ORIGINAL ARTICLE

Atherosclerosis Complications in the Brazilian Population: An Ecological Time Series Study

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Abstract

Background: Atherosclerosis is a serious health problem, and several factors contribute to its occurrence. Longitudinal and qualified monitoring of primary health care (PHC) may contribute to the management of atherosclerosis and reduction of avoidable hospital admissions.

Objective: To estimate the trend in hospitalizations for atherosclerosis and the impact of PHC coverage on its evolution from 2008 to 2018 in Brazil.

Method: An ecological time series analytical study based on the outcomes of hospital admissions for atherosclerosis in Brazil. Time in years, PHC coverage, and Family Health Strategy (FHS) services were considered independent variables. A Prais–Winsten model was used to estimate the outcome trend, and α < 0.05 was adopted.

Results: We observed a mean increase of 1.81 hospitalizations for atherosclerosis per 100 000 inhabitants annually (p = 0.002) in Brazil. This growth was evidenced in the Northeast (p < 0.001), Southeast (p = 0.003), and South (p < 0.001) regions, being stable in the North (p = 0.057) and Midwest (p = 0.62) regions. Men presented twice the growth in hospitalizations from the fifth decade of life on (p < 0.01). An inversely proportional relationship was observed for PHC coverage (B = -0.71; p < 0.001) and the proportion of FHS services (B = -0.59; p < 0.001) with the rate of admissions due to atherosclerosis in Brazil.

Conclusion: Although hospitalizations for atherosclerotic complications are increasing in Brazil, they present regional and individual gender and age discrepancies, as well as a mitigating effect exerted by PHC coverage.

Keywords: Atherosclerosis/ complications; Population; Brazil/ epidemiology; Ecology; Ecosystem; Environmental Health; Time Series Studies.

Introduction

Atherosclerosis is a chronic inflammatory disease of multifactorial etiology. It results from endothelial aggression and affects the tunica intima of medium and large caliber arteries.^{1,2} Several factors that contribute to the development of this disease are modifiable, such as systemic arterial hypertension, diabetes, dyslipidemia, smoking, obesity, and sedentary lifestyle. The main non-modifiable risk factors are genetics, male gender, and age.³ The atherogenic process begins in the early stages of life and, together with the spread of Western habits, is considered responsible for the increased prevalence of dyslipidemias in childhood and adolescence in several countries.⁴ This scenario requires longitudinal monitoring of those at risk, based on modifiable and non-modifiable factors, in order to mitigate these events.

Mortality from cardiovascular diseases (CVD) is on the rise, mainly due to population growth and ageing, as well as to the failure of health systems. In Brazil, CVD is the leading cause of death.⁵ High rates

Mailing Address: Johnnatas Mikael Lopes Campus UNIVASF Paulo Afonso Rua Liberdade, S/N, Bairro Sal Torrado, Paulo Afonso-BA - Brazil. E-mail: johnnatas.lopes@univasf.edu.br of atherosclerosis represent a serious life-threatening health problem, as complications of this disease include mitral regurgitation, ventricular fibrillation, stroke, heart failure, ischemia of the lower extremities, among other conditions.⁶ The early diagnosis of atherosclerosis is capable of providing great benefits to the patient's health as treatment can be initiated at early stages, which reduces the risk of premature cardiovascular events.⁷

Brazil is currently going through a demographic transition, in which the older population is projected to numerically surpass the young population.⁸ In addition, the country suffers from a triple burden of diseases (infectious, chronic, and external causes), with a predominance of chronic non-communicable diseases (CNCDs). This health scenario demands the presence of robust health care networks, with foundations in primary health care (PHC), as desired for the Brazilian Unified Health System (SUS).⁹

PHC development, especially considering the Family Health Strategy (FHS), has major implications in the prevention and treatment of atherosclerosis. Its strengthening not only favors the implementation of SUS' principles and guidelines,¹⁰ but also brings several other positive results to the country, such as a reduction in potentially avoidable hospital admissions through longitudinal monitoring.¹¹

Therefore, this study aimed to estimate the temporal trend of complications from atherosclerosis that led to hospitalization and the impact that PHC coverage and FHS, through actions to promote health and prevent atherosclerosis risk factors, had on its evolution from 2008 to 2018 in Brazil.

