

## ORIGINAL ARTICLE

## Cardiovascular Risk and Metabolic Syndrome in Individuals with Mental Disorders

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### Abstract

**Background:** Patients with mental disorders are more susceptible to cardiovascular diseases and metabolic disorders compared to the general population.

**Objective:** To evaluate cardiovascular risk and metabolic syndrome in individuals with mental disorders.

**Materials and methods:** A cross-sectional study, conducted at the Psychosocial Care Centers. Socioeconomic, clinical, biochemical and anthropometric data were collected using a standard form. Cardiovascular risk was assessed by the Framingham risk score. Metabolic syndrome (MS) was determined by the World Health- Organization (WHO), the National Cholesterol Education Program (NCEP) and the International Diabetes Federation (IDF) criteria. Data were analyzed by descriptive statistics, and associations were evaluated by the chi-square test and Fisher's exact test, as well as Odds Ratio. The significance level adopted for all statistical tests was 5%.

**Results:** The chance of individuals diagnosed with MS be at intermediate-to-high cardiovascular risk was greater (12.22, 8.01 and 6.23 times higher according to WHO, NCEP and IDF criteria, respectively) than those without MS.

**Conclusion:** A high percentage of patients with mental disorders were at intermediate / high cardiovascular risk, and this was significantly associated with MS. (Int J Cardiovasc Sci. 2019;32(5):517-523)

**Keywords:** Cardiovascular Diseases/physiopathology; Mental Disorders; Metabolic Syndrome; Mental Health; Patient Care Team Psychosocial Support Systems.

### Introduction

Psychiatric reform in Brazil was implemented with the objective of changing the model of mental health assistance from a hospital-centered one to a community-centered model, based on the principles of the Brazilian Unified Health System and focused on a humanized psychosocial rehabilitation.<sup>1</sup> The Psychosocial Care Centers (CAPS) have become the main actors in this process, providing multidisciplinary care, social interaction, active participation of the families,<sup>2</sup> and sociocultural inclusion of patients by intersectoral actions.<sup>3</sup>

Studies have reported that individuals with mental disorders (MDs) are more likely to develop metabolic syndrome (MS) and coronary disease, especially due to poor access to a well-balanced diet and physical exercise, and also to pharmacotherapy, mainly psychotropics.<sup>4,5</sup>

Metabolic syndrome is composed by several conditions, many of them commonly seen in MD patients, including hypertension, glucose intolerance, visceral fat accumulation, and dyslipidemia. Together, these factors have a negative impact on metabolism, increasing the risk for type 2 diabetes mellitus and cardiovascular disease, and affecting patient's quality of life.<sup>6</sup>

Metabolic syndrome has gained much attention not only because of the high prevalence of its components, but also because of their association with cardiovascular risk. The syndrome is associated with a risk two times greater for cardiovascular diseases, such as infarction, stroke and cardiovascular mortality.<sup>7</sup> Grover et al.,<sup>8</sup> and Speyer et al.,<sup>9</sup> confirmed the high prevalence of cardiovascular risk factors and MS in MD patients, and reported premature death in this population, especially among schizophrenic patients.

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In the present study we evaluated cardiovascular risk and MS in individuals with psychiatric disorders attending CAPS in the city of Teresina, Brazil.

## Methods

This was a cross-sectional, analytical study conducted from October 2015 and February 2016.

The sample was composed of 729 individuals of both sexes, older than 18 years, that attended weekly CAPS of Teresina, Brazil, as part of the multidisciplinary treatment program. The sample size calculated to allow estimation of the parameters with an error margin of 5% and 95% confidence level was 298 participants. The sample was selected using Thompson parameters, by simple random sampling (shuffling) and proportionally stratified according to the district zone.

The eligibility criteria were the presence of the tutor and/or caregiver with the patient and agreement with participation in all phases of the study – 1) interview for the collection of sociodemographic (sex, age, race, educational level, family situation and income) and clinical (psychiatric diagnosis and smoking status) data; 2) blood sample collection for laboratory measurements (glucose, HDL cholesterol, LDL cholesterol and triglycerides); 3) obesity-related anthropometric measurements (weight, height, body mass index – BMI – waist circumference, abdominal circumference, hip circumference, waist-to-hip ratio – WHR); and 4) blood pressure measurement.

