Factors Related to Adherence to Therapy in Patients Using Oral Anticoagulants in Outpatient Follow-Up

# Factors Related to Adherence to Therapy in Patients Using Oral Anticoagulants in Outpatient Follow-Up\*

\* Article stemming from the doctoral thesis entitled "Development and validation of technologies for telenursing management in oral anticoagulation," presented to the Associated Postgraduate Nursing Program, at the Universidade de Pernambuco-Universidade Federal da Paraíba, Brazil.

#### ⊠ Xênia Sheila Barbosa Aguiar Queiroz

https://orcid.org/oooo-ooo3-3218-4759 Universidade de Pernambuco, Brazil sheila\_tshe@hotmail.com

#### Nataly Lins Sodré

https://orcid.org/0009-0007-0811-3260 Universidade de Pernambuco, Brazil nataylsodre@gmail.com

#### Isabel Cristina Ramos Vieira Santos

https://orcid.org/0000-0002-5458-4334 Universidade de Pernambuco, Brazil isabel.santos@upe.br

#### Maria Beatriz Araújo Silva

https://orcid.org/oooo-ooo2-5730-5425 Universidade de Pernambuco, Brazil beatriz.silva@upe.br

#### Rebeka Maria de Oliveira Belo

https://orcid.org/0000-0001-6489-3002 Universidade de Pernambuco, Brazil rebeka.belo@upe.br

#### Simone Maria Muniz da Silva Bezerra

https://orcid.org/0000-0002-6301-8457 Universidade de Pernambuco, Brazil simone.muniz@upe.br

#### DOI: 10.5294/aqui.2024.24.4.6

Para citar este artículo / To reference this article / Para citar este artigo

Theme: Health promotion

Contribution to the field: The identification of factors related to therapy adherence may enable nurses and the multi-professional team working with patients using oral anticoagulants to understand the sociodemographic and clinical profile of these individuals, as well as the elements that facilitate or hinder adherence to the proposed treatment. This knowledge is essential for the improvement of therapeutic follow-up, for supporting clinical decision-making, and for implementing educational interventions designed to prevent complications related to the use of oral anticoagulants, reduce hospitalization rates, promote measures that improve treatment adherence, and encourage changes in habits, resulting in an improvement in patients' quality of life.

### **Abstract**

Introduction: Factors related to therapy adherence can influence the complexity of care for patients using anticoagulants. Objective: To identify the factors related to patient adherence to oral anticoagulant treatment in outpatient follow-up. Materials and Methods: This is a descriptive, cross-sectional study with a quantitative approach, conducted at the oral anticoagulation outpatient clinic of a cardiology reference hospital in northern and northeastern Brazil. A questionnaire with sociodemographic and clinical variables and an instrument measuring treatment adherence were employed. The data was analyzed using the Statistical Package for the Social Sciences and the Chi-squared and Fisher's exact statistical tests. All the statistical tests applied a significance level of 5%. Results: 202 patients were screened, 66.3% of whom were classified as adherent. Patients with a clinical referral for valve replacement, a treatment time longer than five years, and an international normalized ratio (INR) value outside the therapeutic target showed greater adherence to treatment. In addition, having a sedentary lifestyle and the use of antiarrhythmic medication were significantly associated with adherence. Variables such as sex, income, occupation, level of education, and the presence of complications were not significantly associated with treatment adherence. Conclusion: This study's findings highlight that adherence to treatment with anticoagulants hinges more on clinical factors and health behavior than on sociodemographic characteristics. Although traditionally studied, these are not necessarily reliable predictors of adherence. The essential factor seems to be more closely related to health education and medical and family support, which emphasizes the need for individualized support for these patients, with a focus on awareness and regular clinical follow-up.

#### **Keywords (Source: DeCS)**

Anticoagulants; cooperation and treatment adherence; health promotion; cardiovascular nursing.

# Factores relacionados con la adherencia terapéutica en pacientes tratados con anticoagulantes orales en el seguimiento ambulatorio

\* Artículo derivado de la tesis doctoral titulada "Elaboração e validação de tecnologias para gerenciamento da telenfermagem em anticoagulação oral", presentada al Programa de Postgrado Asociado de Enfermería, de la Universidade de Pernambuco-Universidade Federal da Paraíba, Brasil.

#### Resumen

Introducción: los factores relacionados con la adherencia terapéutica pueden influir en la complejidad de la atención a los pacientes que utilizan anticoagulantes. Objetivo: identificar los factores relacionados con la adherencia de los pacientes al tratamiento anticoagulante oral durante el seguimiento ambulatorio. Materiales y métodos: estudio descriptivo, transversal, con enfoque cuantitativo, realizado en el ambulatorio de anticoagulación oral de un hospital de referencia en cardiología del Norte y Nordeste de Brasil. Se utilizó un cuestionario con variables sociodemográficas y clínicas y un instrumento de medición de la adherencia al tratamiento. Los datos se analizaron utilizando el Statistical Package for the Social Sciences y las pruebas estadísticas chi-cuadrado y exacta de Fisher. Todas las pruebas estadísticas utilizaron un nivel de significación del 5 %. Resultados: se evaluaron 202 pacientes, de los que el 66,3 % se clasificaron como adherentes. Los pacientes con una indicación clínica de sustitución valvular, un tiempo de tratamiento superior a cinco años y un valor de la razón internacional normalizada fuera del objetivo terapéutico mostraron una mayor adherencia al tratamiento. Además, un estilo de vida sedentario y el uso de medicación antiarrítmica se asociaron significativamente con la adherencia. Variables como el sexo, los ingresos, la ocupación, la escolaridad y la presencia de complicaciones no se asociaron significativamente con la adherencia al tratamiento. Conclusión: los hallazgos de este estudio subrayan que la adherencia al tratamiento con anticoagulantes depende más de factores clínicos y conductas de salud que de características sociodemográficas. Aunque tradicionalmente se han estudiado, éstas no son necesariamente predictores fiables de la adherencia. El factor esencial parece estar más relacionado con la educación en salud y el apoyo médico y familiar, lo que refuerza la necesidad de un apoyo individualizado para estos pacientes, centrado en la toma de conciencia y el seguimiento clínico regular.