Method

This is an ecological study of mixed design: time series and multiple comparison, with an analytical approach conducted between 2008 and 2018. The collected information covered all Brazilian regions.

Data collection

In order to study the number of hospitalizations for atherosclerosis and a possible relationship of these events with PHC coverage and the proportion of FHS services within this system, we analyzed authorizations for hospital admissions with the I-70 diagnostic code according to the International Classification of Diseases, 10th edition (ICD-10). This information was retrieved from the Hospital Information System of the Information Technology Department of the Unified Health System (DATASUS),¹² which contains secondary data without patient identification. It is noteworthy that this information is freely available to the public, therefore this study did not require approval by an ethics committee according to Resolution 510/2016 of the National Health Council.

To obtain the number of hospitalizations for atherosclerosis, we used functions of epidemiological information and general hospital morbidity by place of residence. Demographic data were collected from the Brazilian Institute of Geography and Statistics (IBGE) database.¹³ Data on PHC coverage and the proportion of FHS services were collected from the Primary Care Information and Management System (e-Gestor AB).¹⁴

Data on hospitalizations for atherosclerosis were stratified according to region, sex, and age group. Stroke and acute myocardial infarction events were excluded from the analysis. The annual cumulative incidence rate was obtained through the ratio between the number of hospitalizations for atherosclerosis per year and the estimated population for that year according to the IBGE, multiplied by the constant for every 100 000 inhabitants. To avoid possible errors when collecting information from the databases, an audit was carried out by a second group of researchers using a random sample from the bank.

Statistical analysis

The dependent variable in this study was the accumulated incidence of hospitalization for atherosclerosis, and the independent variables were year, PHC coverage (proportion of population coverage by PHC), and the relationship between FHS coverage and PHC coverage (FHS/PHC coverage). The "year" variable (year–2013.5) was adjusted by the mean year of the time series so as not to produce a serial correlation with the outcome and modify the intercept of the analysis curve. The "PHC coverage" variable was expressed as the percentage of covered population, and the "FHS/PHC coverage" variable revealed the proportion of PHC services that were FHS.

In the process of analyzing data trends, regression modeling used the Prais-Winsten method due to its high statistical relevance and greater ease of interpretation; we also extracted from the model the effect of the serial correlation of the time series. Therefore, a linear y = B0 245

+B1x equation was estimated, where x represented the "year" independent variable.

The mean outcome observed in the period, regardless of the year, was characterized as B0; B1 was the regression coefficient, which informed the mean annual evolution and the slope of the line. The sign of the slope determines an increasing trend (+) or decreasing trend (-) of the outcome. In addition to the equation, the adjusted coefficient of determination (R^2_{adjus}) is presented, which specifies the degree of explanation of the model with the observed data, ranging from 0 to 1.

To verify the impact of the interaction between PHC coverage and the proportion of FHS coverage within PHC services ("PHC-FHS coverage interaction" variable) on the trend of hospitalizations for atherosclerosis in Brazil, we used a generalized estimating equations approach, an extension of generalized linear models (GLM) for correlated data. A robust covariance matrix and an autoregressive (ARIMA) or unstructured working correlation matrix were assumed to estimate the effects of independent variables, depending on the quality of the model based on the quasi-likelihood independence criterion (QIC) of the model. The gamma link function was used to connect independent variables and the outcome in the model. The sign of the model coefficients (B) would indicate the effect of the independent variables and their significance estimated by the Wald chi-squared test (χ^2). R software was also used to adjust the polynomial curves and build the GLM. A 5% significance level was considered to minimize type I error in curve adherence and modeling processes. R software was used for data analysis.

