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## Original Research

# Medication regimen complexity in adults and the elderly in a primary healthcare setting: determination of high and low complexities

Juliana M. FERREIRA, Dayani GALATO, Angelita C. MELO.

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### ABSTRACT\*

**Background:** The complexity of a medication regimen is related to the multiple characteristics of the prescribed regimen and can negatively influence the health outcomes of patients.

**Objective:** To propose cut-off points in the complexity of pharmacotherapy to distinguish between patients with low and high complexities seen in a primary health care (PHC) setting to enable prioritization of patient management.

**Methods:** This is a cross-sectional study, which included 517 adult and elderly patients, analyzing different cut-off points to define the strata of low and high pharmacotherapy complexities based on percentiles of the population evaluated. Data collection began with the solicitation of prescriptions, followed by a questionnaire that was administered by an interviewer. The complexity of a medication regimen was estimated from the Medication Regimen Complexity Index (MRCI). High complexity pharmacotherapy scores were analyzed from patient profiles, the use of health services, and pharmacotherapy. The criteria for subject inclusion in the sample population were as follows: inhabitant of the area covered by the municipality, 18 years or older, and being prescribed at least one drug during the collection period. Exclusion criteria at the time of collection were the use of any medication whose prescription was not available. All medications were accessed through the Primary Healthcare Service (PHS).

**Results:** The median total pharmacotherapy complexity score was 8.5. High MRCI scores were correlated with age, medications taken with in the Brazilian PHS, having at least one potential drug-related problem, receiving up to eight years of schooling, number of medications and polypharmacy (five or more medicines), number of medical conditions, number of medical appointments, and number of cardiovascular diseases and endocrine metabolic diseases. We suggest different complexity tracks according to age (e.g., adult or elderly) that consider the pharmacotherapy and population coverage characteristics as high complexity limits. For the elderly patients, the tracks were as follows:  $MRCI \geq 25.4$ ,  $MRCI \geq 20.9$ ,  $MRCI \geq 17.5$ ,  $MRCI \geq 15.7$ ,  $MRCI \geq 14.0$ , and  $MRCI \geq 13.0$ . For adult patients, the limits of high complexity were  $MRCI \geq 25.1$ ;  $MRCI \geq 23.8$ ;  $MRCI \geq 21.0$ ;  $MRCI \geq 17.0$ ;  $MRCI \geq 16.5$ ; and  $MRCI \geq 15.5$ .

**Conclusion:** The medication regimen complexity is associated with the patient's illness profile and problems with the use of drugs; therefore, the proposed scores can be useful in prioritizing patients for clinical care by pharmacists and other health professionals.

**Keywords:** Drug Administration Schedule; Pharmaceutical Preparations; Polypharmacy; Pharmacoepidemiology; Brazil

### INTRODUCTION

The existence of higher-complexity therapies is related to recent changes in the epidemiological profile and the wide availability of drugs on the market, as pharmacotherapy is the main therapeutic tool to cure and control diseases.<sup>1,2</sup> Several studies have evaluated the negative effect of a high medical regimen complexity in treating different diseases and specific population groups.<sup>3-5</sup> However, the complexity of pharmacotherapy has various definitions, despite being related to a regimen's characteristics.

The Medication Regimen Complexity Index (MRCI) was developed by George *et al.* (2004)<sup>6</sup> and validated in Portuguese version in 2007 by Melchior *et al.*<sup>1</sup> in order to standardize a method to quantify this attribute. This index assumes that factors, such as dosage form, dose frequency, and additional instructions that direct the mode of use, contribute to the complexity.<sup>6</sup> This index has shown satisfactory validity for classifying the regimen complexity over a simple medication count, with application to clinical research.<sup>7</sup>

Despite the time elapsed since the development of the MRCI, scores have not yet been established that define its relationship with patient profiles and also problems with a pharmacotherapy, which therefore affect its utility in prioritization of patients to a pharmacist or other healthcare professional. The aim of this study was to propose different MRCI index score ranges and to analyze the relationship of the strata of high complexity pharmacotherapies with patient characteristics and potential health problems in an adult population in a primary healthcare setting.

### METHODS

In this part of the study, we analyzed MRCI score tracks and their characteristics. The original study was a cross-sectional, population-based research study that examined pharmacotherapy in primary health care (PHC) patients in a medium-size city in the central-western portion of the Brazilian state of Minas Gerais. Minas Gerais is the second most populous Brazilian state, as well as being the third most economically important state. Additionally, the

\* **Juliana M. FERREIRA.** Pharmacy Department, Federal University São João Del-Rei. Divinópolis, MG (Brasil). ju.mirandaferreira@gmail.com

**Dayani GALATO.** Pharmacy Department, University of Brasília. Brasília (Brazil). dayani.galato@gmail.com

**Angelita C. MELO.** Pharmacy Department, Federal University São João Del-Rei. Divinópolis, MG (Brasil). angelitamelo@ufsj.edu.br

city under study serves as a regional hub for health care for 55 cities.

