



Polypharmacy in older patients at primary care units in Brazil

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Received: 18 June 2018 / Accepted: 31 December 2018 / Published online: 25 January 2019
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Abstract

Background Despite extensive studies of polypharmacy in older patients, no consensus regarding the definition of this practice exists in the literature. Several studies have defined polypharmacy as problematic when considering only the numbers of medications used by patients. **Objective** This study aimed to assess the prevalence of polypharmacy prescribing by comparing two different definitions (quantitative and qualitative) and evaluating factors associated with this practice in older patients. **Setting** Twenty-three basic health units. **Method** A cross-sectional study involving 386 older adults who received a prescription after a medical consultation. Multivariate analyses were conducted using a Poisson regression with robust variance. **Main outcome measure** The main outcome measures included patients with a prescription of five or more medications (quantitative polypharmacy) and those with a prescription of five or more medications including at least one drug considered potentially inappropriate for older adults (qualitative polypharmacy). **Results** The frequency of quantitative polypharmacy was 20.5%. The results of an adjusted analysis showed that the frequency of quantitative polypharmacy was associated with a higher number of self-reported morbidities and the prescription of potentially inappropriate drugs. The prevalence of qualitative polypharmacy was 10.4%, and after adjustment, this outcome remained significantly associated with the presence of three or more self-reported morbidities. **Conclusions** The presence of multiple comorbidities was identified as the main factor associated with the prescription of both quantitative and qualitative polypharmacy.

Keywords Brazil · Older people · Polypharmacy · Potentially inappropriate medications · Prescription drugs · Primary health care

Impacts on practice

- The use of a purely quantitative definition of polypharmacy is controversial because polypharmacy may be appropriately indicated for treating multiple comorbidities;

- The prevalence of polypharmacy differs when comparing the quantitative and qualitative criteria

Introduction

Older people are the greatest consumers of medicines, especially prescription drugs, and are more likely to consume multiple drugs concomitantly [1, 2], a practice known as polypharmacy. Despite the wide practice of polypharmacy, this term has been used to describe various concepts in the scientific literature, and no consensus has been reached regarding the number of concomitant drugs required to achieve the designation of polypharmacy [3, 4]. Furthermore, some authors have referred to polypharmacy as the use of a greater number of drugs than clinically indicated [5, 6] to overcome controversies surrounding the use of purely quantitative definitions because the concomitant use of multiple drugs may be appropriately indicated for treating

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certain clinical conditions or various comorbidities in an individual [3]. This lack of consensus regarding the concept of polypharmacy makes it difficult to compare findings among studies and has led to divergent findings and statistics regarding its prevalence [7, 8]. Moreover, the practice of both quantitative (referring to the quantity of medications used) and qualitative polypharmacy (referring to the use of several medications without all medications having been indicated) among older people can be associated with negative outcomes, including increased costs related to medications, adverse drug reactions, drug interactions, non-compliance with medical treatment, decreased functional status, and development of geriatric syndromes [3].

Aim of the study

This study aimed to evaluate the prevalence of prescribed polypharmacy, compare two different definitions of the term (qualitative and quantitative polypharmacy), and evaluate the factors associated with this practice in older patients receiving care at primary care units within a municipality in the Northeast Region of Brazil.

Ethics approval

This study was approved by the Research Ethics Committee of the Multidisciplinary Health Institute, Federal University of Bahia (technical opinion number 378.198), and all patients provided informed consent prior to participating.

Methods

Study design and participants

This prospective cross-sectional study analysed the prescriptions provided to older patients at primary health care units. Eligible patients were aged 60 years or older and treated by doctors at 23 primary health care units in a municipality in the Northeast Region of Brazil.

Individuals who met the age restriction and were waiting to receive medical care at a health care unit were invited to participate in the study. Those who agreed to participate by providing signed informed consent were directed to the first stage of the interview. The interviews were completed after a health consultation. Patients with hearing impairments and/or severe cognitive deficits who were not accompanied by a person who could respond to the interview questionnaire were excluded.