Patients who did not attend CAPS weekly, who received medical care seen at home, pregnant women or those with previous pregnancy in the last six months were considered ineligible.

Diagnosis of psychiatric disorders were grouped into eight categories according to the International Classification of Diseases ICD 10: F00-F09 Organic Mental Disorders; F20-F29 Schizophrenia, schizotypal disorder, and persistent delusional disorders; F30-F39 Mood (affective) disorders; F50-F59 Behavioral syndromes; F60-F69 Disorders of adult personality and behavior; F70-F79 Intellectual disabilities; F80-F89 Psychological Developmental Disorder; and unspecified ICD-10 codes.<sup>10,11</sup> In case of two or more diagnoses, we considered the first diagnosis recorded in the medical records.

Smoking was defined as any smoking, i.e., independent of the number, frequency (daily or occasionally) and duration of the habit.<sup>12</sup>

BMI was calculated by dividing body weight (kg) by height (m) squared.<sup>13</sup> Body weight was measured using a weighing scale (180 kg capacity; 100 precision), and height was measured using a stadiometer (graduated in cm), with maximum height measurement of 200 cm.

Waist circumference was measured using a measuring tape at the smallest point between the rib and the iliac crest (hip bone). Abdominal circumference was determined at the midpoint between the tenth rib and the iliac crest, and hip at the maximum protrusion of the gluteal region.<sup>14</sup>

Blood pressure was measured using a semi-automated, digital device, from the individual at rest, in sitting position. Three measures were taken, with a minimal interval of one minute between them, and the mean of these measurements was considered for analysis.

Metabolic syndrome was defined according to the World Health Organization (WHO), the National Cholesterol Education Program (NCEP) and the International Diabetes Federation (IDF) criteria. According to the WHO, MS was defined as the presence of diabetes, glucose intolerance or insulin resistance, in addition to two or more of the following: central obesity (waist-to-hip ratio > 0.90 in men and > 0.85 in women, and/or BMI  $\geq 30$  kg/m<sup>2</sup>; systolic blood pressure  $\geq 140$  or diastolic blood pressure  $\geq 90$  mmHg or treatment for hypertension; plasma triglycerides  $\geq 150$  mg/dL or HDL cholesterol < 35 mg/dL in men and < 39 mg/dL in women.<sup>13</sup>

For NCEP, MS was defined as the presence of three or more of the following: glucose > 110 mg/dL; central obesity (waist circumference > 102 cm in men and > 88 cm in women); systolic blood pressure  $\geq 130$  or diastolic blood pressure  $\geq 85$  mmHg; plasma triglycerides  $\geq 150$  mg/dL or HDL cholesterol < 40 mg/dL in men and < 50 mg/dL in women.<sup>15</sup>

The International Diabetes Federation criteria for MS consider waist circumference > 90 cm in men and > 80 cm in women together with the presence of two or more of the following: glucose  $\geq 100$  mg/dL or previous diagnosis of diabetes, triglycerides  $\geq 150$  mg/dL or treatment for dyslipidemia, HDL cholesterol < 40 mg/dL in men or < 50 mg/dL in women or treatment for dyslipidemia, systolic blood pressure  $\geq 130$  mmHg or diastolic blood pressure  $\geq 85$  mmHg or treatment for hypertension.<sup>16</sup>

Cardiovascular risk was determined according to the Framingham risk score – a low, intermediate or high 10-year risk were defined as a risk  $\leq 10\%$ , 10-20% and  $\geq$

20%, respectively, for coronary heart disease, based on sex, age, HDL and LDL cholesterol levels, systolic and diastolic blood pressure, diabetes and smoking.<sup>17</sup>

An informed consent form, containing detailed information about the study, and assuring confidentiality and protection from harm or complications, was signed by each participant or their tutors. The study was submitted and approved by the ethics committee of Piau Federal University.

### Statistical analysis

We conducted a descriptive, analytical study. Categorical data were expressed as relative (%) and absolute (n) frequency, and 95% confidence interval. Distribution of quantitative variables was tested for normality using the Kolmogorov-Smirnov test. Continuous variables with normal distribution were presented as dispersion measures (mean and standard deviation) and measures of central tendency (minimum and maximum values).

