

Complexity of pharmacotherapeutic regimens for older adults in primary care in Brazil: a cross-sectional study

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Abstract

Aims: Adherence to prescribed treatment is important for obtaining the desired outcomes in older people care. Polypharmacy is strictly associated with adherence, and complex pharmacotherapy can lead to poor adherence and unexpected outcomes, which are aggravated by older age. The medication regimen complexity index has been proven to be a valid and reliable tool for quantifying the complexity of medication regimens. The objective of the present study was to evaluate the therapeutic complexity of drugs used by older people in a primary care setting in Brazil. **Methods:** This was a cross-sectional study conducted in 22 basic health units in Brazil. Older people from this sample who were treated in a primary care setting were interviewed after a consultation with a family practice physician. Data were collected from September 2016 to March 2019. Patients aged ≥ 60 years who visited the primary care units were included in the study. Pharmacotherapeutic complexity was assessed according to the medication regimen complexity index. **Results:** In all, 675 individuals with a mean age of 70 years (± 7.1 years) were included. The mean number of drugs prescribed per capita was 2.9 (± 1.8). The median medication regimen complexity index for the sample was 8.0, and 26.1% of the patients interviewed had a high medication regimen complexity index. **Conclusion:** The complexity of the drug regimen was high in almost one-third of the prescriptions analysed. This high complexity might contribute to non-adherence to medication regimens, leading to safety- and effectiveness-related issues. **Key words:** drug prescriptions, geriatrics, pharmaceutical preparations, polypharmacy, primary health care, older patient.

Introduction

Lifestyle, biological decline, and socioeconomic conditions hinder older patients' ability to recover from illness and compromise daily functions to different degrees ¹. Thus, polypharmacy and prolonged treatments are common among older people ². Polypharmacy could cause adverse events, especially in older people². However, the quantity factor is not the only associated with the negative events of pharmacotherapy; complexity has been known to influence treatment adherence and lead to unexpected outcomes ³. The medication regimen complexity index (MRCI) has proven to be a valid and reliable tool for quantifying the complexity of medication regimens ⁴. It comprises direct evaluation of the factors necessary for drug administration, including dosage forms, number of daily doses, and instructions for use. Treatment adherence decreases as the complexity of the medication regimen increases; therefore, complexity is considered one of the main causes of treatment non-adherence ². The risk of adverse effects, and at the same time, the need for complex

pharmacotherapeutic schemes in older patients requires preventive actions.

Aim of the study

The present study was aimed at evaluating the therapeutic complexity of drugs used by older people in primary care settings in Brazil.

Method

This was a cross-sectional study conducted in 22 public basic health units in the municipality of Vitória da Conquista, Bahia, Brazil. Data were retrieved from a randomized clinical trial titled *Development and evaluation of a mobile application for supporting the prescription of appropriate medications to the elderly*. These units are part of the Brazilian healthcare system. Data were collected from September 2016 to March 2019 by using a multidimensional questionnaire adapted from an instrument used in a project named Health, Wellbeing, and Aging in Latin America and the Caribbean⁵. A digital data collection platform (*Kobotoolbox*®) was used to administer the questionnaire. Interviews were conducted in two different moments: prior and after their appointment. All patients aged 60 years or older, that were in the waiting room of the primary care facilities, were included in the study only after accepting and signing informed consent. Patients without a medical prescription, unaccompanied patients with hearing and/or severe cognitive impairments, or accompanied by a caregiver that could not answer the questionnaire were not included in the study.

The assessment of pharmacotherapeutic complexity was performed according to the MRCI⁴ divided into three sections: the first (A) pertained to correspondence to information on dosage forms; the second (B) pertained to the frequency of doses; and the third (C) pertained to additional information, such as specific times and use with food. Drugs with more than one instruction, as described in the *Medscape*® database and/or leaflet consultations, were scored for each aspect. The cut-off points for MRCI used to distinguish complexity were as follows: values of <2.7 were considered very low; 2.7 to 5.0 as low; 5.0 to 12.0 as average; 12.0 to 24.5 as high; > 24.5 as very high⁶. The sociodemographic parameters included in the assessment were education level and skin colour (white vs. other). The clinical and functional parameters assessed were cognitive impairment (assessed using the Mini-Mental State Examination⁷, considering different cut-off points according to educational level), self-reported hearing impairment and polypharmacy (characterized as five or more drugs in a prescription)⁸.

