

Polypharmacy, socioeconomic indicators and number of diseases: results from ELSA-Brasil

Polifarmácia, indicadores socioeconômicos e número de doenças: resultados do ELSA-Brasil

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ABSTRACT: *Objective:* To estimate the prevalence of polypharmacy, describe the pharmacotherapeutic classes used, and investigate whether polypharmacy is associated with demographic and socioeconomic indicators, regardless of the number of diseases, among participants in the Brazilian Longitudinal Study of Adult Health (ELSA-Brasil) baseline (2008–2010). *Method:* In this analysis, 14,523 adults and elderly (35–74 years) participated. Polypharmacy was characterized as regular use of five or more medicines. The demographic and socioeconomic indicators analyzed were: gender, age, education level, *per capita* family income, and access to private health insurance. The independent association between demographic and economic indicators and polypharmacy was estimated by binary logistic regression. *Results:* The prevalence of polypharmacy was 11.7%. The most used drugs were those with action on the cardiovascular system. After adjustments, including by number of diseases, the chances of being on polypharmacy treatment were significantly higher among women, older participants and those with greatest number of diseases. Individuals without health insurance had lower chance to be under polypharmacy, as well as those with lower income. *Conclusion:* The occurrence of polypharmacy among ELSA-Brasil baseline participants was mainly due to drugs for the treatment of chronic diseases. The relation between polypharmacy and the female gender, as well as its association with old age, are in consonance with the results obtained in other studies. Despite the absence of an association between polypharmacy and education level, the income and health insurance results reinforce the existence of social inequalities regarding drug use.

Keywords: Pharmacoepidemiology. Polypharmacy. Population Health. Drug utilization.

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RESUMO: *Objetivo:* Estimar a prevalência de polifarmácia, descrever as classes farmacoterapêuticas utilizadas e investigar se a polifarmácia está associada a indicadores demográficos e socioeconômicos, independentemente do número de morbidades, entre os participantes na linha de base do Estudo Longitudinal de Saúde do Adulto (ELSA-Brasil) (2008–2010). *Métodos:* Participaram desta análise 14.523 adultos e idosos (35–74 anos). A polifarmácia foi caracterizada como uso regular de cinco ou mais medicamentos. Os indicadores demográficos e socioeconômicos analisados foram: sexo, idade, escolaridade, renda familiar *per capita* e acesso a plano de saúde particular. A associação independente entre os indicadores demográficos e econômicos e polifarmácia foi estimada por meio de regressão logística binária. *Resultados:* A prevalência de polifarmácia foi de 11,7%. Os medicamentos mais utilizados foram aqueles com ação no sistema cardiovascular. Após ajustes, incluindo número de doenças, a chance de estar sob tratamento com polifarmácia foi significativamente maior entre mulheres, participantes mais velhos e aqueles com maior número de doenças. Participantes de baixa renda e aqueles sem plano privado de saúde, no entanto, tiveram menor chance de estar sob polifarmácia. *Conclusão:* A ocorrência de polifarmácia entre os participantes da linha de base do ELSA-Brasil deveu-se principalmente a medicamentos para o tratamento de doenças crônicas. A relação entre polifarmácia e sexo feminino, bem como sua associação com maior idade, estão em consonância com os resultados obtidos em outros estudos. Apesar da ausência de associação entre a polifarmácia e a escolaridade, os resultados de renda e plano privado de saúde reforçam a existência de desigualdades sociais em relação ao uso de medicamentos.

Palavras-chave: Farmacoepidemiologia. Polifarmácia. Saúde da população. Uso racional de medicamentos.

INTRODUCTION

The increasing worldwide use of multiple drugs is related to several factors, such as extended life expectancy and the consequent increase in multimorbidity prevalence. In addition, excessive drug use, usually referred to as polypharmacy, is also affected by the greater availability of medical treatments and therapeutic guidelines that recommend the use of more than one medication in dealing with several health conditions, such as hypertension and diabetes *mellitus*¹. If appropriately prescribed, drug association for treatment of different diseases may be required and beneficial to the patient². However, some drug combinations are inappropriate and may lead to clinically relevant adverse reactions and drug interactions³.