In the original study, the sampling parameters included 4% accuracy, 5% statistical significance and an outcome occurrence of non-adherence to therapy rate of 36.8%<sup>8</sup>, and it included 427 individuals. This 20% was added to the total, due to stratifications and possible losses, resulting in 517 patients who were interviewed. For the patient selection, this sample was proportional to the dispensation amount in one of five public pharmacies. The patients were selected by a random draw. The original sample size was 80.97% of power, with continuity correction, to compare adult and elderly patients.

Data collection was conducted using a structured and coded instrument by Pharmacy scholars who trained under the supervision of a Pharmacist between May-June 2012 on weekdays at different times. This began with the solicitation of patient prescriptions (all of which were conducted by hand), followed by a questionnaire that was administered by an interviewer who subsequently guided the patient on how to use the drugs. In the Brazilian PHS system, electronic prescriptions were not used.

The criteria for subject inclusion in the sample were as follows: inhabitant of the area covered by the municipality, 18 years of age or older, and having been prescribed at least one drug during the collection period. The exclusion criteria were as follows: the person who was interviewed was not the patient (removal of medication by a third party) or the patient was using medication whose prescription was not available for consultation.

The dependent variable was the total pharmacotherapy complexity score, which was evaluated directly from a patient's prescriptions, with reference to the MRCI.<sup>6</sup> We analyzed all of the patients' active prescriptions at the time of data collection. Prescriptions from the PHS could be dispensed over a six-month period.

The MRCI is an instrument used to measure a treatment regimen complexity for an individual patient, and it is divided into three sections: A, B, and C. Section A corresponds to the information on the dosage forms; section B includes information regarding the dose frequency; and section C corresponds to additional information, such as specific times and use with food.<sup>3,6</sup> In this last section, if a prescription did not include instructions, then we did not attribute a value score. Each section is scored based on the pharmacotherapy analysis of the patient, and the complexity index was obtained by summing the points (scores) of the three sections. The median of the total score and separate scores percentiles were estimated in order to determine what would be the cut-off points to categorize patients with a usual complexity, as well as low and high pharmacotherapy complexities.

The percentiles that were used as range limits were as follows: a) P2.5 and P97.5 (95% of the patients had usual complexities); b) P5.0 and P95.0 (90% had usual complexities); c) P10 and P90 (80% had

usual); d) P15 and P85 (70% had usual complexities); e) P20 and P80 (60% had usual complexities); f) P25 and P75 (50% had usual complexities).<sup>9</sup>

The independent variables that were collected were patient related, which included age (65 years or over), gender, years of schooling, number of clinical conditions, presence of cardiovascular or endocrine metabolic disease, number of medical appointments (year before interview) and medicines, and polypharmacy (usage of five or more medications)<sup>10-12</sup>, all medications were accessed through the PHS, having at least one potential drug-related problem (PDRP)<sup>13</sup>, and self-reported adherence. In the PDRP analysis, we took the following into consideration: 1) the patient's clinical conditions and medicines in use, 2) the presence of potential drug interactions of clinical importance, 3) the therapeutic range of the drug, and 4) self-reported adherence. The dosages were analyzed with Micromedex.<sup>14</sup>

The collection of self-reported adherence information was carried out for each medication with the question: "Patients often forget to take their medications. How often can you follow the dosage instructions of this medicine?" The answer was collected on the Likert scale ("every time", "most often", "sometimes", "almost no time", or "never"). For the purpose of this analysis, the membership report for each drug was grouped into an adherence if a patient made use of the drug "every time" and "in most cases" and did not adhere to other alternatives. Non-adherence to pharmacotherapy (all drugs) was categorized as reported noncompliance with at least one drug in the regimen. For those patients starting pharmacotherapy, the first prescription and medication adherence could not be evaluated; therefore, it was assigned the code 'does not apply'.

The information analysis consisted of descriptive statistics with median, percentile, and proportion estimates. To evaluate the association between the complexity scores and explanatory variables, we adopted the chi-squared test with the Bonferroni correction and a statistical significance of 5%. Correlations were evaluated with the Spearman correlation coefficient. Multivariable analysis was conducted with the Statistical Learning Theory with the Pearson's chi-square test and Bonferroni adjustments. This analysis, although it is very scarce, is helpful for profile determinations and cut-off estimations. The parameters included the exhaustive CHAID (chi-squared automatic interaction detector) algorithm, a statistical significance of 5.0%, a total of 50 cases in the parent node and 30 cases in the child node, and up to three hierarchical levels, as well as cross-validation by 10 sub folds. For constructing the database and analyses, the SPSS program was used.

This study was conducted in accordance with ethical standards, and it was approved by the Ethics Committee on Human Research of the Hospital São João de Deus under the number, 154/2011.

