

## ORIGINAL ARTICLE

## Therapeutic Adherence According to the Morisky Scale in Patients with Hypertension

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## Abstract

**Background:** In view of the high prevalence of hypertension and the importance of adequate drug therapy in the prevention of complications, it is necessary to know the adherence to drug treatment in this population.

**Objective:** To verify adherence to antihypertensive drug treatment in Brazilian patients with hypertension using the Morisky-Green Test (MGT), relating it with demographic data.

**Methods:** Prospective, observational, multicenter, national registry study, with 2,578 hypertensive patients participating in study I, the Brazilian Cardiovascular Registry of Arterial Hypertension (I-RBH), recruited in the five regions of Brazil. The analyses carried out on the data were descriptive statistics, qui-square tests, ANOVA, and logistic regression, adopting 5% as the significance level for the tests.

**Results:** The research shows that 56.13% of patients in the sample were female; 56.71% were elderly ( $\geq 65$  years); 55.86% were White; 52.37% were from the Southeast Region; and 59.74% were non-adherent. Logistic regression showed an independent relationship between patients' age, ethnicity, and region with medication adherence.

**Conclusion:** Adherence to treatment is the key to reducing high rates of cardiovascular complications. The study brings a successful outcome in the relationship between the factors ethnicity, age, and region of patients with hypertension and medication adherence. To this end, it is necessary to understand these factors, considering systematic evaluation in the care of patients with hypertension and other chronic non-communicable diseases. This study is a significant contribution to multidisciplinary teams, as it highlights which risk factors interfere with medication adherence, incorporating better strategies in health education.

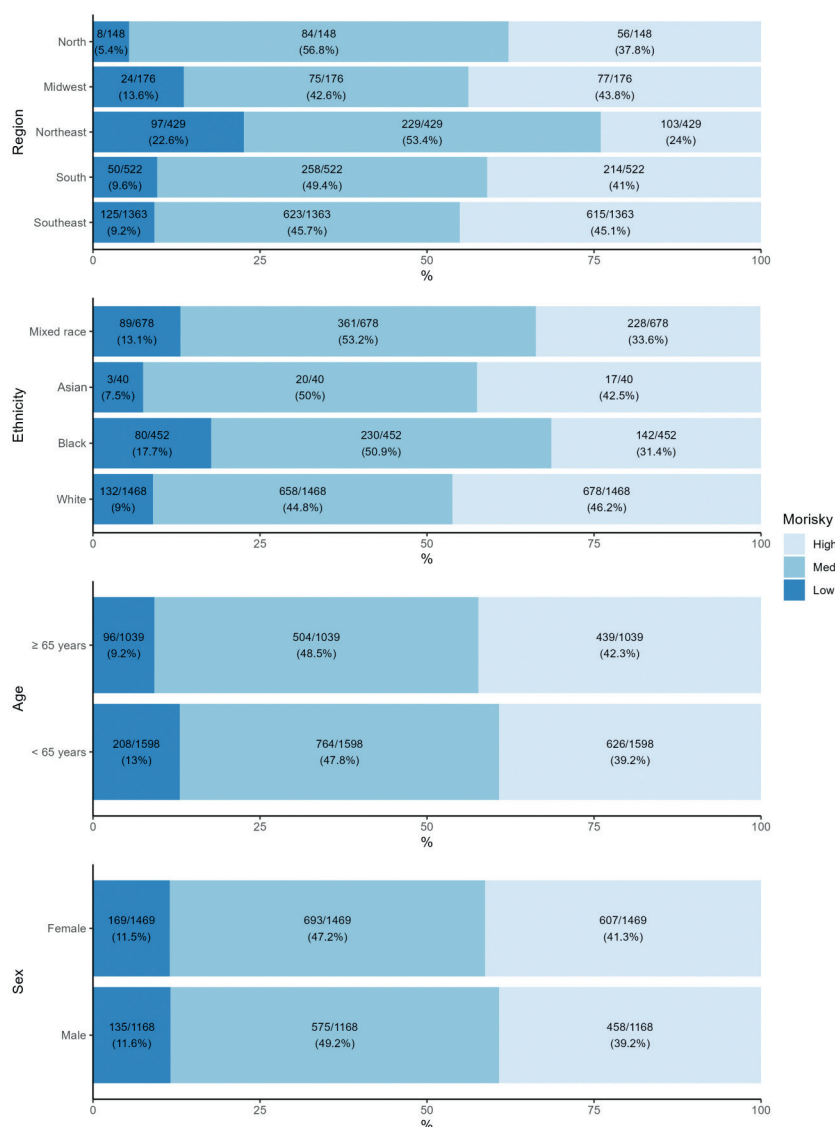
**Keywords:** Hypertension; Medication Adherence; Cardiovascular Diseases.