Polypharmacy has been defined in different ways, and one of the most common definitions is the concomitant use of five or more drugs⁴⁻⁹. The use of multiple medications makes administering them difficult, reduces adherence to pharmacotherapy, and contributes to therapeutic duplication. In addition, polypharmacy has also been associated with increased risk of falls¹⁰, fractures¹¹, hospitalizations¹², and mortality¹³, as well as with a significant increase in social and household health expenditures^{14,15}.

Studies that investigated polypharmacy are still limited, most of which focus on specific populations, such as the elderly^{6,7,9,16-18}. Well-known factors associated with polypharmacy include an increase in age and a higher number of diseases^{9,18-24}. Polypharmacy prevalence may reach 60% among people aged 65 years and older^{25,26}, although high prevalence rates

have also been observed among younger adults²⁷⁻²⁹. Comparatively, fewer studies investigated if socioeconomic characteristics, regardless of the presence of diseases, are associated with polypharmacy^{20,22,24}, and the few existing results show diverging and inconclusive results. For example, a positive association between polypharmacy and education levels among adults and the elderly was detected in Greece²⁴. However, a negative association was detected among the elderly in Belgium³⁰ and Sweden²⁰, while other studies detected no association between education levels and polypharmacy²².

From a clinical and public health standpoint, it is important to investigate the prevalence of polypharmacy among the middle-aged population, as it is a marker for multimorbidity, medication use quality, and potential adverse reactions. In addition, no information about the prevalence and the determinants of polypharmacy in Brazil, within this specific group, is available. Additionally, it generates opportunities to evaluate and intervene in pharmacotherapy that avoids exposing these individuals to polypharmacy for long periods of time, especially in vulnerable socioeconomic population, considering the existence of potential inequities in medication use demonstrated in some studies. In addition, no information about the prevalence and the determinants of polypharmacy in Brazil, within this specific group, is available. Therefore, this study is designed to estimate the prevalence of polypharmacy and to investigate if demographic and socioeconomic characteristics, regardless of the presence of diseases, are associated with polypharmacy among a large sample of Brazilians between 35 and 74 years of age.

METHODS

This is a cross-sectional study with participants in the Brazilian Longitudinal Study of Adult Health (ELSA-Brasil) baseline. ELSA-Brasil is a prospective cohort study that monitors active and retired public servants in public higher education and/or research institutions located in six state capitals in the Northeast, South, and Southeast regions of Brazil³¹. Data collection in ELSA-Brasil's baseline was conducted between 2008 and 2010, and it consists of 15,105 participants from 35 to 74 years of age. Detailed information about the ELSA-Brasil design and baseline participant characteristics have been provided in earlier publication³¹. In the present study, ELSA-Brasil baseline included participants who exhibited valid data about demographic and socioeconomic characteristics, and who submitted complete information about their use of medications.

Like most national^{5-7,9,17,32,33} and international^{4,8,22} studies that have investigated the prevalence of polypharmacy, in the present work, polypharmacy was characterized by the use of five or more different drugs, used regularly, excluding phytotherapy preparations and homeopathic medications. Participants were instructed to bring all prescriptions, packages, inserts, and/or blisters for the medications they had used in the previous two weeks to the ELSA-Brasil Research Center. All medications, prescription or non-prescription, used regularly, produced industrially or by pharmacy compounding, in any form, were recorded

here³¹. The use of natural products, medicinal plants, or other preparations of the kind were not considered during the interview.

The following demographic and socioeconomic variables were also collected: gender (male/female); age (as a continuous variable); *per capita* household income (distributed by quintiles); education level (divided into years of study: under 8, from 8 to 10, from 11 to 13, and 14 or more); and health insurance (yes/no).

The variable number of chronic diseases was built taking into account the presence of any of the diseases listed as follow and was divided by the number of identified diseases: none (reference), one, two, or three or more. The diseases were defined by self-reported previous medical diagnosis for: diabetes; hypertension; dyslipidemia; cardiovascular disease, which corresponded to at least one of the clinical conditions: acute myocardial infarction, angina, congestive heart failure, cerebrovascular accident or stroke, and myocardial revascularization; as well as musculoskeletal disorders, that is, reports of rheumatoid arthritis and/or osteoarthritis and/or lupus erythematosus. We also included depression, constructed from face-to-face interviews, and then the sum of all types and severity of depressive episodes was determined by the Clinical Interview Schedule — Revised-CIS-R.