Results

Figure 1 shows the pattern of hospitalizations for atherosclerosis in Brazil and allows us to analyze the situation considering this disease. A constant increase is seen in cases in men and an initial decline is observed among women, with subsequent growth from 2012 on. An average increase of 1.81 cases per 100 000 inhabitants (B = 1.81; p = 0.002) is seen in the general population, with cases among men (p < 0.001) growing more than twice those in women (p = 0.019) (Table 1).

When analyzing the time series by the country's regions, a relatively steady scenario is identified in the Midwest (p = 0.62) and North (p = 0.057) regions, with evidence of a decline in hospitalizations for atherosclerosis among women (B=-0.02; p=0.013). Conversely, the South

(B = 0.65; p < 0.001), Southeast (B = 0.61; p = 0.003), and Northeast (B = 0.56; p < 0.001) regions showed a growth in hospitalizations for atherosclerosis (Table 1).

Atherosclerosis complications that led to hospitalization were decreasing in men under the age of 40 (p < 0.01) and in women under 50 (p < 0.01). Both sexes showed an increase in hospitalizations starting at the fifth decade of life (p < 0.01). However, between the fifth and eighth decade of life, men showed almost twice the increase in hospitalizations presented by women (Table 2).

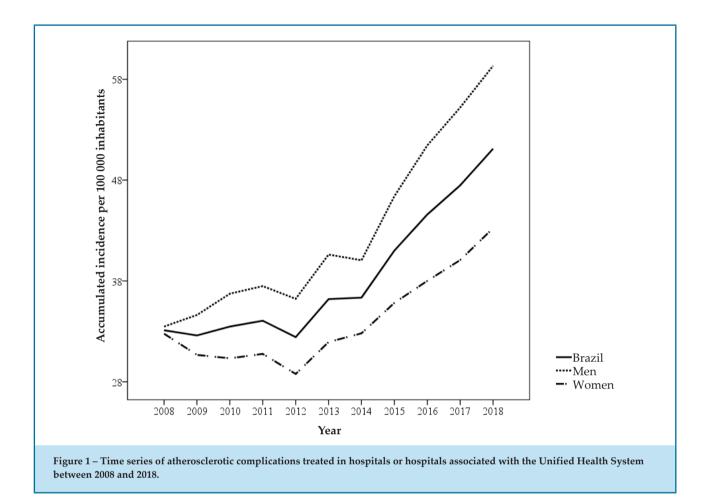
Despite the context of increased hospitalizations for atherosclerosis in the Brazilian population, greater PHC coverage and the proportion of FHS services within PHC showed inverse relationships with hospitalization rates ($B_{PHC} = -0.71$; $B_{FHS/PHC} = -0.59$), thus exerting a mitigating effect on these acute events in Brazil. These effects were more prominent in the North ($B_{PHC} = -1.62$; $B_{FHS/PHC} = -1.38$) and Midwest ($B_{PHC} = -0.99$; $B_{FHS/PHC} = -0.67$; $B_{FHS/PHC} = -0.55$) and Southeast regions ($B_{PHC} = -0.41$; $B_{FHS/PHC} = -0.31$). The South region ($B_{PHC} = 0.41$; $B_{FHS/PHC} = 0.47$) was the only one that did not show a mitigating effect of PHC on hospitalizations for atherosclerosis (Table 3).

Discussion

We aimed to estimate the trend of hospitalizations for atherosclerosis in the Brazilian population and the effects of PHC coverage on its evolution. An increase in atherosclerosis complications requiring hospitalization was observed, especially in men and people aged over 50 years. Regional discrepancies were also evident: the South, Southeast, and Northeast regions showed the worst evolutions. However, this scenario is alleviated by the performance of PHC services, which mitigated the growth of these complications.

The increase in hospitalizations for atherosclerosis in the Brazilian population, especially from 2012 on, may be a reflection of 3 main aspects: the progressive population ageing taking place in the current demographic transition⁹; an increase in Brazilian family incomes accompanied by changes in food consumption and the adoption of urban and less healthy lifestyle habits¹⁵; and public health policies limited by funding and publicprivate partnerships¹⁶, which interact with each other and form a complex causal network.