#### Palabras clave (DeCS)

Anticoagulantes; cooperación y adherencia al tratamiento; promoción de la salud; enfermería cardiovascular.

# Fatores relacionados à adesão terapêutica de pacientes em uso de anticoagulante oral em acompanhamento ambulatorial\*

\* Artigo derivado da tese de doutorado "Elaboração e validação de tecnologias para gerenciamento da telenfermagem em anticoagulação oral", apresentada ao Programa Associado de Pós-Graduação em Enfermagem, Universidade de Pernambuco-Universidade Federal da Paraíba, Brasil.

#### Resumo

Introdução: fatores relacionados à adesão terapêutica podem influenciar na complexidade do cuidado aos pacientes que fazem uso de anticoagulantes. Objetivo: identificar os fatores relacionados à adesão de pacientes ao tratamento com anticoagulante oral em acompanhamento ambulatorial. Materiais e método: estudo descritivo, transversal, com abordagem quantitativa, realizado no ambulatório de anticoagulação oral de um hospital de referência em cardiologia do Norte e Nordeste do Brasil. Utilizaram-se o questionário com variáveis sociodemográficas e clínicas e o instrumento de medida de adesão ao tratamento. Os dados foram analisados pelo programa Statistical Package for the Social Sciences e pelos testes estatísticos qui-quadrado e teste exato de Fisher. Todos os testes estatísticos aplicados adotaram nível de significância de 5 %. Resultados: 202 pacientes foram avaliados, dos quais 66,3 % classificados como aderentes. Pacientes com indicação clínica de troca valvar, tempo de tratamento maior que cinco anos e valor da RNI fora do alvo terapêutico apresentaram maior adesão ao tratamento. Além disso, sedentarismo e uso de medicações antiarrítmicas foram significativamente associados à adesão. Por sua vez, variáveis como sexo, renda, ocupação, escolaridade e presença de complicações não demonstraram associação significativa com a adesão ao tratamento. Conclusão: os achados do presente estudo sublinham que a adesão ao tratamento com anticoagulantes depende mais de fatores clínicos e comportamento de saúde do que de características sociodemográficas. Embora tradicionalmente estudadas, não são necessariamente preditoras confiáveis para a adesão. O fator essencial parece estar mais relacionado à educação em saúde, ao suporte médico-familiar, o que reforça a necessidade de apoio individualizado para esses pacientes, com foco na conscientização e no monitoramento clínico regular.

#### Palavras-chave (Fonte DeCS)

Anticoagulantes; cooperação e adesão ao tratamento; promoção da saúde; enfermagem cardiovascular.

# Introduction

Chronic non-communicable diseases (CNCDs) are the leading cause of death worldwide, representing approximately 70% of deaths among individuals aged from 30 to 70 years. Within the CNCDs setting, cardiovascular diseases (CVDs) are of significant importance, as they are the leading cause of death and are among the factors that influence disability and years of life lost, having a significant social and economic impact on the population's quality of life (1).

For some of these CVDs, the use of oral anticoagulants (OACs) is recommended, as these medications are widely used in patients with clinical conditions that undesirably activate blood coagulation, acting both to prevent and treat thromboembolic events, such as pulmonary and venous thromboembolism, atrial fibrillation, acute myocardial infarction, and heart valve prostheses, among others (2, 3).

Laboratory tests are used to monitor blood coagulation, such as partial thromboplastin time and prothrombin time, expressed by the international normalized ratio [INR] (4). As the risk of bleeding from excessive doses or thrombus formation at low doses is high, strict control of INR is required on a monthly, fortnightly, or weekly basis, through laboratory tests, as well as guidance on the normal range and effective therapeutic adherence, making oral anticoagulation therapy effective in preventing and treating thromboembolic events (5, 6).

In the case of individuals who are using OACs, therapeutic adherence is an even greater challenge, as it is for the healthcare professionals who work in this setting, as it encompasses important aspects such as prescribed medication and adequate control, as well as changes in dietary habits (7). In the presence of CVDs, a low adherence rate not only increases the mortality and hospitalization rate but also significantly reduces the effectiveness of treatments (8).

The World Health Organization (WHO) defines adherence to medication therapy as the extent to which a person's behavior (taking medication, following a diet and/or making lifestyle changes) corresponds to the recommendations agreed upon with a healthcare professional (9). Adherence to any proposed treatment includes patient adaptation through active participation that goes beyond strictly following medication therapy and is associated with lifestyle changes, education, knowledge about the treatment, and various intervening sociodemographic and clinical factors (10, 11).

In this context, outpatient clinics specializing in OACs aim to provide patients with follow-up care and guidance on the necessary medication, as well as on the factors that can interfere with the therapy (12). The systematic review by Salmasi et al. (2020) shows that up to 30% of patients with atrial fibrillation are non-adherent, suggesting that there is a significant therapeutic challenge for this patient population. The work of professional nurses has been a distinguishing factor in this scenario since educational measures that improve

patients' knowledge, developed by such professionals, can contribute to adherence to therapy, and specialized services for the follow-up of these patients favor the development of these measures, which enables a closer relationship between professionals and patients (13).

In light of the above, the complexity of the management and follow-up of patients using OACs is remarkable since several factors can influence adherence to therapy, exposing them to the risk of hemorrhagic or thromboembolic events and associated complications, increasing the number of hospitalizations, as well as morbidity and mortality.