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**Central Illustration:** Therapeutic Adherence According to the Morisky Scale in Patients with Hypertension

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**Introduction**

Systemic arterial hypertension (SAH) is characterized by high and sustained levels of blood pressure, considered a multifactorial clinical condition. Structural and/or functional changes in target organs (heart, brain, kidneys, and blood vessels) and metabolic changes are often associated, consequently increasing the risk of fatal and non-fatal cardiovascular events.<sup>1</sup> In this context, cardiovascular diseases are responsible for 29.4% of all deaths recorded in Brazil yearly. This represents more than

308,000 people who died from acute myocardial infarction and stroke. The high rate of these diseases places Brazil among the 10 countries with the highest rate of deaths from cardiovascular disease.<sup>2</sup>

SAH is considered an important public health problem. It is often asymptomatic and silent, and in most cases its diagnosis is late.<sup>3</sup> Professionals who care for patients with SAH should know that the asymptomatic nature of the disease tends not to stimulate the memory of using medication. However, clarification about the disease and its natural history

is a key element to persuade patients to use their medication correctly and to have periodic follow-up with the health team.<sup>4</sup>

Several factors influence medication adherence. They may be related to the patient, the doctor-patient interaction, the doctor, other professionals involved in care, the organization of health services, and the therapy itself. Regarding the therapy itself, it influences the possibility of acquiring the medication in the public network, its price, dosage adequacy, effectiveness, and the occurrence of adverse effects.<sup>4,5</sup>

There is no consensus regarding the definition of adherence to drug treatment, but it is understood as the use of prescribed drugs in at least 80% of the total, observing schedules, doses, and treatment time.<sup>6</sup>

Although there are different themes related to the health-disease-care process, they have been driving the creation and adaptation of instruments, which, once validated, allow an approximation with reality in order to subsidize more effective interventions. Despite various strategies for assessing adherence to hypertension treatment, there is no consensus on a gold standard. The methods can be direct, such as the dosage of the drug's active/metabolic principle, or indirect, such as pill counting and user reports.<sup>7</sup>

To assess adherence to drug treatment, the Morisky-Green Test (MGT), a low-cost and easy-to-apply questionnaire, is useful to differentiate low adherence to drug treatment and non-response to antihypertensive treatment, despite its low sensitivity and accuracy.<sup>8</sup> The MGT is easy to measure and has been validated in English, Spanish, and Portuguese. However, it is not efficient to relate controlled blood pressure levels and a positive attitude towards taking antihypertensive medication. The lack of correlation between MGT and clinical outcomes motivated Morisky to expand this questionnaire, adding 4 more questions to the original ones. Each of the 8 items on the Morisky Medication Adherence Scale (MMAS-8) measures specific medication-taking behavior, and a Portuguese version of the MMAS-8 was validated by Oliveira Filho et al. in 2012.<sup>8</sup>

This study is justified by the high prevalence of cardiovascular disease, including hypertension, and its relationship with antihypertensive medication adherence. Given the high prevalence of SAH and the importance of adequate drug therapy in preventing complications, it is necessary to know the adherence to drug treatment in the population. Therefore, the objective

of this study was to verify adherence to antihypertensive drug treatment in Brazilian patients with hypertension using the MGT, relating it with demographic data.

## Methods

This is a prospective, observational, national-level, multicenter registry study.

The primary study from which the research originates is entitled Brazilian Cardiovascular Registry of Arterial Hypertension (I-RBH),<sup>9</sup> sponsored by the Brazilian Society of Cardiology (SBC) with the involvement of 49 research centers, distributed throughout the 5 regions of the Brazilian territory. Its main objective is to document the current clinical practice for the treatment of SAH in Brazil.