Setting

The selected municipality has a population of 340,199 residents, of whom 280,800 (82.54%) have primary care health coverage. Approximately 34,000 residents with health coverage are older adults [9]. To ensure a representative sample, all basic health care units in the urban area of the municipality were included in the study.

Sample description

Non-probabilistic sampling was used in this study; here, the sample was obtained by convenience and comprised older patients who attended medical visits at family health care units. The sample calculation in the present study was based on the following parameters: accuracy of 5%, confidence level of 95%, and prevalence of 50%. These figures considered the heterogeneity of the events to be measured and assumed a loss of 30% after the pilot interview; accordingly, a sample of 494 older people was targeted for interviews. This sample was divided proportionally by the number of physicians who offered treatment at the selected health care units. For the purpose of this study, the analysis included only older patients who were provided medical prescriptions after their consultations (n = 386).

Data collection

Data were collected from September 2016 to July 2017 using semi-structured questionnaires adapted from a previous study [10]. Some variables were collected based on medical prescriptions. The participants' cognitive status was evaluated using a version of the Mini Mental State Examination (originally developed by Folstein et al. in 1975) that was modified and updated for use in the Brazilian population in 2003 by Bruck et al. [11, 12]. The Katz Index was applied to evaluate the participants' functional capacity [13, 14].

As noted above, individual interviews were conducted before and after the medical consultations at health care units. Portable computers and tablets (e.g., Samsung Galaxy Tab 3 Lite) compatible with the Android platform and the application Kobo Collect, version 1.4.8 were used in the offline mode. If any health-related impediment to the interview existed, such as deafness or a mild-to-moderate cognitive deficit, the information was obtained from the patient's companion, relative, or caregiver.

Variables

Quantitative polypharmacy refers to the presence of five or more medications taken concomitantly. Qualitative

polypharmacy refers to the presence of five or more medications taken concomitantly, of which at least one is categorised as a potentially inappropriate medication (PIM). The definition of PIM was adopted from the Brazilian Consensus of PIM for the older population: “An inappropriate prescription covers the use of medicines which present a significant risk of adverse events, when there is evidence of an equal or more effective alternative and with less risk for treating the same condition” [15].

The study questionnaire included items regarding sociodemographic characteristics, health conditions, the use of health services, indicators of geriatric syndromes, and medical prescriptions. Information about the prescribed medications issued during the health consultation was obtained by asking the question: “Could you show me the prescription that the doctor gave you?” For participants who answered “yes,” we recorded the medication name, pharmaceutical form, quantity, dose, means of administration, and frequency of prescription. Subsequently, the pharmaceutical specialties were classified by the anatomical (level 1) and therapeutic (level 2) levels according to the Anatomical Therapeutic Chemical (ATC) Classification System [16]. Medications that lacked ATC coding, such as some herbal medicines, were excluded from the analyses.

Data analysis

Two analytical models were created, and the dependent variables were determined based on the two definitions of polypharmacy. The individual was the unit of analysis. Differences between the proportions were tested using Pearson’s Chi square distribution or the Chi square test for linear trend. The prevalence rates of quantitative and qualitative polypharmacy according to the above definitions were calculated based on the number of participants who obtained these types of prescriptions, divided by the total number of older patients analysed. A Poisson regression with robust variance was used to establish the potential relationships of the dependent variables with possible outcomes of interest [17]. All variables included in the bivariate analysis were associated with the dependent variables at a significance level of < 20%. A significance level of 5% was used for all tests and to determine the permanence of variables in the final model. The models were compared using the Akaike and Bayesian information criteria. The adequacy of the model was assessed using a Chi square test. The Statistical Package for Social Sciences, version 23 (IBM, Inc., Armonk, NY, USA) and STATA software, version 14 (Stata Corp., College Station, TX, USA) were used for the data analysis.

