Patient Preference and Adherence

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ORIGINAL RESEARCH

Medication Adherence In Patients With Arterial Hypertension: The Relationship With Healthcare Systems' Organizational Factors

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Purpose: Arterial hypertension is one of the most common diseases in the world, presenting a great impact on global mortality. Despite having good medication, the best control depends on patient's adherence. Our aim is to characterize the relationship of adherence to medication in hypertensive patients with consultation length and other organizational factors of healthcare systems.

Patients and methods: We performed a comprehensive review of literature using the MeSH terms "hypertension" and "medication adherence". 61 articles were selected for inclusion and adherence parameters were extracted, allowing us to estimate the mean adherence for each country. The adherence was then correlated with organizational aspects of healthcare systems: consultation length, number of health providers (doctors, nurses and pharmacists), number of hospital beds, health expenditure and general government expenditure.

Results: Adherence to medication ranged between 11.8% in Indonesia and 85.0% in Australia. There is much heterogeneity in methodology, but the Morisky Medication Adherence Scale was the preferred method, used in 63.6% of the cases. We found no relation with consultation length, but a significant one with the greater number of health professionals available. Some differences were observed when considering European countries or Morisky Medication Adherence Scale alone.

Conclusion: The better the drugs, the better the control of blood pressure, if patients take them. Rather than investing in the prescription of more drugs, it is important to address non-adherence and reduce it to promote better blood pressure control. Organizational factors are relevant constraints and depend on administrative and political decisions. Although they are not always considered, they greatly impact the adherence to medication.

Keywords: high blood pressure, medication adherence, primary care, health services administration

Introduction

Arterial Hypertension, defined by the World Health Organization (WHO) as systolic blood pressure ≥140 mmHg and/or diastolic blood pressure ≥90 mmHg, is a chronic disease that affected about 22% of the adult population in 2015.[1] The highest prevalence of the disease occurs in developing regions and lower numbers are found in more developed regions.[1] Every year, it accounts for approximately 7.5 million deaths worldwide and has harmful consequences, especially in countries with low capacity for health investment.[2]

The treatment and the control of hypertension include lifestyle changes, such as decreased food salt intake and antihypertensive medication, a strategy required in

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most patients.[3] Adherence is defined as "the extent to which a person's behavior – taking medication, following a diet, and/or executing lifestyle changes, corresponds with agreed recommendations from a healthcare provider", ergo it has a preponderant role in the management of this disease.[4] It is estimated that among hypertensive patients whose disease is not controlled, about half of them do not take medication correctly.[3] Several factors influence adherence to pharmacological and non-pharmacological therapeutic measures and can be related to social and economic context, disease-related, patient-related, healthcare-related and therapy-related.[4]

In addition to the multidimensionality and evident complexity inherent to the adherence process, which may explain its undesired values, the evaluation of adherence to therapy is not always systematically approached in consultation. This fact can result in the loss of opportunities to diagnose and correct non-adherence. On the other hand, the evaluation of adherence is a complex process, since several methods can be used, and there is no standardized method better than the other.[5,6] Detection of the drug in the blood or urine is the most accurate, but it is difficult to apply in clinical practice and has higher costs. Indirect methods, such as questionnaires, are simpler to apply, but often underestimate poor adherence.[3] Although frequently inaccurate and biased by patients' behavior, their value remains, because they provide opportunities to identify patients in need for counselling and to educate them according to their individual barriers, questions or doubts.[5,7] No specific questionnaire is recommended to assess adherence, but most researchers use Morisky Medication Adherence Scale (MMAS). The original MMAS is a 4-item questionnaire, which evaluates 4 reasons for non-adherence: forgetting to take medication, being careless about it, starting do feel better and feeling worse because of possible side effects. Other versions of MMAS were then created, allowing it to be a more consistent instrument.[8,9]

During consultation, counting tablets/prescriptions, introducing specific questionnaires, verifying the expected clinical response to the medication or evaluating physiological markers are possible strategies to evaluate adherence.[10] But it is not enough to evaluate, it is also necessary to take this information and proceed to improve the situation, creating or maintaining a good relationship between doctor and patient, promoter of literacy and better health behaviors.[4,11] Time spent in consultation is crucial to achieve this goal. Longer consultation times are associated with better prescribing and better counseling for lifestyle and preventive behaviors.[12] Although time should not be the decisive factor leading the consultation, there are multiple constraints affecting the way the schedules are programmed or even imposed, turning it in an organizational problem more than a clinical determinant.

The primary aim of this study was to characterize the relation between mean time of consultation, as well as other variables associated with the organization of health systems, and adherence to antihypertensive medication. Secondarily, we sought to define an average adherence to antihypertensive therapy and to characterize the variation between the different methods used to assess it.

Materials And Methods

We searched Pubmed, Scopus and SciELO databases using the MeSH terms "hypertension" and "medication adherence". Subsequently, one author eliminated duplicates and excluded articles by study design and by country. The two authors, independently, read the titles and abstracts of the selected articles, applying the remaining inclusion criteria for full-text reading. Then, we excluded the articles that were unfitting for the objective and a quality evaluation of each one was carried out. All the divergences that emerged during the process were resolved by discussion and consensus.