The data was analysed using SPSS version 27 (serial number 10101161149). To perform prevalence ratio (PR) the R statistical software was used. To summarise results, descriptive analyses of the variables were executed. The association between categorical variables and the strength of the association were determined by chi-square teste and PR. The level of statistical significance adopted was a P value <0.05 and a 95% confidence interval.

Results

We interviewed 854 older patients, 179 were excluded due to absence of a prescription after medical consultation, totalling 675 interviewed individuals, with a mean age of 70 years (± 7.1 years). Of the patients included, 69.2% were women, 24% had white skin colour, and 41% did not attend school (Table 1). Cognitive impairment was found in 65.9% of older patients; 34.1%, 12.4%, and 90.7% of the patients reported hearing deficits, hospitalisation in the last year, and noncommunicable diseases (NCD), respectively.

[Insert Table 1]

The mean number of drugs prescribed per capita was 2.9 (± 1.8). In terms of the dosage form, capsules/tablets for oral use were the most prescribed (88.5%). Regarding dosage frequency, the most common was once daily (57.6%). The most identified instructions for use were take/use at specified time/s (69.3%) and relation to food (18.3%) (Table 2).

[Insert Table 2]

Regarding MRCI, the section on dose frequency had the greatest influence on the score, with a median of 4.0. The sample was considered to have an average MRCI, with a median value of 8.0 (Table 3).

[Insert Table 3]

In this sample, 26.1% of the participants had a high MRCI (Table 4).

[Insert Table 4]

Discussion

In this study, we evaluated the pharmacotherapeutic complexity of drug regimens used by older people in primary care settings in Brazil based on the MRCI. We found that almost one-third of the prescriptions were associated with a high MRCI. Although this index does not have established cut-off points, several studies have investigated its relationship with negative health outcomes and the need for intervention^{6,9}. A high MRCI (>20.0) has been associated with older age, more comorbidities, better cognitive status, higher prevalence of self-reported pain, impaired dexterity, and greater likelihood of receiving help for using their drugs¹⁰. Additionally, in institutionalised and hospitalised older people, the mean MRCI was 30.27 and 18.2, respectively^{6,9}.

The level of pharmacotherapeutic complexity has been associated with the number of clinical conditions, number of drugs, and polypharmacy⁶. Polypharmacy and higher medication complexity have been associated with medication non-adherence rates in 50% of older patients³. In our study, 90.7% of patients had NCD and 2.5% received medication regimens with very high complexity; polypharmacy was identified in 18.9% of the patients. These findings are similar to those obtained in older patients in a hospital context, suggesting a need for the attention and review of the drugs used⁶. Higher complexity might be related to the aspects of older people care, such as more complex dosage forms, more frequent dosing, and higher consumption of drugs.

Although older adults with high pharmacotherapeutic complexity are commonly found in health facilities with higher complexity of care, the individuals in this study were those in primary care settings, of which 28.6% had high and very high MRCI. Among them, 37.2% did not know how to use at least one prescribed drug, 66.3% presented with some degree of cognitive impairment, and 35.2% had hearing impairment. Solid oral dosage forms and once or twice daily dosing were more frequent among our patients, which could be related to greater availability of these dosage forms and the intention to provide better therapeutic comfort in terms of the dosing schedule⁶. The scores obtained for the section on dose frequency indicated that the section had the maximum impact on the final score of the MRCI¹¹. In another study conducted among patients in primary care settings, a similar result (median = 8.5) was obtained for the complexity index⁶. Although the two studies are comparable in terms of population, in the cited study, scores were assigned for the instructions for use section only to what was prescribed, which may compromise the estimation of the actual pharmacotherapeutic complexity and affect the quality of prescriptions. The additional instructions complement the necessary information for the appropriate use of drugs and converge approximate the results of MRCI to the real challenges of pharmacotherapy follow-up that must be addressed by health professionals at all levels of care. This suggests that even in primary care settings, it is important to review aspects of pharmacotherapy and other factors such as dosage forms, frequencies, and instructions in prescriptions to reduce pharmacotherapeutic complexity. The optimization of drug prescription in this population is a priority due to the significant clinical and economic costs of drug-related complications.

Strengths and limitations

This study has several potential limitations. This study is a secondary analysis of the baseline data from another study, which was not designed for our specific objectives. Furthermore, a non-probability sampling procedure was used, and some data were obtained through self-reporting. We did not explore other prescriptions and over the counter drugs.