Results

A total of 386 older patients were examined. The interviewees had a mean age of 70 years (SD = 7.17). Of them, 67.9% were women and more than half (54.1%) were aged between 60 and 69 years. Approximately 52.3% of the patients reported that they were married or in a stable relationship. Nearly all patients reported having no health plan (96.6%), and 65.3% exhibited evidence of cognitive decline (Table 1).

More than half of the included older patients (68.9%) had a consultation time of less than 15 min, and nearly a third (31.3%) received PIM prescriptions independent of the clinical condition. In addition, 20.5% of the older patients met the above definition of quantitative polypharmacy. Additionally, 10.4% of the individuals met the above definition of qualitative polypharmacy (Table 1).

Quantitative polypharmacy was significantly associated ($p < 0.05$) with the female sex, a higher number of self-reported morbidities, a medical consultation time exceeding 15 min, and the administration of PIM prescriptions independent of the clinical condition (Table 2). In contrast, this variable was not associated with a better self-reported health status or better self-assessment of distance vision. Meanwhile, qualitative polypharmacy was positively associated with the female sex, a higher number of self-reported morbidities, and a duration of medical consultation exceeding 15 min.

The following factors were independently associated with quantitative polypharmacy: a higher number of self-reported morbidities and PIM prescription independent of the clinical condition. Furthermore, qualitative polypharmacy was positively associated with having at least three self-reported morbidities (Table 3).

Discussion

The prevalence of quantitative polypharmacy (20.5%) was similar to that reported in other studies conducted in Brazil [18, 19]. However, this prevalence was much less in the present study than in the international context, as evidenced by reports from Serbia (37%) [20], Portugal (59.2%) [7], Italy (60.3%) [8], and Spain (72.9%) [21]. These differences can be explained by the longer life expectancies of individuals in European countries [22], which suggest that the European population faces a greater incidence of chronic disease and consequently a greater use of medications [23].

Qualitative polypharmacy was less common in this study than in studies conducted previously in Spain

Table 1 Sociodemographic characteristics related to the health status, use of health services, and prescription medications in the studied population (PIM Project, Brazil, 2017)

Variables	Total	
	n	%
Sex		
Male	124	32.1
Female	262	67.9
Age		
60–69 years	209	54.1
70 years or older	177	45.9
Marital status		
Single	184	47.7
Married/stable relationship	202	52.3
Skin colour/race		
Not black	96	24.9
Black/brown/indigenous	283	73.3
Education (years of study completed)		
0	143	37.0
1–4 years	161	41.7
5 years or more	80	20.7
Actively employed		
Working	72	18.7
Not working	314	81.3
Income in terms of minimum wage (MW)		
No income	43	11.1
Less than the MW	10	2.6
1–2.99 times the MW	324	83.9
3 or more times the MW	3	0.8
Health plan		
No	373	96.6
Yes	13	3.4
Cognitive decline		
No decline	134	34.7
Decline	252	65.3
Physical performance in basic activities of daily life (BADL)		
Very dependent	15	3.9
Moderate level of dependence	16	4.1
Independent	355	92.0
Self-perception of status of health		
Very bad/bad	88	22.8
Normal	192	49.7
Good/very good	104	26.9
Pain during the last 3 months		
No	123	31.9
Yes	263	68.1
Long-range vision		
Blind/bad/very bad	85	22.0
Normal	82	21.2
Good/very good	219	56.7
Close-range vision		
Blind/bad/very bad	94	24.4

Table 1 (continued)