Study Selection Criteria

We included systematic reviews and observational studies. The study by Irving et al, 2017[13] provided a list of 67 countries for which data on the average consultation time in Primary Health Care were available. This list was our basis for collecting data on other variables. The full-text reading of the articles allowed us to select those with percentage measurements of adherence to medication, regardless of the method used and the type of drugs prescribed.

Extraction Of Data On Medication Adherence

We studied the percentage of adherence to antihypertensive therapy, the method of assessment of adherence and the respective classification criteria in adherence or non-adherence for each article. One of the authors extracted data, which was, then, validated by both authors.

Medication adherence, in general and by country, was estimated by the average of the available results. From the articles included in the review, we extracted data about the different methods used to evaluate adherence to medication and we characterized their use among the studied countries.

Other Variables Studied

The review by Irving et al, from 2017,[13] provided the estimation of the average time of consultation in primary care for each country with available data.

Besides consultation length, many factors can interfere with hypertensive patients' adherence to prescribed medication. Amongst them are health-related human, logistical and financial resources. We studied the number of health professionals (doctors, nurses and pharmacists) per 1000 inhabitants, the number of hospital beds per 10,000 inhabitants, current health expenditure as a percentage of Gross Domestic Product (GDP), current health expenditure per capita, out-of-pocket expenditure per capita and general government expenditure. These data were obtained from WHO's Global Health Observatory.

Quality Assessment

The quality of the studies was assessed by an adaptation of the National Heart, Lung and Blood Institute Assessment Tool, including 4 questions: "1) Was the research question or objective in this paper clearly stated?"; "2) Was the study population clearly specified and defined?"; "11) Were the outcome measures (dependent variables) clearly defined, valid, reliable, and implemented consistently across all study participants?"; "14) Were key potential confounding variables measured and adjusted statistically for their impact on the relationship between exposure(s) and outcome(s)?". Each question was classified with yes or no and the scale of quality evaluation was defined as: Very Good, if it answered yes to the 4 questions; Good, if 3 of the questions were satisfactory; Sufficient if 2 questions were positively answered or Insufficient if less than 2.[14] The classifications obtained from each author were compared and the divergences resolved by discussion and consensus. Articles classified as insufficient were excluded.

Statistical Analysis

The correlations between variables were calculated by the Spearman's Rank Correlation Coefficient (represented by ρ), using the IBM SPSS Statistics 24®. Statistical significance was established when $p < 0.05$.

Results

We identified 2995 articles in database search, to which we added 6 others identified in the references of some of the articles. After applying the inclusion and exclusion criteria, 63 articles were submitted to quality assessment: two thirds had good quality and, among the others, 5 were very good, 14 were sufficient and 2 were insufficient. The 2 insufficient articles were excluded. This process is described in a PRISMA flow diagram[15] (Figure 1).

The 31 countries included in this review represent those who presented studies evaluating adherence to therapy among the 67 described in the review by Irving et al[13]. The mean adherence to antihypertensive therapy ranged from 11.8% in Indonesia to 85.0% in Australia. Overall, the median therapeutic adherence corresponded to 55.3% (Figure 2). In 19 countries (61.3%) medication adherence is estimated to range between 50% and 75% and in 7 countries (22.6%) between 25% and 50%. Only 2 countries (6.4%) are below 25% and 3 (9.7%) are above 75%.

We found 66 assessments of adherence, using 24 different methods. The Morisky Medication Adherence Scale (MMAS) questionnaire and its several adaptions were the most used (63.6%). The original version, MMAS-4, was present in 20 studies and its first adaptation, MMAS-8, in 17 cases. The remaining versions have a less significant representation: MMAS-7 appears 3 times and MMAS-5 only one, as well as MMAS-6. The remaining 36.4% of adherence measurements were grouped and dealt with together. This group included different methods, such as other validated questionnaires (Qualiaids Team Non-Compliance Questionnaire, Batalla Test, Brief Medication Questionnaire, Hill-Bone Compliance Scale, Drug Attitude Inventory 10, Martin-Bayarre-Grade Questionnaire, and Medication Adherence Rating Scale 6) and non-validated, comparing records, calculating ratios (Medication Possession Ratio and Proportion of Days Covered), electronic monitoring (MEMS® cap) and composed measures.

Table 1 presents the detailed results of the review.

No relation between adherence to therapy and mean time of consultation was found ($\rho = 0.140$; $p = 0.451$). However, we found a significant correlation with the number of physicians in the population ($\rho = 0.587$, $p = 0.001$) and a weaker one with the number of nurses ($\rho = 0.394$, $p = 0.031$). When we analysed only the results of the questionnaires based on the Morisky Medication Adherence Scale (MMAS), in all its variants, the correlation is weaker for the number of physicians ($\rho = 0.460$; $p = 0.031$) and not significant for the number of nurses ($\rho = 0.387$, $p = 0.075$). None of the other variables studied showed a significant correlation with adherence to therapy (Table 2).