Conclusion

The complexity of the drug regimen was high in almost one-third of the prescriptions analysed. This high complexity might contribute to non-adherence to medication regimens, leading to safety- and effectiveness-related issues. Certainly, there is potential for pharmacists' intervention to reduce the complexity as part of the medication review routine. The MRCI proved to be a useful tool in identifying factors that contribute to treatment difficulties.

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Ethics

This study was performed according to the tenets of the Declaration of Helsinki. The study protocol (technical opinion number 378.198) was approved by the Research Ethics Committee of the Multidisciplinary Health Institute of Federal University of Bahia. The patients signed an informed consent form.

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Disclosures

The authors declare that they have no conflicts of interests.

References

1. Galvão O, Ferreira L, Maciel SC, et al. Active Aging and Its Relationship To Functional. *Text Context Nurs* . 2008;21(3):513-518.
2. González-Bueno J, Calvo-Cidoncha E, Sevilla-Sánchez D, Molist-Brunet N, Espauella-Panicot J, Codina-Jané C. Patient-centered prescription model to improve therapeutic adherence in patients with multimorbidity. *Farm Hosp* . 2018;42(3):128-134. doi:10.7399/fh.10961
3. Hajjar ER, Cafiero AC, Hanlon JT. Polypharmacy in elderly patients. *Am J Geriatr Pharmacother* . 2007;5(4):345-351. doi:10.1016/j.amjopharm.2007.12.002
4. George J, Phun YT, Bailey MJ, Kong DCM, Stewart K. Development validation of the medication regimen complexity index. *Ann Pharmacother* . 2004;38(9):1369-1376. doi:10.1345/aph.1D479
5. Lebrão ML, Laurenti R. Saúde, bem-estar e envelhecimento: o estudo SABE no Município de São Paulo. *Rev Bras Epidemiol* . 2005;8(2):127-141. doi:10.1590/S1415-790X2005000200005
6. Ferreira JM, Galato D, Melo AC. Medication regimen complexity in adults and the elderly in a primary healthcare setting: Determination of high and low complexities. *Pharm Pract (Granada)* . 2015;13(4):1-9. doi:10.18549/PharmPract.2015.04.659
7. Bertolucci PHF, Brucki SMD, Campacci SR, Juliano Y. O Mini-Exame do Estado Mental em uma população geral: impacto da escolaridade. *Arq Neuropsiquiatr* . 1994;52(1):01-07. doi:10.1590/S0004-282X1994000100001
8. Gomes MS, Amorim WW, Morais RS, et al. Polypharmacy in older patients at primary care units in Brazil. *Int J Clin Pharm* . 2019;41(2):516-524. doi:10.1007/s11096-018-00780-5
9. Lino VTS, Pereira SRM, Camacho LAB, Ribeiro Filho ST, Buksman S. Cross-cultural adaptation of the Independence in Activities of Daily Living Index (Katz Index). *Cad Saude Publica* . 2008;24(1):103-112. doi:10.1590/s0102-311x2008000100010

10. Wimmer BC, Johnell K, Fastbom J, Wiese MD, Bell JS. Factors associated with medication regimen complexity in older people: A cross-sectional population-based study. *Eur J Clin Pharmacol* . 2015;71(9):1099-1108. doi:10.1007/s00228-015-1883-2

11. Remondi FA, Cabrera MAS, de Souza RKT. Não adesão ao tratamento medicamentoso contínuo: Prevalência e determinantes em adultos de 40 anos e mais. *Cad Saude Publica* . 2014;30(1):126-136. doi:10.1590/0102-311X00092613

Tables

Table 1. Sociodemographic and clinical characteristics of participants together and separate by Medication Regimen Complexity Index (n = 675) (2016-2019)

Characteristics MRCI ⁺	Characteristics MRCI ⁺	Characteristics MRCI ⁺	Characteristics MRCI ⁺	Univariate analysis
		Very low to Average 71.4% (482)	High to very high 28.6% (193)	PR (95% CI) P value -
Distribution of patients	Distribution of patients			
Sex				
Female	69.2% (467)	68.5% (330)	71% (137)	1.09 (0.84, 1.42) 0.52
Male	30.8% (208)	31.5% (152)	29% (56)	1.0
Skin colour				
White	24% (160)	22.9% (109)	26.6% (51)	1.0
Other (such as Black, and Brown)	76% (507)	77.1% (366)	73.4% (141)	0.87 (0.67, 1.14) 0.32
Education level				
Illiterate	41% (268)	40.9% (191)	41.4% (77)	1.01 (0.79, 1.30) 0.91
Literate	59% (385)	59.1% (276)	58.6% (109)	1.0
Clinical characteristics				
NCD⁺⁺				
Yes	90.7% (612)	90.2% (435)	91.7% (177)	1.14 (0.73, 1.77) 0.56
No	9.3% (63)	9.8% (47)	8.3% (16)	1.0
Cognitive impairment				
Yes	65.9% (444)	65.7% (316)	66.3% (128)	1.02 (0.79, 1.31) 0.88
No	34.1% (230)	34.3% (165)	33.7% (65)	1.0
Hearing impairment				
Yes	34.1% (230)	33.7% (162)	35.2% (68)	1.05 (0.82, 1.35) 0.70
No	65.9% (444)	66.3% (319)	64.8% (125)	1.0
Misunderstanding of medication dosage regimen instructions				