One of the secondary objectives of the I-RBH is to estimate adherence to drug treatment using the MGT.

Patients were screened and evaluated in outpatient clinics of internal medicine and specialties, during the 12-month follow-up period. Data were collected from May 2013 to October 2015.

Study participants were patients over 18 years of age, of both sexes, diagnosed with SAH for at least 4 weeks. Inclusion criteria were: age greater than 18 years; diagnosis of arterial hypertension for at least 4 weeks, with systolic blood pressure  $\geq 140$  mmHg and/or diastolic blood pressure  $\geq 90$  mmHg in the sitting position, according to the protocol presented in the 2020 Brazilian Guidelines on Arterial Hypertension, or on antihypertensive medication; and patients with hypertension regularly enrolled at the participating site/institution.

Exclusion criteria were: patients with renal failure undergoing dialysis; hospitalization at the time of inclusion or in the last 30 days; patients who were hemodynamically unstable and had been using vasoactive drugs in the last 30 days; heart failure functional class III or IV; pregnant and/or breastfeeding women; psychiatric illnesses that prevented compliance with the protocol; history of stroke or acute myocardial infarction up to 30 days prior to study enrollment; serious diseases and/or cancer accompanied by a prognosis of less than 1 year; and patients who withdrew from the research at any time during the study.

The study interruption criteria were individuals who no longer wished to participate in the study, who died, or who presented one or more exclusion criteria.

A total of 2,643 outpatients were recruited, and participation in the study began after signing an informed consent form. At the inclusion visit, information was collected through an interview. The questionnaire that was used consisted of the following: demographic data; personal background; family background; history of SAH; clinical evaluation, with 2 blood pressure measurements performed in the sitting position with an interval of at least 1 minute between them; the medications that the patient was using during the last 30 days; laboratory data and electrocardiogram in the last 6 months, if available; other exams performed within the last year; lifestyle; ambulatory blood pressure monitoring, in the last 6 months, if available; and adherence to treatment verified through MGT.

The MGT is a questionnaire composed of 4 questions that assess adherence by application. The questions are as follows: 1) Do you ever forget to take your medicine? 2) Are you sometimes careless about the time you take your medication? 3) When you feel well, do you ever stop taking your medicine? 4) When you feel bad with the medicine, do you sometimes stop taking it? Patients were classified in the high degree of adherence group when the answers to all questions were negative. When 1 or 2 answers were affirmative, the patients were classified in the medium adherence group, and patients with 3 or 4 affirmative answers were classified in the low adherence group.<sup>6</sup>

This research analyzed sociodemographic data (age, sex, color, and region of Brazil where the patient was recruited) and medication adherence using the MGT, information that is part of the electronic clinical record (e-CRF).

## Statistical analysis

Data were submitted to descriptive statistical analysis and presented in tables in the form of absolute and percentage frequencies.<sup>10</sup>

In descriptive statistics, frequencies were distributed (absolute and relative) across all variables and presented as the mean and standard deviation only for the following variables: age, sex, ethnicity, and region of Brazil. Comparisons with Morisky scale were performed with qui-squared tests and one-way ANOVA (for age). The normality assumption of ANOVA was verified with quantile-quantile (QQ) residual plots.

The relationships between adherence (low, medium, and high) and sociodemographic characteristics were analyzed using logistic regression models.

Statistical analyses were performed using R Software 4.2.1 (Vienna, Austria, 2023), and a 5% significance level was used in hypothesis tests.

The logistic regression analysis was carried out to identify the effect on medication adherence defined as zero points on the Morisky scale, that is, patients who answered at least 1 question affirmatively were considered non-adherent, and those who answered negatively to all questions were considered adherent.

## Results

Between May 2013 and October 2015, 2,675 patients were recruited from this national registry, of which 97 (3.62%) were excluded from clinical follow-up, because they did not answer the questions of the variables analyzed in the research.

