Ciência & Saúde Coletiva
cienciaesaudecoletiva.com.br
ISSN 1413-8123. v.29, n.8
DOI: 10.1590/1413-81232024298.19282022EN

Adherence to antihypertensive drug treatment in Brazil: a systematic review and meta-analysis

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Abstract *This article aims to evaluate the adherence to antihypertensive treatment prevalence in the Brazilian population based on peer-reviewed studies which used instruments exclusively designed and/or adapted for this purpose. A systematic review with meta-analysis based on the recommendations of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA). The search was carried out in the BDENF, SciELO, Cuiden, PsycINFOe, CINAHL, Embase, LILACS, and MEDLINE databases, as well as the AgeLine, Google Scholar and ScienceDirect academic search engines. The protocol was registered with PROSPERO (CRD42021292689). Random effects models were used for a meta-analysis of the prevalence obtained from individual studies. A total of 104 studies were included in the meta-analysis on antihypertensive treatment in the Brazilian population, totaling 38,299 patients. The most used instrument was the four-item Morisky-Green Test (49.5%). The adherence prevalence estimated by the meta-analysis was 44.4% (95%CI: 39.12%-49.94%, I_2 = 91.17, $p < 0.001$), showing high heterogeneity. The adherence to antihypertensive treatment prevalence found in national studies was unsatisfactory, demonstrating that this problem continues to be a major challenge.*

Key words *Hypertension, Medication adherence, Evaluation of research programs and instruments, Prevalence, Meta-analysis*

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Introduction

Lack of adherence to antihypertensive medication treatment is one of the main causes of inadequate blood pressure control. Systemic Arterial Hypertension (SAH) affects around 1.28 billion adults between 30 and 79 years old worldwide[1] and around 31.0% of the adult population in Brazil[2], being the main modifiable risk factor for cardiovascular diseases.

Pharmacological treatment for SAH has proven efficacy and effectiveness, however there is a low prevalence of Blood Pressure (BP) control in middle and low-income countries[3]. It was estimated in 2019 that only 10.3% (95%CI 9.6-11.0%) of hypertensive patients in these countries had blood pressure control.

Adherence to pharmacological treatment is among the protective factors associated with blood pressure control[1-3]. According to the World Health Organization (WHO), a patient adheres to antihypertensive pharmacological treatment when he or she uses 80% or more of the prescribed medications[1,2].

Adherence is a complex phenomenon influenced by factors associated with the disease, treatment, the patient and the healthcare system, and can be measured directly through an analysis of drug metabolites or biological markers in urine/blood, or indirectly through interviews, self-report instruments, diaries or pill counting[4,5].

In this sense, a systematic review brought together studies that used different strategies to assess adherence to antihypertensive treatment, and estimated the worldwide non-adherence prevalence with a wide variation, from 3.3% to 86.1%. The differences in the non-adherence percentage evidenced in this study can be explained by the different methods and instruments used to measure adherence, sociodemographic characteristics, different clinical conditions and the health system of the populations under study[5].

There are few population-based studies in Brazil which estimate the adherence to pharmacological treatment prevalence in hypertensive patients, which is necessary information to optimize treatment and achieve blood pressure control goals. Thus, the present study aimed to evaluate the adherence to antihypertensive treatment prevalence in the Brazilian population, based on peer-reviewed studies which used instruments exclusively designed and/or adapted for this purpose.

Methods

Study design

This is a systematic review with meta-analysis based on the recommendations of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA)[6]. The guiding question consisted of: what is the adherence to antihypertensive pharmacological treatment prevalence in the Brazilian population, based on peer-reviewed Brazilian studies that used instruments exclusively designed and/or adapted for this purpose? The protocol for this meta-analysis was registered in PROSPERO, with identification CRD42021292689.

Literature sources and search strategies

The search in the databases included articles published until November 22, 2021. The following electronic data sources were used to select the articles: Nursing Databases (BDENF), Online Electronic Scientific Library (SciELO), Cuiden, PsycINFO, Cumulative Index to Nursing and Allied Health Literature (CINAHL), Excerpta Medica dataBASE (Embase), Latin American and Caribbean Literature in Health Sciences (LILACS), Medical Literature Analysis and Retrieval System (MEDLINE), as well as academic search engines (AgeLine, Google Scholar and ScienceDirect). Descriptors were identified in the Medical Subject Headings (MeSH), Health Sciences Descriptors (Decs) and Embase Subject Headings (Emtree). Controlled descriptors specific to each database were used as a search strategy.

Outcomes

Primary outcome: national estimate of the adherence to antihypertensive medication treatment prevalence, assessed using instruments for this purpose.

Secondary outcomes: national estimate of the adherence to antihypertensive drug treatment prevalence according to decade of publication, geographic region of the study, and the instruments used.

Eligibility criteria

Quantitative studies submitted to peer review, developed in Brazil, in Portuguese, English and Spanish, carried out with adults (age ≥ 18 years old), without restrictions on year of publication

or sample size, which addressed the adherence to antihypertensive drug treatment prevalence using instruments exclusively designed and/or adapted for this purpose, and validated for use in the Brazilian population were selected.

Studies with pregnant women, those which did not evaluate pharmacological adherence or did not consider the prevalence of pharmacological adherence exclusively for arterial hypertension and studies that used the same database were excluded. In addition, review, theoretical, methodological and qualitative articles, as well as publications considered gray literature (theses, dissertations, conference annals, technical standards, commercial literature, websites, among others) were excluded.

Study selection and data extraction

Duplicate articles were identified and excluded in the first selection stage. Next, titles and abstracts were read to evaluate the eligibility criteria and determine the reason for exclusion in the second stage. When the information contained in the title and abstract was not sufficient to make a decision, the articles were kept for reading in full. The last stage consisted of reading the articles in full that did not contain exclusionary information in titles and abstracts.

The steps were performed by two independent reviewers (AK and RJ), and in case of divergence, the analysis was carried out by a third examiner (MC). Data collection took place using a Microsoft Excel spreadsheet covering the following variables: authors, title, year of publication, journal, place of study, type of study, methods of evaluating pharmacological adherence (direct and/or indirect and their respective measuring instruments). It is noteworthy that the proportion of adherence measured by indirect methods was considered in the present study. Only the prevalence of initial adherence to the study was considered in relation to clinical trials; and in relation to studies which used the four-item Morisky-Green Test in conjunction with other indirect method(s) or instrument(s) of self-report, only the prevalence of the Morisky-Green Test was considered for the meta-analysis, as it is the most used method in studies assessing adherence to treatment.