Table 1. Adults and elderly characteristics attending the PHC of a midsize city of Minas Gerais, 2012.

Characteristics	Adults (n=363)		Elderly (n=149) <sup>5</sup>	
	% (n)	p value <sup>4</sup>	% (n)	p value <sup>4</sup>
Socio-demographic				
Female	79.1 (287)	>0.05	61.1 (91)	>0.05
Studied for up to 8 years	57.9 (210)	>0.05	73.1 (109)	>0.05
Lives with a partner	56.2 (204)	>0.05	52.1 (78)	>0.05
Number of inhabitants per household <sup>1</sup>	3.0 (2.0;4.0)	>0.05	2.0 (2.0;4.0)	>0.05
Clinical conditions				
Diseases <sup>1</sup> P <sub>50</sub> (P <sub>25</sub> ; P <sub>75</sub> ) <sup>2</sup>	2.0 (1.0;3.0)	<0.01	3.0 (2.0;4.0)	<0.01
Cardiovascular diseases <sup>1,2</sup>	1.0 (1.0;1.0)	=0.04	1.0 (1.0;1.0)	>0.05
Endocrine & metabolic diseases <sup>1,3</sup>	1.0 (1.0;2.0)	<0.01	1.0 (1.0;2.0)	>0.05
Access and use of health care services				
Private Health care assistance	69.1 (251)	>0.05	57.7 (86)	>0.05
All medicines were accessed by PHS	89.5 (325)	0.01	88.6 (132)	>0.05
Medical appointments <sup>1</sup>	3.0 (2.0;5.0)	>0.05	3.0 (2.0;4.0)	>0.05
Pharmacotherapy				
Number of medicines <sup>1</sup>	3.0 (2.0;4.0)	<0.01	4.0 (3.0;5.0)	<0.01
Polypharmacy	21.2 (77)	<0.01	38.9 (58)	<0.01
PDRP <sup>b</sup>	50.1 (182)	<0.01	60.4 (90)	<0.01
Adherence	72.5 (263)	>0.05	78.5 (117)	>0.05

<sup>1</sup>Median (Percentile 25; Percentile 75); <sup>2</sup>n adults=166; n Elderly=95; <sup>3</sup>n adults=244; n elderly=124;

<sup>4</sup>Pearson's chi-square with Bonferroni adjustment; <sup>5</sup>Five patients did not know their birthday date

## RESULTS

For the 517 patients in the PHC, in general, the majority were females (73.5%), the median age was 57.2 years (range 18-86 years), and a median of up to three years between medical appointments took place. Most had no consultations with a pharmacist in the last year (78.3%) (data not shown in the table).

The adult and elderly patient characteristics are presented in Table 1. Most patients in both groups were women, received up to 8 years schooling, and lived with a partner. The median inhabitants per household were larger for the adult patients than for the elderly. As expected, the median disease number for the elderly patients was largest. The cardiovascular and endocrine metabolic disease medians were the same for both groups. In relation to access and use of health care services in both groups, most of the patients had PHC assistance, they had a median of three medical appointments in the last year, and they accessed all medications through the PHS. Polypharmacy represented the smallest percentage while presence of PDRP and adherence represented the largest percentages. For the adult patients, the characteristics with statistically significant complexity score differences included presence of cardiovascular disease, endocrine metabolic disease, medication number, polypharmacy and PDRP. For the elderly patients, the dependent variables were clinical condition number, medication number, polypharmacy and PDRP.

The 517 patients had 1,788 medications in their prescriptions, a per capita consumption of 3.5 drugs. By analyzing the complexity of these medications by MRCI<sup>6</sup>, we observed that Section A provided the most complete prescription record (100% information). In contrast, in Section C, there was little record of instructions to the patient, which included only 255 instances (for approximately 14.3% of drugs) (Table 2).

Section A identified that the oral route of administration and 'tablet or capsule' pharmaceutical form occurred in 95.1% (n=1701) of

the medications. No prescriptions for ophthalmic and rectal routes were observed. Four of the 1,788 medicines prescribed did not have any Section B information. In this section, the majority of registered dosages were 'once a day' (61.0% of the medications, n=1,088). In Section C, there were few written records (approximately 14.3% of the drugs included written records). The most frequent additional instruction, in Section C, was 'relationship with food', which was found in 60.0% of the instructions (n=153) (Table 2).

The different samples included a curve that provided the limits for low and high complexities from the percentile definitions. These are shown in Table 3. The low complexity MCRI values for the adult patients had a minimum value of 2.0 and a maximum of 4.5. For the elderly patients, the minimum and maximum low complexity MRCI values were 2.0 and 7.0, respectively. The high complexity MCRI values for the adult patients had tracks of 13.0 to 25.4. For the elderly patients, the minimum track value was 15.5, and the maximum value was 25.1.