Initially, demographic and socioeconomic characteristics, diseases, and the total number of drugs were distributed among the entire population, and by the occurrence of polypharmacy. Categorical variables were described in proportion, and the continuous variable was described by average and standard deviation (SD). The comparison among proportions was conducted using the chi-squared test. Averages and their respective 95% confidence intervals (95%CI) were estimated in raw form and adjusted by age, using linear regression, based on the number of diseases category. Absolute and relative drug frequencies, based on the first level of Anatomical Therapeutic Chemical (ATC) classification³⁴, were distributed among the participants under polypharmacy treatment.

The association between polypharmacy and demographic and socioeconomic indicators was estimated by logistic regression and displayed as odds ratios (OR) with 95% confidence intervals (95%CI). Initially, a univariate analysis was performed for each one of the demographic and socioeconomic characteristics, as well as for the number of diseases and polypharmacy variables (model 0). After this, gender and age were added (model 1), and, then, model 1 was adjusted by *per capita* household income, education level and health insurance (model 2). Finally, the number of diseases was included (model 3). All variables that remained statistically associated with the response variable ($p < 0.05$) were maintained in the final model after all adjustments. This strategy made it possible to understand the effect of each variable on the model, which is important for understanding the phenomenon studied. All analyses were performed with the software Stata 12.0 and GraphPad Prism 7.

ELSA-Brasil was approved by the Research Ethics Committees at the learning and research institutions, as well as the National Research Ethics Committee, under the register number 976/2006, and all interviewees signed the free and informed consent form.

This study was part of a master's thesis by the first author, entitled *Polifarmácia e indicadores socioeconômicos: análise transversal do estudo longitudinal de saúde do adulto (ELSA-BRASIL)*,

defended in April 2017 in the Post-graduate Program in Health Sciences at the Federal University of São João del-Rei.

RESULTS

Of the 15,105 ELSA-Brasil baseline participants, 118 (0.78%) were excluded from the analysis because they did not adequately respond to the medication use questionnaire. Another 464 (3.07%) questionnaires were not included in this study because they presented missing information on socioeconomic and demographic variables. Therefore, 14,523 (94.15%) participants were included in the regression models. The majority were females (54.4%) and had at least a college education (52.1%). The average age of the population was 52.0 years (SD = 9.1).

Polypharmacy prevalence was 11.7%. Participants under polypharmacy treatment were significantly older, the majority of whom were women with lower education levels and higher *per capita* household income and, additionally, most of them had health insurance ($p < 0.001$), if compared to the participants who used fewer than five drugs. In addition, the number referent to the frequency of disease was significantly higher ($p < 0.001$) among participants undergoing polypharmacy treatment (Table 1).

The recorded number of drugs used by participants was 727. The number of medications varied between 0 and 35. The average of drugs used by the participants increased linearly according to the number of diseases, even after the age had been adjusted (Figure 1).

The most frequent drug classes used among the patients undergoing polypharmacy treatment were, in this order, those that act on the cardiovascular system, the digestive tract and metabolism, the nervous system, and the genitourinary system (Supplementary Table 1).

In this univariate analysis, women exhibited more likelihood to be under polypharmacy treatment if compared to men ($p < 0.001$). A positive dose-response gradient was detected in the association between age and polypharmacy ($p < 0.001$). Individuals with a lower education level (8 years of schooling or less) exhibited a greater chance of polypharmacy when compared to the group with a higher education level (14 years of schooling or more) ($p < 0.001$). In terms of income, a negative gradient was detected in the association magnitude: the lower the income, the lower the chance of polypharmacy ($p < 0.001$). Individuals without health insurance had lower chance to be under polypharmacy when compared to those who have it. The occurrence of polypharmacy also increased based directly on the number of diseases, suggesting a dose-response gradient in the association ($p < 0.001$) (Table 2).

After being adjusted based on demographic and socioeconomic characteristics, all associations present in the univariate analysis were maintained. There was no substantial change in the associations' magnitudes, nor in their statistical significances. By adding the number of diseases variable to the previous model, the association between education level and polypharmacy lost its statistical significance, and the magnitudes of the associations between polypharmacy and age and the number of diseases suffered important reduction (Table 2).