Assessment of the quality of studies

The studies were individually evaluated for methodological quality considering internal and external validity, response rate and generalization of study results using the 10-item Rating Scale developed by Hoy et al. (2012)[7] for cross-sectional studies, adapted by Bigna et al. (2017)[8]. A corresponding score was used for each item, with 1 (one) point for "Yes" and 0 (zero) for "No". At the end, the points were added up and evaluated within a score from zero to 10, which was categorized as follows: 8-10 = low risk of bias, 5-7 = medium risk of bias, and 0-4 = high risk of bias. Articles that had a high risk of bias were excluded from the meta-analysis, however all studies were included in the qualitative synthesis.

Data analysis

The characteristics of the studies were described by absolute and relative frequencies. The estimated adherence to treatment rate for arterial hypertension was expressed as prevalence. The prevalence of grouped adherence was calculated using a generalized linear mixed effects model with a restricted maximum likelihood estimator, a method which has shown better fit when the outcome is the proportion. The models are accompanied by residual heterogeneity statistics, divided by unmodeled variability (I^2), and subgroup analysis for decade of publication, geographic region in which the study was conducted and the instrument used to assess adherence to antihypertensive drug treatment. The confidence level adopted was 95% and all analyzes were performed in the R 4.1.1 statistical software program using the 'meta' and "metafor" package, version 5.0-0.

Results

The database search retrieved 2,735 articles, but 972 duplicates were removed, resulting in 1,761 articles for evaluation. After analyzing titles and abstracts, 1,526 studies were excluded, totaling 235 for full-text evaluation. After evaluating the full texts, 129 were discarded as they did not meet the eligibility criteria for this study, as detailed in Figure 1. Thus, 106 studies which were part of the qualitative synthesis were selected for the final sample (Figure 1).

It is noteworthy that a high percentage of these studies were found between 2011 and 2021 (89.6%), published in national journals (87.7%) and concentrated in journals in the areas of Nursing, Public Health and Cardiology (70. 0%) (Chart 1). Regarding the Brazilian region in which the

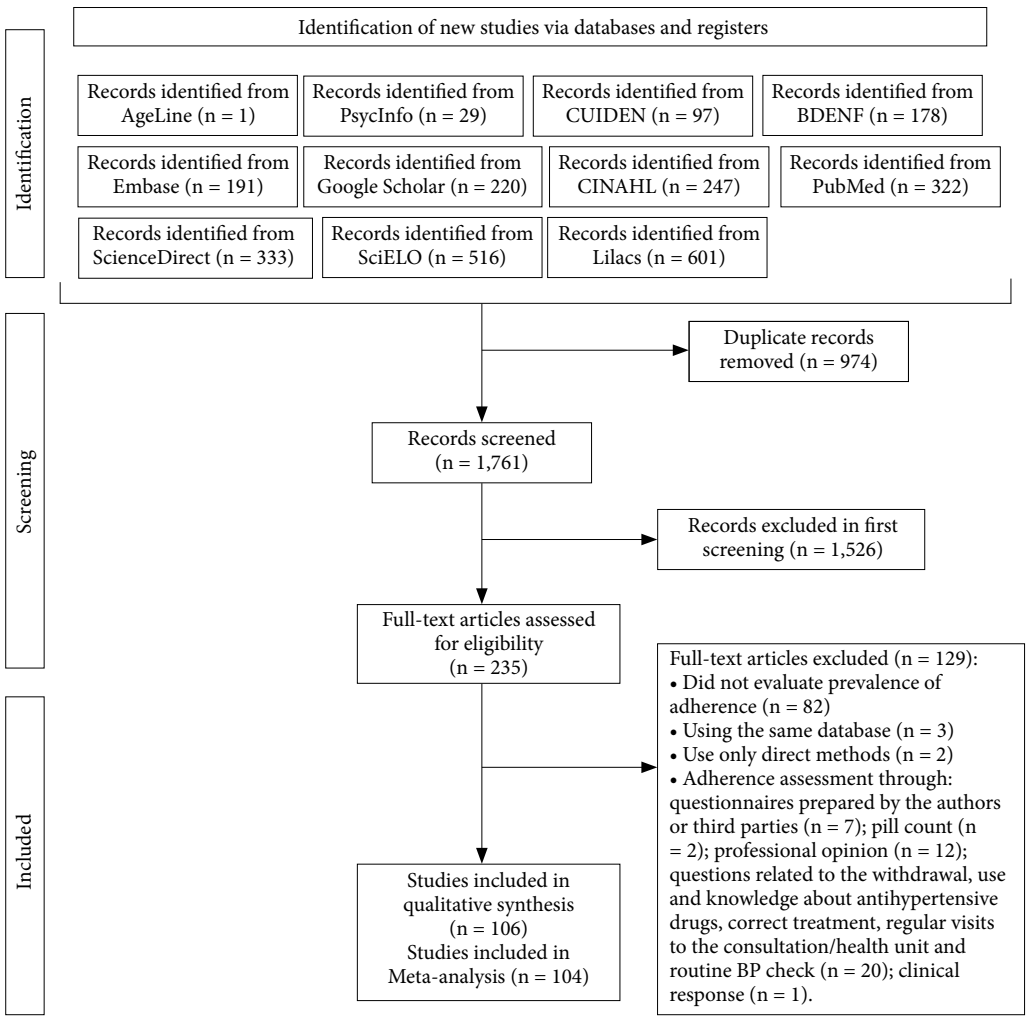

Figure 1. Flowchart of the search and selection process for articles on the adherence to antihypertensive pharmacological treatment prevalence in Brazil, 2023.

Source: Authors.

study was conducted, there was an absence of studies carried out exclusively in the North Region, while 38.5% occurred in the Southeast, 33.7% in the Northeast, 21.2% in the South and 4.8% in the Center-West regions (Chart 1).

After analyzing the risk of bias, it was found that 1.9% (n = 2) of the studies presented a high risk of bias, 51.9% moderate risk (n = 55) and 46.2% low risk (n = 49) (Chart 1). Therefore, 104 studies were included in the meta-analysis, as they presented a moderate or low risk of bias.

A total of 38,299 patients were obtained among the studies selected for the meta-analysis, whose median sample size of the studies was 145 (interquartile range = 100-299), with a minimum value of 14 patients and a maximum of 1,029. Among the 104 studies, 79.8% were cross-sectional, 5.8% were cohort studies and 12.5% were clinical trials (Chart 1).