Variables	Total	
	n	%
Normal	80	20.7
Good/very good	212	54.9
Difficulty sleeping		
No	193	50.0
Yes	191	49.5
Experienced a fall after age 60		
No	159	41.2
Yes	219	56.7
Urinary incontinence during the last month		
No	287	74.4
Yes	99	25.6
Number of self-reported morbidities		
One or none	142	36.8
Two	108	28.0
Three or more	136	35.2
Hospitalisation during the last 12 months		
None	339	87.8
One or more	46	11.9
Number of medical consultations in last 12 months		
None	47	12.2
One or more	338	87.6
Duration of medical consultation		
Less than 15 min	266	68.9
More than 15 min	119	30.8
Prescription of potentially inappropriate medication		
No	265	68.7
Yes	121	31.3
Prescription of five or more medications		
No	307	79.5
Yes	79	20.5
Prescription of five or more medications and a potentially inappropriate medication		
No	346	89.6
Yes	40	10.4

(37.3%) [21] and Portugal (37%) [7]. However, the analyses in both earlier studies included certain PIMs that should be avoided regardless of clinical condition, as well as PIMs for which the appropriateness depends on certain diagnoses. Notably, the prevalence of qualitative polypharmacy in this study was similar to that reported in an investigation of older individuals in São Paulo, Brazil who had private health plans (33.4%), which also analysed PIM regardless of the clinical condition [24].

In this study, 10.4% of the older patients met the definition of qualitative polypharmacy. Previously, a similar finding (9.3%) was reported in an American study [25]. However, that study described polypharmacy as the concomitant

Table 2 Prevalence and prevalence ratio (PR) for the prescription of five or more drugs and the prescription of five or more drugs, including at least one potentially inappropriate medication (PIM), according to the evaluated variables (PIM Project, Brazil, 2017)

Variable	Prescription of five or more medications		Prescription of five or more medications and at least one PIM [§]	
	%	PR (95% CI)	%	PR (95% CI)
Sex				
Male	11.3	1.00	4.8	1.00
Female	24.8	2.19 (1.28–3.76)*	13.0	2.70 (1.16–6.22)*
Age				
60–69 years	21.1	1.00	11.0	1.00
70 years or older	19.8	0.94 (0.63–1.40)	9.6	0.87 (0.48–1.58)
Marital status				
Single	22.8	1.00	12.5	1.00
In a relationship	18.3	0.80 (0.54–1.19)	8.4	0.67 (0.37–1.22)
Skin colour/race				
Not black	20.8	1.00	9.4	1.00
Black	20.5	0.98 (0.63–1.55)	10.6	1.13 (0.58–2.30)
Education (years of study completed)				
0	20.3	1.00	10.5	1.00
1–4 years	19.9	0.98 (0.63–1.54)	11.8	1.13 (0.59–2.13)
5 years or more	22.5	1.11 (0.66–1.87)	7.5	0.72 (0.29–1.77)
Actively employed				
Not working	20.1	1.00	10.2	1.00
Working	22.2	1.10 (0.68–1.80)	11.1	1.09 (0.52–2.27)
Income, minimum wage (MW)				
Less than the MW	28.3	1.00	11.3	1.00
More than the MW	19.6	0.69 (0.43–1.12)	10.4	0.92 (0.41–2.08)
Health plan				
No	20.6	1.00	10.2	1.00
Yes	15.4	0.75 (0.21–2.71)	15.4	1.51 (0.41–5.60)
Cognitive decline				
No decline	23.1	1.00	7.5	1.00
Decline	19.0	0.82 (0.55–1.23)	11.9	1.59 (0.80–3.16)
Physical performance of BADL				
Independent	19.7	1.00	9.6	1.00
Moderately/very dependent	29.0	1.47 (0.82–2.65)	19.4	2.02 (0.92–4.44)
Self-perception of status of health				
Very bad/bad	29.5	1.00	14.8	1.00
Normal	19.3	0.65 (0.42–1.01)	10.4	0.70 (0.37–1.35)
Good/very good	15.4	0.52 (0.30–0.91)*	6.7	0.45 (0.19–1.09)
Pain during the last 3 months				
No	14.6	1.00	6.5	1.00
Yes	23.2	1.58 (0.98–2.56)	12.2	1.87 (0.89–3.94)
Long-range vision				
Blind/bad/very bad	29.4	1.00	14.1	1.00
Normal	23.2	0.79 (0.47–1.32)	12.2	0.86 (0.39–1.89)
Good/very good	16.0	0.54 (0.35–0.85)*	8.2	0.58 (0.29–1.16)
Close-range vision				
Blind/bad/very bad	24.5	1.00	13.8	1.00
Normal	13.8	0.56 (0.29–1.08)	7.5	0.54 (0.22–1.36)
Good/very good	21.2	0.87 (0.56–1.35)	9.9	0.72 (0.37–1.37)
Difficulty sleeping				
No	18.7	1.00	9.8	1.00