The MCRI profiles for sections A, B, and C for the different high complexity cut-offs can be observed in Table 3. For Section A, a direct proportional relationship between the high complexity scores (MRCI $\geq$ 13.5 up MRCI $\geq$ 25.0) and the drug numbers was observed, as well as the proportion of topical dosage forms, such as 'cream', 'gel', 'ointment', 'tincture', 'solution' and 'vaginal cream'. In Section C, the most common instruction to the strata was a high complex 'relationship with food'. We observed a direct relationship between the high complexity scores and the frequency of the instruction to 'decrease/increase dose gradually' (Table 4).

In Tables 5 and 6, the proposed high complexity score tracks for the adult and elderly patients, respectively, are correlated with some patient and pharmacotherapy characteristics. In Table 5, the adult patients of the proposed high scores were mostly women who received up to eight years of schooling and had a cardiovascular disease median of 1. The median clinical conditions and drug

Table 2. Pharmacotherapy characteristics of patients attending the PHC of a midsize city of Minas Gerais, 2012			
Characteristics		Scores MRCI <sup>1</sup>	Medicines % (n)
<b>Section A: Dosage forms (n= 1788)</b>			
<b>Oral (n= 1724)</b>			
Capsules/ Tablets		1.0	95.1 (1701)
Gargles/ Mouthwashes/ Gums/ Lozenges/ Liquids/ Powders/ Granules/ Sublingual Spray/Tabs		2.0	1.3 (23)
<b>Topical (n= 13)</b>			
Creams/ Gels/ Ointments/ Paints/ Solutions		2.0	0.7 (12)
Patches		2.0	0.1 (1)
Sprays		1.0	-
Dressing/ Pastes		3.0	-
<b>Injections (n= 27)</b>			
Ampoules/ Vials		4.0	1.5 (27)
Prefilled		3.0	-
<b>Nasal (n= 11)</b>			
Spray		2.0	0.6 (11)
Drops/ Creams/ Ointments		3.0	-
<b>Inhalation (n= 9)</b>			
Metered dose inhalers		4.0	0.5 (9)
Accuhalers/ Aerolizers/ Turbuhaler/ Other DPIs/ Oxygen/ Concentrator		3.0	-
Nebuliser		5.0	-
<b>Vaginal(n= 3)</b>			
Creams		2.0	0.2 (3)
<b>Ear(n= 1)</b>			
Drops/ creams/ ointments		3.0	0.1 (1)
<b>Section B: Dosing Frequency (n = 1784)<sup>2</sup></b>			
Once daily		1.0	61.0 (1088)
Twice daily		2.0	9.8 (175)
Three times daily		3.0	1.5 (27)
Four times daily		4.0	0.5 (9)
q 12h		2.5	19.8 (354)
q 8h		3.5	4.4 (78)
q 6h		4.5	1.1 (19)
q 4h		6.5	0.2 (3)
prn/ sos		0.5	1.7 (31)
<b>Section C: Additional Directions (n = 255)<sup>2</sup></b>			
Relation to food		1.0	60.0 (153)
Break or crush tablet / Multiple units at one time		1.0	34.5 (88)
Alternating dose		2.0	5.1 (13)
Tapering or increasing dose		2.0	0.4 (1)

<sup>1</sup> Suggested by George *et al.* (2004) <sup>2</sup>Missing information.

numbers increased as the scores increased. The proportion of patients with polypharmacy and at least one PDRP had a clear and direct relationship with higher MRCI scores. There was no linear relationship between adherence or 'all medicines are accessed by PHS' and high complexity. In Table 6, we could perceive the same variable tendencies but with higher complexity scores than the adults.

## DISCUSSION

In relation to the elements that constitute the pharmacotherapy complexity for more MRCI proposal, in this study, information that was essential to a drug dispensation came at the expense of those who instructed the correct use of the drug to the patient. Oral therapies, in single or twice daily administrations, were predominant, even

for the high complexity scores. The different proposed strata were related to age (65 years or over), receiving up to eight years of schooling, disease number, having at least one cardiovascular disease, having at least one endocrine metabolic disease, physician visit number, medication number, polypharmacy, had medications removed by the PHS, and having at least one PDRP. No relationship between complexity and self-reported adherence was found.

The complexity index was lower than in other studies, particularly in elderly patients who were in a hospital or institutionalized setting, and these index scores were 18.2 and 30.27, respectively.<sup>7,15</sup> Our study differs from most because it examined patients in a primary healthcare setting rather than specific groups.