The null hypothesis (H0) was that the data had a normal distribution, whereas the alternative hypothesis (H1) was that data did not have a normal distribution (Kolmogorov test). Student's t-test was used for comparisons of the means of data with normal distribution, and the non-parametric Mann-Whitney U test used for data without normal distribution (rejecting the null hypothesis).

To verify whether the variables were independent (i.e., unrelated), we used the chi-square test of independence and the Fisher's exact test (when more than 25% of the expected frequency was lower than 5 or if any of the expected frequencies was lower than 1). The odds ratio was used to test the strength of the association between two variables. The level of significance was set at 0.05.

Data were organized and analyzed using the IBM Statistical Package for the Social Sciences software, version 20.0.<sup>18</sup>

### Results

A total of 298 individuals participated in the study, 176 (59.1%) were women. Most men (57.38%) were aged between 18 and 40 years, and most women (55.11%) between 40 and 60 years. Most participants (65.4%) self-reported "Pardo". Regarding school attainment, 46% completed elementary school, 75.9% were single, living

with family members, and 36.2% of them gained < 1 minimum wage (Table 1).

The frequency of MS was 5.4%, 41.3% and 46% according to the WHO, NCEP and IDF criteria, respectively. A higher frequency of MS was seen among women according to these three definitions, although a statistically significant difference between men and women was seen with the NCEP criteria only ( $p = 0.0094$ ) (Table 2).

Schizotypal disorders and persistent delusional disorders were the most prevalent conditions (50%; 60.7% in men), followed by mood disorders (39.3%; 50.0% in women). No cases of behavioral syndromes, disorders of adult personality and behavior, intellectual disabilities, or psychological developmental disorders were found. A higher frequency of MS was observed in patients with schizotypal disorders and persistent delusional disorders - 50%, 47.2% and 48.2% according to WHO, NCEP and IDF criteria, respectively (Table 3).

In addition, regarding the 10-year risk for coronary diseases, most patients (81.9%) showed a low cardiovascular risk, 13.8% and intermediate risk, and 4.4% a high risk. Therefore, an intermediate or a high cardiovascular risk was seen in 18.12% of the sample, 75.07% among women.

The factors used for the Framingham score calculation are described in Table 4. All variables were significantly associated with cardiovascular risk, except for smoking.

Significant association between the variables was found in the analysis of the relationship of the intermediate/high risk for coronary disease with MS ( $p < 0,01$ ). Analysis of the data revealed that the chance of individuals with MS, according to the WHO criteria, being at an intermediate or high risk for cardiovascular disease was 12.22 times greater than those without MS, and 8.01 and 6.23 times greater based on NCEP and IDF criteria for MS, respectively (Table 5).

### Discussion

Although many studies have investigated MS or cardiovascular risk in psychiatric patients,<sup>19-21</sup> this is the first study to evaluate the classification of cardiovascular risk and its association with MS in MD patients at secondary health care in Brazil.

The present study confirmed data in the literature showing an association between MDs and social indicators, such as a higher frequency of female

**Table 1 - Sociodemographic profile of the study population by sex**

	Sex				Total (n = 298)
	Male (n = 122)		Female (n = 176)		
Age	N	%	N	%	n (%)
> 18 e < 40	70	(57.38)	58	(32.95)	128 (42.95)
> 40 e < 60	46	(37.70)	97	(55.11)	143 (47.99)
> 60 e < 74	6	(4.92)	21	(11.93)	27 (9.06)
<b>Race</b>					
White	10	(8.2)	12	(6.8)	22 (7.4)
Pardo	69	(56.6)	126	(71.6)	195 (65.4)
Black	43	(35.2)	38	(21.6)	81 (27.2)
<b>School attainment</b>					
Illiterate	12	(9.8)	7	(4.0)	19 (6.4)
Literate	6	(4.9)	3	(1.7)	9 (3.0)
Elementary school	60	(49.1)	77	(43.8)	137 (46.0)
High school	37	(30.4)	83	(47.1)	120 (40.2)
Higher education	7	(5.7)	6	(3.4)	13 (4.4)
<b>Civil status</b>					
Living with a partner (with/without children)	8	(6.6)	43	(24.5)	51 (17.1)
Living with family members (without a partner)	110	(90.2)	116	(65.9)	226 (75.9)
Living with other people (without a partner)	1	(0.8)	5	(2.8)	6 (2.0)
Living alone	3	(2.5)	12	(6.8)	15 (5.0)
<b>Income</b>					
No income	3	(2.5)	7	(4.0)	10 (3.4)
< 1 MW	32	(26.2)	76	(43.2)	108 (36.2)
> 1 MW and < 2 MWs	39	(32.0)	47	(26.7)	86 (28.9)
> 2 and < 3 MWs	29	(23.8)	34	(19.3)	63 (21.1)
> 3 and < 5 MWs	15	(12.3)	8	(4.5)	23 (7.7)
> 5 MWs	4	(3.3)	4	(2.3)	8 (2.7)