After meta-analysis of the 104 included studies, an adherence to antihypertensive pharmacological treatment prevalence was estimated at 44.4% (95%CI: 39.1-49.9). The heterogeneity between the estimated prevalence rates was high and statistically significant ($I^2 = 97.90\%$; $p<0.001$) (Figure 2).

Chart 1. Studies selected for meta-analysis according to author, journal, year of publication, type of study, sample size and assessment of risk of bias, Brazil, 2023.

Authors	Year of publication	Journal	Study type	Sample size	Adhesion evaluation method	Risk of bias of the study*
1. Strelec MAAM et al.	2003	*Arq Bras Cardiol*	Cross-sectional	130	Four-item Morisky-Green Test	7
2. Prado Júnior JC et al.	2007	*J Hum Hypertens*	Cross-sectional	109	Four-item Morisky-Green Test	8
3. Bloch KV et al.	2008	*Cad Saude Publica*	Cross-sectional	200	Four-item Morisky-Green Test	7
4. Dosse C et al.	2009	*Rev Latino-Am Enfermagem*	Cross-sectional	123	Four-item Morisky-Green Test	7
5. Medeiros ACD et al.	2009	*Lat Am J Pharm*	Cross-sectional	450	Four-item Morisky-Green Test	7
6. Souza WA et al.	2009	*J Clin Hypertens (Greenwich)*	Uncontrolled trial (quasi-experimental)	44	Four-item Morisky-Green Test	7
7. Santa-Helena ET et al.	2010	*Cad Saude Publica*	Cross-sectional	595	Medication Adherence Questionnaire - Qualaids (MAQ-Q)	9
8. Santos BRM et al.	2010	*Braz J Pharm Sci*	Cross-sectional	102	Four-item Morisky-Green Test	7
9. Ungari AQ et al.	2010	*Braz J Pharm Sci*	Cross-sectional	109	Four-item Morisky-Green Test	9
10. Amarante LC et al.	2010	*Rev Ciênc Farm Básica Apl*	Controlled trial (experimental without randomization)	27	Four-item Morisky-Green Test	4- excluded from meta-analysis
11. Helena ETS et al.	2010	*Saúde Soc*	Cross-sectional	595	Medication Adherence Questionnaire - Qualaids (MAQ-Q)	10
12. Obreli-Neto PR et al.	2011	*Int J Clin Pharm*	Clinical trial	194	Four-item Morisky-Green Test	7
13. Cavalari E et al.	2012	*Rev. Enferm. UERJ*	Cross-sectional	75	Four-item Morisky-Green Test	7
14. Demoner MS et al.	2012	*Acta Paul Enferm*	Cross-sectional	150	Four-item Morisky-Green Test	7
15. Aguiar PM et al.	2012	*J Am Pharm Assoc*	Controlled trial (experimental without randomization)	35	Four-item Morisky-Green Test	6
16. Oliveira-Filho AD et al.	2012	*Arq Bras Cardiol*	Cross-sectional	223	Morisky eight-item Medication Adherence Scale (MMAS-8)	8
17. Bastos-Barbosa RG et al.	2012	*Arq Bras Cardiol*	Cross-sectional	60	Four-item Morisky-Green Test	4 - excluded from meta-analysis
18. Massierer D et al.	2012	*Arq Bras Cardiol*	Cross-sectional	106	Four-item Morisky-Green Test	7
19. Pucci N et al.	2012	*Arq Bras Cardiol*	Cross-sectional	260	Four-item Morisky-Green Test	6
20. Rufino DBR et al.	2012	*J Health Sci Inst*	Cross-sectional	50	Four-item Morisky-Green Test	8

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Authors	Year of publication	Journal	Study type	Sample size	Adhesion evaluation method	Risk of bias of the study*
21. Eid LP et al.	2013	*Rev Eletrônica Enferm*	Cross-sectional	90	Four-item Morisky-Green Test	7
22. Silva CS et al.	2013	*Rev Esc Enferm USP*	Cross-sectional	340	Primary Care Assessment Tool (PCAT)	8
23. Ferreira FM et al.	2013	*Rev APS*	Cross-sectional	51	Treatment Adherence Measure (TAM)	8
24. Nascimento ACG et al.	2013	*Rev APS*	Cross-sectional	72	Martín-Bayarre-Grade (MBG)	8
25. Martins BPR et al.	2013	*Braz J Pharm Sci*	Uncontrolled trial (quasi-experimental)	14	Four-item Morisky-Green Test	6
26. Oliveira DC et al.	2013	*Rev Soc Bra Clín Méd*	Cross-sectional	850	Four-item Morisky-Green Test	8
27. Grezzana GB et al.	2013	*Arq Bras Cardiol*	Cross-sectional	143	Four-item Morisky-Green Test	6
28. Silva LOL et al.	2013	*Cad Saude Colet*	Cross-sectional	99	Four-item Morisky-Green Test	6
29. Bezerra ASM et al.	2014	*Rev Bras Enferm*	Cross-sectional	77	Treatment Adherence Measure (TAM)	8
30. Jannuzzi FF et al.	2014	*Rev. Latino-Am. Enfermagem*	Cross-sectional	100	Four-item Morisky-Green Test	6
31. Raymundo ACN et al.	2014	*Rev Esc Enferm USP*	Controlled trial (experimental without randomization)	283	Four-item Morisky-Green Test	8
32. Martins AG et al.	2014	*Acta Paul Enferm*	Cross-sectional	140	Four-item Morisky-Green Test	7
33. Silva LFRS et al.	2014	*Rev Ciênc Farm Básica Apl*	Cross-sectional	117	Four-item Morisky-Green Test	5
34. Souza CS et al.	2014	*Arq Bras Cardiol*	Cross-sectional	353	Four-item Morisky-Green Test	8
35. Martins BCC et al.	2014	*Rev Bras Hipertens*	Uncontrolled trial (quasi-experimental)	23	Four-item Morisky-Green Test	6
36. Vieira LB et al.	2014	*Rev Bras Cardiol*	Cross-sectional	32	Four-item Morisky-Green Test	6
37. Weber D et al.	2014	*Rev Bras Hipertens*	Retrospective cohort	100	Four-item Morisky-Green Test	8
38. Dias TK et al.	2014	*Geriatr, Gerontol Aging*	Cross-sectional	504	Four-item Morisky-Green Test	9
39. Medeiros ARC et al.	2014	*Saúde Debate*	Cross-sectional	118	Medeiros Test	6
40. Barreto MS et al.	2015	*Rev Bras Enferm*	Cross-sectional	422	Medication Adherence Questionnaire - Qualaids (MAQ-Q)	10
41. Magnabosco P et al.	2015	*Rev Latino-Am Enfermagem*	Cross-sectional	247	Medication Adherence Questionnaire - Qualaids (MAQ-Q)	9
42. Mantovani MF et al.	2015	*Rev enferm UFPE on line*	Cross-sectional	100	Brief Medication Questionaire (BMQ)	7