Considering that sociodemographic and clinical variables can influence therapeutic adherence, the aim of this study was to identify the factors related to patient treatment adherence with OACs in outpatient follow-up.

# **Materials and Methods**

# **Study Type and Setting**

This is a descriptive, cross-sectional study, with a quantitative approach. The study was conducted at the oral anticoagulant outpatient clinic of the Emergency Cardiology Unit of the Universidade de Pernambuco, which is a reference center for cardiology in northern and northeastern Brazil, located in the city of Recife, Pernambuco.

The study is part of a larger project entitled "Development and Validation of Technologies for Telenursing Management in Oral Anticoagulation."

# **Population and Sample**

The population consisted of patients using OACs receiving follow-up at an outpatient clinic specializing in anticoagulation. The sample was calculated for finite populations, considering an N of 245 patients, with a confidence interval of 95% and a sampling error of 5%. The calculated sample consisted of 175 patients. The sample analyzed consisted of 202 patients.

#### Inclusion and Exclusion Criteria

Patients aged 18 or over, undergoing OAC treatment, and receiving follow-up at the outpatient clinic, who had been using OACs for three months, were included in the study. Patients with cognitive deficits, confirmed by the application of the Mini-Mental State Examination (MMSE), according to the criteria established by Brucki et al. (14), did not participate in this study, as they ren-

dered the study impossible to understand as well as to apply the questionnaires. The MMSE sets the following cut-off points: 17 for illiterate individuals; 22 for individuals who have between 1 and 4 years of education; 24 for those who have between 5 and 8 years of education; and 26 when they have more than 9 years of education or are over 69 years old. These measurements correspond to the average cut-off score for each education level found in the study by Brucki et al (14), minus one standard deviation.

#### **Data Collection**

Individuals who were waiting for an appointment at the research location during the data collection period and those who met the aforementioned inclusion criteria were invited by the researchers to participate in the study. After the research objectives were presented and participants consented by signing the informed consent form, the questionnaires were administered via interview. The data collection period ranged from July to November 2022, and the instrument duration was approximately 15 minutes. Two questionnaires were used as data collection instruments:

- A semi-structured questionnaire prepared by the study's researchers, covering sociodemographic and clinical variables, such as sex, age, ethnicity, marital status, origin, occupation, monthly income, level of education, number of people living in the same household, cost of transportation to the outpatient clinic, cost of medication, prescription of OACs use, type of OAC, dosage, length of treatment, INR, complications, length of treatment, personal history, and medications in use;
- An instrument for measuring treatment adherence, which has been adapted and validated by Carvalho et al. in 2010 for the OACs use setting (15, 16), and with its internal consistency measured by a Cronbach's alpha of o.6, which found the presence of a maximum effect in the answers to all the items. The instrument consists of seven items, as follows: How many times have you forgotten to take the anticoagulant? How many times have you taken the anticoagulant out of the timetable? How many times have you stopped taking the anticoagulant because you were feeling better? How many times have you stopped taking the anticoagulant because you were feeling worse or causing problems? How many times have you changed the anticoagulant dose because you forgot to take it the day before? How many times have you stopped taking the anticoagulant due to a shortage of the medicine? How many times have you stopped taking the anticoagulant for reasons beyond your control? These items assess the individual's behavior regarding the daily use of the medication. The answers are collected using a six-point ordinal scale, ranging from 1 - "always" to 6 - "never". The response values for the seven items are added together and then divided by the

total number of items, resulting in a score ranging from 1 to 6. Subsequently, values equal to or above 5 are categorized as adherent on this scale, while the remaining values are classified as 0, which indicates non-adherence. Thus, the scale is converted into a dichotomous "yes/no" format, that is, adherent/non-adherent, respectively.

## **Data Treatment and Analysis**

The SPSS version 25.0 (Statistical Package for the Social Sciences) for Windows and Microsoft Excel 365 software were used to analyze the collected data. All the statistical tests employed a significance level of 5% (p-value  $\leq$  0.05), with p-values lower than or equal to 0.05 being considered statistically significant.

The results are presented in tabular format, with the respective absolute and relative frequencies for the categorical variables, providing a clear view of the data distribution. For the numerical variables, central tendency measurements (mean, median) and dispersion measurements (standard deviation and range) were used, providing a detailed description of the behavior of the quantitative variables.

To verify the existence of associations between the categorical variables, the Chi-squared test and Fisher's exact test were used, the latter being applied in cases where the expected frequencies in the contingency table cells were lower than 5. These tests enabled the evaluation of the relationships between the variables and the identification of statistically significant associations in the data set analyzed.

# **Ethical Aspects**

The study was conducted in compliance with Resolution 466/2012 of the National Health Council and approved by the Research Ethics Committee with the Certificate of Ethical Appraisal No. 59677322.5.0000.5192 and Opinion No. 5.512.060.

# **Results**

A total of 202 patients using OACs and receiving specialized outpatient follow-up participated in the study. Most of them were female (58.40%), with a mean age of 61.74 years (± 11.84), of mixed ethnicity (59.40%), and with a partner (54.50%). There was also a prevalence of patients with a low income of up to 1 times the minimum wage (78.20%), who were unemployed (83.16%), and with incomplete primary education (50.50%). In addition, 86.10% of the individuals came from the Metropolitan Region of Recife and reported that they had to pay for transportation (52.55%) and medication (83.2% [Table 1]).