MW: minimum wage.

patients, low educational attainment, low income, white ethnicity and single.<sup>22,23</sup> With respect to age, in the study by Andrade et al.,<sup>24</sup> patients aged between 25 and 59 years were more likely to develop MDs. This would have a great impact on economy, since this

age group represents the majority of the economically active population.

There is strong evidence that women have a higher propensity to seek health care than men.<sup>25</sup> In addition, studies have indicated an association of MS with female

**Table 2 - Frequency of metabolic syndrome according to the World Health Organization, National Cholesterol Education Program and International Diabetes Federation criteria by sex**

Qualitative variables	Sex				Total (n = 298)		p-value
	Male (n = 122)		Female (n = 176)		N	(%)	
	N	%	N	%	N	(%)	
MS – WHO							
No	118	(96.7)	164	(93.2)	282	(94.6)	0.2839
Yes	4	(3.3)	12	(6.8)	16	(5.4)	
MS – NCEP							
No	83	(68.0)	92	(52.3)	175	(58.7)	0.0094**
Yes	39	(32.0)	84	(47.7)	123	(41.3)	
MS – IDF							
No	74	(60.7)	87	(49.4)	161	(54.0)	0.056
Yes	48	(39.3)	89	(50.6)	137	(46.0)	

*p-value – chi-square test with Yates' correction and Fisher's exact test; \* significant at 5%; \*\* significant at 10%. MS: metabolic syndrome; WHO: World Health Organization; NCEP: National Cholesterol Education Program; IDF: International Diabetes Federation.*

sex. The causes of such association have not been defined, although there are evidences of a social and biological predisposition, in which both neuroendocrine and social play a role in increasing the susceptibility in women.<sup>26</sup> Besides, women are generally more influenced by psychological and hormonal factors.<sup>27</sup> On the other hand, some authors have not found an association between sex and MS, indicating the need for further investigations, aiming at better elucidating the relationship between these variables.<sup>28,29</sup>

Educational attainment is known to contribute to a better quality of life, in addition to influence healthy behaviors. Consequently, it can improve the access of patients to healthcare, facilitating the early identification of health changes, including metabolic ones, and timely treatment.<sup>30</sup>

Job instability, low salaries, and lack of social benefits and protection of labor laws can contribute to the development of anxiety and depression among informal workers or unemployed individuals.<sup>31</sup> These factors could explain the relatively higher frequency of individuals with a low family income in our study. Also, being a member of lower income families is associated with the incidence of and mortality for cardiovascular diseases, probably due to the combination of risk factors.<sup>32</sup>

Although the purpose of the present study was not to analyze specific diagnosis of the study population, Gonçalves et al.,<sup>22</sup> have reported the high prevalence of anxiety disorders in Brazil and attribute this finding to the generalized urban violence and adverse socioeconomical conditions. Besides, the high levels of noise and the lack of recreational areas in Brazilian big cities may be also be related.<sup>22</sup>

The prevalence of MS was markedly different considering the different evaluation criteria, i.e., WHO, NCEP and IDF's. The lower frequency of MS by the WHO criteria compared with NCEP and IDF criteria is explained by the fact that diabetes mellitus was considered a criterion for MS definition by the WHO only.