Table 2 (continued)

Variable	Prescription of five or more medications		Prescription of five or more medications and at least one PIM [§]	
	%	PR (95% CI)	%	PR (95% CI)
Yes	22.5	1.20 (0.81–1.79)	11.0	1.12 (0.62–2.00)
Experienced a fall after age 60				
No	17.6	1.00	9.4	1.00
Yes	22.8	1.30 (0.86–1.96)	11.0	1.17 (0.63–2.14)
Urinary incontinence during the last month				
No	20.2	1.00	10.5	1.00
Yes	21.2	1.05 (0.67–1.64)	10.1	0.96 (0.49–1.90)
Number of self-reported morbidities				
One or none	7.7	1.00	4.2	1.00
Two	20.4	2.64 (1.33–5.19)*	8.3	1.98 (0.72–5.38)
Three or more	33.8	4.39 (2.36–8.08)*	18.4	4.38 (1.84–10.3)*
Hospitalisation in last 12 months				
None	20.1	1.00	10.6	1.00
One or more	23.9	1.19 (0.68–2.08)	8.7	0.82 (0.31–2.19)
Number of medical consultations during the last 12 months				
None	19.1	1.00	10.6	1.00
One or more	20.7	1.08 (0.50–1.73)	10.4	0.98 (0.40–2.36)
Duration of medical consultation				
Less than 15 min	16.1	1.00	7.9	1.00
More than 15 min	30.3	1.88 (1.28–2.76)*	16.0	2.03 (1.13–3.63)*
PIM [§]				
No	14.7	1.00		
Yes	33.1	2.25 (1.53–3.30)*		

*Significant values ($p < 0.05$); BADL, basic activities of daily life; PR, prevalence ratio; CI, confidence interval; §PIM, potentially inappropriate medication

Table 3 Results from a final multivariate analysis of factors associated with the prescription of five or more medications and the prescription of five or more medications including a potentially inappropriate medication (PIM) (PIM Project, Bahia, Brazil, 2017)

Variable	Prescription of five or more medications	Prescription of five or more medications and at least one PIM [§]
	PR (95% CI)	PR (95% CI)
Duration of the medical consultation		
Less than 15 min	1.00	1.00
More than 15 min	1.44 (1.00–2.10)	1.70 (0.93–3.08)
Number of self-reported morbidities		
One or none	1.00	1.00
Two	2.56 (1.30–5.01)*	1.84 (0.67–5.01)
Three or more	3.89 (2.11–7.18)*	3.95 (1.62–9.52)*
PIM [§]		
No	1.00	–
Yes	2.03 (1.40–2.96)*	

*Significant values ($p < 0.05$), Wald test (Z); §PIM, potentially inappropriate medication; PR, prevalence ratio; CI, confidence interval

use of six or more medications and the presence of at least one PIM. The authors of that study argued that when considering only the numbers of medications, polypharmacy is

associated with a high rate of false positives and does not specify how or whether medications are used inappropriately [25].

In this context, the use of a purely quantitative definition of polypharmacy is controversial because polypharmacy may be appropriately indicated for treating multiple comorbidities, especially in the older population. Such comorbidities include chronic heart failure and diabetes, which require multidrug therapy according to the therapeutic guidelines for these conditions [3, 25]. Data from the present study demonstrate that the use of a quantitative concept of polypharmacy may overestimate the occurrence of this phenomenon. Accordingly, when a qualitative concept was applied, the prevalence of polypharmacy was reduced by half. Several studies have established associations of polypharmacy with important variables, some of which may have exhibited statistical significance; however, these associations did not demonstrate the clinical importance or plausible explanations based on solid scientific evidence [26].

