

# PREVALENCE OF QUANTITATIVE AND QUALITATIVE POLYPHARMACY IN OLDER ADULTS WITH ALZHEIMER DEMENTIA

## Prevalência da polifarmácia quantitativa e qualitativa em idosos com demência de Alzheimer

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### ABSTRACT

**BACKGROUND:** Polypharmacy can be defined quantitatively or qualitatively. One of the concepts underlying the quantitative definition of polypharmacy is the use of two or more medications. The qualitative definition, in turn, takes into account the rationalization of pharmacotherapy. **OBJECTIVES:** Based on these two concepts, this study aimed to determine the prevalence of polypharmacy in older adults with dementia and correlate it with sociodemographic, clinical, and pharmacological characteristics. **METHODS:** A cross-sectional study was conducted in a center of excellence for dementia care in the Federal District, including 97 older adults with a diagnosis of Alzheimer dementia. Prevalence rates were determined for quantitative and qualitative polypharmacy. The presence of polypharmacy was correlated with the characteristics of the sample by univariate analysis. Descriptive statistics were calculated for all dependent and independent variables. The correlation between secondary variables and polypharmacy was determined by prevalence ratio. Univariate analysis was performed using the following statistical tests: Pearson's  $\chi^2$  test, Kruskal-Wallis test, and Wilcoxon-Mann-Whitney (WMW) test. **RESULTS:** The prevalence of quantitative polypharmacy was 92.8%, of which 37.2% were characterized as minor, 25.8% as moderate, and 29.8% as major. The prevalence of qualitative polypharmacy was 49.5%. Sociodemographic and clinical characteristics were not associated with quantitative or qualitative polypharmacy. **CONCLUSION:** Both quantitative and qualitative polypharmacy were highly prevalent among older adults with dementia. The delivery of multidisciplinary care to older outpatients through a methodology that identifies and characterizes polypharmacy both quantitatively and qualitatively seems to be a useful tool to promote the rational use of medications. **KEYWORDS:** aged; health of the aged; Alzheimer disease.

### RESUMO

**INTRODUÇÃO:** A polifarmácia pode ser classificada como quantitativa e qualitativa. Entre os conceitos para a quantitativa, está a utilização de dois ou mais medicamentos. Por sua vez, a polifarmácia qualitativa considera a racionalização da terapia farmacológica. **OBJETIVOS:** Com base nos dois conceitos apresentados, este estudo objetivou avaliar a prevalência da polifarmácia em idosos com demência e correlacioná-la às características socioclínicas, demográficas e farmacológicas. **MÉTODOS:** Foi realizado um estudo transversal em um centro de referência em demência no Distrito Federal, incluindo 97 idosos com diagnóstico de demência de Alzheimer. Foram identificadas as prevalências da polifarmácia quantitativa e da qualitativa, e, valendo-se da análise univariada, correlacionou-se a presença de polifarmácia às características da população. A estatística descritiva foi calculada para todas as variáveis, as dependentes e as independentes. A correlação entre as variáveis secundárias e a polifarmácia foi determinada pela razão de prevalências. Para a análise univariada, utilizaram-se os seguintes testes estatísticos:  $\chi^2$  de Pearson, Kruskal-Wallis e Wilcoxon-Mann-Whitney (WMW). **RESULTADOS:** A prevalência da polifarmácia quantitativa foi de 92,8%, sendo 37,2% leve, 25,8% moderada e 29,8% grave, e a da qualitativa foi de 49,5%. Analisando-se os dados, as características socioclínicas e demográficas não estiveram associadas nem com a polifarmácia quantitativa nem com a qualitativa. **CONCLUSÃO:** A polifarmácia quantitativa e a qualitativa foram prevalentes entre os idosos com demência. O atendimento ambulatorial multiprofissional aos idosos mediante a metodologia de identificação e qualificação das polifarmácias quantitativa e qualitativa parece ser uma ferramenta útil para promover o uso racional de medicamentos. **PALAVRAS-CHAVE:** idoso; saúde do idoso; Doença de Alzheimer.

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## INTRODUCTION

Currently, 80% of persons older than 65 years have chronic medical conditions that require long-term drug therapy. In addition, complex medical conditions and the presence of comorbidities often involve the use of multiple medications.<sup>1</sup>

Due to conceptual differences in existing definitions, there is a large heterogeneity in the prevalence rates of polypharmacy. A study using a quantitative definition of polypharmacy reported a prevalence of 42% of this problem in older adults.<sup>2</sup> A Finnish study of older persons aged  $\geq 75$  years showed a prevalence of 67% of polypharmacy, defined as  $> 5$  medications in use.<sup>3</sup> A Brazilian study conducted in a long-term care institution found that polypharmacy occurred in 78% of patients.<sup>4</sup>

Few prospective studies have examined predictors of polypharmacy in older adults. Over a 4-year period, Veehof et al.<sup>2</sup> evaluated quantitative polypharmacy in older patients and found that the best predictor of polypharmacy was the number of long-term drugs that a patient used at the start of the study. An also important finding was the detection of an increased risk of polypharmacy in patients with hypertension and atrial fibrillation, who had, respectively, a 37.3 and a 19.6 times higher risk of developing polypharmacy than patients without these disorders.