Table 1. Descriptive characteristics of the study population according polypharmacy occurrence, Longitudinal Study of Adult Health (ELSA-Brasil) (2008–2010).

	Total (n = 14,523)	No polypharmacy* (n = 12,821)	Polypharmacy** (n = 1,702)
Gender (%)			
Male	45.6	46.9	35.1
Female	54.4	53.1	64.9
Age (years) (%)			
35–44	22.2	24.3	6.5
45–54	39.5	41.3	26.2
55–64	27.9	26.5	38.7
65+	10.4	7.9	28.6
Education level (years) (%)			
14+	52.1	52.0	52.8
11–13	35.1	35.5	31.8
8–10	6.9	6.8	7.5
< 8	5.9	5.7	7.9
Per capita household income (quintiles) (%)			
5 (highest)	16.1	14.9	25.5
4	22.5	22.2	24.4
3	20.7	21.0	18.3
2	20.3	20.9	15.7
1 (lowest)	20.4	21.0	16.1
Health insurance (%)			
Yes	67.9	66.8	76.2
No	32.1	33.2	23.8
Number of diseases*** (%)			
None	22.6	25.0	4.9
1	37.7	40.7	16.5
2	24.3	23.6	29.4
3+	15.4	10.7	49.2
Number of drugs (mean ± SD)	1.8 ± 2.3	1.1 ± 1.3	6.7 ± 2.3

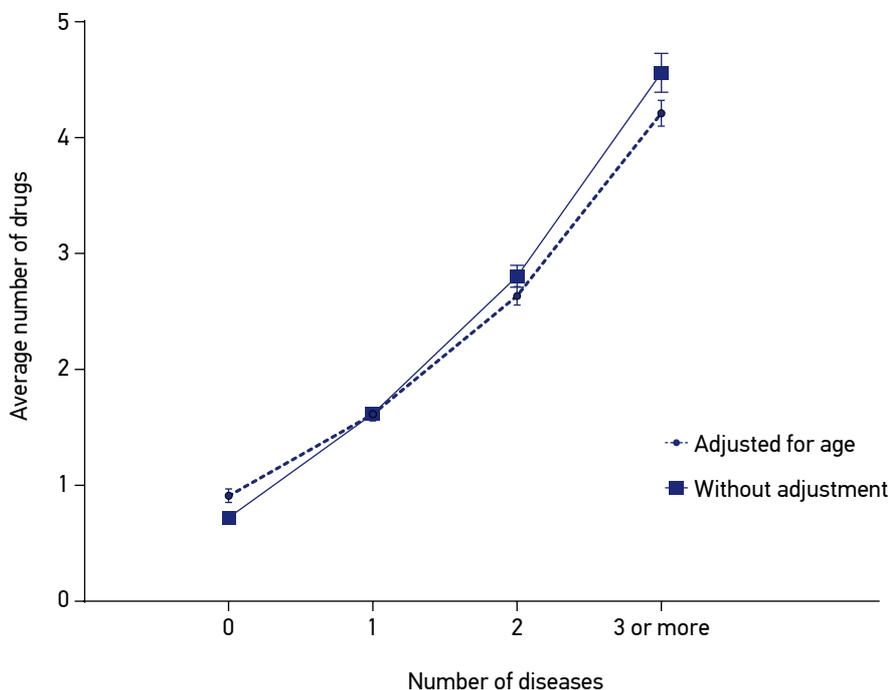
*Non-polypharmacy: use of 0 to 4 medications; **Polypharmacy: use of 5 or more medications; ***diabetes *mellitus* and/or hypertension and/or cardiovascular disease and/or dyslipidemia and/or depression and/or musculoskeletal disease. Differences between participants with and without polypharmacy were statistically significant for all variables presented in the table ($p < 0.001$). The presentation of the average number of drugs used is descriptive and not compared between groups in polypharmacy and non-polypharmacy.

DISCUSSION

This study, conducted with a large sample of Brazilian adults and elderly people, showed that approximately one in ten participants in the baseline was under polypharmacy treatment. After adjustments, including by number of diseases, the chances of being under polypharmacy treatment was significantly higher among women and older participants. Lower income participants without health insurance, however, had fewer chances of being under polypharmacy.