We analysed separately the subgroup of European countries, since their health systems are quite similar, based on the European Social Model, whether with public or private funding. There was a positive

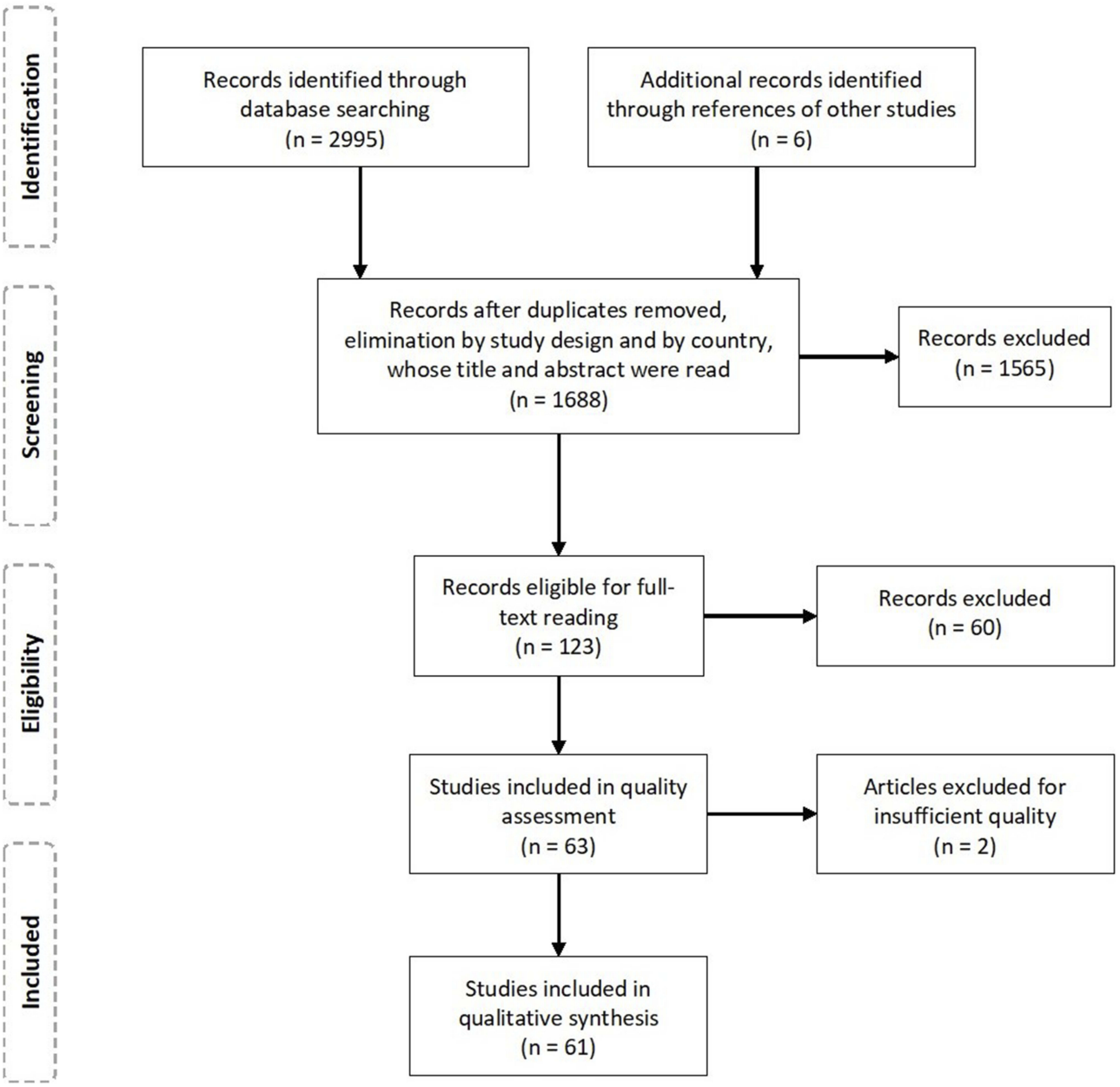

Figure 1 PRISMA flow diagram.

correlation between adherence to antihypertensive therapy and increased government spending on health, both in relation to Gross Domestic Product (ρ = 0.742, p = 0.004) and per capita (ρ = 0.819, p = 0.001), which becomes more pronounced when only adherence measurements by MMAS were considered. The higher public investment in the country is also associated with a better adherence to therapy (ρ = 0.670; p = 0.012) and, once again, there are differences regarding the form of evaluation of adherence: in the questionnaires based on the MMAS scale this relation is more evident. Concerning health professionals, we found a positive and significant correlation of adherence with the number of physicians (ρ = 0.581, p = 0.037), but not with the number of nurses (ρ = 0.467; p = 0.108), nor the number of pharmacists (ρ = −0.324, p = 0.280); considering only the MMAS, nurses' density appeared to be related with higher adherence, but nor doctors', nor pharmacists'. Once more, no relation was found with the mean consultation time, the number of hospital beds per 10,000 inhabitants and the individual health expenditure per capita (Table 2).