However, studies focusing mainly on older persons with dementia are still scarce. The present study aimed to determine the prevalence of polypharmacy in older adults with dementia, using both quantitative and qualitative polypharmacy definitions, and correlate it with sociodemographic, clinical, and pharmacological characteristics.

## METHODS

This was a cross-sectional study of older patients with Alzheimer dementia treated by the health care team of the Center for Geriatric Medicine at Hospital Universitário de Brasília (HUB), located in Brasília, the Federal District of Brazil. The study was approved by the Research Ethics Committee of the School of Health Sciences at Universidade de Brasília (UnB) (project number 079/2005; approval number 0261.0.012.000-05 of October 11, 2005).

All older adults seeking care at HUB Center for Geriatric Medicine were screened for eligibility. After obtaining written informed consent, a semi-structured interview was conducted to obtain sociodemographic data, such as age (in years), sex, and level of education (in full years of school attendance), and specific data on pharmacotherapy, such as use of prescription and non-prescription medications, route of administration, adverse events, and simultaneous follow-up by different

medical specialties. Additional data were collected from the patients' medical records.

Eligible participants were all older adults aged  $\geq 60$  years with a diagnosis of cognitive impairment of possible or probable Alzheimer's disease according to the criteria adopted by the American Psychiatric Association in the Diagnostic and Statistical Manual of Mental Disorders, fourth edition (DSM-IV).<sup>5</sup> The severity of dementia was stratified into mild, moderate, and severe according to the Clinical Dementia Rating (CDR) scale.<sup>6</sup> Older patients referred from other health care facilities in the Federal District and those whose caregivers and/or legally authorized representatives refused consent for the patient's participation in the study were excluded.

Polypharmacy was defined and evaluated quantitatively and qualitatively as follows:

- quantitative polypharmacy: defined as the concomitant use of 2 or more medications and characterized as minor (use of 2-3 medications), moderate (use of 4-5 medications), and major (use of  $> 5$  medications);<sup>2</sup>
- qualitative polypharmacy: defined as the prescription, administration or use of more medications than are clinically indicated in a given patient.<sup>7</sup> The implicit method was used for this evaluation, which is characterized by a clinical review of the medications in use taking into account the practices considered appropriate according to a review of the medical literature on the specific disease of the patient.<sup>8</sup> Based on the clinical review of medications, the reasons for polypharmacy were divided into two subcategories: lack of indication and therapeutic duplication.<sup>9</sup>

After determining the prevalence of polypharmacy according to its quantitative and qualitative definitions, epidemiological, social, demographic, and pharmacological variables were examined for possible associations with the prevalence of both quantitative and qualitative polypharmacy.

All regularly scheduled medications taken by the patient and those taken as needed for the treatment of acute illness within 5 weeks before the application of the questionnaire were considered in the analysis. Potentially inappropriate medications in the older population were defined as those whose adverse events outweigh the benefits of treatment, according to the Beers criteria.<sup>10</sup> These same criteria have been recently published in Brazil.<sup>11</sup>

Descriptive statistics were calculated (mean, median, mode, standard deviation, and percentages) for all dependent and independent variables. The correlation between secondary variables and polypharmacy was determined by prevalence

ratio. Statistical analyses were performed using SPSS, version 23.0. Univariate analysis was performed using the following statistical tests: Pearson's chi-square test, Kruskal-Wallis test, and Wilcoxon-Mann-Whitney (WMW) test. The significance level was set at  $p < 0.05$  for all analyses.

## RESULTS

A total of 97 older adults with Alzheimer dementia were included in the study, of whom 69.1% ( $n = 67$ ) were women. Patient age ranged from 60 to 94 years, with a median age of 78 years. The median age was 78 years for women (range, 60 to 94 years) and 79 years for men (range, 65 to 93 years). Age did not differ significantly between women and men ( $p = 0.364$ ). Of the total sample, 49.5% ( $n = 48$ ) had moderate dementia (CDR = 2), 34.0% ( $n = 33$ ) had severe dementia (CDR = 3), and only 16.5% ( $n = 16$ ) had mild dementia (CDR = 1).