Some studies involving the general population conducted in other countries that used the same polypharmacy classification^{4,35} reported the prevalence of polypharmacy between 15.0 and 24.4%, that is, much higher than that observed for the ELSA-Brasil baseline. One of the possible explanations for this difference is that drug use investigation in these studies referred to a 30-day⁴ and 12-month³⁵ period, which is greater than the period considered in the ELSA-Brasil study, which was 2 weeks. As is well-known, prevalence is a function of time, that is, the longer the time period considered, the higher an event's prevalence will be.

When compared to studies using the same reference period on drug use, the prevalence of polypharmacy found in the present study is also markedly lower than that observed in



*Comorbidities: diabetes mellitus and/or systemic arterial hypertension and/or cardiovascular disease and/or dyslipidemia and/or depression and/or musculoskeletal disease.

Figure 1. Average of drugs used by participants according to the number of disease comorbidities*.

cross-sectional studies conducted in municipalities in the Southeastern^{18,36,37}, Midwest⁷, South^{38,39} and Northeast¹⁶ of Brazil. This difference was expected, given that the population interviewed in these studies was concentrated in elderly individuals. Moreover, these are

Table 2. Univariate and multivariate analysis of the number of diseases and demographic and socioeconomic characteristics and diseases associated with polypharmacy in Longitudinal Study of Adult Health (ELSA-Brasil) (n = 14,523).

	Model 0 OR (95%CI)	Model 1 OR (95%CI)	Model 2 OR (95%CI)	Model 3 OR (95%CI)
Gender				
Male	Reference	Reference	Reference	Reference
Female	1.63 (1.47 – 1.82)*	1.78 (1.59 – 1.98)*	1.72 (1.54 – 1.93)*	1.79 (1.58 – 2.02)*
Age (years)	1.10 (1.09 – 1.11)*	1.10 (1.09 – 1.11)*	1.09 (1.08 – 1.10)*	1.05 (1.04 – 1.06)*
Education level (years)				
14+	Reference	-	Reference	Reference
11–13	0.88 (0.79 – 0.99)*	-	1.34 (1.17 – 1.55)*	1.08 (0.93 – 1.26)
8–10	1.08 (0.88 – 1.31)*	-	1.24 (0.98 – 1.57)	0.95 (0.74 – 1.23)
< 8	1.36 (1.12 – 1.66)*	-	1.44 (1.13 – 1.83)*	1.09 (0.84 – 1.43)
Per capita household income (quintiles)				
5 (highest)	Reference	-	Reference	Reference
4	0.64 (0.55 – 0.74)*	-	0.89 (0.77 – 1.05)	0.84 (0.70 – 0.99)**
3	0.51 (0.44 – 0.60)*	-	0.77 (0.65 – 0.92)*	0.67 (0.55 – 0.82)*
2	0.44 (0.37 – 0.52)*	-	0.64 (0.53 – 0.78)*	0.52 (0.42 – 0.64)*
1 (lowest)	0.45 (0.38 – 0.53)*	-	0.65 (0.53 – 0.80)*	0.51 (0.41 – 0.65)*
Health insurance				
Yes	Reference	-	Reference	Reference
No	0.63 (0.56 – 0.71)*	-	0.72 (0.63 – 0.82)*	0.75 (0.64 – 0.77)*
Number of diseases***				
None	Reference	-	-	Reference
1	2.06 (1.59 – 2.67)*	-	-	1.63 (1.25 – 2.12)*
2	6.33 (4.95 – 8.11)*	-	-	4.31 (3.34 – 5.57)*
3 +	23.43 (18.36 – 29.90)*	-	-	14.91 (11.51 – 19.28)*

Model 0: crude analysis; model 1: gender + age (continuous); model 2: model 1 + educational level + *per capita* household income + health insurance; model 3: model 2 + number of diseases; OR: *odds ratio*; 95%CI: interval of confidence of 95%; *P < 0.001; **P < 0; ***diabetes *mellitus* and/or hypertension and/or cardiovascular disease and/or dyslipidemia and/or depression and/or musculoskeletal disease.

unicentric studies and, although some were conducted in large Brazilian capitals, such as São Paulo⁹, Rio de Janeiro⁴⁰ and Porto Alegre³⁸, they had a markedly less sample diversity than ELSA-Brasil. This limits the comparability of their results with those found in this paper.