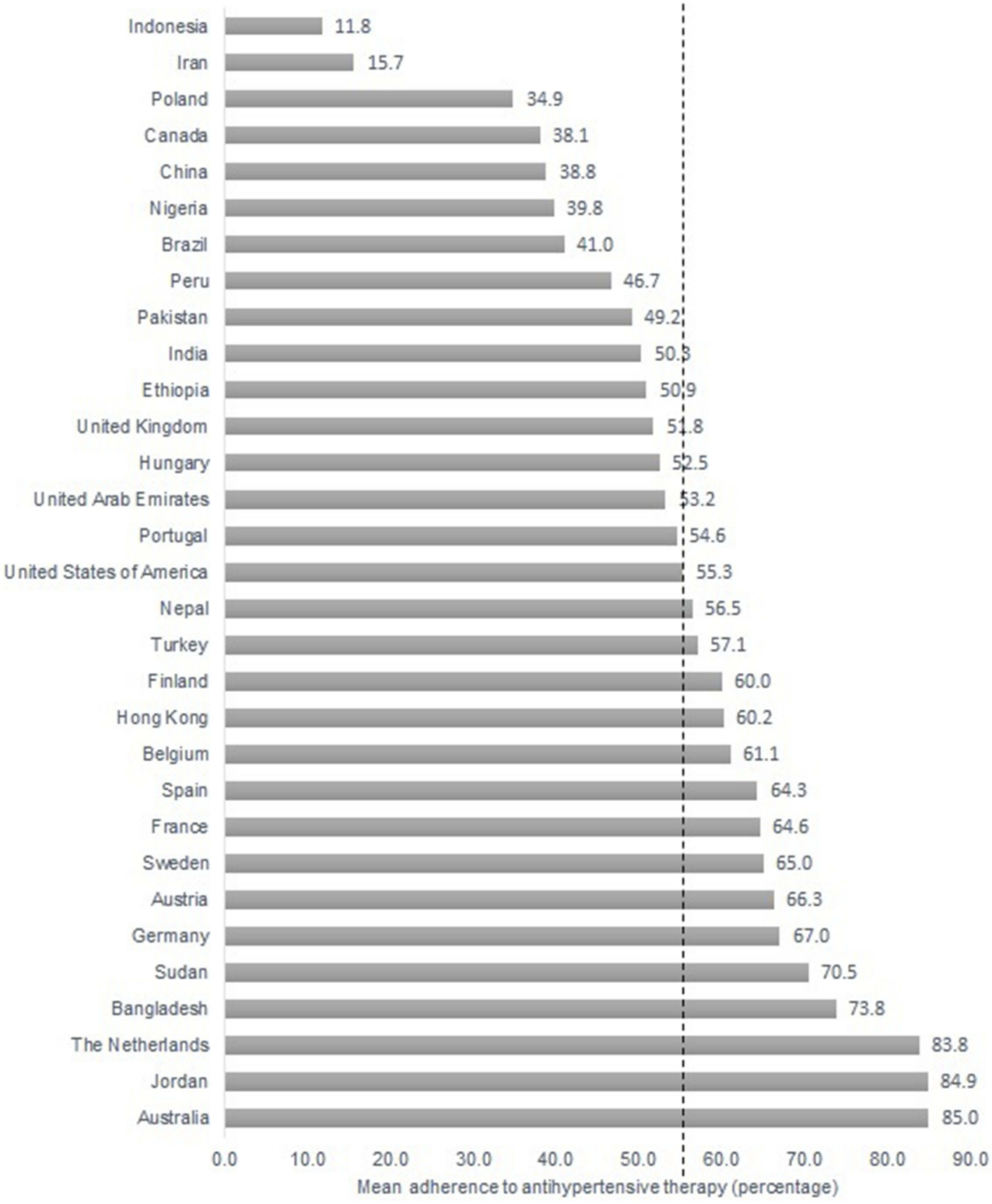

Figure 2 Graphic representation of mean adherence to medication by country.
Note: Dashed line represents median adherence for all countries.

Discussion

According to our results, the median adherence to drug therapy in Arterial Hypertension is 55.3%, which is in line with the global prevalence described by the WHO and ranges from 50% to 70%.[4] The range between countries is very large (73.2%), with most of them showing