Characteristics MRCI ⁺	Characteristics MRCI ⁺	Characteristics MRCI ⁺	Characteristics MRCI ⁺	Univariate analysis
Yes	36,2% (242)	35.8% (171)	37.2% (71)	1.04 (0.82, 1.34)
No	63.8% (427)	64.2% (307)	62.8% (120)	0.73
Hospitalization in the last year				1.0
Yes	12.4% (84)	12.4% (60)	12.4% (24)	1.00 (0.70, 1.43)
No	87.6% (591)	87.6% (422)	87.6% (169)	1.00
				1.0

⁺MRCI: Medication Regimen Complexity Index; ⁺⁺NCD: non-communicable disease

Table 2. Characteristics of pharmacotherapy for Medication Regimen Complexity Index calculation (2016-2019)

Characteristics	MRCI ⁺	Drugs % (n)
Section A: Dosage forms (n = 1972)		
Oral		
Capsules/tablets	1	88.5 (1746)
Liquids	2	4.5 (89)
Powders/granules	2	0.2 (4)
Topical		
Creams/gels/ointments	2	2.6 (51)
Paints/Solutions	2	0.1 (1)
Ear, eye, and nose		
Ear drops/creams/ointments	3	0.2 (3)
Eye drops	3	0.2 (4)
Nasal spray	2	0.4 (7)
Inhalation		
Aerolizers	3	0.3 (6)
Metered dose inhalers	4	0.7 (14)
Nebuliser	5	0.2 (4)
Others dry-powder inhalers	3	0.1 (1)
Others		
Injections: Prefilled	3	0.9 (17)
Injections: Ampoules/Vials	4	1.0 (19)
Suppositories	2	0.1 (2)
Vaginal creams	2	0.2 (4)
Section B: Dosing frequency (n = 1972)		
Once daily	1	57.6 (1136)
Twice daily	2	27.3 (539)
Three times daily	3	8.8 (173)
Four times daily	4	3.3 (65)
On alternate days or less frequently	2	3.0 (59)
Section C: Additional directions (n = 1969) ⁺⁺		
Break or crush tablet	1	0.1 (2)
Dissolve tablet/powder	1	0.3 (5)
Multiple units at one time (e.g. 2 tablets, 2 puffs)	1	2.7 (53)
Take/use at a specified time/s (e.g. morning, night, 8 AM)	1	69.3 (1364)

Characteristics	MRCI ⁺	Drugs % (n)
Relation to food (e.g. with food)	1	18.3 (360)
Take with specific fluids	1	0.2 (4)
Take/use as directed	2	9.2 (181)

⁺MRCI: Medication Regimen Complexity Index; ⁺⁺medicines with more than one instruction were scored for each instruction.

Table 3. Medication Regimen Complexity Index scores distributed by sections (2016-2019)

MRCI ⁺	Median	Interquartile range	Minimum	Maximum
Dosage forms	1.0	1.0	0	13.0
Dosing frequency	4.0	4.0	0.5	20.0
Additional directions	2.0	4.0	0	16.0
MRCI ⁺ final score	8.0	7.0	2.0	39.0

⁺MRCI: Medication Regimen Complexity Index

Table 4. Categorized Medication Regimen Complexity Index⁺ (2016-2019)

Classification	Total MRCI score	Frequency % (n)
Very low MRCI ⁺	≤2.6	2.2% (15)
Low MRCI ⁺	2.7–5.0	27% (182)
Average MRCI ⁺	5.1–11.9	42.2% (285)
High MRCI ⁺	12.0–24.5	26.1% (176)
Very high MRCI ⁺	>24.6	2.5% (17)
⁺ MRCI: Medication Regimen Complexity Index	⁺ MRCI: Medication Regimen Complexity Index	⁺ MRCI: Medication Regimen Complexity Index