Sociodemographic variables	Mean	(± sd)
Age	61.74	11.84
-	N	%
Sex		
Female	118	58.40
Male	84	41.60
Ethnicity		
Mixed	120	59.40
White	42	20.80
Black	34	16.80
Indigenous	6	3.0
Marital status		
With a partner	110	54.50
Without a partner	92	45.50
Income		
Up to the minimum wage	158	78.20
More than the minimum wage	44	21.80
Occupation		
No employment	168	83.16
With employment	34	16.84
Education		
Illiterate	6	3.0
Incomplete primary education	102	50.50
Complete primary education	28	13.90
Incomplete secondary education	14	6.90
Complete secondary education	52	25.70
Origin		
Metropolitan Region	174	86.10
Countryside	28	13.90
Expenses with transportation		
Yes	106	52.50
No	96	47.50
Expenses with medication		
Yes	168	83.20
No	34	16.80

**Source**: Prepared by the authors.

Regarding the clinical characterization of individuals based on their OACs therapy, the main referral was for valve replacement (53.90%), followed by atrial fibrillation (40.60%), with a treatment time longer than six months (94.04%), and undergoing Marevan® therapy (85.10%). In addition, 52.50% of patients interviewed had an INR outside the therapeutic target, requiring adjustments to the medication dosage, 28.70% stated that they had already suffered hemorrhagic complications, and 23.80% had suffered thromboembolic complications. The most frequent comorbidities and medications with multiple responses were systemic arterial hypertension (91.10%), followed by having a sedentary lifestyle (59.40%), and dyslipidemia (39.60%), with the use of the following medications: antihypertensives (91.10%), statins (37.60%), and others (24.50% [Table 2]).

**Table 2.** Clinical Characteristics of Patients Using OACs (N = 202). Recife, Pernambuco, 2022

Clinical Variables	N	%
Referral		
Valve replacement	109	53.90
Atrial fibrillation	82	40.60
Chagas disease	6	3.0
Others	5	2.5
Length of treatment		
Up to six months	12	5.96
Over six months	190	94.04
Type of OAC		
Marevan®	172	85.10
Warfarin®	30	14.90
Therapy target		
Below the recommended target	62	30.70
Normal*	96	47.50
Above the recommended target	44	21.80
Complications		
Hemorrhagic	58	28.70
Thromboembolic	48	23.80
None	96	47.50
Comorbidities**		
Systemic arterial hypertension	184	91.11
Dyslipidemia	80	39.60
Sedentary lifestyle	118	58.40
Stress***	56	27.70
Diabetes mellitus	30	14.90

Clinical Variables	N	%
Chronic kidney disease	6	3.0
Smoking	18	8.90
Medications in use**		
Antihypertensive	184	91.11
Statin	76	37.60
Hypoglycemic	28	13.90
Antiarrhythmic	52	25.70
Antidepressant	8	4.0
Others	54	26.80

Note: \*Dose adjustment not needed according to clinical prescription; \*\*Multiple answers; \*\*\* Self-reported.

Source: Prepared by the authors.

In the assessment of adherence to therapy, using the ATMT (15, 16), 66.3% of patients were classified as adherent and 33.7% as non-adherent, as shown in Table 3.

**Table 3.** Evaluation of Pharmacological Adherence of Patients Undergoing OACs Treatment (N = 202). Recife, Pernambuco, 2022

Pharmacological adherence (ATMT)	N	%
Adherent	134	66.30
Non-adherent	68	33.70

**Source**: Prepared by the authors.

The analysis in Table 4, which evaluates the relationship between sociodemographic and clinical conditions with the scores for adherence to OAC therapy in patients, yielded significant results for some variables. Clinical referral showed a statistically significant association with adherence (p < 0.001), with patients with a referral for valve replacement showing greater adherence compared to those with a referral for atrial fibrillation and other conditions.

The length of treatment was also relevant (p = 0.001), with greater adherence among those who had been undergoing treatment for more than five years. The therapeutic target showed a significant association (p < 0.001), with greater adherence among patients outside the therapeutic target. In addition, comorbidities (such as having a sedentary lifestyle) and the use of antiarrhythmic medication were also significantly associated with adherence (p = 0.003 and p < 0.001, respectively).

In turn, variables such as sex, income, occupation, level of education, and the presence of complications showed no significant association with treatment adherence.

**Table 4.** Relationship between Sociodemographic and Clinical Conditions and ATMT Scores in Patients Undergoing OAC Treatment (N = 202). Recife, Pernambuco, 2022

Variables	Adherence		
	Yes n (%)	No n (%)	p-value
Sex			
Female	54 (64.3)	30 (35.7)	0.603*
Male	80 (67.8)	38 (32.2)	
Income			
Up to the minimum wage	102 (64.6)	56 (35.4)	0.310 *
More than the minimum wage	32 (72.7)	12 (27.3)	
Occupation			
No employment	110 (65.5)	58 (34.5)	0.565 *
With employment	24 (70.6)	10 (29.4)	
Education			
Illiterate	4 (66.7)	2 (33.3)	1.000 **
Primary education (complete/incomplete)	86 (66.2)	44 (33.8)	
Secondary education (complete/incomplete)	44 (66.7)	22 (33.3)	
Referral			
Atrial fibrillation	40 (51.3)	38 (48.7)	< 0.001 **
Valve replacement	82 (78.8)	22 (21.2)	
Chagas disease	2 (33.3)	4 (66.7)	
Others	10 (71.4)	4 (28.6)	
Length of treatment			
Up to five years	20 (45.5)	24 (54.5)	0.001*
Over five years	114 (72.2)	44 (27.8)	
Therapeutic target			
Outside the therapeutic target	84 (79.2)	22 (20.8)	< 0.001*
Within the therapeutic target	50 (52.1)	46 (47.9)	
Complications			
Yes (hemorrhagic/thromboembolic)	68 (64.2)	38 (35.8)	0.490 *
No	66 (68.7)	30 (31.3)	
Comorbidities (sedentary lifestyle)			
Yes	88 (74.6)	30 (25.4)	0.003*
No	46 (54.8)	38 (45.2)	
Medications in use (antiarrhythmics)			
Yes	22 (42.3)	30 (57.7)	< 0.001 *
No	112 (74.7)	38 (25.3)	

Note: \* Chi-squared; \*\* Fisher's exact.