Table 1 Summary Of Data Collected From The Studies Included In This Review

Country	Author	Year	Adherence Level	Method Used To Assess Adherence	Adherence Criteria	Quality Assessment
Australia	Mc Namara et al[16]	2014	A: 85.0% NA: 15.0%	MMAS-4 (Y or N)	A: 0 Yes NA: ≥ 1 Yes	Good
Austria	Morrison et al[17]	2015	A: 66.3% NA: 33.7%	MMAS-4 (Y or N)	A: 0 Yes NA: ≥ 1 Yes	Good
Bangladesh	Khanam et al[18]	2014	A: 73.8% NA: 26.2%	Discontinuation of medication at any time since the beginning of therapy (Y or N)	A: No NA: Yes	Good
Belgium	Morrison et al[17]	2015	A: 61.1% NA: 38.9%	MMAS-4 (Y or N)	A: 0 Yes NA: ≥ 1 Yes	Good
Brazil	Barreto et al[19]	2015	A: 57.4% NA: 42.6%	QAM-Q (3 questions)	A: taking 80 to 120% of predicted doses	Good
	Ben et al[20]	2012	A: 38.8% NA: 61.2%	MMAS-4 (Y or N)	A: 0 Yes NA: ≥ 1 Yes	Good
	Bezerra et al[21]	2012	A: 87.0% NA: 13.0%	MMAS-7 (Y or N)	A: 0 or 1 Yes NA: > 1 Yes	Good
	Carvalho et al[22]	2012	A: 22.5% NA: 77.5%	Batalla Test (3 questions)	A: 3 correct answers NA: <3 correct answers	Good
	de Oliveira-Filho et al[23]	2014	A: 20.3% NA: 79.7%	MMAS-8 (7 Y or N + 1 Likert scale)	A: 8 points NA: <8 points	Very Good
	de Santa-Helena et al[24]	2010	A: 46.9% NA: 53.1%	QAM-Q (3 questions)	A: taking 80 to 120% of predicted doses	Good
	Demoner et al[25]	2012	A: 36.0% NA: 64.0%	MMAS-4 (Y or N)	A: 0 Yes NA: ≥ 1 Yes	Good
	Magnabosco et al[26]	2015	A: 38.1% NA: 61.9%	QAM-Q (3 questions)	A: taking 80 to 120% of predicted doses	Good
	Oliveira-Filho et al[27]	2012	A: 19.7% NA: 80.3%	MMAS-8 (7 Y or N + 1 Likert scale)	A: 8 points NA: <8 points	Good
	Ungari et al[28]	2010	A: 43.1% NA: 56.9%	MMAS-4 (Y or N)	A: 0 Yes NA: ≥ 1 Yes	Good
Canada	Evans et al[29]	2012	A: 38.1% NA: 61.9%	MPR (by questionnaire)	A: > 80% NA: ≤ 80%	Very Good
China	Ma et al[30]	2016	A: 21.3% NA: 78.7%	MMAS-4 (Y or N)	A: 0 Yes NA: ≥ 1 Yes	Good
	Strand et al[31]	2017	A: 60.0% NA: 40.0%	Questionnaire about medication taken, frequency and dose and subsequent comparison with standard frequency and dosage for each drug	A: Responses given by participants match the standard	Insufficient
	Yang et al[32]	2016	A: 43.5% NA: 56.5%	MMAS-4 (Y or N)	A: 0 Yes NA: ≥ 1 Yes	Sufficient
	Yue et al[33]	2015	A: 51.7% NA: 48.3%	MMAS-8 (7 Y or N + 1 Likert scale)	A: 8 points NA: <8 points	Good

(*Continued*)

Table 1 (Continued).

Country	Author	Year	Adherence Level	Method Used To Assess Adherence	Adherence Criteria	Quality Assessment
Ethiopia	Ambaw et al[34]	2012	A: 64.6% NA: 35.4%	MMAS-4 (Y or N)	A: 0 or 1 Yes NA: > 1 Yes	Good
	Berhe et al[35]	2017	AT: 21.0% NA: 79.0%	MMAS-8 (7 Y or N + 1 Likert scale)	A: 8 points NA: <8 points	Good
	Mekonnen et al[36]	2017	A: 67.2% NA: 32.8%	MMAS-8 (7 Y or N + 1 Likert scale)	A: ≥6 points NA: <6 points	Good
Finland	Nabi et al[37]	2008	A: 60.0% NA: 40.0%	PDC (by clinical records)	A: coverage for 365 days NA: coverage for <365 days	Good
France	Hamdidouche et al[38]	2017	A: 85.0% NA: 15.0%	MMAS-4 (Y or N)	A: 0 Yes NA: ≥1 Yes	Good
	Korb-Salvodelli et al[39]	2012	AT: 44.2% NA: 55.8%	MMAS-8 (7 Y or N + 1 Likert scale)	A: 8 points NA: <8 points	Very Good
Germany	Morrison et al[17]	2015	A: 66.8% NA: 33.2%	MMAS-4 (Y or N)	A: 0 Yes NA: ≥1 Yes	Good
	Ude et al[40]	2013	A: 58.2% NA: 41.8%	MMAS-5 (Y or N)	A: 0 points NA: ≥1 point; (1 positive answer = 1 point)	Good
			A: 71.9% NA: 28.1%	MMAS-6 (Y or N)		
	Van de Steeg et al[41]	2009	A: 71.1% NA: 28.9%	MMAS-4 (Y or N)	A: 0 Yes NA: ≥ 1 Yes	Sufficient
Hong Kong (Special Administrative Region)	Kang et al[42]	2015	A: 55.2% NA: 44.8%	MMAS-8 (7 Y or N + 1 Likert scale)	A: >6 points NA: ≤6 points	Good
	Lee et al[43]	2013	A: 65.1% NA: 32.6%	MMAS-8 (7 Y or N + 1 Likert scale)	A: >6 points NA: ≤6 points	Good
Hungary	Doró et al[44]	2011	A: 75.2% NA: 24.8%	(Number of prescribed doses – Number of doses not taken)/Number of prescribed doses x 100 + MEMS® track cap + MMAS-4 (Y or N)	A: ≥80% NA: <80% + A: ≥80% NA: <80% + A: 0 Yes NA: ≥1 Yes	Sufficient
	Morrison et al[17]	2015	A: 29.7% NA: 70.3%	MMAS-4 (Y or N)	A: 0 Yes NA: ≥ 1 Yes	Good
India	Choudhary et al[45]	2016	A: 54.6% NA: 45.4%	Questionnaire (non-specified)	No information	Insufficient
	Dennis et al[46]	2011	A: 50.3% NA: 49.7%	BMQ (5 questions)	A: 0 points NA: ≥1 point	Good
Indonesia	Sulistiyowatiningsih et al[47]	2017	A: 11.8% NA: 88.2%	MMAS-8 (7 Y or N + 1 Likert scale)	A: 8 points NA: <8 points	Good