Population ageing is a paradigm that has been experienced since the 1960s–1970s in Brazil and was expressed in this research with the growth of



atherosclerotic complications in individuals aged 50 years and older, both men and women. The current challenge seems to be related to reversing the health worsening that men and women over the age of 50 have experienced throughout their lives and that inflates hospitalizations for atherosclerosis in this population.

Only recently has the Brazilian State, through the SUS, been concerned with harmful events produced by population ageing. Therefore, more efficient pharmacological strategies and approaches to therapeutic adherence, along with non-pharmacological actions, will have to be implemented to mitigate harmful events and a reduction in quality of life in this population. This is a generation that requires differentiated care from the health system.

Younger people (under 50 years old) show a decline in atherosclerotic events and this may be directly linked to the adoption of healthier lifestyles in this age group in recent decades, such as a reduction in smoking rates, regular physical activity, and protective health policies for childhood and adolescence. It is important that these trends continue in the next life cycles and are consolidated in the coming decades in order to counterbalance the effects of aging and an unfavorable social context.

However, the evolution of hospitalizations for atherosclerotic events was not homogeneous in men and women. Complications increased to a lesser extent in women, which is probably due to social aspects of gender (such as the greater tendency of women to seek health services)¹⁷ and biological features, such as protective factors for cardiovascular events in fertile women¹⁸. Estrogens have a cardiovascular protective effect, act on lipid metabolism, and contribute to the stabilization of atheromatous plaques. Women of reproductive age are at low risk of CVD, especially considering diseases related to the carotids.¹⁸ Seeking health monitoring may also be a determining factor for the development of CVD and other diseases, and men present a low adherence to health care practices.¹⁷

Another contribution to discrepancies in sex and age arises from ecological/contextual conditions such as those provided by the country's regions. The regional analysis

Region		equation	В	R ² adjus	р	Trend
BRAZIL	Total	1.81x - 39.34	0.84	0.64	0.002	Increasing
	Men	2.55x+43.70	0.89	0.75	< 0.001	Increasing
	Women	1.09x+35.03	0.71	0.39	0.019	Increasing
NORTH	Total	-0.15x + 2.41	-0.61	0.22	0.057	Stationary
	Men	-0.08x+2.35	-0.53	0.11	0.100	Stationary
	Women	-0.02x+2.31	-0.71	0.46	0.013	Decreasing
NORTHEAST	Total	0.56x + 6.60	0.99	0.98	< 0.001	Increasing
	Men	0.64x+6.68	0.98	0.96	< 0.001	Increasing
	Women	0.48x+6.54	0.99	0.97	< 0.001	Increasing
MIDWEST	Total	0.10x + 6.86	0.17	0.21	0.620	Stationary
	Men	0.19x+7.24	0.30	0.13	0.390	Stationary
	Women	0.01x+6.33	0.02	0.24	0.940	Stationary
SOUTHEAST	Total	0.61x+9.62	0.82	0.60	0.003	Increasing
	Men	0.77x+10.93	0.83	0.62	0.003	Increasing
	Women	0.45x+8.29	0.81	0.56	0.005	Increasing
SOUTH	Total	0.65x +13.93	0.98	0.96	< 0.001	Increasing
	Men	0.95x+16.65	0.98	0.95	< 0.001	Increasing
	Women	0.38x+11.31	0.97	0.94	< 0.001	Increasing

Table 1 – Trend modeling of hospitalizations for atherosclerosis in Brazil and its regions between 2008 and 2018

B: standardized regression coefficient; R²: adjusted linear coefficient of determination; p: statistical significance.