**Source**: Prepared by the authors.

# **Discussion**

Regarding the sociodemographic variables of the patients receiving care at the OAC outpatient clinic, there was a prevalence of females aged over 60, corroborating the findings of other studies in which, in the setting of OAC use, the female population was more prevalent (6, 17, 18). The increased use of anticoagulants in women may be associated with various factors, from their use during reproductive age to their increased use of healthcare services compared to men, as well as their higher susceptibility to cardiovascular diseases (19).

Regarding the questions, most patients had an income of up to the minimum wage and were unemployed, a result also prevalent in other studies (13, 20). This may be due to the prevalence of individuals considered to be retired or pensioners, either due to unemployment or the physical limitations imposed by the comorbidity, influencing the lack of job opportunities.

In terms of education, the study participants had a low level of education, with most of them having incomplete primary education, a result found in other studies conducted with patients undergoing OAC treatment in the public sector (7, 21). Patients with a lower level of education may have limited knowledge about their medication and its importance, leading to a lack of understanding and motivation to adhere to the prescribed treatment, challenges in understanding and managing potential medication interactions, dietary restrictions, and other factors that can affect the effectiveness of OACs. These limitations can contribute to poor adherence and potentially compromise the maintenance of INR within the therapeutic range.

Regarding the clinical variables, the main referral for anticoagulant therapy was valve replacement surgery (mechanical and biological). Furthermore, the length of treatment with OACs was longer than six months, similar to findings in other studies (13, 22). Oral anticoagulation with vitamin K antagonists has been the gold standard for preventing thromboembolism in replaced heart valves since the 1960s. However, more recent studies report that newer OACs are contraindicated for patients with mechanical heart valves due to higher rates of thromboembolism and bleeding events compared to conventional oral anticoagulation (23).

Regarding the associated comorbidities, hypertension stood out in the clinical profile of the individuals, which is in line with other studies (21, 24). This was followed by dyslipidemia and having a sedentary lifestyle, which are risk factors for developing other cardiovascular diseases. Comorbidities have an important role in favoring the use of OACs. In addition, they are prescribed for heart diseases with high embolic flow, while antiaggregant treatment may be sufficient for the prevention of low-risk heart diseases and for the treatment of large and small artery diseases (25).

Regarding treatment adherence, participants were adherent to OAC therapy according to the ATMT scale, a satisfactory result that is in

line with other studies where individuals were also considered to be adherent to treatment (20, 26). Thus reasserting the effectiveness of specialized multi-professional outpatient care and follow-up for individuals who use OACs, favoring therapeutic adherence, which contributes to the quality of life and promotion of self-care.

In the evaluation of pharmacological adherence and the relationship between sociodemographic and clinical conditions and adherence to OACs, patients with a clinical referral for valve replacement, a length of treatment of more than five years, and an INR value outside the therapeutic target showed greater adherence to treatment.

It should be noted that adherence was self-reported, which may contain some bias. It is worth noting that poor adherence can lead to unsatisfactory therapy results and excessive medical care costs. Adherence is a multidimensional concept influenced by a range of factors, including the medical doctor-patient relationship, the characteristics of the disease, and the patient's belief system. It is therefore essential to ensure a high-quality knowledge base, skills, and motivation at the level of the healthcare system for assessing and improving adherence (27). Adherence is not just a matter of achieving a specific INR value, but also of shared decision-making, therapeutic alliance, and the overarching success of the therapy.

Valve replacement is associated with a higher thromboembolic risk, and the use of OACs is essential to prevent serious complications such as thrombosis and systemic embolism. Studies show that patients undergoing valve replacement are more aware of the need for continuous use of anticoagulants since any interruption or lack of treatment adherence can result in serious health risks (28). This understanding leads to greater adherence to the therapeutic regimen, as the patient understands the critical importance of anticoagulation for the adequate function of the valve prosthesis.

In addition, a length of treatment of more than five years is associated with increased adherence due to several factors, including greater familiarity with the therapeutic regimen, dosage adjustment, and incorporation of the medication into the daily routine (29). Over time, patients tend to adapt to the regular use of their medication, monitor their state of health, and realize the long-term benefits of adequate INR management. This behavior is supported by evidence showing that patients with longer treatment times develop a more stable routine, reducing the incidence of complications and the risk of non-adherence (30).

The management of the INR outside the therapeutic target is also a relevant factor in improving adherence to OAC treatment. When the INR is imbalanced, whether too low or too high, there

is an increased risk of both thrombosis and bleeding, which tends to cause concern among patients and motivates them to strictly follow the prescribed treatment to avoid these complications (31). Monitoring it regularly and making the necessary adjustments encourages patients to remain adherent to the treatment to stabilize the INR within the desired therapeutic range.

Regarding having a sedentary lifestyle, a study that assessed therapeutic adherence and the knowledge of anticoagulated patients found that it is possible that patients do not attribute to physical activity its true value in maintaining adequate INR values, which minimizes the risk of complications related to the use of anticoagulants (13). Given that a sedentary lifestyle can be considered a risk factor for developing CVDs, it can be inferred that sedentary patients using OACs are more likely to develop complications related to treatment and the setting of cardiovascular risk imposed by the disease that requires therapy, thus interfering with treatment adherence.