(*Continued*)

Table 1 (Continued).

Country	Author	Year	Adherence Level	Method Used To Assess Adherence	Adherence Criteria	Quality Assessment
Iran	Behnood-Rod et al[48]	2016	A: 16.4% NA: 83.5%	MMAS-8 (7 Y or N + 1 Likert scale)	A: 8 points NA: <8 points	Good
	Moharamzad et al[49]	2015	A: 15.0% NA: 85.0%	MMAS-8 (7 Y or N + 1 Likert scale)	A: 8 points NA: <8 points	Very Good
Jordan	Al-daken et al[50]	2017	A: 84.9% NA: 15.1%	HBC (14 items assessed by Likert scale)	A: >80% NA: ≤80%	Good
Nepal	Bhandari et al[51]	2015	A: 56.5% NA: 43.5%	MMAS-4 (Y or N)	A: 0 or 1 Yes NA: >1 Yes	Good
The Netherlands	Morrison et al[17]	2015	A: 75.9% NA: 24.1%	MMAS-4 (Y or N)	A: 0 Yes NA: ≥1 Yes	Good
	Van Onzenoort et al[52]	2010	A: 91.6% NA: 8.4%	Monitoring the medication box's opening every 24 hrs, by MEMS® track cap	A: medication box opened in >90% of the days	Good
Nigeria	Adeyemo et al[53]	2013	A: 77.0% NA:33.0%	Pill counting (pills taken/pills prescribed) + Urine detection	A: Miss less than 2 doses or drug detected in urine	Good
	Iloh et al[54]	2013	A: 42.9% NA: 57.1%	5 items questionnaire (0 to 4 points)	A: 4 points NA: <4 points	Sufficient
	Okwuonu et al[55]	2014	A: 7.5% NA: 92.5%	MMAS-8 (7 Y or N + 1 Likert scale)	No information	Sufficient
	Okwuonu et al[56]	2015	A: 31.8% NA: 68.2%	MMAS-8 (7 Y or N + 1 Likert scale)	A: >4 points NA: <4 points	Good
Pakistan	Arshad et al[57]	2015	A: 70.7% NA: 29.3%	MMAS-4 (Y or N)	A: 0 Yes NA: ≥1 Yes	Good
	Hashmi et al[58]	2007	A: 77.0% NA: 23.0%	Pills taken in a period of time/Pills prescribed in the same period of time	A: ≥80% NA: <80%	Good
	Saleem et al[59]	2012	A: 0.0% NA: 100.0%	DAI-10 (10 Y or N, scoring between 10 and −10)	A: ≥6 points NA: <6 points	Good
Peru	Rodríguez-Abt et al[60]	2017	A: 46.7% NA: 53.3%	MBG (12 questions with a 5 option Likert scale, scoring between 0 and 48)	A: 38 to 48 points NA: 0 to 37 points	Good
Poland	Jankowska-Polan et al[61]	2016	A: 36.4% NA: 63.6%	MMAS-8 (7 Y or N + 1 Likert scale)	A: 8 points NA: <8 points	Very Good
	Morrison et al[17]	2015	A: 42.4% NA: 57.6%	MMAS-4 (Y or N)	A: 0 or 1 Yes NA: >1 Yes	Good
	Wilinski et al[62]	2013	A: 26.0% NA: 74.0%	MMAS-4 (Y or N)	A: 0 or 1 Yes NA: >1 Yes	Sufficient
Portugal	da Costa et al[63]	2015	A: 54.6% NA: 45.4%	MMAS-7 (Y or N)	A: 0 or 1 Yes NA: >1 Yes	Sufficient

(*Continued*)

Table 1 (Continued).

