82,7.40)	-0.64 (-1.07,0.22)	<.01	0.02 [c]
Yes	6.47	(6.15,6.79)			
Uses sweeteners					
No	6.43	(6.18,6.68)	1.18 (0.72,1.64)	<.01	<.01 [c]
Yes	7.62	(7.23,8.00)			
Use of Psychotropic drugs					
No	6.18	(5.93,6.42)	1.88 (1.42,2.33)	<.01	<.01 [c]
Yes	8.05	(7.66,8.44)			

(a) Adjusted by age; (b) Adjusted by gender; (c) Adjusted by age and gender; OTC: Over-the-counter drugs; ADE: Adverse drug event

approximately 48% of the interviewees used more than six drugs, whilst in another Brazilian study this prevalence was only 11% (Rozenfeld, Fonseca, Acurcio, 2008). This high number of drugs used favored the risk of problems related to pharmacotherapy, such as drug interactions (Janchawee *et al*., 2005), adverse drug reactions (Nguyen *et al*., 2006; Obreli-Neto *et al.,* 2012a) and the use of inappropriate drugs (Buck *et al*., 2009; Lai *et al*., 2009).

The high prevalence of the use of drugs for the cardiovascular system stands out amongst the similarities for the use of drugs in this age range (Ribeiro *et al*., 2008; Crentsil *et al*., 2010; Correr *et al*., 2007). Drugs that act on the cardiovascular system are important causes of adverse drug reactions (ADR) amongst the elderly, mainly affecting the central nervous system and the gastrointestinal and vascular systems (Mohebbi *et al*., 2010; Faulx MD, Francis, 2008), which suggests the

need for appropriate medication therapy management in these patient to prevent and detect negative therapeutic outcomes early. Drugs that act on the alimentary tract and metabolism and on the nervous system are also frequently prescribed in our study and in other Brazilian studies. These ATC codes were also frequently involved in adverse drug reactions in elderly outpatients (Gurwitz *et al.*, 2003).

Dypirone was the drug most frequently used in self-medication, followed by caffeine and diclofenac. Considering these drugs used for self-medication, the use of non-steroidal anti-inflammatory drugs (NSAID) stands out. NSAIDs show considerable potential for drug interactions (Micromedex, 2011) and adverse reactions, such as an increase in cardiovascular risk (Hudson, Richard, Pilote, 2005) and increases in renal dysfunction in patients with chronic kidney disease, a condition that tends to occur with greater incidence in elderly patients (Kuo *et al.*, 2010). Apart from the NSAIDs, the use of carisoprodol should also be highlighted, since this drug is considered inappropriate for the elderly, on account of it showing a high risk of causing anticholinergic adverse effects, sedation, weakness and risk of fractures (American Geriatrics Society, 2012).

In the present study, the statistical analysis indicated that polypharmacy was probably multifactorial. Different to the study of Hovstadius *et al.* (2010), we found that female sex was a predictor of polypharmacy, whereas when we observe the age, the data corroborate with those in the literature, the use of drugs increasing with increasing age (> 75 years) (Janchawee *et al.*, 2005; Hovstadius *et al.*, 2010; Bardel, Wallander, Svardsudd, 2000). However another Brazilian study carried out with institutionalized elderly subjects found no association between polypharmacy and increasing age amongst the three age ranges analyzed (Lucchetti *et al.,* 2010). These divergent findings suggest that polypharmacy has regional characteristics.

The absence of physical activity amongst the elderly can be considered as an indicator of polypharmacy, corroborating with available data which shows that the practice of physical exercises reduces the risk of chronic diseases (Haskell *et al.*, 2007), which can hence reduce the need for drug use (Veehof *et al.*, 2000).

The number of health problems was the most important statistical indicator of polypharmacy, hypertension and diabetes mellitus being the most common ones. Previous studies identified these morbidities as indicators that favored the use of polypharmacy amongst the elderly (Rozenfeld, Fonseca, Acurcio, 2008), which confirms the strong correlation between polypharmacy

and the number of health problems found in our study. In addition, we found that the use of sweeteners had a significant relationship with polypharmacy. However, it is important to consider that this could be associated with the presence of diabetes mellitus, since this morbidity favors the use of various drugs (Rozenfeld, Fonseca, Acurcio, 2008; Veehof *et al.*, 2000).

The number of medical appointments is a well-known indicator of polypharmacy (Haider *et al.*, 2008; Rozenfeld, Fonseca, Acurcio, 2008), nevertheless in clinical practice this evidence deserves a critical evaluation of the rationality of pharmacotherapy, since in geriatrics a physiological alteration inherent to the ageing process can be confounded with a health problem, leading to an unnecessary prescription.

Analyzing the drug categories used by the elderly, it can be seen that the use of OTCs and of psychotropic drugs was also correlated with polypharmacy. The relationship of polypharmacy with the use of OTCs could be related to self-medication, since the drugs in this category were those showing the greatest prevalence of use amongst those not prescribed by a doctor. Moreover, it is important to remember that the use of polypharmacy and psychotropic drugs together are risk factors for falls in elderly patients (Baranzini *et al.*, 2009).

Considering the consequences of polypharmacy to the health of the elderly, it is important to highlight the need for new studies that evaluate if all the drugs used by the elderly justify the clinical indication (Rozenfeld, Fonseca, Acurcio, 2008). If on one hand the use of various medications could indicate the guarantee of access to the medication, on the other hand it could indicate excessive and irrational use. These questions provide an impulse for new investigations and new hypotheses to be tested by analytical studies.

CONCLUSIONS

From the data obtained in the interviews with the elderly outpatients, it was observed that they were exposed to various factors that could have contributed to the use of polypharmacy, such as a high prevalence of health problems, elevated number of doctors' appointments, self-medication, and the use of psychotropic drugs and OTC. The exposition to all these factors justified the high prevalence of polypharmacy amongst the interviewees, with 47.9% using more than six drugs. This showed the need to adopt clinical intervention and educational and managerial measures to analyze and promote rationality in the use of drugs amongst the elderly users of the Brazilian Public Health System.

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CONFLICTS OF INTEREST

None to declare.

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