Regarding the research finding that antiarrhythmics are facilitators for better adherence, this has also been noted in other studies (22, 31), which may be justified by the medication interaction with OACs since Amiodarone, the most commonly used antiarrhythmic, reduces hepatic metabolism and prothrombin time, increasing the effect of Warfarin® in the body, which can interfere with and increase the risk of bleeding, making the patient more susceptible to being outside the recommended therapeutic target, to complications, and the need for hospitalization, requiring this patient to adhere to the treatment more rigorously.

Several studies have researched the relationship between sociode-mographic variables—such as sex, income, occupation, level of education, and the presence of complications—and adherence to OAC treatment. However, the results show that these variables alone have no significant association with treatment adherence.

Concerning sex, research indicates that men and women tend to behave similarly in terms of treatment adherence, especially when they are adequately informed and monitored (32). Continued education regarding anticoagulant therapy seems to neutralize gender-related differences so that both sexes equally understand the importance of adherence to the therapeutic regimen.

Income and occupation also showed no significant association with adherence. Although it is common to assume that patients with a higher income or formal occupations have increased access to healthcare and therefore have better adherence, the data does not consistently support this hypothesis. Patients from varying income ranges and occupations seem to have similar levels of treatment adherence when they receive adequate support and education about the treatment (21).

In the case of education, although it is expected that patients with a higher level of education will have easier access to understanding the importance of anticoagulant therapy, this does not necessarily translate into better adherence. Adherence is more reliant on factors such as social support, adequate medical follow-up, and the patient's continued education about the treatment than on their level of education alone (33).

Treatment adherence is a complex behavior that entails multiple factors, including personal motivation, access to the healthcare system, and continued professional support, which seem to be more determinant than the mere presence of complications (34). These findings suggest that although sociodemographic and clinical variables have traditionally been studied, they are not necessarily reliable predictors of adherence to treatment with anticoagulants. The key factor for adherence seems to be more closely related to health education, medical and family support, and continued follow-up for the patient during treatment.

From this perspective, it is essential to develop educational strategies that encourage understanding the aspects such as the reason why treatment is prescribed and necessary, the follow-up of laboratory control, the adequate INR values based on the clinical condition, the possible complications (risk of bleeding and thromboembolic events), dietary advice, medication interactions, as well as the necessary lifestyle changes (13).

Nurses, as integral members of the multi-professional team that provides care to patients using anticoagulants, should work to develop educational measures to improve the orientation process and understanding of individuals (13). These professionals' efforts should also be aimed at providing comprehensive care, in which individual needs are assessed and patients are encouraged to expose their challenges in relation to medication use to allow them to develop ideal coping strategies (35).

Identifying these factors could enable nurses and the multi-professional team who work with OAC users to learn about patients' sociodemographic and clinical profiles, as well as the factors that contribute to and hinder adherence to the established therapy, helping with therapeutic follow-up, decision-making, and the implementation of educational interventions designed to prevent complications related to OAC use, reduce hospital admissions, implement measures to strengthen adherence to treatment and change habits, improving patients' quality of life and the related biopsychosocial factors.

Finally, it should be noted that patients tend to overestimate their medication adherence, therefore this study may be limited in quantifying self-reported adherence. In addition, the study may not consider all the relevant variables that influence adherence, since it is based on an exploratory study of the local reality, and further studies with a broader scope are recommended.

# **Conclusion**

The present study identified the factors related to adherence to OAC therapy in outpatient follow-up, covering the complexity involved in OAC treatment, and enabled the characterization of the population receiving follow-up at the outpatient clinic specializing in OAC, as well as identifying that clinical factors such as valve replacement, length of treatment of more than five years, INR outside the therapeutic target, having a sedentary lifestyle, and use of antiarrhythmics are important determinants of improved adherence to OAC treatment.

These findings highlight the importance of continuous follow-up and health education in managing anticoagulation in patients who face a higher risk of complications, especially those who have undergone valve replacement and have a long treatment history.

Furthermore, sociodemographic variables such as sex, income, occupation, level of education, and the presence of complications were not significantly associated with treatment adherence. These data suggest that treatment adherence with anticoagulants is more reliant on clinical factors and health behavior than sociodemographic characteristics, which highlights the need for individualized support for patients using anticoagulants, with a focus on awareness and regular clinical follow-up.

These results provide input for clinical practice, showing that follow-up strategies should prioritize patients with longer treatment times and uncontrolled INR, as well as improving education and continued support to maintain long-term therapeutic adherence.

Conflicts of interest: None declared.