Table 2 – Modeling the trend of hospitalizations for atherosclerosis in Brazil by region and sex between 2008 and 2018

			Men					Women		
	Equation	β	р	$R^2_{\ adjus}$	Trend	Equation	β	р	$R^2_{\ adjus}$	Trend
≤ 19 years	-0.009x+0.17	-0.71	0.020	0.38	Decreasing	-0.017x+0.18	-0.83	0.003	0.61	Decreasing
20–29 years	-0.038x+0.53	-0.92	< 0.001	0.81	Decreasing	-0.056x+0.54	-0.88	0.001	0.72	Decreasing
30–39 years	-0.047x+1.32	-0.70	0.020	0.37	Decreasing	-0.117x+1.45	-0.79	0.007	0.53	Decreasing
40-49 years	-0.019x+4.39	-0.19	0.590	-0.20	Stationary	-0.100x+4.49	-0.72	0.010	0.41	Decreasing
50–59 years	0.69x+18.91	0.86	0.001	0.67	Increasing	0.296x+11.86	0.80	0.005	0.54	Increasing
60–69 years	3.257x+50.79	0.92	< 0.001	0.82	Increasing	1.130x+29.04	0.85	< 0.001	0.67	Increasing
70–79 years	3.964x+81.09	0.89	< 0.001	0.74	Increasing	1.875x+54.46	0.92	< 0.001	0.82	Increasing
\geq 80 years	2.949x+92.56	0.73	0.010	0.42	Increasing	2.271x+72.32	0.76	0.010	0.47	Increasing

B: standardized regression coefficient; R²: adjusted linear coefficient of determination; p: statistical significance.

Table 3 – Association of primary health care (PHC) coverage and the proportion of family health strategy (FHS) services within PHC with hospitalizations for atherosclerosis in Brazil and its regions between 2008 and 2018

		Standard	Wald 95% CI		Hypothesis test		
Parameter	В	error	Inferior	Superior	x² Wald	df	р
BRAZIL							
Interception	52.96	5.069	43.03	62.90	109.17	1	< 0.001
Year	0.03	0.007	0.01	0.04	17.72	1	< 0.001
PHC coverage	-0.71	0.074	-0.86	-0.572	93.95	1	< 0.001
FHS/PHC coverage	-0.59	0.066	-0.72	-0.467	80.74	1	< 0.001
Interaction FHS/PHC coverage	0.009	0.001	0.007	0.011	80.50	1	< 0.001
Scale	0.002						
MIDWEST							
Interception	72.48	4.993	62.69	82.26	210.68	1	< 0.001
Year	0.07	0.020	0.03	0.11	12.34	1	< 0.001
PHC coverage	-0.99	0.072	-1.13	-0.85	189.32	1	< 0.001
FHS/PHC coverage	-0.80	0.048	-0.89	-0.70	268.04	1	< 0.001
Interaction FHS/PHC coverage	0.01	0.0007	0.01	0.01	251.98	1	< 0.001
Scale	0.02						
NORTHEAST							
Interception	54.61	12.777	29.56	79.65	18.26	1	< 0.001
Year	0.09	0.001	0.09	0.09	6515.56	1	< 0.001
PHC coverage	-0.67	0.152	-0.97	-0.37	19.62	1	< 0.001
FHS/PHC coverage	-0.55	0.136	-0.82	-0.28	16.36	1	< 0.001
Interaction FHS/PHC coverage	0.007	0.001	0.004	0.01	18.82	1	< 0.001
Scale	0.002						
NORTH							
Interception	115.66	1.620	112.49	118.84	5093.87	1	< 0.001
Year	-0.09	0.018	-0.12	-0.05	25.08	1	< 0.001
PHC coverage	-1.62	0.011	-1.64	-1.59	19994.23	1	< 0.001
FHS/PHC coverage	-1.38	0.014	-1.41	-1.35	8639.16	1	< 0.001
Interaction FHS/PHC coverage	0.02	7.71.10-5	0.01	0.02	64387.21	1	< 0.001
Scale	0.01						
SOUTHEAST							
Interception	27.89	0.949	26.03	29.75	863.70	1	< 0.001
Year	0.12	0.003	0.11	0.12	1305.91	1	< 0.001
PHC coverage	-0.41	0.007	-0.43	-0.40	2907.77	1	< 0.001
FHS/PHC coverage	-0.31	0.018	-0.35	-0.27	277.59	1	< 0.001
Interaction FHS/PHC coverage	0.005	0.0002	0.005	0.006	677.81	1	< 0.001
Scale	0.002						
SOUTH							
Interception	-30.82	9.271	-48.99	-12.65	11.05	1	0.001
Year	0.09	0.004	0.08	0.10	474.71	1	< 0.001
PHC coverage	0.41	0.111	0.19	0.63	13.79	1	< 0.001
FHS/PHC coverage	0.47	0.128	0.22	0.72	13.68	1	< 0.001
Interaction FHS/PHC coverage	-0.006	0.001	-0.009	-0.003	14.47	1	< 0.001
Scale	0.003						