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Authors	Year of publication	Journal	Study type	Sample size	Adhesion evaluation method	Risk of bias of the study*
43. Nunes MGS et al.	2015	*Acta Paul Enferm*	Cross-sectional	458	Four-item Morisky-Green Test	8
44. Ribeiro IJS et al.	2015	*Revista Baiana Enferm*	Cross-sectional	92	Four-item Morisky-Green Test	7
45. Vancini-Campanharo CR et al.	2015	*Rev Latino-Am Enfermagem*	Cross-sectional	116	Four-item Morisky-Green Test	8
46. Rigoni CC et al.	2015	*Braz J Pharm Sci*	Uncontrolled trial (quasi-experimental)	40	Four-item Morisky-Green Test	7
47. Oliveira-Filho AD et al.	2015	*Rev Ciênc Farm Básica Apl*	Cross-sectional	173	Morisky eight-item Medication Adherence Scale (MMAS-8)	9
48. Aiolfi CR et al.	2015	*Rev. Bras. Geriatr Gerontol*	Cross-sectional	124	Morisky eight-item Medication Adherence Scale (MMAS-8)	8
49. Rocha TPO et al.	2015	*Int J Cardiovasc Sci*	Cross-sectional	502	Four-item Morisky-Green Test	10
50. Souza FFR et al.	2015	*Rev bras hipertens*	Cross-sectional	356	Four-item Morisky-Green Test	8
51. Barreto MS et al.	2016	*Esc Anna Nery*	Cross-sectional	392	Medication Adherence Questionnaire - Qualaids (MAQ-Q)	10
52. Maciel APF et al.	2016	*Acta Paul Enferm*	Cross-sectional	720	Four-item Morisky-Green Test	9
53. Pierin AMG et al.	2016	*Rev Esc Enferm USP*	Cross-sectional	290	Four-item Morisky-Green Test	8
54. Santos JFS et al.	2016	*Enferm Foco (Brasília)*	Cross-sectional	155	Treatment Adherence Measure (TAM)	8
55. Tavares DMS et al.	2016	*Rev Bras Enferm*	Cross-sectional	1029	Four-item Morisky-Green Test	5
56. Ferreira MA et al.	2016	*Rev Min Enferm*	Cross-sectional	150	Treatment Adherence Measure (TAM)	7
57. Moura AA et al.	2016	*Enferm Glob*	Cross-sectional	138	Four-item Morisky-Green Test	7
58. Corrêa NB et al.	2016	*J Am Soc Hypertens*	Prospective cohort	21	Morisky eight-item Medication Adherence Scale (MMAS-8)	6
59. Jesus NS et al.	2016	*Arq Bras Cardiol*	Cross-sectional	96	Four-item Morisky-Green Test	8
60. Mansour SN et al.	2016	*Epidemiol Serv Saúde*	Cross-sectional	106	Treatment Adherence Measure (TAM)	6
61. Machado ALG et al.	2017	*Rev Enferm UFPE on line*	Cross-sectional	145	SAH Treatment Adherence Questionnaire (SAHTAQ)	6
62. Maciel APF et al.	2017	*Rev Enferm UFPE on line*	Controlled trial (experimental without randomization)	720	Four-item Morisky-Green Test	7

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Authors	Year of publication	Journal	Study type	Sample size	Adhesion evaluation method	Risk of bias of the study*
63. Fritzen JS et al.	2017	*Rev Saúde Pública*	Cross-sectional	414	Brief Medication Questionaire (BMQ)	7
64. Righi CG et al.	2017	*J Clin Hypertens (Greenwich).*	Cross-sectional	416	Morisky eight-item Medication Adherence Scale (MMAS-8)	8
65. Aquino GA et al.	2017	*Rev Bras Geriatr Gerontol*	Cross-sectional	279	Four-item Morisky-Green Test	8
66. Pereira MG et al.	2017	*Rev Baiana Saúde Pública*	Cross-sectional	60	Four-item Morisky-Green Test	6
67. Rocha ML et al.	2017	*Rev APS*	Cross-sectional	405	Borges	9
68. Klafkea A et al.	2017	*Rev Bras Med Fam Comunidade*	Cross-sectional	128	Borges	9
69. Albuquerque NLS et al.	2018	*Rev Bras Enferm*	Cross-sectional	270	Four-item Morisky-Green Test	5
70. Feriato KT et al.	2018	*Rev Bras Enferm*	Cross-sectional	108	Four-item Morisky-Green Test	9
71. Ghelman LG et al.	2018	*Rev Enferm UFPE on line*	Cross-sectional	60	Four-item Morisky-Green Test	6
72. Sousa ASJ et al.	2018	*Rev Enferm UERJ*	Cross-sectional	602	Four-item Morisky-Green Test	8
73. Gewehr DM et al.	2018	*Saúde Debate*	Cross-sectional	145	Brief Medication Questionaire (BMQ)	8
74. Falcão AS et al.	2018	*Rev Bras Promoc Saúde*	Cross-sectional	254	SAH Treatment Adherence Questionnaire (SAHTAQ)	6
75. Dallacosta FM et al.	2019	*Rev Pesqui Cuid Fundam (Online)*	Cross-sectional	72	Brief Medication Questionaire (BMQ)	8
76. Santana BS et al.	2019	*Esc Anna Nery*	Cross-sectional	133	Four-item Morisky-Green Test	5
77. Birck MG et al.	2019	*Sao Paulo Med J*	Prospective cohort	15.105	Four-item Morisky-Green Test	8
78. Almeida ALJ et al.	2019	*Rev APS*	Cross-sectional	114	Treatment Adherence Measure (TAM)	9
79. Andrade DDBC et al.	2019	*REVISA (Online)*	Cross-sectional	261	Morisky eight-item Medication Adherence Scale (MMAS-8)	7
80. Santos LMC et al.	2019	*Rev Psicol Saúde*	Cross-sectional	100	Morisky eight-item Medication Adherence Scale (MMAS-8)	7
81. Amaral MMB et al.	2019	*Rev Salud Pública*	Controlled trial (experimental without randomization)	14	SAH Treatment Adherence Questionnaire (SAHTAQ)	7
82. Gouveia Neto JR et al.	2019	*Nursing (São Paulo)*	Cross-sectional	112	Morisky eight-item Medication Adherence Scale (MMAS-8)	8