Thus, 2,578 patients with SAH confirmed evidence of the inclusion criteria, listed in this registry, in 49 Brazilian research centers. In Table 1 – Demographic data in number and percentage, the sociodemographic characteristics of the recruited patients were analyzed, and it was observed that 56.13% of patients were female; 56.71% were elderly ( $\geq 65$  years); 55.86% were White; and 52.37% were from the Southeast Region. With respect to elderly patients, 54.58% were from the Southeast Region; 48.11% had average medication adherence, and 59.74% were not adherent. For more details on patient characteristics, see Table 1 – Demographic data in number and percentage.

A relationship was also observed between sociodemographic characteristics and adherence to drug treatment.

Regarding the sex of the patients, the chi-square test showed no evidence of a relationship between medication adherence and sex. The application of the test about age group and medication adherence provided evidence of the relationship between these characteristics. In this case, the Marascuilo procedure indicates that there was a significant difference between medium and high adherence and low adherence, but medium and high adherence did not differ; the same happened for elderly patients.

Furthermore, medication adherence was related to the ethnicity of the patients. For White and Black patients, all levels of medication adherence differed from each other; regarding Asian patients, there was no significant difference between the levels of medication

**Table 1 – Demographic data per Morisky classification**

Characteristic	Low (3 or 4) 304/2638 (11.5%)	Medium (2 or 1) 1269/2638 (48.1%)	High/adherent (0) 1065/2638 (40.4%)	Total	p value
<b>Sex</b>					
Female	135/304 (44.4%)	575/1269 (45.3%)	458/1065 (43.0%)	<b>1168/2638 (44.3%)</b>	0.535
Male	169/304 (55.6%)	694/1269 (54.7%)	607/1065 (57.0%)	<b>1470/2638 (55.7%)</b>	
<b>Age</b>					
Mean ± SD	59.5 ± 12.0*	61.4 ± 11.9*	62.3 ± 11.8*	<b>61.6 ± 11.9*</b>	0.001
Elderly (≥ 65)	96/304 (31.6%)	504/1268 (39.7%)	439/1065 (41.2%)	<b>1039/2637 (39.4%)</b>	0.009
<b>Ethnicity</b>					
White	132/304 (43.4%)	658/1269 (51.9%)	678/1065 (63.7%)	<b>1468/2638 (55.6%)</b>	< 0.001
Mixed race	80/304 (26.3%)	230/1269 (18.1%)	142/1065 (13.3%)	<b>452/2638 (17.1%)</b>	
Black	3/304 (1.0%)	20/1269 (1.6%)	17/1065 (1.6%)	<b>40/2638 (1.5%)</b>	
Asian	89/304 (29.3%)	361/1269 (28.4%)	228/1065 (21.4%)	<b>678/2638 (25.7%)</b>	
<b>Region</b>					
Southeast	125/304 (41.1%)	623/1269 (49.1%)	615/1065 (57.7%)	<b>1363/2638 (51.7%)</b>	< 0.001
South	50/304 (16.4%)	258/1269 (20.3%)	214/1065 (20.1%)	<b>522/2638 (19.8%)</b>	
Northeast	97/304 (31.9%)	229/1269 (18.0%)	103/1065 (9.7%)	<b>429/2638 (16.3%)</b>	
Midwest	24/304 (7.9%)	75/1269 (5.9%)	77/1065 (7.2%)	<b>176/2638 (6.7%)</b>	
North	8/304 (2.6%)	84/1269 (6.6%)	56/1065 (5.3%)	<b>148/2638 (5.6%)</b>	
<b>Elderly by region</b>					
Southeast	39/96 (40.6%)	281/505 (55.6%)	267/439 (60.8%)	<b>587/1040 (56.4%)</b>	< 0.001
South	15/96 (15.6%)	80/505 (15.8%)	79/439 (18.0%)	<b>174/1040 (16.7%)</b>	
Northeast	32/96 (33.3%)	95/505 (18.8%)	50/439 (11.4%)	<b>177/1040 (17.0%)</b>	
Midwest	9/96 (9.4%)	18/505 (3.6%)	22/439 (5.0%)	<b>49/1040 (4.7%)</b>	
North	1/96 (1.0%)	31/505 (6.1%)	21/439 (4.8%)	<b>53/1040 (5.1%)</b>	
(*) age was compared with analysis of variance (ANOVA). SD: standard deviation.					