In Brazil, the first population studies, representative of the five regions in the country, which investigated polypharmacy among urban area residents, used data from the National Survey on Access, Use, and Promotion of Rational Use of Medicines (PNAUM). Ramos et al.¹⁸, investigating polypharmacy using PNAUM data, observed an 18% polypharmacy prevalence in individuals 60 to 65 years of age or older. If the ELSA-Brasil elderly group (65–74 years of age) is considered alone ($n = 1,504$), a polypharmacy prevalence of 32.3% is detected, which is almost double the PNAUM prevalence, even taking into account that this study's sample does not include the oldest group (75 years of age or more). However, it is important to note that PNAUM data included only continuous-use medication for the treatment of specific chronic diseases, while the ELSA-Brasil study included all medications used regularly, prescription or non-prescription, regardless of the therapeutic indication, which may well explain the detected differences.

Polypharmacy in the PNAUM was investigated exclusively among adults (18 years of age or older) and the elderly who use the primary health care services at the Brazilian Unified Health System (SUS). Although the time interval considered to investigate the use of medication (30 days) is longer than that adopted for ELSA-Brasil, the prevalence of polypharmacy in the primary healthcare services in the PNAUM was 6.9%⁴¹, lower than that detected in the present study. In addition, the fact that the PNAUM study involves younger adults (starting at the age of 18) tends to reduce the global polypharmacy prevalence, considering that age, both in the PNAUM and the ELSA-Brasil study, was a factor associated with the occurrence.

The most frequent drug classes used among the patients undergoing polypharmacy treatment were, in this order, those that act on the cardiovascular system; the digestive tract and metabolism; and the nervous system. These results are similar to those observed in the adult and elderly groups included in the PNAUM⁴¹ and are compatible with the prevalence of other chronic conditions that affect these systems, considering that 40% of the participants in ELSA-Brasil were affected by at least two noncommunicable diseases (NCDs), which include those affecting the cardiovascular system (hypertension and/or cardiovascular disease), metabolism (diabetes or dyslipidemia), and the nervous system (depression). Another explanation would be prescribing doctors' adherence, in general, to the guidelines for treating these diseases. It is worth pointing out that guidelines and clinical protocols for treating NCD, despite being necessary, disregard certain specific circumstances in patient care. The prescription model that defines an individual drug therapy for each disorder has not often taken into account the population's aging and consequent increase of multimorbidity, resulting in an excessive use of medications observed in recent years⁴¹.

Results in this study corroborate other national^{7,9,32,39,41} and international^{42,43} studies that detected a higher chance of polypharmacy among women. Part of this association may be explained by the fact that the women use healthcare services more often⁴⁴, for preventive care or for reproductive health purposes³⁶, which creates different opportunities for

diagnosis and, consequently, for drug prescription. In addition, women tend to adhere to prescribed treatments more than men, justifying why the association remained after adjusting for number of chronic diseases^{38,44}.

In agreement with other studies' results^{4,9,16,24,32,37,43,45}, polypharmacy was strongly associated with an increase in age and with a dose-response gradient. This result was independent on the adjustment by number of chronic diseases, which increases with aging⁴⁶. Wastesson et al.⁴⁷ estimated, based on the analysis of a drug dispensation database, that, after 75 years of age, Swedish elderly people would have been under polypharmacy treatment for more than half of the remaining period of life. Fragmentation of the biomedical model for the health approach, it should be noted, contributes to the increase in drug prescription and polypharmacy, as each specialist is responsible for treating a given morbidity, disregarding the overall realm of health problems exhibited by the individual⁴⁸.

It is important to emphasize that, although association magnitude has been significantly reduced, and residual confounding may be present (adjustment by categories), age was maintained in strong association with polypharmacy, even after the adjustment by number of diseases, demonstrating that part of the effect of age on the occurrence of polypharmacy would not be explained by the higher number of diseases. Similarly, the number of diseases and polypharmacy, even when magnitude is reduced, remain strongly associated with one another, after adjustment by age. In addition, the average number of drugs grows linearly in line with the number of diseases, regardless of age. This suggests that, in fact, there is an effect, regardless of these two variables in the event of polypharmacy. These results reinforce the importance of discussing the healthcare practice called deprescribing⁴⁹, which proposes revising pharmacotherapy and discontinuing previously prescribed drugs⁵⁰.