B: adjusted regression coefficient; CI: confidence interval; x^2 : Wald chi-squared test; df : degrees of freedom; p: statistical significance; PHC coverage: proportion of the population covered by primary health care; FHS/PHC coverage: proportion of FHS coverage within primary health care; interaction FHS/PHC coverage: interaction between the proportion of Family Health Strategy coverage within PHC and PHC coverage.

of hospitalizations for atherosclerosis demonstrates clear differences, probably due to characteristics that are inherent to each country region, which include economic, demographic, cultural and social dimensions.¹⁵ Comparing the five Brazilian regions, the South and Southeast had more hospitalizations for atherosclerosis as these regions have historically had greater economic development and were thus associated with contextual effects of urbanization and a precarious lifestyle;¹⁹⁻²¹ their populations are also older. A smaller effect of PHC coverage was observed in these regions when compared to the others, which limits longitudinal monitoring of individual and collective health necessary for the control of chronic health conditions.

On the other hand, there is a large offer of predominantly private outpatient medical services in the Southeast and South regions of Brazil.22 This scenario is a consequence of the public-private relationship in the health sector of the most economically developed regions of Brazil,¹⁶ where a socioeconomic ecosystem pressures the health system to follow models of individual-outpatient-curative actions provided by private services/insurers, whereas less longitudinal and preventive follow-up is offered by the public system, especially PHC. This is driven by less public funding for health protection due to the bias of greater private access to health. However, the objectives of the private subsystem are to minimize expenses, reducing service provision, and to transfer health responsibilities to the individual.¹⁶

In addition to economic and organizational aspects of the health system, the Southeast and South regions of Brazil present individual factors such as an atherogenic diet and excess abdominal adiposity,²³ a high prevalence of smoking (24.5% among men and 19.7% among women), and a prevalence of hypertension above 30%. Regarding obesity, its prevalence was higher than the national average, and the physical inactivity rate was 41.73%; cardiovascular risk was thus classified as moderate for women (11.8%) and high for men (24.7%).²⁴

In the South, older women presented lack of physical activity as the most prevalent cardiovascular risk factor. Among men, the main cardiovascular risk factor was the limited intake of fruits and vegetables, although alcohol abuse and smoking were also significant.²⁵ The Southeast region had similar results, where men aged 20 to 49 years had 2 or more risk factors for cardiovascular disease,²⁶ mainly obesity and physical inactivity.²⁷

The Northeast region had the greatest PHC coverage in the country. However, this coverage was not able to prevent the progression of complications caused by atherogenic disease, despite mitigating their damage. Greater health service coverage also requires social support actions for the adoption of healthy behaviors, as well as intersectoral measures that improve quality of life and access to food, which are still limited in the SUS.¹⁶

The confluence of strong PHC and impacting intersectoral policies could circumvent factors such as low educational and economic levels among PHC users in the Northeast and North of Brazil,28 as CNCDs more intensely affect people from vulnerable groups.²⁹ A study with students from Campina Grande-PB indicated a percentage of regular or occasional smokers of 9.8% and 31.3% of experimental smokers.³⁰ A study in the state of Sergipe indicated that 77.5% of the participants practiced insufficient physical activity, 57.5% drank soft drinks excessively, 15.5% were overweight or obese, and 49.2% claimed to have consumed alcohol in the previous 30 days.³¹ In the analysis of older age groups, the scenario was also severe, with sedentary lifestyle being reported by 39% of adults and 67.5% of the older population.³²