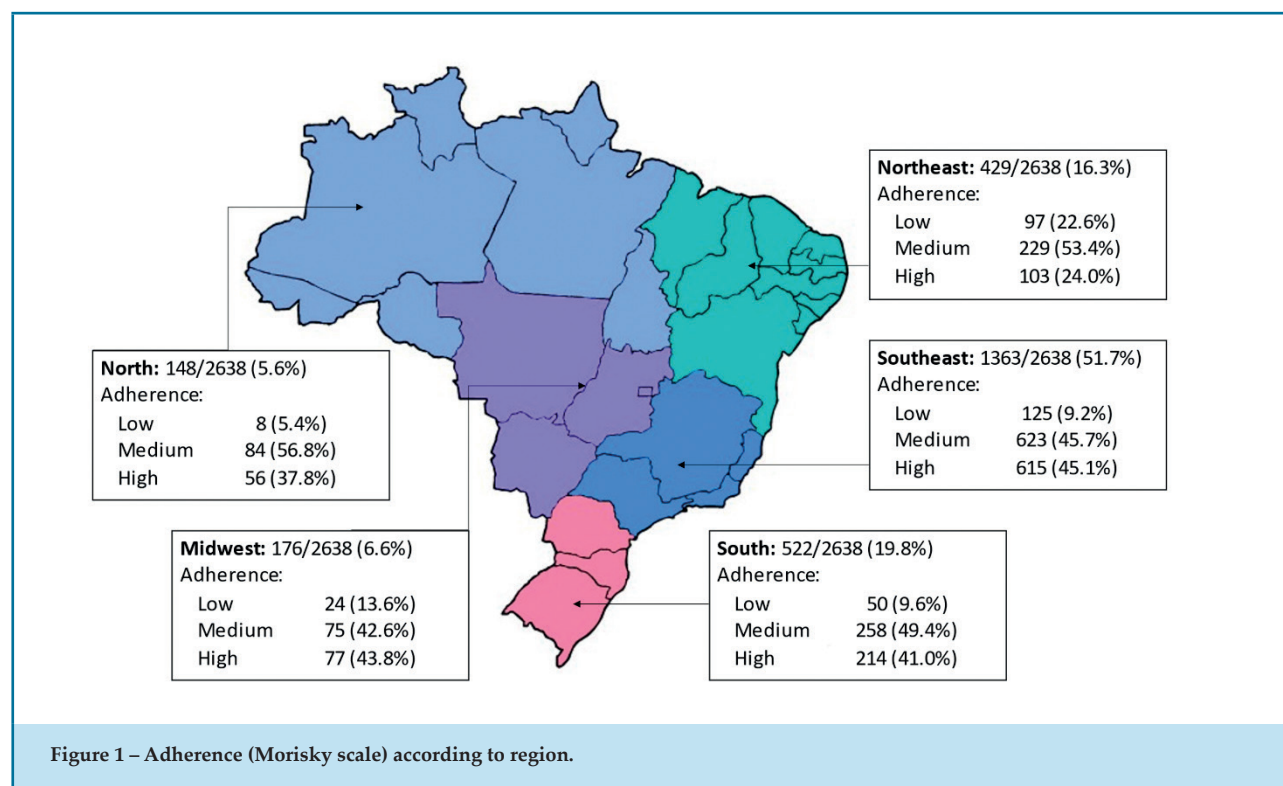
adherence (Table 1). As for mixed race patients, there was a difference between high medication adherence and medium and low adherence, which in turn did not differ from each other (Table 1).

Medication adherence was related to the patients' region of Brazil. For the Midwest and South Regions, there was no significant difference between levels of medication adherence. As for the Northeast and Southeast Regions, there was a significant difference

between all levels of medication adherence (Table 1 and Figure 1). With regard to the North Region, low medication adherence had a significant difference in relation to medium and high medication adherence, and there was no significant difference between the two, according to the Marascuilo procedure.

In the Central Illustration – Variables associated to medication adherence, the results obtained are shown in graphical form.