Table 3. Adults and elderly estimates of cut-offs for low and high MRCI (score)				
Usual Range	Low complexity [score (n)]		High complexity [score (n)]	
	Adult	Elderly	Adult	Elderly
P <sub>2.5</sub> e P <sub>97.5</sub> (95%)	<2.0 (41)	< 2.0 (16)	<25.4 (9)	< 25.1 (4)
P <sub>5</sub> e P <sub>95</sub> (90%)	<2.0 (41)	< 4.0 (15)	<20.9 (17)	< 23.8 (9)
P <sub>10</sub> e P <sub>90</sub> (80%)	<2.0 (41)	< 4.0 (15)	<17.5 (35)	< 21.0 (15)
P <sub>15</sub> e P <sub>85</sub> (70%)	<3.3 (54)	< 5.0 (24)	<15.7 (54)	< 17.0 (26)
P <sub>20</sub> e P <sub>80</sub> (60%)	<4.0 (87)	< 6.0 (33)	<14.0 (69)	< 16.5 (30)
P <sub>25</sub> e P <sub>75</sub> (50%)	<4.5 (92)	< 7.0 (42)	<13.0 (82)	< 15.5 (36)



Table 4. Strata of high complexity and characteristics of the pharmacotherapy of patients attending the PHC of a midsize city of Minas Gerais, 2012

Characteristic of MRCI Sections	Median complexity	High Complexity					
MRCI's cut-off	8,5	25,0	21,6	18,0	16,5	14,5	13,5
Number of medicines <sup>1</sup>	1275	127	208	402	541	697	812
Section A: Dosage forms % (n)							
Oral (Capsule/ Tablet)	94.7 (1207)	93.7 (119)	92.3 (192)	95.3 (383)	94.5 (511)	94.7 (660)	94.3 (766)
Othersolid orais <sup>2</sup>	1.3 (17)	3.9 (5)	3.4 (7)	2.0 (8)	1.7 (9)	1.4 (10)	1.6 (13)
Topical <sup>3</sup> (cream/gel/ointment/ paint/ solution)	0.6 (8)	-	-	-	0.4 (2)	0.3 (2)	0.2 (2)
Ear % (drops/ creams/ ointments)	0.1 (1)	-	-	-	-	0.1 (1)	0.1 (1)
Nasal % (spray)	0.6 (8)	-	0.5 (1)	0.2 (1)	0.2 (1)	0.1 (1)	0.2 (2)
Injection% (ampoule/ vial)	2.0 (25)	2.4 (3)	2.4 (5)	1.7 (7)	2.8 (15)	2.6 (18)	2.6 (21)
Vaginal % (cream)	0.1 (1)	-	0.5 (1)	0.2 (1)	0.2 (1)	0.1 (1)	0.1 (1)
Inhalation % (metered dose inhaler)	0.6 (8)	-	1.0 (2)	0.5 (2)	0.4 (2)	0.6 (4)	0.7 (6)
Section B: Dosing Frequency % (n) <sup>4</sup>							
Instructions on dosage (n)	1274	126	209	403	540	695	810
Oncedaily	56.3 (717)	50.8 (64)	48.8 (102)	48.6 (196)	52.6 (284)	53.4 (371)	52.6 (426)
Twicedaily	10.8 (137)	8.7 (11)	10.0 (21)	11.4 (46)	10.7 (58)	10.9 (76)	11.6 (94)
Threetimes daily	1.7 (22)	-	1.9 (4)	2.7 (11)	2.6 (14)	2.3 (16)	2.1 (17)
Four times daily	0.5 (7)	0.8 (1)	1.4 (3)	1.0 (4)	0.7 (4)	0.7 (5)	0.6 (5)
q 12h	22.3 (284)	28.6 (36)	24.9 (52)	23.8 (96)	22.4 (121)	21.7 (151)	22.7 (184)
q 8h	5.6 (71)	7.9 (10)	9.1 (19)	9.2 (37)	8.1 (44)	7.9 (55)	7.0 (57)
q 6h	1.3 (17)	1.6 (2)	1.4 (3)	1.0 (4)	0.9 (5)	1.3 (9)	1.5 (12)
q 4h	0.2 (3)	-	0.5 (1)	0.5 (2)	0.6 (3)	0.4 (3)	0.4 (3)
prn/ sos	1.3 (16)	1.6 (2)	1.9 (4)	1.7 (7)	1.3 (7)	1.3 (9)	1.5 (12)
Section C: Additional Directions % (n) <sup>4</sup>							
Additional Directions (n)	226	27	44	77	106	129	146
Relationtofood	61.8 (126)	57.7 (15)	55.0 (22)	51.5 (35)	52.1 (49)	55.3 (63)	57.3 (75)
Break or crush tablet / Multiple units at one time	31.9 (65)	26.9 (7)	35.0 (14)	35.3 (24)	37.2 (35)	35.1 (40)	34.4 (65)
Alternating dose	5.9 (12)	15.4 (4)	10.0 (4)	11.8 (8)	9.6 (9)	8.8 (10)	7.6 (10)
Tapering or increasing dose	0.5 (1)	-	-	1.5 (1)	1.1 (1)	0.9 (1)	0.8 (1)

<sup>1</sup>Patients with this score had this number of medicines in prescriptions. <sup>2</sup>Gargle / mouthwash / gum / Tablet / Liquid / Powder / Granules / Spray / Sublingual Tablet. <sup>3</sup>Not was prescribed patched. <sup>4</sup>Not there was information for all medications, informed the "n" for each stratum