Regarding investigations on the prevalence of MS in patients with MT, Teixeira et al.,<sup>33</sup> conducted a systematic review of MS prevalence in patients with schizophrenia and schizotypal disorders. The review included eleven studies, with a prevalence varying from 28.4% to 62.5% (NCEP) in 9 studies. The lowest prevalence (28.4%) was observed in a study conducted in the Netherlands, which was twice the prevalence of MS in the general population in the country, according to the authors.<sup>33</sup>

Similar to recent studies,<sup>34,35</sup> the present study confirm the increased prevalence of MS among women with

**Table 3 - Prevalence of metabolic syndrome by psychiatric diagnosis**

Psychiatric diagnostic groups	Metabolic syndrome						Total
	WHO		NCEP		IDF		
	Yes	No	Yes	No	Yes	No	
	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	
Organic MDs*	0 (0.0)	2 (0.7)	1 (0.7)	1 (0.6)	1 (0.7)	1 (0.6)	2 (0.7)
Schizotypal MDs*	8 (50.0)	141 (50.0)	58 (47.2)	91 (52.0)	66 (48.2)	83 (51.6)	149 (50.0)
Mood disorders	7 (43.8)	110 (39.0)	53 (43.1)	64 (36.6)	58 (42.3)	59 (36.6)	117 (39.3)
Neurotic disorders	1 (6.2)	7 (2.5) (2.5)	4 (3.3)	4 (2.3)	4 (2.9)	4 (2.5)	8 (2.7)
Intellectual disabilities	0 (0.0)	17 (6.0)	4 (3.3)	13 (7.4)	4 (2.9)	13 (8.1)	17 (5.7)
Unspecified	0 (0.0)	5 (1.8)	3 (2.4)	2 (1.1)	4 (2.9)	1 (0.6)	5 (1.7)
Total	16 (5.4)	282 (94.6)	123 (41.3)	175 (58.7)	161 (46.0)	137 (54.0)	298 (100.0)

\*MDs- mental disorders; WHO: World Health Organization; NCEP: National Cholesterol Education Program; IDF: International Diabetes Federation.

MDs, especially in schizophrenic patients compared with patients with other psychiatric disorders.<sup>34,35</sup>

The higher prevalence of MS in psychiatric patients is explained by the fact that the cause of the MS is multifactorial, including factors related to life style (healthy eating and sedentarism), genetics, perinatal, neurochemical and hormonal factors, in addition to side effects of psychopharmaceuticals, such as dyslipidemia, insulin resistance, hyperglycemia and weight gain.<sup>6</sup>

The prevalence of risk factors for cardiovascular disease, including MS in patients with MDs is high. However, some of these risk factors are modifiable and could prevent many of the deaths caused by these conditions.<sup>36</sup>

Surprisingly, smoking was not significantly associated with cardiovascular risk classification. This may be due to the considerable decrease in the percentage of smokers in Brazil in the last decades as a result of several actions

of the National Tobacco Control Policy in Brazil.<sup>37</sup> Thus, the possibility that psychiatric patients are included in this percentage cannot be ruled out.

The prediction of cardiovascular risk in cardiovascular prevention has been well explored in the last decades.<sup>38</sup> Estimation of the 10-year absolute risk of cardiovascular risk in primary and secondary prevention enables the development of preventive measures, particularly by guiding population strategies and detection of high risk individuals. Also, it can motivate treatment adherence and modulate risk reduction efforts.<sup>39</sup>

According to the World Heart Federation,<sup>40</sup> men are more likely to develop cardiovascular diseases than women, but the risk increases in post-menopausal women and is practically the same as in men. This could explain the higher prevalence of high cardiovascular risk

**Table 4 - Clinical and laboratory data by ten-year cardiovascular risk classification (Framingham risk score) in individuals with psychiatric disorders**

	Cardiovascular risk			p-value
	Low (n = 244)	Intermediate (n = 41)	High (n = 13)	
Sex				
Male	108 (88.5)	10 (8.2)	4 (3.3)	0.042*
Female	136 (77.3)	31 (17.6)	9 (5.1)	
Age	40 ± 10.9 (19 - 75)	55.6 ± 8.76 (24 - 79)	59.9 ± 8.53 (44 - 76)	< 0.001**
LDL cholesterol	123.6 ± 100 (41 - 1324)	169 ± 105.2 (97.2 - 608)	143.5 ± 50.2 (67.2 - 241)	< 0.001**
HDL cholesterol	47.6 ± 14.1 (21 - 94)	42.7 ± 11.3 (24 - 85)	37.1 ± 8.06 (26 - 51)	0.003**
Systolic blood pressure	111 ± 14.4 (71 - 175)	121.7 ± 24.2 (85 - 230)	118 ± 11.1 (102 - 140)	0.003**
Diastolic blood pressure	73.7 ± 11.2 (46 - 131)	78.5 ± 9.68 (57 - 100)	73.3 ± 18.1 (51 - 115)	0.013*
Glycemia	85.9 ± 25.9 (53 - 274)	101.6 ± 40.8 (46 - 318)	111.4 ± 26.5 (71 - 146)	< 0.001**
Smoking				
Yes	196 (65.8)	33 (11.1)	9 (3.0)	0.574
No	48 (16.1)	8 (2.7)	4 (1.3)	