Regarding the results of the logistic regression, the variables sex and age group were not observed to be risk factors for patients' medication adherence, since the confidence interval of these variables has the value 1 as a possible value with 95% reliability. The variables ethnicity, region, and age in years are risk factors for medication adherence by multivariable analysis (Table 2 – Result of logistic regression of variables associated with medication adherence). Thus, there is evidence that patients who are Black or mixed race, from the South or Northeast Region, and with advanced age are groups more likely to not adhere to medication.

## Discussion

This is the first Brazilian registry of hypertension with prospective follow-up of a hypertensive population in Brazil. The results show gaps in the treatment of the hypertensive Brazilian population and creates possibilities to implement interventions that improve care and clinical practice for these patients. Due to the lack of information about these indicators in the studied population, the data obtained will serve as a reference and gold standard in the management of Brazilian patients with hypertension. The findings of this study are the first, unique and innovative for the

hypertensive Brazilian population, and they should guide researchers to correlate and explore the different classes of antihypertensive drugs and their relationship with blood pressure levels.

**Table 2 – Result of logistic regression of variables associated with medication adherence**

Coefficient	Odds ratio	Confidence interval (95%)	p value
Sex (female)	1.06	0.91 - 1.25	0.449
Age (years)	1.01	1.00 - 1.01	0.026
<b>Race/ethnicity (ref. White)</b>	<b>1.00</b>	<b>-</b>	<b>-</b>
Black	0.63	0.49 - 0.79	<0.001
Asian	0.90	0.47 - 1.70	0.746
Mixed race	0.70	0.57 - 0.86	<0.001
<b>Region (ref. Southeast)</b>	<b>1.00</b>	<b>-</b>	<b>-</b>
South	0.80	0.64 - 0.98	0.032
Northeast	0.46	0.35 - 0.59	<0.001
Midwest	0.97	0.70 - 1.34	0.853
North	0.81	0.56 - 1.14	0.232

Worldwide, it is possible to observe the high prevalence of SAH. Studies carried out in Canada, the United States, and Europe showed high numbers of SAH, mainly in the elderly population (between 30% and 35%). The emphasis on the elderly population corroborates the 2020 Brazilian Guidelines on Arterial Hypertension, which estimated that more than 60% of the elderly are hypertensive.<sup>1,11</sup>

Another result to be highlighted in this study is the high prevalence of female patients (56.13%). Several studies have shown that women seek health services more and claim that, because they survive longer than men, they are more likely to suffer from chronic diseases. Other authors justify this higher prevalence in women because this group presents an increase in risk factors with a decrease in the production of steroid hormones, leading to an increase in the vascular tone of the peripheral arteries and causing SAH in postmenopausal women.<sup>12</sup>

Men, on the other hand, often discover that they are hypertensive only after suffering a serious clinical event, such as a heart attack or stroke.<sup>13</sup>

A survey carried out by VIGITEL (Surveillance of Risk and Protection Factors for Chronic Diseases by Telephone Survey) in 2011 showed that the diagnosis of hypertension is more common in women (25.4%) than in men (19.5%). This finding is expected, as there is a greater share of women in the population, especially in the elderly.<sup>14</sup>

The relationship between MGT and sex did not show a statistically significant difference. Similar results were found in research on factors associated with patients' non-adherence to the treatment of SAH. A study that measured patients' adherence to therapy using another method showed that there was greater adherence in females than in males.<sup>15</sup>

The White color or race was present in the largest share in this study (86.7%), which corroborates the results of the 2010 Demographic Census on the distribution of color or race groups throughout Brazilian territory. Regarding skin color, it can be observed that non-White individuals were more exposed to non-adherence to medication; this fact is possibly related to other socioeconomic characteristics, such as low income, lower level of education, and greater difficulty in accessing health services. A study carried out in the city of Salvador, Bahia, with 200 low-income individuals with SAH, observed a growing trend of non-adherence, with 46.4% among White patients, 67.0% among mixed race patients, and

80.3% among Black patients. Data from the study on adherence and ethnicity show the importance of more detailed analyses of their associations, in view of the possibility that Black patients may more often choose to abandon or not adhere to treatment.<sup>16</sup>

It should be noted that no other studies were found that so clearly demonstrated the association between ethnicity and non-adherence to antihypertensive treatment.