The presence of oral solid dosage forms and dosage schedules in single or double doses taken per day were the most prevalent, including in the high complexity strata. This may be related to increased availability of drugs in pharmaceutical form, the study population characteristics, as well as greater convenience and administration ease. Similar findings were found in other primary health studies.<sup>16,17</sup> Other studies have shown that most drugs used by patients were 'capsules/tablets', demonstrating the superiority of this drug type in clinical routines.<sup>15,18</sup>

The absence of instructions to the patients as to the appropriate use of medications in a prescription was similar to another study.<sup>19</sup> One possible explanation for this is the lack of an electronic prescription system in the Brazilian PHS. These prescriptions are done by hand. Electronic prescription systems can put in mandatory fields and, thus, improve the quality of the information. In addition to causing incorrect use of medications, this omission may compromise the actual complexity estimate. Hypotheses to explain the lack of the educational aspects in prescribing include deficiencies in their provision to the patient and oral provisions.<sup>17,20-22</sup> Whatever the cause, the provision of written instructions assists in patient compliance with

therapeutic regimens and reduces medication errors. Some authors claim problems may be caused in medical training, such as the information provided for a pharmacotherapy.<sup>23,24</sup>

These findings reinforce the need for multi-professional teamwork because in the absence of these instructions given by the prescriber, the pharmacist at the time of dispensing of medicines can help with any doubts that a patient has through health education and the provision of other services.<sup>25</sup>

Despite the negative effect of high therapy complexity in treatment adherence<sup>26</sup>, this relationship was not found in the present work; however, self-reported adherence was criticized by other authors to have low accuracy.<sup>27,28</sup>

The MRCI scores were strongly positively correlated with the medication numbers ( $p=0.931$ ; data not shown in table). This was also observed in studies by Libby *et al.* (2013), Mansur *et al.* (2012) and Melchior *et al.* (2005).<sup>3,7,29</sup> However, a greater number of medications do not always mean a higher complexity index. This confirms the index's ability to emphasize the different regimen complexities with the same number of drugs and demonstrates that the MRCI goes beyond the mere quantification of drugs.<sup>15,30</sup>

Table 5. Strata of high complexity and characteristics of PHC in adult patients attending a mid-sized city of Minas Gerais, 2012

Characteristic % (n)	High Complexity					
	MRCI ≥25.4	MRCI ≥20.9	MRCI ≥17.5	MRCI ≥15.7	MRCI ≥14.0	MRCI ≥13.0
Number of patients	9	18	35	54	69	82
Female	77.8 (7)	83.3 (15)	80.0 (32)	81.5 (44)	78.7 (59)	78.5 (73)
Studied for up to 8 years	77.8 (7)	72.2 (13)	67.5 (27)	68.6 (37)	64.0 (48)	65.6 (61)
Number of clinical conditions <sup>1</sup>	6.0 (4.5;6.0)	4.5(3.8;6.0)	4.0(3.0;5.0)	4.0 (3.0;5.0)	4.0 (3.0;5.0)	3.0 (3.0;4.0)
Cardiovascular disease <sup>1</sup>	1.0 (1.0;1.0)	1.0 (1.0;1.0)	1.0 (1.0;1.0)	1.0 (1.0;1.0)	1.0 (1.0;1.0)	1.0 (1.0;1.0)
Endocrine metabolic disease <sup>1</sup>	2.0 (1.0; 3.0)	2.0 (1.5; 2.0)	2.0 (1.0; 2.0)	2.0 (1.0; 2.0)	2.0 (1.0;2.0)	2.0 (1.0;2.0)
Number of medical appointments per year <sup>1</sup>	3.0 (2.0;5.8)	2.0 (2.0;3.5)	3.0 (2.0;5.0)	3.0 (2.0;6.0)	3.0 (2.0;6.0)	3.0 (2.0;6.0)
Number of drugs <sup>1</sup>	10.0 (9.0;11.5)	8.0 (7.0;10.0)	6.5 (5.3;8.0)	6.0 (5.0;8.0)	6.0 (5.0;7.0)	5.0 (4.0;7.0)
Polypharmacy	100 (9)	100 (18)	87.5 (35)	87.0 (47)	78.7 (59)	74.2 (69)
All medicines were accessed by PHS	55.6 (5)	72.7 (13)	80.0 (32)	75.9 (41)	80.0 (60)	80.6 (75)
Has at least one PDRP	100 (9)	94.4 (17)	80.0 (32)	81.5 (44)	84.0 (63)	78.5 (73)
Adherence	44.4 (4)	61.1 (11)	72.5 (29)	72.2 (39)	70.7 (53)	72.0 (67)

<sup>1</sup>Median (Percentile 25; Percentile 75)