Country	Author	Year	Adherence Level	Method Used To Assess Adherence	Adherence Criteria	Quality Assessment
Spain	Baena-Díez et al[64]	2011	A: 48.7% NA: 51.3%	MMAS-4 (Y or N)	A: 0 or 1 Yes NA: >1 Yes	Good
	Calderón-Larrañaga et al[65]	2016	A: 79.8% NA: 20.2%	MPR (by questionnaire)	A: >80% NA: ≤80%	Good
Sudan	Omar et al[66]	2018	A: 70.5% NA: 29.5%	MMAS-8 (7 Y or N + 1 Likert scale)	A: 0 to 2 Yes NA: ≥3 Yes	Good
Sweden	Qvarnström et al[67]	2013	A: 65.0% NA: 35.0%	Follow-up of medicines purchased in the pharmacy	A: ≤30 days without purchasing prescribed medicines	Good
Turkey	Karaeren et al[68]	2009	A: 72.0% NA: 28.0%	Questionnaire	No information	Sufficient
	Karakurt et al[69]	2012	A: 42.1% NA: 57.9%	Questionnaire	No information	Sufficient
United Arab Emirates	Bader et al[70]	2015	A: 54.4% NA: 45.6%	MMAS-4 (Y or N)	A: 0 or 1 Yes NA: >1 Yes	Good
	Fahey et al[71]	2006	A: 52.0% NA: 48.0%	MMAS-7 (Y or N)	A: 0 or 1 Yes NA: >1 Yes	Good
United Kingdom	Horne et al[72]	2010	A: 45.0% NA: 55.0%	MARS-6 (6 items with Likert scale, scoring between 6 and 30)	No information	Sufficient
	Morrison et al[17]	2015	A: 58.5% NA: 41.5%	MMAS-4 (Y or N)	A: 0 or 1 Yes NA: >1 Yes	Good
United States Of America	Fortuna et al[73]	2018	AT: 29.7% NA: 70.3%	MMAS-8 (7 Y or N + 1 Likert scale)	A: 8 points NA: <8 points	Sufficient
	Grigoryan et al[74]	2012	A: 65.4% NA: 34.6%	Monitoring of taken dose in 30 days, by MEMS® track cap	A: ≥80% NA: <80%	Sufficient
	Haley et al[75]	2016	A: 38.8% NA: 61.2%	MMAS-8 (7 Y or N + 1 Likert scale)	A: 8 points NA: <8 points	Good
	Pittman et al[76]	2010	A: 74.6% NA: 25.4%	MPR (by questionnaire)	A: ≥80% NA: <80%	Sufficient
	Roberts et al[77]	2014	A: 52.0% NA: 48.0%	PDC (by clinical records)	A: ≥80% NA: <80%	Good
	Roberts et al[77]	2014	A: 52.0% NA: 48.0%	PDC (by clinical records)	A: ≥80% NA: <80%	Good
	Whittle et al[78]	2016	A: 71.2% NA: 28.8%	In an interview, participants report the medication taken so far	A: ≥80% NA: <80%	Sufficient

Abbreviations: A, Adherence; NA, Non-Adherence; Y/N, Yes or No; MMAS, Morisky Medication Adherence Scale; QAM-Q, *Questionário de Não-Adesão a Medicamentos da Equipa Qualiaids*; MPR, Medication Possession Ratio; MEMS, medication events monitoring systems; PDC, proportion of days covered; BMQ, brief medication questionnaire; HBC, Hill-Bone Compliance Scale; DAI-10, the drug inventory; MBG, Martin-Bayarre-Grau Questionnaire; MARS-6, medication adherence report scale.

adherence levels between 25% and 75%. This discrepancy is associated with the great diversity of economic, social and individual factors among all the countries. Amongst the factors we analysed, there seems to be no relation to

Table 2 Correlation Between The Determinants Of Organization Of Healthcare Systems And Adherence To Therapy In Patients With Arterial Hypertension

	All Countries		European Countries	
	All Methods	MMAS	All Methods	MMAS
Mean Consultation Time (Minutes)	0.140	0.170	−0.011	−0.018
	(0.401)	(0.409)	(0.972)	(0.960)
Hospital Beds (per 10,000 Inhabitants)	0.248	0.188	0.198	0.200
	(0.185)	(0.402)	(0.517)	(0.580)
Number Of Doctors (Per 1000 Inhabitants)	0.587	0.460	0.581	0.358
	(0.001)	(0.031)	(0.037)	(0.310)
Number Of Nurses (Per 1000 Inhabitants)	0.394	0.387	0.467	0.733
	(0.031)	(0.075)	(0.108)	(0.016)
Number Of Pharmacists (Per 1000 Inhabitants)	0.339	0.144	−0.324	−0.418
	(0.067)	(0.523)	(0.280)	(0.229)
Health Expenditure (% GDP)	0.289	0.279	0.742	0.879
	(0.115)	(0.198)	(0.004)	(0.001)
Health Expenditure (Per Capita)	0.334	0.316	0.819	0.939
	(0.071)	(0.152)	(0.001)	(0.000)
Out-Of-Pocket Expenditure (Per Capita)	0.233	0.141	0.368	0.200
	(0.215)	(0.533)	(0.219)	(0.580)
General Government Expenditure (%)	0.247	0.197	0.670	0.855
	(0.189)	(0.379)	(0.012)	(0.002)

Notes: Calculated spearman correlations (ρ). The value in brackets corresponds to the significance (P), considering a bilateral distribution.
Abbreviations: MMAS, Morisky Medication Adherence Scale; GDP, Gross Domestic Product.

the average time of consultation. However, the greater number of health professionals available, the investment and the health expenditures of each country appear as promoters of adherence to medication.