Chi-square test, Fisher's exact test, Mann-Whitney test; \*Statistically significant at 5%; \*\* Statistically significant at 1%.

**Table 5 - Association between metabolic syndrome and moderate or high risk for cardiovascular diseases in patients with mental disorders**

Classification of MS	Intermediate / high cardiovascular risk			
	N (%)	p-value	OR	95%CI
OMS	11(68.8%)	< 0.01	12.228	4.047 – 36.951
NCEP	43 (35.0%)	< 0.01	8.014	3.924 – 16.367
IDF	43(31.4%)	< 0.01	6.238	3.065 – 12.696

MS: metabolic syndrome; WHO: World Health Organization; NCEP: National Cholesterol Education Program; IDF: International Diabetes Federation.

in women than men in our study, since mean age was higher in the former than in the latter.

Based on the Framingham Heart Study, it is important to consider the percentage of intermediate/high risk for cardiovascular diseases in our study population. Although apparently low – 18.12% – the percentage was meaningful considering the importance of the diagnosis. Besides, this result cannot be compared with that reported in previous studies and populations, since our study is a pioneer study on the theme.

The chance of the patients diagnosed with MS be at intermediate/high risk for cardiovascular disease was elevated according to the three evaluation criteria for MS. In addition, it is worth pointing out that, although the IDF criteria have been the most widely described in the literature, despite the most conservative, the WHO criteria were the most sensitive in showing that individuals with MS were at intermediate/high risk for cardiovascular disease.

Considering these data and the study by Tseng et al.,<sup>21</sup> which showed a higher prevalence not only of MS but also of cardiovascular disease in individuals with MDs, it is reasonable to suggest that the percentage of intermediate/high risk for cardiovascular disease and of cardiovascular risk is higher in psychiatric population as compared with the general population.

Limitations of the study correspond to limitations of the Framingham risk score, including – the absolute cardiovascular risk in participants in the Framingham study is not necessarily the same that observed in other populations; some risk factors known to be important in cardiovascular diseases were not considered in the development of the score such as diet, body weight and physical exercise; finally, the risk has a one-way relationship, i.e. the reduction in one risk factor does not necessarily reduces cardiovascular risk. In addition, differences in the cut-off points for the risk factors used by the different MS criteria may be a source of bias between the associations. Also, limitations intrinsic of cross-sectional studies make it difficult to establish a causal relationship, in this case, between risk factor exposure and development of disease.

Although much effort has been devoted to determine the risk factors to which the psychiatric population are exposed, there are still many challenges to guarantee the right to health for this population. These data can serve as a basis for the planning of actions that contribute to

increase life expectancy and improve the quality of life of these patients.

## Conclusion

Our findings confirm the sociodemographic profile of social disadvantage and the vulnerability for cardiovascular risk factors in patients attending CAPSs.

The prevalence of MS, established by the NCEP and the IDF diagnostic criteria, was high in this population, especially in patients with schizotypal disorders. In addition, our results indicate a high prevalence of intermediate/high cardiovascular risk in psychiatric patients and its significant association with MS.

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## Author contributions

Conception and design of the research: Cabral SMR, Santos MM. Acquisition of data: Cabral SMR. Analysis and interpretation of the data: Cabral SMR, Santos MM. Writing of the manuscript: Cabral SMR. Critical revision of the manuscript for intellectual content: Cabral SMR, Santos MM.

## Potential Conflict of Interest

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

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## Study Association

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## Ethics approval and consent to participate

This study was approved by the Ethics Committee of the Universidade Federal do Piauí under the protocol number 985.376. All the procedures in this study were

in accordance with the 1975 Helsinki Declaration, updated in 2013. Informed consent was obtained from all participants included in the study.

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