The prevalence of quantitative polypharmacy was 92.8% ( $n = 90$ ). In 37.2% ( $n = 36$ ) of cases, polypharmacy was characterized as minor, in 25.8% ( $n = 25$ ) as moderate, and in 29.8% ( $n = 29$ ) as major.

The prevalence of qualitative polypharmacy was 49.5% ( $n = 48$ ). Seventy-eight medications were considered clinically unnecessary, with a median of 1 (range, 1 to 5). In approximately 95% ( $n = 74$ ) of cases, the reason for a medication being considered clinically unnecessary was lack of indication, while therapeutic duplication accounted for 5.1% ( $n = 4$ ) of cases.

After analyzing polypharmacy based on its quantitative and qualitative definitions, we observed that all participants with qualitative polypharmacy ( $n = 48$ ) also had quantitative polypharmacy. Only seven participants did not have polypharmacy, neither quantitative nor qualitative. This difference between groups was statistically significant ( $p = 0.007$ ).

Data on sex, age, education, and income were analyzed in relation to the presence of quantitative and qualitative polypharmacy, but there was no statistically significant difference between the groups (Tables 1 and 2). Regarding the severity of dementia and polypharmacy, there was also no statistically significant difference between the groups ( $p_{\text{quanti}} = 0.129$ ;  $p_{\text{quali}} = 0.065$ ).

## DISCUSSION

In the present study, the prevalence of polypharmacy in older adults with Alzheimer dementia treated in a center of excellence for dementia care was 92.8% and 49.5% for its

quantitative and qualitative definitions, respectively. The high prevalence of quantitative polypharmacy may have resulted from the presence of multiple comorbidities in our older patients with dementia or from the criteria used to identify the problem. A total of 283 medical conditions were identified, with a median of 3 (range, 1 to 8). Despite the

**Table 1** Relationship between the prevalence of quantitative polypharmacy and the sociodemographic and clinical characteristics of older adults with dementia.

Variables	Quantitative polypharmacy (%)				p-value
	No polypharmacy	Minor	Moderate	Major	
Sex*					
Female	6.2	23.7	16.5	22.7	0.515
Male	1.0	13.4	9.3	7.2	
Total (%)	7.2	37.1	25.8	29.9	100
Age* (years)					
60–69	3.1	5.2	4.1	1.0	0.243
70–79	3.1	18.6	11.4	10.2	
≥ 80	2.1	13.4	9.3	18.5	
Total (%)	8.3	37.2	25.8	29.7	100
Education* (years)					
Never studied	0.0	6.3	3.2	5.2	0.813
≤ 3	4.1	18.8	8.4	9.4	
> 3 and ≤ 7	1.0	8.3	4.2	6.2	
> 7 and ≤ 11	1.0	1.0	5.3	3.1	
> 11	1.0	4.2	4.1	5.2	
Total (%)	7.1	38.6	25.2	29.1	100
Income* (MW**)					
≤ 1	1.1	14.9	7.4	7.4	0.168
> 1 and ≤ 5	2.1	14.9	8.5	8.5	
> 5 and ≤ 10	1.1	7.4	7.4	7.4	
> 10	3.2	1.1	3.2	3.2	
Total (%)	7.5	38.3	26.5	27.7	100
Severity of dementia*					
Mild	1.0	7.2	6.2	2.1	0.129
Moderate	4.1	14.4	16.5	14.4	
Severe	2.1	15.5	3.1	13.4	
Total (%)	7.2	37.1	25.8	29.9	100

\*Analyzed by the  $\chi^2$  test; \*\*MW: minimum wage.

differences observed between the prevalence rates for quantitative and qualitative polypharmacy in the current study, the intake of multiple medications may be associated with the consumption of clinically unnecessary medications, since all older adults with qualitative polypharmacy also had quantitative polypharmacy, and this association was statistically significant ( $p = 0.007$ ).

Quantitative polypharmacy was also investigated in older persons with cognitive impairment, with a prevalence

**Table 2** Relationship between the prevalence of qualitative polypharmacy and the sociodemographic and clinical characteristics of older adults with dementia.