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Authors	Year of publication	Journal	Study type	Sample size	Adhesion evaluation method	Risk of bias of the study*
83. Luz MM et al.	2019	*Rev Soc Cardiol Estado de São Paulo*	Cross-sectional	110	Morisky eight-item Medication Adherence Scale (MMAS-8)	7
84. Barbosa MEM et al.	2019	*Rev enferm UERJ*	Cross-sectional	257	Borges	9
85. Nascimento MO et al.	2020	*Texto Contexto Enferm*	Cross-sectional	421	Morisky eight-item Medication Adherence Scale (MMAS-8)	8
86. Silva LM et al.	2020	*Rev Esc Enferm USP*	Cross-sectional	193	Four-item Morisky-Green Test	8
87. Macedo C et al.	2020	*Arq Bras Cardiol*	Cross-sectional	146	Morisky eight-item Medication Adherence Scale (MMAS-8)	6
88. Silva ÂTM et al.	2020	*Res Nurs Health*	Clinical trial	94	SAH Treatment Adherence Questionnaire (SAHTAQ)	6
89. Rosa GS et al.	2020	*Rev Enferm UFPI*	Cross-sectional	105	Four-item Morisky-Green Test	7
90. Rosa RS et al.	2020	*Rev Cuid*	Cross-sectional	302	Morisky eight-item Medication Adherence Scale (MMAS-8)	5
91. Mata JGF et al.	2020	*Saude e Pesqui (Impr)*	Cross-sectional	213	Four-item Morisky-Green Test	8
92. Cavalcante LR et al.	2020	*Rev Bras Promoc Saúde*	Cross-sectional	286	Four-item Morisky-Green Test	7
93. Araújo LBS et al.	2020	*Int J Cardiovasc Sci*	Retrospective cohort	216	Morisky eight-item Medication Adherence Scale (MMAS-8)	7
94. Luz ALA et al.	2020	*Rev Bras Geriatr Gerontol*	Cross-sectional	384	Brief Medication Questionaire (BMQ)	7
95. Barletta PH et al.	2021	*Int J Cardiovasc Sci*	Cross-sectional	181	Morisky eight-item Medication Adherence Scale (MMAS-8)	8
96. Girão AC et al.	2021	*Rev Enferm Cent-Oeste Min*	Cross-sectional	242	Morisky eight-item Medication Adherence Scale (MMAS-8)	6
97. Carvalho BL et al.	2021	*REVISA (Online)*	Cross-sectional	103	Morisky eight-item Medication Adherence Scale (MMAS-8)	8
98. Soares MM et al.	2021	*Cad Saúde Pública*	Cross-sectional	641	Four-item Morisky-Green Test	10
99. Vieira LB et al.	2021	*Einstein (São Paulo)*	Uncontrolled trial (quasi-experimental)	32	Four-item Morisky-Green Test	8
100. Silva GF et al.	2021	*Esc Anna Nery*	Cross-sectional	306	Martín-Bayarre-Grade (MBG)	7
101. Pinhati R et al.	2021	*Int J Clin Pract*	Prospective cohort	311	Four-item Morisky-Green Test	8

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Chart 1. Studies selected for meta-analysis according to author, journal, year of publication, type of study, sample size and assessment of risk of bias, Brazil, 2023.

Authors	Year of publication	Journal	Study type	Sample size	Adhesion evaluation method	Risk of bias of the study*
102. Volpi SS et al.	2021	*Peer J*	Uncontrolled trial (quasi-experimental)	49	Martín-Bayarre-Grade (MBG)	7
103. Pinhati RR et al.	2021	*Int Urol Nephrol*	Cross-sectional	485	Four-item Morisky-Green Test	7
104. Steffen PLS et al.	2021	*Am J Prev Med*	Clinical trial	189	Martín-Bayarre-Grade (MBG)	6
105. Barletta PHAAS et al.	2021	*Int J Cardiovasc Sci*	Cross-sectional	120	Morisky eight-item Medication Adherence Scale (MMAS-8)	5
106. Wachholz PA et al.	2016	*Acta Sci, Health Sci*	Prospective cohort	213	Treatment Adherence Measure (TAM)	8

* Risk of study bias: low risk = 8 to 10 points; moderate risk = 5 to 7 points; high risk risk = 0 to 4 points.

Source: Authors.

The subgroup analysis showed no statistically significant difference in the adherence prevalence between the period in which the studies were carried out (2001-2010 vs. 2011-2021, p=0.704), respectively, presenting the following prevalence rates of 42% (95%CI: 28.76-56.69) and 44.7% (95%CI: 39.01-50.60) (Table 1).

The adherence prevalence assessment according to geographic region identified a lower adherence prevalence in studies carried out in the Central-West and in multicenter studies (conducted in more than one location in Brazil). There was no significant difference in the proportion of adherence to treatment between the South, Southeast, North and Northeast regions. However, there was a difference between the prevalence evidenced in the multicenter study compared to studies carried out in the South, Southeast and Northeast Regions. Nevertheless, this finding must be analyzed with caution, as only two studies were multicenter (Table 1).

The instruments used in the studies selected in this meta-analysis were the: four-item Morisky-Green Test, Morisky eight-item Medication Adherence Scale (MMAS-8), Treatment Adherence Measure (TAM), Brief Medication Questionnaire (BMQ), Medication Adherence Questionnaire – Qualiaids (MAQ-Q), SAH Treatment Adherence Questionnaire (SAHTAQ), Martín-Bayarre-Grade (MBG), Haynes-Sackette Test and Primary Care Assessment Tool (PCAT), Assessment instrument of non-adherence to arterial hypertension treatment developed by Borges, and the Medeiros test.

A higher medication adherence prevalence was observed in the study which used the Primary Care Assessment Tool (89.1%), followed by those that used the SAH Treatment Adherence Questionnaire – SAHTAQ (88.3%) and the Treatment Adherence Measure - TAM (74.1%). Lower prevalence was found in studies which used the Martín-Bayarre-Grade (MBG) (30.5%), the four-item Morisky-Green Test (36.9%) and the eight-item Morisky Medication Adherence Scale (MMAS-8) (36.8%) (Figure 3).