The direct relationship of increasing pharmacotherapy complexity and the number of chronic medical conditions the patient has would be in addition to elements that contribute to the identification of patients at risk. This could indicate those with a greater need for clinical management as well as specialized care by professionals, such as physicians and pharmacists.<sup>30,31</sup> Furthermore, Stange suggested that the intervention of a qualified health professional, such as pharmacists, could be effective in reducing the treatment complexity.<sup>32</sup>

Advinha *et al.* (2014)<sup>15</sup> emphasizes that although MRCI is an open-ended index, with no maximum value, there is an absence of articles or authors who tried to establish a cut-off, a figure related to negative health outcomes and the need to intervene. Most studies are made on specific population groups and only show the complexity mean. In our study, the complexity mean was 9.9 (minimum=2.0, maximum=51.0,  $\pm$  6.5). Advinha *et al.* (2014)<sup>15</sup> analyzed elderly patients in nursing homes and found a mean of 18.2 ( $\pm$  9.6). Libby *et al.*<sup>3</sup> evaluated patients in defined populations with chronic diseases. The mean patient-level MRCI score for hypertension was 17.80 ( $\pm$  9.13), 25.44 ( $\pm$  11.67) for geriatric depression, 21.76 ( $\pm$  12.49) for HIV, and 22.98 ( $\pm$  11.58) for diabetes. Martinez & Ferreira (2012)<sup>33</sup> observed a complexity mean of 19 ( $\pm$  8.9) in diabetics patients. Our study differs from

most because it examines adult and elderly patients in a primary healthcare setting rather than specific groups.

According to this complexity, patients with a higher MRCI profile tended to be female; received up to eight years of schooling; had an average of four clinical conditions, which included the presence of cardiovascular and endocrine metabolic disease; had about three medical appointments per year; used an average of seven drugs; had polypharmacy features; had medications removed by the PHS; had at least one PDRP, and did not adhere to pharmacotherapy. These patients used drugs whose dosage form was mostly an oral solid, in a single administration or twice a day, with instructions concerning the relation to food and the crushing of tablets or taking multiple units together.

Other cut-off point proposals have been presented. Olson *et al.* (2014)<sup>34</sup> suggested a score cut-off point of 33, which included an analysis of elderly patients in nursing homes from cut-off points that were previously selected based on clinical experience and the review of the research literature that distinguished patients at high and low risk of re-hospitalization. This study showed that High Risk Medication Regimen calculations were optimized by increasing the MRCI cut-off point that distinguishes patients by their medication-related risks for hospital readmissions.<sup>34</sup> Dierich *et al.* (2011)<sup>35</sup> analyzed

Table 6. Strata of high complexity and characteristics of PHC elderly attending a mid-sized city of Minas Gerais, 2012

Characteristic % (n)	High Complexity					
	MRCI ≥25.1	MRCI ≥23.8	MRCI ≥21.0	MRCI ≥17.0	MRCI ≥16.5	MRCI ≥15.5
Number of patients	4	7	15	26	30	39
Female	50 (2)	57.1(4)	60.0 (9)	53.8 (14)	56.7 (17)	61.5 (24)
Studied for up to 8 years	50 (2)	57.2 (4)	66.6 (10)	65.3 (17)	66.7 (20)	66.7 (26)
Number of clinical conditions <sup>1</sup>	4.5 (3.3;5.8)	5.0 (3.0;6.0)	4.0 (3.0;5.0)	4.0 (2.8;5.0)	3.5 (2.0;5.0)	4.0 (2.0;4.0)
Cardiovascular disease <sup>1</sup>	1.0 (1.0;1.8)	1.5 (1.0;2.3)	1.0 (1.0;2.0)	1.0 (1.0;1.5)	1.0 (1.0;1.0)	1.0 (1.0;1.0)
Endocrine/metabolic disease <sup>1</sup>	2.5 (1.3;3.0)	2.0 (1.0;3.0)	1.0 (1.0;2.0)	2.0 (1.0;2.0)	2.0 (1.0;2.0)	2.0 (1.0;2.0)
Number of medical appointments per year <sup>1</sup>	4.0 (3.0;6.0)	4.0 (3.0;7.5)	3.0 (2.0;4.8)	4.0 (2.0;9.0)	4.0 (2.0;8.0)	3.5 (2.7;8.0)
Number of drugs <sup>1</sup>	9.0 (8.3;9.8)	9.0 (7.0;9.0)	7.0 (6.0;9.0)	7.0 (6.0;7.3)	7.0 (5.0;7.0)	6.0 (5.0;7.0)
Polypharmacy	100 (4)	100 (7)	100 (15)	92.3 (24)	93.3 (28)	94.9 (37)
All medicines were accessed by PHS	50 (2)	71.4 (5)	66.7 (10)	80.8 (21)	80.0 (24)	82.1(32)
Has at least one PDRP	100 (4)	100 (7)	93.3 (14)	88.5 (23)	86.7 (26)	87.2 (34)
Adherence	100 (4)	100 (7)	80.0 (12)	80.8 (21)	83.3 (25)	84.6 (33)

<sup>1</sup>Median (Percentile 25; Percentile 75)

older patients in a home care setting and found a mean MRCI of 35.4 (75% of them had scores >20), a relationship between readmission and higher polypharmacy, potentially inappropriate medications, and high complexity scores. Cut-off points are very dependent upon the studied population, which may explain the differences found.