Despite the growing number of hospitalizations for atherosclerosis in Brazil, it is worth highlighting the role of PHC, and specifically FHS services, in the clinical management, management of risk factors, and detection, treatment, and planning of preventive actions. From the perspective that Brazil will have 21.7% of the population aged over 60 years by the year 2040, obesity and diabetes control, as well as individual and collective anti-smoking approaches, become a priority within PHC and FHS practices, such as the promotion of physical activities, dietary guidance, and longitudinal monitoring.³³

The adoption of such measures can not only reduce the rate of hospitalizations for CVDs but also minimize spending on health care, given that CVDs are responsible for most costs of hospital admissions in the SUS.^{34,35} It is stipulated that a 10% reduction in worldwide mortality from CVDs could result in savings of up to 25 billion dollars per year.³⁶ Considering that this is the second leading cause of death in Brazil, the amount saved nationally could be invested in expanding the coverage of the health network, strengthening primary and specialized care and increasing disease prevention and screening.

Based on a more complex approach to the concept of health, valued by the work process and ways of caring within the FHS, the important impact of this health care model on the frequency of CVD in the population is noticed.³⁷ The biological, sociocultural, and economic multi-causality in the manifestation of CNCDs, especially CVDs, indicates the need for action on social determinants of health, in addition to the clinical aspects that are inherent to atherosclerosis and other CVDs. In this sense, the FHS becomes an important health care tool for the Brazilian population.³⁸ Educational interventions aimed at the most affected population evaluated in this study can be valuable instruments for the empowerment of these people and for strengthening social support networks, thus generating capital and social cohesion to reduce risk factors and encourage healthier lifestyle habits.39

As for the limitations of this study, it is possible that the ability to diagnose acute events associated to atherosclerosis without complementary examinations is limited in the most economically vulnerable regions, which could lead to underdiagnosis because of the difficulty in accessing sensitive complementary exams related to the cause of acute events. Furthermore, it is not possible to infer that individuals from a region with more records of atherosclerosis complications are at greater risk of developing it, which would constitute an ecological fallacy. Studies with other methodological designs are important to directly define cause and risk relationships for atherosclerosis.

Conclusion

The incidence of atherosclerosis complications in Brazil is rising, possibly motivated by individual lifestyle and health care aspects as well as ecological conditions related to geographic regionalization and distinct socioeconomic and cultural components within the country. There is an evident need for public health policies that are differentiated by age group and sex due to the different magnitudes of hospitalization trends for atherosclerosis, especially from the fifth decade of life on. The effect of PHC in mitigating the progression of atherosclerotic complications is noteworthy, being notably influenced by its coverage potential and, possibly, by its quality of care. This result could be expanded with the implementation of comprehensive and intersectoral policies that address conditions of production and work, food, leisure, and physical activity, given that more socioeconomically developed regions had the worst trends in hospitalizations in standardized comparisons.

Author contributions

Conception and design of the research: Silva EJ, Gomes Junior FS, Firmiano JVB, Silva NR, Carlini WA, Lopes JM. Acquisition of data: Silva EJ, Gomes Junior FS, Firmiano JVB, Silva NR, Carlini WA. Analysis and interpretation of the data: Silva EJ, Gomes Junior FS, Firmiano JVB, Silva NR, Carlini WA, Lopes JM, Guedes MBOG, Lopes MR. Statistical analysis: Lopes JM. Writing of the manuscript: Silva EJ, Gomes Junior FS, Firmiano JVB, Silva NR, Carlini WA, Lopes JM, Guedes MBOG, Lopes MR. Critical revision of the manuscript for intellectual content: Lopes JM, Guedes MBOG, Lopes MR.

Potential Conflict of Interest

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

Sources of Funding

There were no external funding sources for this study.

Study Association

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

Ethics approval and consent to participate

This article does not contain any studies with human participants or animals performed by any of the authors.

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