Regarding the region of the country with the highest prevalence of arterial hypertension, the Southeast was in first place with 23.3%, confirming the result found in this study.<sup>17</sup>

The present study found that the prevalence of non-adherence to antihypertensive treatment (72.2%) was similar to studies carried out with hypertensive patients, which evaluated adherence by MGT.<sup>15</sup>

However, a study carried out in Santa Catarina in 2012, which evaluated adherence to medication in elderly patients with hypertension using the MGT, showed a higher prevalence of adherence to treatment.<sup>18</sup>

Although Monane et al. estimated adherence to medication treatment using another method, they observed that older age was associated with better adherence.<sup>19</sup> The results corroborate a study carried out in São José do Rio Preto, São Paulo with patients with hypertension, which evaluated medication adherence using the MGT, finding that only 28% of the individuals in the study adhered to the treatment.<sup>20</sup>

In another survey carried out with patients with hypertension enrolled in the Family Health Program in Ribeirão Preto, São Paulo, 79.8% were classified as adherent to antihypertensive treatment by the MGT.<sup>21</sup> The results indicated adequate levels of medication adherence to the treatment by patients and highlighted the importance of professional-patient interaction, trust, and the attitude of health professionals towards users.

The present study revealed that there is a relationship between medication adherence and some of the sociodemographic data compared, namely, age, ethnicity, and region of Brazil, with emphasis on Black and mixed race patients from the South and Northeast Regions, maintaining, in these cases, a relationship with increasing age and lower adherence.

### Study Limitations

The central study was conducted by several cardiology centers throughout Brazil; therefore, the quality of care

can be overestimated when compared to places with limited resources. The main limitation of the study is highlighted; the MGT, as it is an indirect tool, with low sensitivity and precision, shows results that may not reflect specific health care, such as clinical care environments in primary care and in rural areas. Another important limitation is the lack of centralized evaluation of results.

## Conclusion

Adherence to treatment is the key to reducing high rates of cardiovascular complications. It is necessary to understand this fact, considering systematic evaluation in the care of patients with hypertension and other non-communicable chronic diseases.

This study makes a significant contribution to multidisciplinary teams, as it points out which risk factors interfere with medication adherence, incorporating better strategies in health education.

The research's weakness was that it assessed adherence to drug treatment for SAH using the MGT. As the MGT is considered to have low sensitivity and accuracy, the research incorporated sociodemographic data to make the analysis more robust.

Health professionals should apply low-cost tests, such as the MGT, in order to obtain greater knowledge and control over adherence to drug treatment in patients with hypertension under their care. In addition, it is necessary to continuously promote interdisciplinary strategies to raise awareness among patients with hypertension, aiming to increase adherence to drug treatment and lifestyle adaptations, which are fundamental conditions for improving their life expectancy and quality of life.

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Conception and design of the research: Barroso WKS, Brandão AA, Barbosa ECD, Malachias MVB, Gomes MM, Amodeo C, Povia RMS, Précoma DB, Sousa ACS, Dantas JMM, Cesarino EJ, Silva PGMB, Jardim PCBV, Lopes RD; acquisition of data, analysis and interpretation of the data, statistical analysis and critical revision of the manuscript for intellectual content: Lanza VE, Silva GO, Quiroga CCC, Cavalcante MA, Barroso WKS, Brandão AA, Barbosa ECD, Malachias MVB, Gomes MM, Amodeo C, Povia RMS, Précoma DB, Sousa ACS, Dantas JMM, Cesarino EJ, Silva PGMB, Jardim PCBV, Lopes RD; writing of the manuscript: Lanza VE, Silva GO, Quiroga CCC, Cavalcante MA.

## Potential Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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## Study Association

This study is not associated with any thesis or dissertation work.

## Ethics Approval and Consent to Participate

This study was approved by the Ethics Committee of the Universidade do Oeste Paulista (UNOESTE) under the protocol number 1650/CAAE 13477313.0.2041.5515. All the procedures in this study were in accordance with the 1975 Helsinki Declaration, updated in 2013. Informed consent was obtained from all participants included in the study.

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