Variables	Qualitative polypharmacy (%)		p-value
	No polypharmacy	Qualitative polypharmacy	
<b>Sex*</b>			
Female	37.1	32.0	0.344
Male	13.4	17.5	
Total (%)	50.5	49.5	100
<b>Age* (years)</b>			
60–69	10.3	3.1	0.145
70–79	18.6	24.8	
≥ 80	21.6	21.6	
Total (%)	50.5	49.5	100
<b>Education* (years)</b>			
Never studied	7.2	7.2	0.453
≤ 3	24.7	15.4	
> 3 and ≤ 7	8.2	11.3	
> 7 and ≤ 11	5.3	6.2	
> 11	4.2	10.3	
Total (%)	49.6	50.4	100
<b>Income* (MW**)</b>			
≤ 1	14.9	16.0	0.812
> 1 and ≤ 5	20.2	18.1	
> 5 and ≤ 10	11.7	7.4	
> 10	5.3	6.4	
Total (%)	52.1	47.9	100
<b>Severity of dementia*</b>			
Mild	12.4	4.1	0.065
Moderate	24.7	24.8	
Severe	13.4	20.6	
Total (%)	50.5	49.5	100

\*Analyzed by the  $\chi^2$  test; \*\*MW: minimum wage.

rate 18% lower than that observed in the present study.<sup>12</sup> These authors warned that the lower utilization of medications among older persons with cognitive deficits may represent underuse of medications. Because the present study was conducted in a center of excellence for dementia care, we may assume that there was no underuse of medications, which is supported by the presence of polypharmacy. When qualitative polypharmacy was evaluated in the present study, approximately 5 out of 10 older adults with dementia used at least one medication considered clinically unnecessary. This result is similar to that of previous studies.<sup>9,13,14</sup>

Interestingly, 78 medications were identified as clinically unnecessary in our sample of older adults with dementia, 94.9% due to lack of indication and 5.1% due to therapeutic duplication. Because many of these patients were making their first visit to our center, it is possible that any unnecessary medication use was due to the involvement of several specialists in the previous care of these patients. The literature on this type of analysis is widely scattered. Davis et al.<sup>15</sup> found that 83% of the medications in use lacked a documented indication and 10% duplicated another medication. Conversely, another study conducted in the United States did not find such a high rate of unnecessary medication use. In this study of frail older people, among unnecessary medications, 32% lacked an indication, 18% were ineffective, and 7% were duplicated.<sup>14</sup>

The lack of explicit criteria for identifying qualitative polypharmacy and the fact that this involves a subjective analysis impair the reproducibility of this concept. In the present study, the method used to identify the presence of qualitative polypharmacy in older patients included the identification of medications that were indicated without documented diagnosis of the patient's medical condition and duplication of medications that are used for the same therapeutic indication. A third parameter could have been included in our method to identify polypharmacy qualitatively: an approach involving medication effectiveness, as performed by Hajjar et al.,<sup>14</sup> but this analysis was not possible because of the cross-sectional nature of the present study. Nevertheless, an advantage of the method used in the present study is that it allowed us to evaluate medications in the clinical context of each older patient. Differences between reported prevalence rates may be explained by the lack of a standardized methodology for the evaluation of qualitative polypharmacy.

In the present study, no statistically significant association was found between both quantitative and qualitative polypharmacy and patients' sociodemographic and clinical characteristics (sex, age, education, income, and severity of

dementia). This possibly demonstrates that, in this population, medical indication may have been a determining factor in the occurrence of polypharmacy. Similar results were found by Rossi et al.<sup>9</sup> and Flores and Mengue<sup>16</sup> in older adults when analyzing quantitative polypharmacy in relation only to social characteristics and age groups. Conversely, conflicting results were found by Hajjar et al.,<sup>14</sup> who reported a positive association between qualitative polypharmacy and older patients' age and level of education. Their study had the strength of being a cohort study. In the same vein, Veehof et al.<sup>2</sup> found that only age accounted for the increased consumption of medications among older persons.

The present study has some limitations. First, the cross-sectional nature of the study precludes causal inferences. Also, convenience sampling may have led to the selection of a very homogeneous patient group, taking the research setting away from the Brazilian reality. Finally, the very criteria for polypharmacy are still a matter of debate in the literature.

Prophylactic measures may be taken to minimize polypharmacy in older persons with dementia. One of the problems identified is the lack of regular review of medications, as suggested by Zermansky et al.,<sup>17</sup> who showed that 72% of medical prescriptions are not regularly reviewed for

adequacy of dose or dosage. In this respect, the qualitative analysis of polypharmacy represents an important approach and a differential advantage in the follow-up of patients with Alzheimer dementia.

## CONCLUSIONS

In the present study, the prevalence of quantitative polypharmacy in older adults with dementia treated in a center of excellence for dementia care was 92.8%, while qualitative polypharmacy was present in 49.5% of patients. Sociodemographic and clinical characteristics were not associated with polypharmacy.

Prospective studies are needed to more clearly define the critical stages of the polypharmacy process and thus develop assistance tools aiming to improve the quality of pharmacotherapy and to minimize the vulnerability of older persons with dementia to medication errors and other adverse drug reactions due to polypharmacy.

## CONFLICT OF INTERESTS

The authors declare no conflict of interests.

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