Discussion

The adherence to antihypertensive drug treatment prevalence measured by indirect methods in Brazilian studies was 44.4%. There was no difference in the adherence prevalence between the periods studied and the geographic region in which the study was conducted. It is noteworthy that there were no studies exclusively conducted in the Northern Region of the country, a location with the greatest socioeconomic vulnerability in the country.

The adherence prevalence identified after the meta-analysis was higher than the prevalence of other studies carried out in low- and middle-income countries, whose percentages were around 35.0%[9,10]. However, these studies assessed adher-

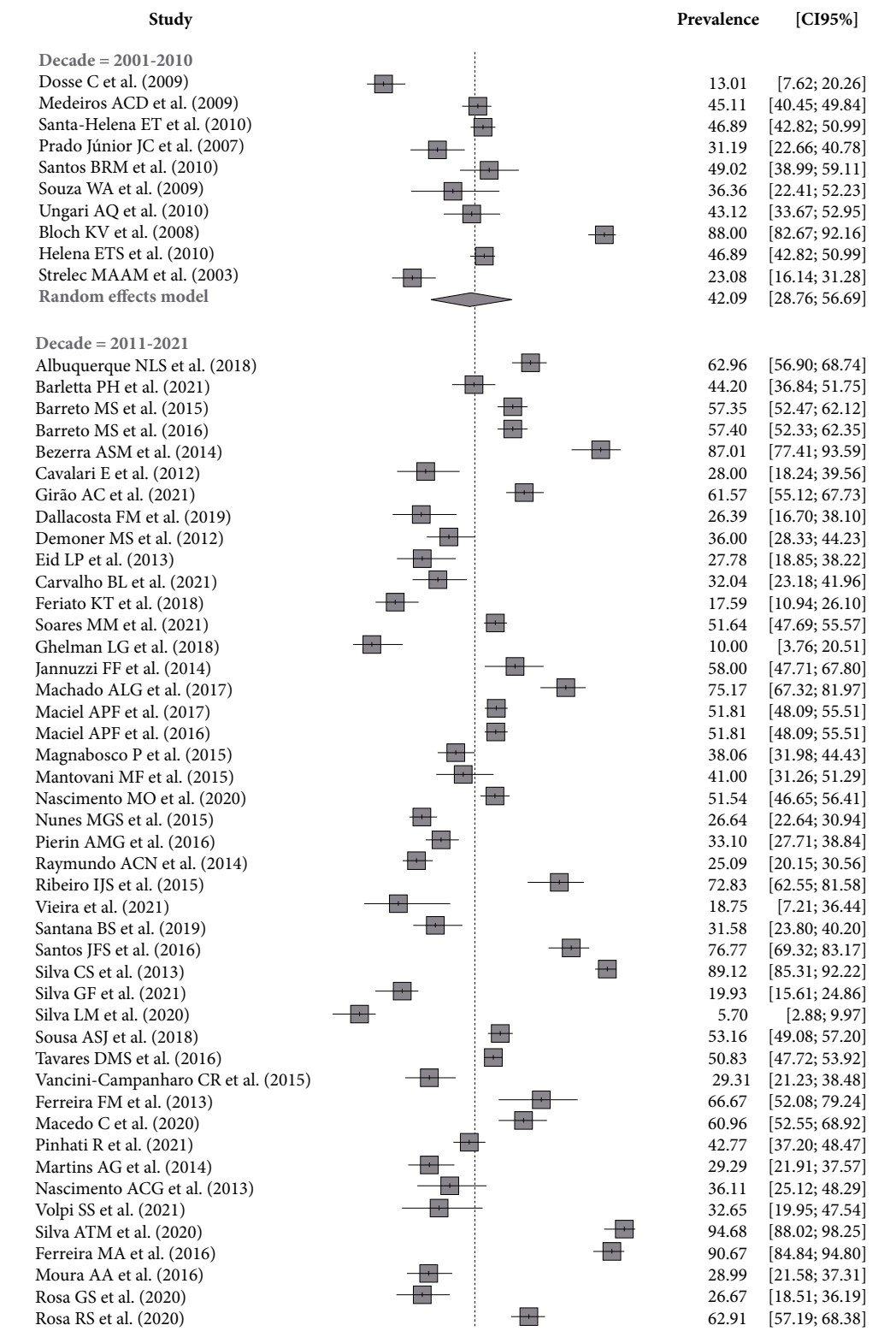

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Figure 2. Forest plot with the adherence to antihypertensive pharmacological treatment prevalence in Brazil stratified by decade of the study, Brazil, 2023.