Regarding the consultation time, it seems intuitive, and it is described in some literature, that the short duration of the consultation hinders the development of a strong relation between doctor and patient, interfering in the clarification of questions related to therapeutics and with the disease itself. Moreover, with less time for consultation, attention is focused on higher priority issues and the assessment of adherence to therapy ends up being postponed.[4,13,60,79] However, our results did not show a significant correlation between these two variables. The data we used may explain this finding. Average consultation times include all consultations in primary healthcare, regardless of their purpose, which may explain very low consultation times in some countries. They are more related to the renewal of prescriptions, to the evaluation of complementary diagnostic exams or to the referral to hospital care, than to more structured consultations and follow-up of chronic diseases.[13] Heterogeneous methods for measuring consultation time may also influence this relation.[13]

Hypertension is a disease mainly managed by primary healthcare and not at hospital level.[80] We used an indicator of access to hospital care, the number of hospital beds, and, as expected, it did not correlate with adherence to medication in hypertension. Although adherence should be a concern for all providers, the primary healthcare is, undoubtedly, in a better position to deal with this issue.

Regarding the health providers, we observed that with a greater number, adherence to therapy improved. We can infer that this eases the access to healthcare, as well as a closer follow-up, contributing to the better adherence of the patients to the medication.[4] The role of physicians seems more preponderant. Doctors are the initial prescribers and take the responsibility to follow and adjust the medication to each case, promoting patient's involvement in therapeutics decisions and stressing its importance. One must dissipate doubts and advise on behaviors that promote a better health.[4,5] Nurses are also crucial in monitoring the medication and in the education for health, reinforcing the relevance of pharmacological and non-pharmacological treatment measures, as well as preventive behaviors.[4] Surprisingly, the number of pharmacists did not show a significant role in the adherence to medication, especially in European countries, making us believe that improving the active participation of pharmacists in the effective control of patient's medications can be a path to follow to address the problem of non-adherence. Cooperation among the various health entities, towards the common goal of caring for a patient, has proved to be essential.[4]

Considering the European countries, with comparable healthcare systems, the strong correlation with increased government expenditure on health means better adherence to antihypertensive therapy. Indeed, a country that can invest in good infrastructures and human resources creates

conditions for the population to be closer to a healthier situation.[4,55] It is, therefore, not surprising that the prevalence of arterial hypertension is higher in the most deprived countries, and in some of them it is still increasing.[1] There is also a positive relation with general public expenditure, including all other areas, such as social security and education. Public investment directed to empower the population in a holistic view, and not only in the fight against diseases, may lead to a more literate population. Thus, they are able to better understand the recommendations and regimens towards their own health, as well as to understand the disease itself and its consequences. Literacy improves adherence to healthy behaviors and may reduce medication errors.[11,19,68] Economic constraints are also a reason for poor adherence to therapy. Governments play a significant role in ensuring the access to healthcare and medication, through strategies of reimbursement on medicines and services, especially in most vulnerable patients, mainly elders or isolated people.[55,63]

The heterogeneity of methods used to estimate adherence through the different studies was an important constraint in this analysis and strongly affected the obtained results. Some of the variations we found may be due to this discrepancy. The Morisky Medication Adherence Scale (MMAS), amongst all the methods represented, seems to obtain the most consensus and, according to literature, it is the most frequently used and the most reliable indirect method by questionnaire.[8,23,49] Overall, the questionnaires were the preferred method, which is in line with their easier application.[6] The choice of the method for adherence evaluation is a relevant factor, affecting our results, according to the instrument used. Other potential bias comes from the heterogeneity of the studies where data were retrieved. However, and considering there is no gold-standard for medication adherence assessment, it becomes a difficult situation to overcome. In this context, it would be important to define a standard to measure adherence to medication, of simple and systematic application in healthcare services.

Nevertheless, we included a set of good quality articles, which increases the robustness of our results, and allows us to infer about the impact of organizational factors in the most relevant determinant of uncontrolled blood pressure in hypertensive patients. Acting on these aspects may improve the adherence to medication and, consequently, reduce the burden of cardiovascular disease for individual patients and healthcare systems.[80]

This study contributes to explain a part of the complexity of determinants associated with adherence to medication. Our results show the impact of administrative and political decisions on hypertensive patients. All over the European countries, but also in other parts of the world, governments and funding agencies are reducing the funds for health, based on the necessity of adjusting them to the metric of the economic models. However, people are not just numbers and this study rises the importance of political decisions on people's health. Nonetheless, this is a macro analysis at a country level and needs to be proven at patient's level, comparing different organizational contexts and considering clinical determinants.

Conclusion

Non-adherence to therapy is a real problem, nowadays. It depends on the interaction of factors related to the patients, the providers and the surrounding context. The doctor's role cannot only be prescribing but addressing all the patient's dimensions to understand the best strategy for each individual person. Promoting adherence becomes as important to populations' health as the act of prescribing. Healthcare systems and organizations have a relevant role creating conditions for populations to evolve into their maximum potential, when it comes to development and health.

Author Contributions

Ana Sofia Carvalho conducted the data analysis. Paulo Santos conducted the statistical analysis. Both authors designed the review, extracted data, drafted and revised the paper, gave final approval of the version to be published, and agreed to be accountable for all aspects of the work.

Disclosure

The authors report no conflicts of interest in this work.

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