Our data demonstrate that an individual was more likely to be prescribed five or more medications if he or she reported having a greater number of self-reported diseases, and this association was confirmed in our adjusted analysis. A similar relationship was confirmed after the dependent variable was changed to the prescription of five or more medications, including a PIM. This association also remained significant in the final model when the number of morbidities was three or more. As the risk of developing certain clinical disorders increases with age, older people are most affected by chronic diseases [27, 28]. Similar findings were reported in other Brazilian studies [29, 30] as well as in international studies [31–33]. In another Brazilian study carried out in a large city, the prevalence of polypharmacy was 29.5%. This difference can be explained by the different contexts of practice, the medication supplied by the local public health network, and differences in the profile of the assisted population [34].

Some studies have reported associations of the use of multidrug combinations with certain conditions such as diabetes mellitus [34, 35], depression, pain, cardiovascular disease [33–35], chronic obstructive pulmonary disease [35], and endocrine and gastrointestinal disorders [33]. These findings reflect that the various medical conditions present in this population often require multidrug therapy.

The prescription of five or more medications was more frequent among those who also received a prescription for a PIM. This effect was confirmed through an adjusted analysis, indicating an independent association of this variable with the prescription of five or more medications. This result was also confirmed by other previous studies [33, 36].

The strong relationship between the use of five or more medications and PIM has been established clearly in the scientific literature [7, 20, 30, 33, 36]. Some authors [37] emphasised that an examination of the relationship between total medication use and other measures of prescription quality, such as PIM, is important to understand the

appropriateness of multiple medication usage, especially in the most vulnerable populations.

Moreover, evidence suggests that the number of medications may not directly indicate the prescription quality in pharmacological therapy [38]. In other words, reducing the number of drugs would not effectively improve the quality of drug use [37, 38]. Therefore, as the term polypharmacy has a negative connotation in the scientific environment, it would be more appropriate to adopt a broader definition that considers both the numerical measure (i.e., use of five or more medications) and a qualitative perspective reflected by the presence of at least one PIM.

The present study had some limitations, including the impossibility of establishing temporality in observed associations due to the cross-sectional nature of the study. Additionally, only a partial analysis of the list of medications in the Brazilian Consensus on PIM was used [15]. We analysed only the presence of PIM prescriptions independent of clinical conditions, and therefore, our reported prevalence of PIM is likely conservative.

In summary, the prescription of five or more medications was associated with a higher number of self-reported diseases and the prescription of a PIM. However, when we considered the prescription of five or more medications, including a PIM, as a dependent variable, only the presence of at least three self-reported illnesses remained an independent variable. These results are plausible when considered in light of the findings from previous international [31–33] and Brazilian studies [29, 30], which identified the presence of multiple comorbidities as the main predictive factor for polypharmacy.

Conclusion

The prevalence of polypharmacy differed in a comparison of the quantitative and qualitative criteria. Notably, the presence of multiple comorbidities was identified as the main factor associated with the prescription of both quantitative and qualitative polypharmacy. The finding that a reasonable proportion of individuals received a PIM prescription suggests the need for practices that would improve the quality of health care provided to older people. Such practices could include electronic prescriptions provided in the context of clinical support comprising the use of tools to confirm pharmacological therapies, as well as continuing education programs regarding older people health that aim to improve the performance of multi-professional teams employed in healthcare units.

Acknowledgements We would like to thank to all the students who assisted us with the interviews of older patients.

Funding This study was funded by the National Council for Scientific and Technological Development (CNPq), the Foundation for Research Support of the State of Bahia (Fapesb), and the Federal University of Bahia.

Conflicts of interest The authors have no conflicts of interest to declare.

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