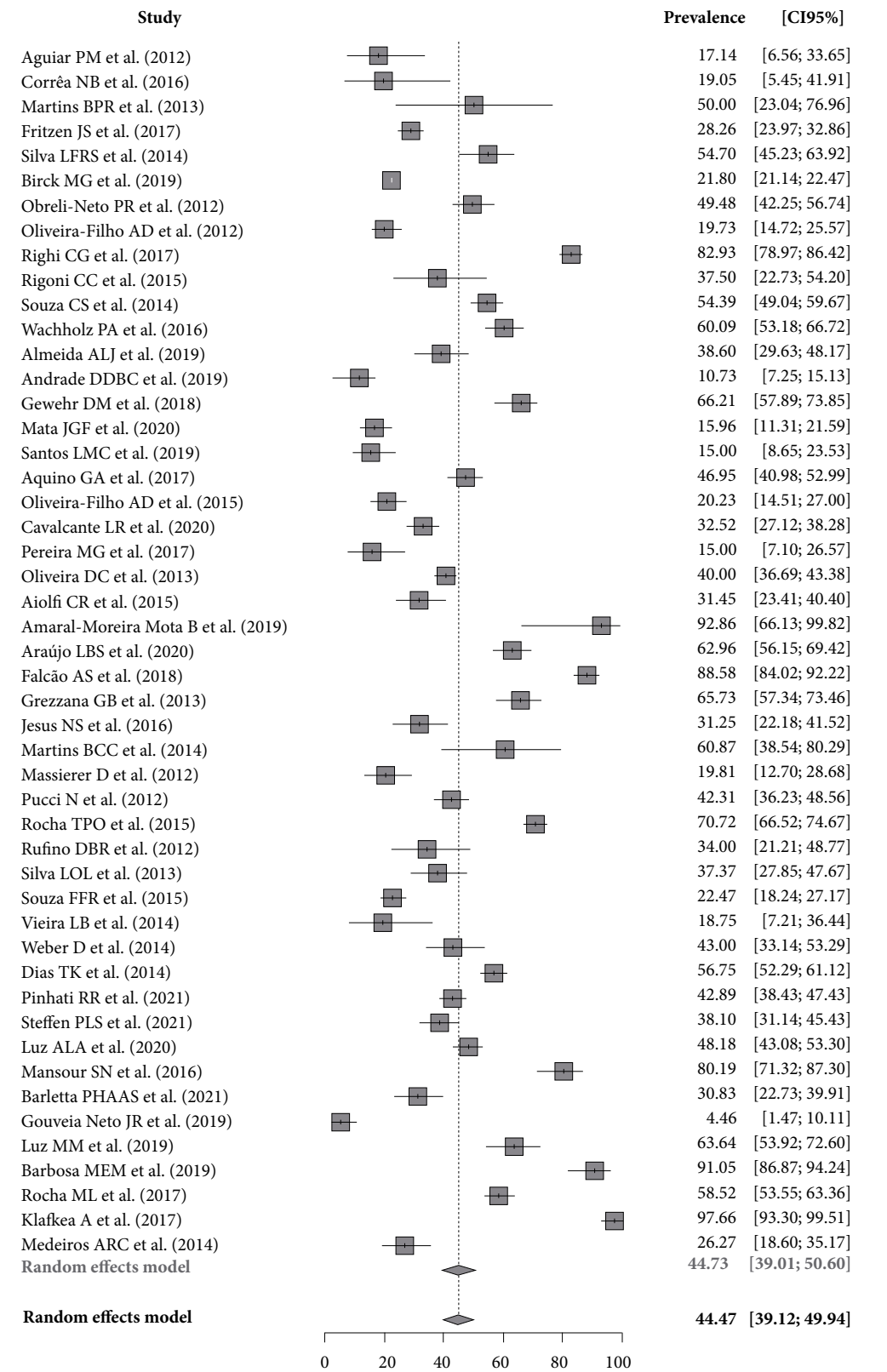

Figure 2. Forest plot with the adherence to antihypertensive pharmacological treatment prevalence in Brazil stratified by decade of the study, Brazil, 2023

Source: Authors.

Table 1. Results of meta-analysis by subgroup according to decade of publication and geographic region in which the study was carried out, Brazil, 2023.

Variables	n	Prevalence (%)	95%CI (%)	I2 (%)	p-value*
Decade					
2001-2010	10	42.09	28.76-56.69	94.90	0.74
2011-2021	94	44.73	39.01-50.60	98.10	
Region					
Center-West	5	26.86	17.26-39.27	89.2	0.001
Multicenter	2	21.86	21.21-22.52	79.5	
Northeast	35	43.88	35.19-52.96	97.1	
Southeast	40	42.07	33.90-50.69	95	
South	22	55.77	43.11-67.73	96.3	

95%CI: 95% confidence interval; I2 = residual heterogeneity statistic, divided by unmodeled variability; test for subgroup differences (generalized linear mixed effects model).

Source: Authors.

ence with Morisky's eight-item Medication Adherence Scale, which also showed a prevalence of approximately 35% in the present study. Developed countries, such as the United States[11] and Canadá[12], show a better scenario, but still not desirable, with adherence prevalence of around 68% and 67% evaluated by the Morisky instruments with eight and four items, respectively.

A greater percentage of the articles included were published in nursing journals which, in the context of hypertensive patients, play a fundamental role in improving adherence to treatment; this is important given that the main proposals currently studied, such as self-measurement of blood pressure, adequacy of dosage schemes and use of Mobile health, require direct nursing action with the patient, justifying the large quantity of research published in journals in the area[11,12].

Despite the efforts observed in recent years, the results of the present study did not indicate a significant improvement in the adherence prevalence when comparing the period from 2001 to 2010 with the historical period from 2011 to 2021. From the 2000s onwards, Noncommunicable Disease (NCD) prevention gained focus, mainly in developing countries. As a result, several national programs and policies were created, such as: the Plan for Reorganization of Care for Arterial Hypertension and Diabetes Mellitus (*Plano de Reorganização da Atenção à Hipertensão Arterial e ao Diabetes Mellitus – HIPERDIA*)[13]; the Brazilian Popular Pharmacy Program (*Programa Farmácia Popular do Brasil – FPB*)[14]; and the Basic Care Booklet and Guidelines and Recommendations for Comprehensive NCD Care (*Caderno de Atenção Básica e as Diretrizes e Recomendações ao Cuidado Integral de DCNT*)[15], with these being directed to Primary Healthcare in order to improve the treatment and prevention of these diseases. These initiatives have brought important advances in the management of chronic diseases, however weaknesses are observed, as what occurred in the South of the country based on the *HIPERDIA* evaluation, in which professionals were observed reporting a much lower number of duties than that established in the protocol, lack of tracking of patients and not prescribing non-pharmacological measures[16].

Pharmacological treatment has a direct relationship with patient adherence in Brazil, and the public health system is based on the universalization of free access to healthcare for the entire population, with decentralization at all levels from prevention to high complexity, shared by federal, state and municipal governments[17]. Antihypertensive medications are available in the Unified Health System (*Sistema* Único *de Saúde – SUS*), with free distribution and a list of medications that include diuretics, beta-blockers, angiotensin-converting enzyme inhibitors and angiotensin receptor blockers through the *Farmácia Popular do Brasil* Program; this program is fundamental for guaranteeing patients' medication treatment, and data indicate a decrease in medication accessed/obtained by patients with high blood pressure in Basic Health Units between 2011 and 2017 due to the increase in obtaining medication through *Farmácia Popular*[18].