# Referências

- Ministério da Saúde (BR); Secretaria de Atenção Primária à Saúde; Departamento de Promoção da Saúde. Estratégia de Saúde Cardiovascular na Atenção Primária à Saúde: instrutivo para profissionais e gestores [recurso eletrônico]. Brasília: Ministério da Saúde; 2022. Disponível em: https://sisapsdoc. saude.gov.br/manual-evc-estrategia-cardio-vascular.pdf
- Silva PGMB, Sznejder H, Vasconcellos R, Charles GM, Mendonça-Filho HT, Mardekian J et al. Anticoagulation therapy in patients with non-valvular atrial fibrillation in a private setting in Brazil: A real-world study. Arquivos Brasileiros de Cardiologia. 2020;114:457-66. DOI: https://doi.org/10.36660/abc.20180076
- 3. Gadde S, Kalluru R, Cherukuri SP, Chikatimalla R, Dasaradhan T, Koneti J. Atrial fibrillation in chronic kidney disease: An overview. Cureus. 2022;14(8). DOI: https://doi.org/10.7759/cureus.27753
- 4. Dorgalaleh A, Favaloro EJ, Bahrein M, Rad M. Standardization of prothrombin time/international normalized ratio (PT/INR). Int J Lab Hematol. 2021;43(1):21-8. DOI: https://doi.org/10.1111/ijlh.13349
- Cannon CP, Kim JM, Lee JJ, Sutherland J, Bachireddy R, Valentine CM et al. Patients and their physician's perspectives about oral anticoagulation in patients with atrial fibrillation not receiving an anticoagulant. JAMA Netw Open. 2023;6(4). DOI: https://doi. org/10.1001/jamanetworkopen.2023.9638
- Nishino T, Narimoto K, Tominaga K, Sano M, Shimbo M, Muraishi N et al. A large adrenocortical adenoma surrounded with a renal arteriovenous malformation. IJU Case Reports. 2021;4(4):224-7. DOI: https://doi.org/10.1002/iju5.12293
- Sousa WJFN, Guimarães NS, Viana CC, Medeiroa AF, Vianna MS, Bertollo CM. Fatores associados à não adesão ao uso de anticoagulantes orais: protocolo de revisão sistemática. Saúde Coletiva (Barueri). 2021;11(69):8618-34. DOI: https://doi.org/10.36489/ saudecoletiva.2021v11i69p8618-8634
- 8. Richane A, Richane A, Ismail HB, Darej C, Moujahed N. Potential of Tunisian carob pulp as feed for ruminants: chemical composition and in vitro assessment. Tropical Animal Health and Production. 2022;54(1):58. DOI: https://doi.org/10.1007/s11250-022-03071-4
- Al-Makki A, DiPette D, Whelton PK, Murad MH, Mustafa RH, Acharya S et al. Hypertension pharmacological treatment in adults: a World Health Organization guideline executive summary. Hypertension. 2022;79(1):293-301. DOI: https://doi. org/10.1161/HYPERTENSIONAHA.121.18192
- Araújo GT, Simonetti SH, Conceição AP. Nursing interventions on oral anticoagulation therapy: An integrative review. Research, Society and Development. 2023;12(3). DOI: https://doi. org/10.33448/rsd-v12i3.40629
- Santos FS, Da Rocha RZ, Da Silva Pereira P. Acolhimento da enfermagem em unidade básica de saúde no programa da hiperdia. Brazilian Journal of Implantology and Health Sciences. 2024;6(6):1248-62. DOI: https://doi.org/10.36557/2674-8169.2024v6n6p1248-1262
- Salmasi S, Loewen P, Tandun R, Andrade JG, Vera MA. Adherence to oral anticoagulants among patients with atrial fibrillation: a systematic review and meta-analysis of observational studies. BMJ Open. 2020;10(4). DOI: https://doi.org/10.1136/bmjopen-2019-034778
- 13. Olaya Muñoz QX, Sánchez JGM, Ortiz RA, Bales CMT, Silvera G, Gorricho GA et al. Adesão e qualidade de vida em pacientes com fibrilação atrial e insuficiência cardíaca anticoagulados com Apixabana. Revista Uruguaya de Medicina Interna. 2023;8(3):59-69. DOI: https://doi.org/10.26445/08.03.6

- Brucki SMD, Nitrini R, Caramelli P, Bertolucci PHF, Okamoto IH. Suggestions for utilization of the mini-mental state examination in Brazil. Arquivos de Neuropsiquiatria. 2003;61(3b):777-81. DOI: https://doi.org/10.1590/S0004-282X2003000500014
- 15. Carvalho ARS, Dantas RAS, Pelegrino FM, Corbi ISA. Adaptação e validação de uma medida de adesão à terapia de anticoagulação oral. Revista Latino-Americana de Enfermagem. 2010;18:301-8. Disponível em: https://www.redalyc.org/articulo. oa?id=281421933002
- 16. Delgado AB, Lima ML. Contributo para a validação concorrente de uma medida de adesão aos tratamentos. Psicologia, Saúde & Doenças. 2001;2(2):81-100. Disponível em: https://www.redalyc. org/articulo.oa?id=36220206
- 17. Braga MAF. Qualidade de vida relacionada à saúde de egressos da unidade de acidente vascular cerebral de hospital público de Belo Horizonte: um estudo longitudinal prospectivo. 2022. Tese (Doutorado em Enfermagem). Universidade Federal de Minas Gerais, Belo Horizonte; 2022.
- 18. Perreault S, Denus S, White-Guau B, Côté R, Schnnitzer ME, Dubé MP et al. Oral anticoagulant prescription trends, profile use, and determinants of adherence in patients with atrial fibrillation. Pharmacotherapy: The Journal of Human Pharmacology and Drug Therapy. 2020;40(1):40-54. DOI: https://doi.org/10.1002/phar.2350
- Corrochano M, Jiménez B, Millón J, Gich I, Rambla M, Gil E et al. Patient self-management of oral anticoagulation with vitamin K antagonists in everyday practice: clinical outcomes in a single centre cohort after long-term follow-up. BMC Cardiovascular Disorders. 2020;20:1-13. DOI: https://doi.org/10.1186/s12872-020-01448-7
- Bavalia R, Middeldorp S, Weisser G, Espinola-Klein C. Treatment of venous thromboembolism in special populations with direct oral anticoagulants. Thrombosis and Haemostasis. 2020;120(06):899-911. DOI: https://doi.org/10.1055/s-0040-1710314
- Lima PRG, Gonçalves GMS, Rodrigues RCM, Oliveira-Kumakura ARS. Fatores relacionados à adesão de pacientes ao uso de novos anticoagulantes orais. Revista da Escola de Enfermagem da USP. 2021;56. DOI: https://doi.org/10.1590/1980-220X-REEUSP-2021-0191
- Sousa Borges TR, Da Silva Meyer MF, Simonetti SH. Adesão ao uso de anticoagulante oral cumarínico por pacientes portadores de fibrilação atrial. Nursing Edição Brasileira. 2021;24(274):5419-32. DOI: https://doi.org/10.36489/nursing .2021v24i274p5419-5432
- Araújo HVS, Meira ACAP, Bem PHN, Anjos RCCBL, Bezerra SMMS, et al. Qualidade de vida de pacientes em tratamento com anticoagulante oral. Revista Eletrônica Acervo Saúde. 2021;13(3). DOI: https://doi.org/10.25248/reas.e6626.2021
- 24. Aikins J, Koomson A, Ladele M, Al-Nusair L, Ahmed A, Ashry A, et al. Anticoagulation and antiplatelet therapy in patients with prosthetic heart valves. Journal of Cardiac Surgery. 2020;35(12):3521-9. DOI: https://doi.org/10.1111/jocs.15034
- 25. Araújo RMM de, Oliveira FA de. Avaliação da efetividade da anticoagulação oral com varfarina em indivíduos atendidos no serviço de hematologia de um hospital público de referência em Fortaleza. (trabalho de conclusão de curso). Centro Universitário Fametro, Fortaleza; 2023. Disponível em: http://repositorio.unifametro.edu.br/handle/123456789/1662
- Pagès A, Sabatier R, Sallerin B. Factors associated with the choice of oral anticoagulant class in older patients: An observational study. Journal of Cardiovascular Pharmacology and Therapeutics. 2020;25(4):332-7. DOI: https://doi. org/10.1177/1074248420917811