Other studies could assess whether a MRCI score that is 18.0 or higher is really suitable to identify high complexities and, thus, a preferential service for specialized care.

## CONCLUSIONS

Identifying patients with a highly complex therapy can be used as an indicator to prioritize patients with multiple chronic health conditions, problems in their pharmacological therapies, and clinical control. The elderly patients had larger MRCI scores than the adult patients in all the suggested cut-offs. The low complexity MRCI scores for the adult patients included a minimum value of 2.0 and a maximum of 4.5, while the elderly patients had scores of 2.0 to 7.0. The high complexity MRCI scores for the adults included tracks of 13.0 to 25.4. For the elderly patients, the minimum value was 15.5, and the maximum value was 25.1.

The MRCI proved to be a good tool for classifying the complexity of care for the population studied, as it identifies factors that contribute to complex treatments and can be used in routine pharmaceutical dispensing to identify problems related to pharmacotherapy. However, additional studies should be conducted in populations with different characteristics to determine these scores.

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## CONFLICT OF INTEREST

We would like to declare that there were no conflicts of interest in conducting this research. All opinions expressed are of the authors themselves and not an official position of the institution.

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## COMPLEJIDAD DEL RÉGIMEN DE MEDICACIÓN EN ADULTOS Y ANCIANOS EN UN CENTRO DE CUIDADOS PRIMARIOS: DETERMINACIÓN DE LA COMPLEJIDAD ALTA Y BAJA

### RESUMEN

**Antecedentes:** La complejidad de un régimen de medicación se relaciona con las múltiples características del régimen prescrito que pueden influenciar negativamente los resultados en salud de los pacientes.

**Objetivo:** Proponer puntos de corte en la complejidad de la farmacoterapia para diferenciar entre pacientes de baja y alta complejidad que permita la priorización de la gestión de los pacientes entre los atendidos en un centro de cuidados primarios.

**Métodos:** Este es un estudio transversal que incluyó 517 adultos y ancianos analizando diferentes puntos de corte para definir los estratos de alta y baja complejidad de la farmacoterapia basándose en los percentiles de la población evaluada. La recogida de datos comenzó con la solicitud de las prescripciones, seguida de un cuestionario administrado por un entrevistador. La complejidad de la medicación se estimó mediante el Medication Regimen Complexity Index (MRCI). En las farmacoterapias de alta complejidad se analizó los perfiles de los pacientes, el uso de servicios de salud, y la farmacoterapia. Los criterios para la inclusión de la muestra fueron: habitantes del área cubierta por el municipio, 18 años o más, y tener prescrito al menos un medicamento durante el periodo de recogida de datos. Los criterios de exclusión durante la recogida de datos fue el uso de algún medicamento que no estaba disponible. Todos los medicamentos eran del Servicio de Cuidados Primarios (PHS).

**Resultados:** La mediana total de puntuación de complejidad de la farmacoterapia fue de 8,5. Las puntuaciones altas del MRCI se correlacionaban con la edad, medicamentos tomados del PHS, tener al menos una interacción potencial medicamento-medicamento, tener más de 8 años de escolaridad, número de medicamentos, polimedicación (cinco o más medicamentos), número de problemas de salud, número de visitas al médico, y número de enfermedades cardiovasculares o metabólicas. Sugerimos diferentes tramos de complejidad de acuerdo a la edad (e.g. adultos o ancianos) que tienen en cuenta las características de la población y la farmacoterapia como límites de alta complejidad. Para los ancianos los tramos eran:  $MRCI \geq 25,4$ ,  $MRCI \geq 20,9$ ,  $MRCI \geq 17,5$ ,  $MRCI \geq 15,7$ ,  $MRCI \geq 14,0$ , y  $MRCI \geq 13,0$ . Para los pacientes adultos los límites de complejidad eran:  $MRCI \geq 25,1$ ;  $MRCI \geq 23,8$ ;  $MRCI \geq 21,0$ ;  $MRCI \geq 17,0$ ;  $MRCI \geq 16,5$ ; y  $MRCI \geq 15,5$ .

**Conclusión:** La complejidad del régimen de medicación se asocia con el perfil de enfermedad del paciente y sus problemas de uso de medicamentos; por tanto, los límites propuestos pueden ser útiles para priorizar pacientes en cuidados clínicos de los farmacéuticos u otros profesionales de la salud.

**Palabras clave:** Esquema de Medicación; Preparaciones Farmacéuticas; Polimedicación; Farmacoepidemiología; Brasil

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