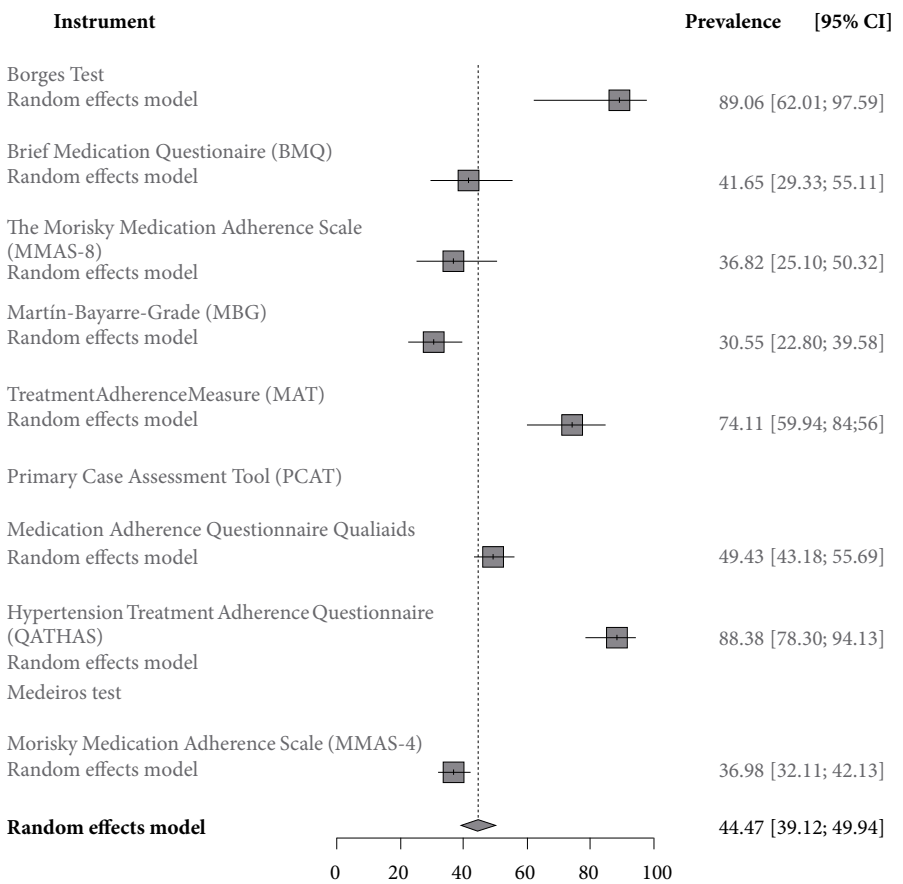

Figure 3. Forest plot with the adherence to antihypertensive pharmacological treatment prevalence in Brazil, stratified by instrument for indirect assessment of adherence to antihypertensive pharmacological treatment, Brazil, 2023.

Source: Authors.

There was also a reduction in the number of hospitalizations and deaths related to systemic arterial hypertension and diabetes mellitus as a result of the program[19], with disparities in the effectiveness and efficacy of these measures according to the level of socioeconomic development and access to health services in the Federative Units of Brazil. On the other hand, polypharmacy stands out in this context, as the program does not include the use of fixed drug combinations which consist of combining antihypertensive drugs, bringing direct benefits in adherence to treatment[20], and consequently better cardiovascular protection[21]. Low adherence to medication treatment is a worrying result, as adherence to 80% or more of prescribed medications reduces the risk of target organ damage[22].

The high heterogeneity between studies stands out as a limitation of this study, which reflected in the wide variation in the adherence prevalence observed in the studies included in the review, with values between 4.46% and 97.66%. Furthermore, results similar to those observed in other reviews on the topic were found[6,23], which highlight that the high heterogeneity is related to the complexity of establishing an ideal method for measurement, being reflected by many self-report instruments developed for this purpose. In this sense, ten different instruments were used in the present study, with the most used be-

ing the four-item Morisky-Green Test, followed by the eight-item Morisky Medication Adherence Scale (MMAS-8). The internal consistency between the instruments varied between 0.61 (Morisky-Green test – 4 items) and 0.89 (Martín-Bayarre-Grade questionnaire). The Brief Medication Questionaire obtained the best results in all domains regarding sensitivity and specificity, ranging from 80.00% to 100.00%.

More recent data indicate greater use of the MMAS-8 worldwide[24], however it is necessary to discuss the applicability of some instruments, as they may require a license fee for use, as is the case with the Morisky instruments. A systematic review evaluated publications around the world, identifying 17 instruments to measure adherence to antihypertensive treatment, of which five were validated in different countries, namely the: Hill-Bone compliance to high blood pressure therapy scale (HB); Morisky-Green-Levine test (MGL); 8-item Self-Reported Medication Adherence Measure (MMAS-8); Medication Adherence Self-Efficacy Scale (MASES); and Treatment Adherence Questionnaire for Patients with Hypertension (TAQPH)[23].

Despite the limitations presented, this study is the first in Brazil to summarize the adherence to medication treatment prevalence for arterial hypertension in peer-reviewed Brazilian studies, carrying out a broad assessment of the literature with studies that presented a medium or low degree of bias. The findings showed low adherence to treatment in Brazil, which is far below (44.4%) the value recommended by the WHO (≥ 80%), with no increase in this percentage in the most recent decade (2011 to 2021), and no differences between regions with lower socioeconomic vulnerability and those with greater vulnerability. Furthermore, there were only two multicenter studies and no studies were carried out in the North Region. These results indicate the need to carry out a national multicenter study in all Federative Units of Brazil using standardized measurement instruments validated for use in the country to facilitate comparing studies, and to identify factors associated with non-adherence to treatment, so that public health actions are planned and evaluated with a view to increasing the adherence to treatment prevalence.

Conclusion

The adherence prevalence found herein showed great variability, highlighting the difficulty in measuring this phenomenon. The four-item Morisky-Green Scale was the most used self-report instrument to assess adherence to antihypertensive treatment in Brazil. In the aggregate result, the overall adherence prevalence in Brazil was unsatisfactory (less than half of patients are suspected of having good adherence to treatment), demonstrating that this challenge continues to be a problem that requires actions at the public health level, which include strategies to minimize polypharmacy and optimize access to treatment for hypertensive patients.

Collaborations

AMG Pierin, JC Coelho, MCLP Guimarães, AKMG Vaz, RJW Lee contributed to the conception, design, writing and revision of the manuscript. KC Meira, J Santos and LF Drager contributed on the writing and critical review of the manuscript. All authors approved the final version of the submitted manuscript and are responsible for all its aspects, including ensuring its integrity.

Funding

This work was carried out with the support of the Coordenação de Aperfeiçoamento de Pessoal de Nível Superior – Brasil (CAPES) – Financing Code 001.

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Article submitted 30/11/2022
Approved 21/08/2023
Final version submitted 23/08/2023

Chief editors: Maria Cecília de Souza Minayo, Romeu Gomes, Antônio Augusto Moura da Silva