- 27. Brízido C, Ferreira AM, Lopes P, Strong C, Mendes GS, Gama FF et al. Adesão à terapêutica com anticoagulantes diretos em doentes com fibrilhação auricular não valvular–uma análise de mundo real. Revista Portuguesa de Cardiologia. 2021;40(9):669-75. DOI: https://doi.org/10.1016/j.repc.2020.10.017
- Hachiro K, Takashima N, Suzuki T. Long-Term Outcomes After Aortic Valve Replacement for Aortic Valve Regurgitation — Importance of Left Ventricular End-Systolic Diameter. Circulation Journal. 2024. Disponível em: https://www.jstage.jst.go.jp/article/circj/advpub/o/advpub\_CJ-24-0081/\_article/-char/ja/
- 29. Queiroz XSBA, Lira ALBC, Queiroz HEO, Oliveira SHS, Sodré NL, Santos ICRV et al. Barreiras na adesão terapêutica de indivíduos em uso de anticoagulantes orais: protocolo de revisão de escopo. Contribuciones a las Ciencias Sociales. 2024;17(3). DOI: https://doi.org/10.55905/revconv.17n.3-223
- 30. Lichota A, Szewczyk EM, Gwozdzinski K. Factors affecting the formation and treatment of thrombosis by natural and synthetic compounds. International Journal of Molecular Sciences. 2020;21(21):7975. DOI: https://doi.org/10.3390/ijms21217975
- Khan F, Tritschler T, Kimpton M, Wells PS, Kearon C, Weitz JI et al. Long-term risk for major bleeding during extended oral anticoagulant therapy for first unprovoked venous thromboembolism:

- A systematic review and meta-analysis. Annals of Internal Medicine. 2021;174(10):1420-9. DOI: https://doi.org/10.7326/M21-109
- 32. Lo FMW, Wong EML, Hong FK. The effects of educational programs on knowledge, international normalized ratio, warfarin adherence, and warfarin-related complications in patients receiving warfarin therapy: an integrative review. Journal of Cardiovascular Nursing. 2022;37(3). DOI: https://doi.org/10.1097/JCN.00000000000000090
- Araújo JA, Souza GC, Siqueira IFB, Cintra LP, Costa JM. Adesão à varfarina em pacientes atendidos em clínicas de anticoagulação do Brasil. Brazilian Journal of Health and Pharmacy. 2023;5(1):11-23. DOI: https://doi.org/10.29327/226760.5.1-2
- 34. Praxedes MFS, Silva JLP, Cruz AJA, Viana CC, Barbosa HC, Guimarães NS et al. Assessment of the relationship between the level of patient knowledge on warfarin therapy and the quality of oral anticoagulation: A systematic review and meta-analysis. PLoS One. 2023;18(8). DOI: https://doi.org/10.1371/journal. pone.0289836
- Ozaki AF, Choi AS, Le QT, Ko DT, Han JK, Park SS et al. Real-world adherence and persistence to direct oral anticoagulants in patients with atrial fibrillation: A systematic review and meta-analysis. Circulation: Cardiovascular Quality and Outcomes. 2020;13(3). DOI: https://doi.org/10.1161/CIRCOUT-COMES.119.0059



#### Available in:

https://www.redalyc.org/articulo.oa?id=74181884006

How to cite

Complete issue

More information about this article

Journal's webpage in redalyc.org

Scientific Information System Redalyc Diamond Open Access scientific journal network Non-commercial open infrastructure owned by academia Sheila Barbosa Aguiar Queiroz, Nataly Lins Sodré, Isabel Cristina Ramos Vieira Santos, Maria Beatriz Araújo Silva, Rebeka Maria de Oliveira Belo, Simone Maria Muniz da Silva Bezerra

Factors Related to Adherence to Therapy in Patients
Using Oral Anticoagulants in Outpatient Follow-Up\*
Factores relacionados con la adherencia terapéutica en
pacientes tratados con anticoagulantes orales en el

seguimiento ambulatorio\*

Fatores relacionados à adesão terapêutica de pacientes em uso de anticoagulante oral em acompanhamento ambulatorial<sup>\*</sup>

Aquichan vol. 24, no. 4, e2446, 2024 Universidad de La Sabana,

ISSN: 1657-5997 ISSN-E: 2027-5374

**DOI:** https://doi.org/10.5294/aqui.2024.24.4.6