In the present study, in the univariate analysis and after adjusting for other demographic and socioeconomic characteristics, an inverse association of polypharmacy with education was observed, that is, lower education was associated with a higher chance of polypharmacy. However, after adjusting for number of diseases, this association did not remain statistically significant, indicating that this association was, in fact, explained by the number of diseases, since the prevalence of this variable is higher among less educated individuals: among those who have completed higher education, 66.0% have one or no disease, whereas in the group of participants with incomplete elementary school, the prevalence of two or more diseases is 58.5%.

Although some international studies do not detect this association^{6,22,39}, national studies have identified similar results to this study's, that is, a lower chance of undergoing polypharmacy for participants with lower incomes and without health insurance, even after adjustment by number of disease^{9,51}. Financially favored (higher incomes with health insurance) individuals tend to have more access to healthcare services, including the use of drugs²². In Brazil, the acquisition of medications in the public system still has deficiencies regarding storage, distribution, and dispensation⁵¹. In addition, public programs for access to pharmacological treatment of chronic diseases were incipient during the data collection phase of the present study. As previously discussed regarding education level, studies show that a

doctor's decision to prescribe medications, especially the most expensive ones, is strongly influenced by the patient's socioeconomic conditions, which means those individuals with higher financial power tend to receive prescriptions with a higher number of drugs, especially newer and more expensive ones⁵².

The National Pharmaceutical Policies of 1998⁵³ guaranteed access to medicine through the national public health care system (NPHS), SUS. Under the Popular Pharmacy of Brazil (Farmácia Popular do Brasil), created in 2004, medicines for hypertension, diabetes, and asthma are distributed free of charge (since 2011), and the Brazilian government covers 90% of the price of other medicines. It is also noteworthy that the data collection of the present study was performed before 2011. It is believed, however, that these policies for expanding access to medicines had no relevant impact on the prevalence of polypharmacy in ELSA-Brasil, considering the majority of baseline participants were covered by a health insurance, being less dependent on the free dispensation of medicines. Further studies in the ELSA-Brasil follow-up population may infer about the influence of these governmental measures on the prevalence of polypharmacy and their association with sociodemographic indicators related to access to medicines in this population.

In the present work, the use of medications was verified based on self-reports. Therefore, measurement errors may have occurred, which is a constraint of this work. To minimize the occurrence of such errors, participants were requested to bring prescriptions and packages for the medications they were using at the time of the interview. To avoid memory effects, participants were questioned about the use of regular medications only during the two weeks prior to the data collection.

The reference category of our polypharmacy classification (use of zero to four drugs *versus* use of five or more drugs) includes non-drug users and those who use less drugs in the same comparison group. However, it is the most used classification in epidemiological studies^{8,22,32} and was adopted in this work to promoting dialogue with other publications. A classification with more than two categories, that would be more discriminatory, was considered during analyzes. However, the number of participants in the category of greatest use of drugs was very small, compromising the sampling power and the adjustment of the model.

Finally, the authors highlight that, although the population of ELSA-Brasil is limited to civil servants of educational and research institutions in the country and does not include unemployed individuals or those in extremely low socioeconomic position, the social, racial and regional diversity demonstrated in this cohort allows the investigation of relevant issues related to health inequities in a large sample of the Brazilian population. Furthermore, the prevalence of chronic conditions and health-related behaviors observed among participants of the ELSA-Brasil baseline was similar to the results found in VIGITEL, the surveillance system for risk and protection factors for chronic diseases by telephone survey held annually in all Brazilian capitals³¹.

The occurrence of polypharmacy among ELSA-Brasil baseline participants was mainly due to drugs for the treatment of chronic diseases. Despite the absence of an association between polypharmacy and education level, the income and health insurance results reinforce

the existence of social inequalities regarding drug use. These findings may subsidize future epidemiological investigations related to excessive or inappropriate drug use, thus opening the door to the development of public policies that promote rational drug use in compliance with specific needs of the Brazilian population.

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